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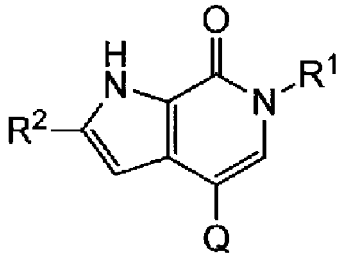
(54) Title: SUBSTITUTED PYRROLOPYRDINES AS INHIBITORS OF BROMODOMAIN



(I)

(57) Abstract: The present invention relates to compounds of formula (I) and to salts thereof, wherein R^1, R^2, and Q 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.

SUBSTITUTED PYRROLOPYRDINES AS INHIBITORS OF BROMODOMAIN

CROSS-REFERENCE TO RELATED APPLICATION

This patent application claims the benefit of priority of U.S. application serial No. 62/077,703, 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).

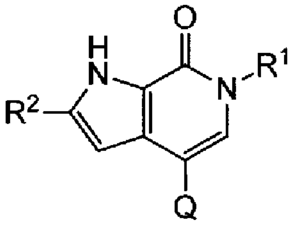
Bromodomains, which are approximately 110 amino acids long, are found in a large number of chromatin-associated proteins and have been identified in approximately 70 human proteins, often adjacent to other protein motifs (Jeanmougin F., et al., *Trends Biochem. Sci.*, 1997, *22*, 5, 151-153; and Tamkun 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 methyl, ethyl, C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl, or heterocyclyl, wherein any methyl of R^1 is substituted with one or more groups R^m, wherein any ethyl of R^1 is substituted with one or more groups R^n, and wherein any C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl 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, or C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b;

Q is carbocyclyl or heterocyclyl, which carbocyclyl or heterocyclyl is optionally substituted with one or more groups R^c;

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 $-N(R^v)-S(O)_2-N(R^v)_2$;

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

each R^m is independently selected from oxo, carbocyclyl, heterocyclyl, -F, $-NO_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, and $-S(O)_2-R^v$, wherein carbocyclyl is optionally substituted with one or more $-O-R^v$;

each R^n is independently selected from oxo, 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)$_2$;

each R^u 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{ua})$_2$, 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^u 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, C$_{1-3}$alkyl and heteroaryl wherein C$_{1-3}$alkyl is optionally substituted with one or more groups independently selected from oxo, hydroxyl, -N(R^{ua})$_2$ and halo and heteroaryl is optionally substituted with one or more -N(R^{ua})$_2$;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{va})$_2$, 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^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;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{wa})$_2$, 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;

each R^{ua} is independently selected from hydrogen and C$_{1-6}$alkyl;

each R^{va} is independently selected from hydrogen and C$_{1-6}$alkyl; and

each R^{wa} is independently selected from hydrogen and C$_{1-6}$alkyl.

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 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, 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. The term heterocyclyl also includes C_3-C_8heterocycloalkyl, which is a saturated or partially unsaturated mono-, bi-, or spiro-ring system comprising 3-8 carbons and one or more (1, 2, 3, or 4) heteroatoms.

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, salicylic 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, piperizine, 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

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

R^1 is methyl, ethyl, C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl, or heterocyclyl, wherein any methyl of R^1 is substituted with one or more groups R^m, wherein any ethyl of R^1 is substituted with one or more groups R^n, and wherein any C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl 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, or C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b;

Q is carbocyclyl or heterocyclyl, which carbocyclyl or heterocyclyl is optionally substituted with one or more groups R^c;

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 $-N(R^v)-S(O)_2-N(R^v)_2$;

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, or 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 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, $-NO_2$, $-N(R^u)_2$, -CN, $-C(O)-N(R^u)_2$,

-S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -O-C(O)-O-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -O-C(O)-N(R^u)$_2$, -N(R^u)-C(O)-OR^u, -N(R^u)-C(O)-N(R^u)$_2$, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u, -N(R^u)-S(O)-N(R^u)$_2$, and -N(R^u)-S(O)$_2$-N(R^u)$_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO$_2$, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^m is independently selected from oxo, carbocyclyl, heterocyclyl, -F, -NO$_2$, -CN, -C(O)-N(R^v)$_2$, -S(O)-N(R^v)$_2$, -S(O)$_2$-N(R^v)$_2$, -C(O)-R^v, -C(O)-O-R^v, -S(O)-R^v, and -S(O)$_2$-R^v, wherein carbocyclyl is optionally substituted with one or more -O-R^v;

each R^n is independently selected from oxo, 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)$_2$;

each R^u 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{ua})$_2$, 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^u 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, C_{1-3}alkyl and heteroaryl wherein C_{1-3}alkyl is optionally substituted with one or more groups independently selected from oxo, hydroxyl, -N(R^{ua})$_2$ and halo and heteroaryl is optionally substituted with one or more -N(R^{ua})$_2$;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{va})$_2$, 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^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;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-N(R^{wa})_2$, 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;

each R^{ua} is independently selected from hydrogen and C_{1-6}alkyl;

each R^{va} is independently selected from hydrogen and C_{1-6}alkyl; and

each R^{wa} is independently selected from hydrogen and C_{1-6}alkyl.

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

R^1 is methyl, ethyl, C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl, or heterocyclyl, wherein any methyl of R^1 is substituted with one or more groups R^m, wherein any ethyl of R^1 is substituted with one or more groups R^n, and wherein any C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl 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, or C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b;

Q is carbocyclyl or heterocyclyl, which carbocyclyl or heterocyclyl is optionally substituted with one or more groups R^c;

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 $-N(R^v)-S(O)_2-N(R^v)_2$;

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, or 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 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^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -O-C(O)-O-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -O-C(O)-N(R^u)$_2$, -N(R^u)-C(O)-OR^u, -N(R^u)-C(O)-N(R^u)$_2$, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u, -N(R^u)-S(O)-N(R^u)$_2$, and -N(R^u)-S(O)$_2$-N(R^u)$_2$, wherein any C$_{1-6}$alkyl, C$_{2-6}$alkenyl, C$_{2-6}$alkynyl, C$_{1-6}$haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO$_2$, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -C(O)-N(R^u)$_2$, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u and C$_{1-6}$alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^m is independently selected from oxo, carbocyclyl, heterocyclyl, -F, -NO$_2$, -CN, -C(O)-N(R^v)$_2$, -S(O)-N(R^v)$_2$, -S(O)$_2$-N(R^v)$_2$, -C(O)-R^v, -C(O)-O-R^v, -S(O)-R^v, and -S(O)$_2$-R^v;

each R^n is independently selected from oxo, 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)$_2$;

each R^u 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{ua})$_2$, 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^u 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{va})$_2$, 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^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;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -N(R^{wa})$_2$, 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;

each R^{ua} is independently selected from hydrogen and C_{1-6}alkyl;

each R^{va} is independently selected from hydrogen and C_{1-6}alkyl; and

each R^{wa} is independently selected from hydrogen and C_{1-6}alkyl.

With respect to the embodiments for formula (I) noted above, the following exemplary values are provided. It is to be understood that two or more embodiments provided herein may be combined.

In certain embodiments R^1 is methyl that is substituted with one or more groups R^m.

In certain embodiments R^1 is ethyl that is substituted with one or more groups R^n.

In certain embodiments R^1 is C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl, wherein any C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl of R^1 is optionally substituted with one or more groups R^a.

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

In certain embodiments R^1 is butyl, 2-cyclopropylethyl, cyclopentylmethyl, 2-penten-1-yl, cyclohexylmethyl, cyclobutylmethyl, 2-cyclohexylethyl, pentyl, 2-methylpropyl, 2-buten-1-yl, butyl, 2-furylmethyl, 3-methylbut-1-yl, 2-propenyl, 3-methyl-2-buten-1-yl, 3-buten-1-yl, 2-methoxyethyl, 3-methoxypropyl, or 4-methoxybenzyl.

In certain embodiments R^2 is H.

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

In certain embodiments R^2 is methyl.

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

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

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

In certain embodiments R^2 is H or C_{1-6}alkyl.

In certain embodiments R^2 is H or C_{1-4}alkyl.

In certain embodiments R^2 is H or methyl.

In certain embodiments Q is carbocyclyl or heterocyclyl, which carbocyclyl or heterocyclyl is optionally substituted with one or more groups R^c.

In certain embodiments Q is carbocyclyl that is optionally substituted with one or more groups R^c.

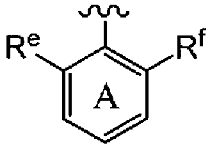
In certain embodiments Q is heterocyclyl that is optionally substituted with one or more groups R^c.

In certain embodiments Q is C_3-C_8cycloalkyl that is optionally substituted with one or more groups R^c.

In certain embodiments Q is aryl that is optionally substituted with one or more groups R^c.

In certain embodiments Q is phenyl that is optionally substituted with one or more groups R^c.

In certain embodiments Q is:



wherein:

ring A is optionally substituted with one or more groups R^g, or ring A is optionally fused with a carbocyclyl or a heterocyclyl to form a polycyclyl that is optionally substituted with one or more groups R^g;

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

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

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

each R^x is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl;

each R^y is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl; and

each R^z 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, cyano, amino, hydroxyl, C_1-C_6alkoxy, carbocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^z 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^e is hydrogen.

In certain embodiments R^f is hydrogen.

In certain embodiments ring A is optionally substituted with one or more groups R^g.

In certain embodiments Q is C_3-C_8heterocycloalkyl that is optionally substituted with one or more groups R^c.

In certain embodiments Q is heteroaryl that is optionally substituted with one or more groups R^c.

In certain embodiments Q is phenyl that is optionally substituted with one or more groups R^c, wherein each R^c is independently selected from C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-N(R^u)$_2$, and -O-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO_2, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -C(O)-N(R^u)$_2$, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments Q is phenyl that is optionally substituted with one or more groups R^c, wherein each R^c is independently selected from C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-N(R^u)$_2$, and -O-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from -O-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments Q is phenyl that is optionally substituted with one group -C(O)-N(R^u)$_2$ and is optionally substituted with one or more groups R^c.

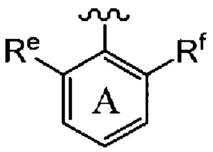
In certain embodiments Q is phenyl that is substituted with a group -C(O)-N(R^u)$_2$, and that is optionally substituted with one or more groups R^c, wherein each R^c is independently selected from C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-N(R^u)$_2$, and -O-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from -O-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments Q is phenyl that is optionally substituted with one or more groups R^c, and that is substituted with a group -C(O)-N(R^u)$_2$ selected from dimethylaminocarbonyl, aminocarbonyl, cyclohexylaminocarbonyl, isopropylaminocarbonyl, tetrahydrofuranylaminocarbonyl, *N*-(2,2-difluoroethyl)-aminocarbonyl, cyclobutylaminocarbonyl, cyclopropylmethyl aminocarbonyl, methylaminocarbonyl, pyrrolidin-1-ylcarbonyl, morpholinocarbonyl, ethylaminocarbonyl, 2-methylpropyl)aminocarbonyl, 2-(dimethylamino)ethylaminocarbonyl, 2-hydroxyethylaminocarbonyl, 1-propylaminocarbonyl, 6-acetyl-2,6-diazaspiro[3.3]heptane-2-ylcarbonyl, 4-methylpiperazin-1-ylcarbonyl, and azetidine-1-carbonyl.

In certain embodiments Q is selected from: 3-(*N,N*-dimethylaminocarbonyl)phenyl, 4-aminocarbonyl-3-fluorophenyl, 3-aminocarbonyl-5-fluorophenyl, 4-*tert*-butylphenyl, 3-(*N*-cyclohexylaminocarbonyl)phenyl, 4-(*N*-cyclohexylaminocarbonyl)phenyl, 3-(*N*-isopropylaminocarbonyl)phenyl, 3-cyano-6-methoxyphenyl, 3-aminocarbonyl-2-fluorophenyl, 3-aminocarbonyl-6-fluorophenyl, phenyl, 3-(*N*-cyclohexylaminocarbonyl)-6-methoxyphenyl, 3-(*N*-tetrahydrofuranylaminocarbonyl)-6-methoxyphenyl, 3-(*N*-(2,2-difluoroethyl)aminocarbonyl)-6-methoxyphenyl, 3-(*N*-cyclobutylaminocarbonyl)-6-methoxyphenyl, 3-(*N*-(cyclopropylmethyl) aminocarbonyl)-6-methoxyphenyl, 4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one-7-yl, 3-(*N,N*-dimethylaminocarbonyl)-5-fluorophenyl, 4-(*N*-methylaminocarbonyl)phenyl, 3-(pyrrolidin-1-ylcarbonyl)phenyl, 3-aminocarbonylphenyl, 4-(methylsulfonlyamino)phenyl, 4-(morpholinocarbonyl)phenyl, 3-(*N,N*-dimethylaminocarbonyl)-6-fluorophenyl, 3-(*N,N*-dimethylaminocarbonyl)-2-fluorophenyl, 3-(*N,N*-dimethylaminocarbonyl)-6-methoxyphenyl, 3-(*N*-ethylaminocarbonyl)-6-methoxyphenyl, 2-methoxy-5-(*N*-*m*ethylaminocarbonyl) phenyl, 2-methoxy-5-(pyrrolidin-1-ylcarbonyl)phenyl, 2-methoxy-5-(*N*-(2-methylpropyl)aminocarbonyl)phenyl, 2-methoxy-5-(*N*-(2-(dimethylamino)ethyl)aminocarbonyl) phenyl, 3-(*N*-(2-hydroxyethyl)aminocarbonyl)-6-methoxy phenyl, 2-methoxy-5-(*N*-prop-1-ylaminocarbonyl) phenyl, 3-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-ylcarbonyl)-6-methoxyphenyl, 4-(1-hydroxy-1-methylethyl)-2-methoxyphenyl, 4-(1-hydroxy-1-methylethyl)phenyl, 4-(4-methylpiperazin-1-

ylcarbonyl)phenyl, 4-(*N*,*N*-dimethylaminocarbonyl)phenyl, 3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl, 3-(*N*-methylaminocarbonyl)phenyl, 4-(hydroxymethyl)phenyl, 3-chloro-4-(*N*,*N*-dimethylaminocarbonyl)phenyl, 3-chloro-4-(aminocarbonyl)phenyl, and 3-(azetidine-1-carbonyl)-6-methoxyphenyl.

In certain embodiments Q is:



wherein:

ring A is optionally substituted with one or more groups R^g, or ring A is optionally fused with a carbocyclyl or a heterocyclyl to form a polycyclyl that is optionally substituted with one or more groups R^g;

R^e is hydrogen, -F, -Cl, -Br, -I, -CN, -O-R^x, C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, -F, -Cl, -Br, -I, -NO_2, -N(R^x)$_2$, -CN, -C(O)-N(R^x)$_2$, -S(O)-N(R^x)$_2$, -S(O)$_2$-N(R^x)$_2$, -O-R^x, -S-R^x, -O-C(O)-R^x, -C(O)-R^x, -C(O)-O-R^x, -S(O)-R^x, -S(O)$_2$-R^x, -N(R^x)-C(O)-R^x, -N(R^x)-S(O)-R^x, and-N(R^x)-S(O)$_2$-R^x,;

R^f is hydrogen, -F, -Cl, -Br, -I, -CN, -O-R^y, C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, -F, -Cl, -Br, -I, -NO_2, -N(R^y)$_2$, -CN, -C(O)-N(R^y)$_2$, -S(O)-N(R^y)$_2$, -S(O)$_2$-N(R^y)$_2$, -O-R^y, -S-R^y, -O-C(O)-R^y, -C(O)-R^y, -C(O)-O-R^y, -S(O)-R^y, -S(O)$_2$-R^y, -N(R^y)-C(O)-R^y, -N(R^y)-S(O)-R^y and -N(R^y)-S(O)$_2$-R^y;

each R^g 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^z)$_2$, -CN, -C(O)-N(R^z)$_2$, -S(O)-N(R^z)$_2$, -S(O)$_2$-N(R^z)$_2$, -O-R^z, -S-R^z, -O-C(O)-R^z, -O-C(O)-O-R^z, -C(O)-R^z, -C(O)-O-R^z, -S(O)-R^z, -S(O)$_2$-R^z, -O-C(O)-N(R^z)$_2$, -N(R^z)-C(O)-OR^z, -N(R^z)-C(O)-N(R^z)$_2$, -N(R^z)-C(O)-R^z, -N(R^z)-S(O)-R^z, -N(R^z)-S(O)$_2$-R^z, -N(R^z)-S(O)-N(R^z)$_2$, and -N(R^z)-S(O)$_2$-N(R^z)$_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO_2, -N(R^z)$_2$, -CN, -C(O)-N(R^z)$_2$, -S(O)-N(R^z)$_2$, -S(O)$_2$-N(R^z)$_2$, -O-R^z, -S-R^z, -O-C(O)-R^z, -C(O)-R^z, -C(O)-O-R^z, -S(O)-R^z, -S(O)$_2$-R^z, -N(R^z)-C(O)-R^z, -N(R^z)-S(O)-R^z, -N(R^z)-S(O)$_2$-R^z and C_{1-6}alkyl and heteroaryl wherein C_{1-3}alkyl is optionally substituted with one or more groups independently selected from oxo, hydroxyl, -N(R^{ua})$_2$ and halo and heteroaryl is optionally substituted with one or more -N(R^{ua})$_2$;

each R^x is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl;

each R^y is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl; and

each R^z 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, heterocyclyl, carbocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^z 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^e is hydrogen.

In certain embodiments R^f is hydrogen.

In certain embodiments the ring A is optionally substituted with one or more groups R^g.

In certain embodiments R^c 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, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -O-R^u, and -N(R^u)-S(O)$_2$-R^u, - wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO$_2$, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

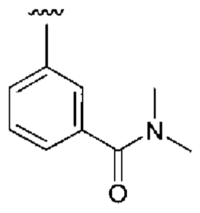
In certain embodiments R^c is independently selected from oxo, C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-N(R^u)$_2$, -O-R^u, and -N(R^u)-S(O)$_2$-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO$_2$, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments R^c is independently selected from oxo, C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-N(R^u)$_2$, -O-R^u, and -N(R^u)-S(O)$_2$-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from -O-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments Q is substituted with one -C(O)-N(R^u)$_2$ group and optionally substituted with one or more R^c groups independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -O-R^u, and -N(R^u)-S(O)$_2$-R^u, - wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO$_2$, -N(R^u)$_2$, -CN, -C(O)-N(R^u)$_2$, -S(O)-N(R^u)$_2$, -S(O)$_2$-N(R^u)$_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -S(O)$_2$-R^u, -N(R^u)-C(O)-R^u, -N(R^u)-S(O)-R^u, -N(R^u)-S(O)$_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments Q is phenyl that is substituted with a group -C(O)-N(R^u)$_2$, and that is optionally substituted with one or more groups R^c, wherein each R^c is independently selected from C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-N(R^u)$_2$, and -O-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from -O-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments Q is selected from:



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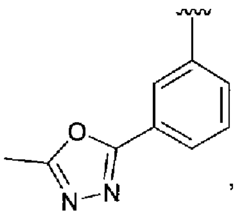

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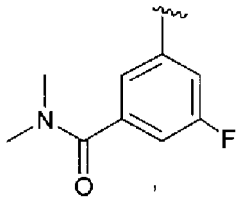

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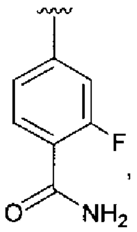

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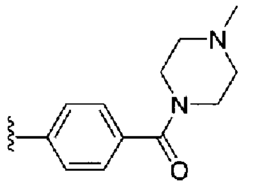

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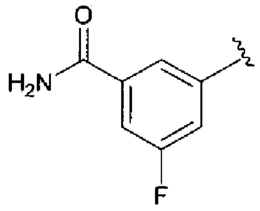

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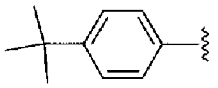

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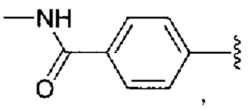

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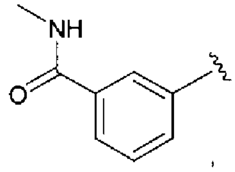
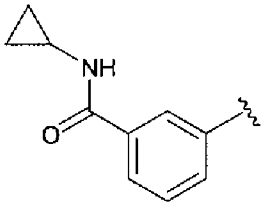
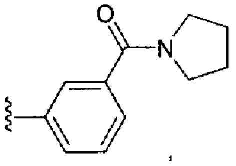
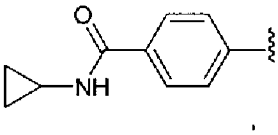
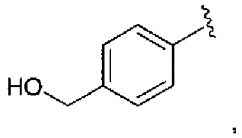
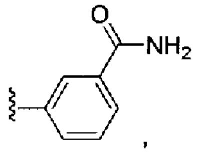
,

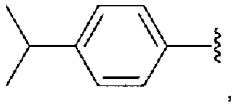
,

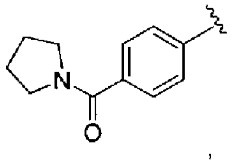
,

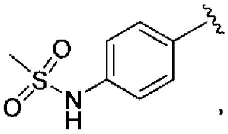
,

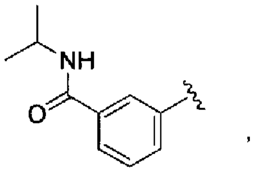
,

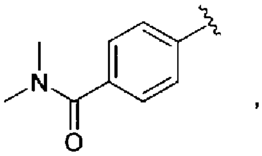
,

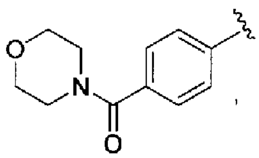
,

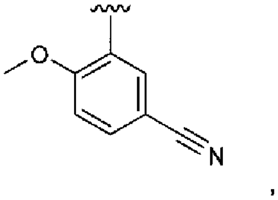
,

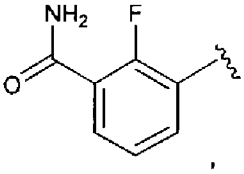
,

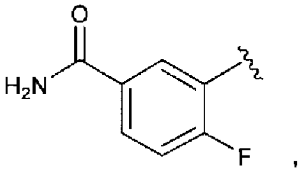
,

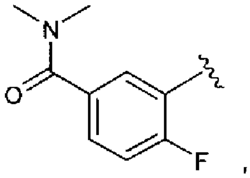
,

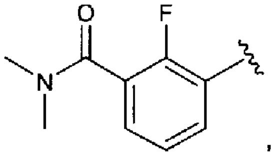
,

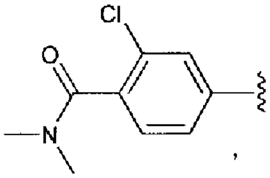
,

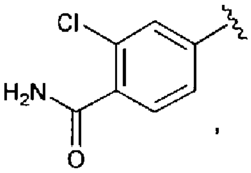
,

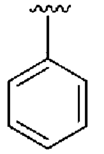
,

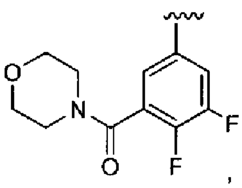
,

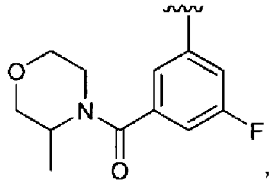
,

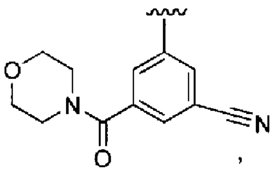
,

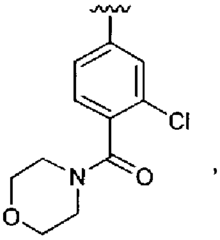
,

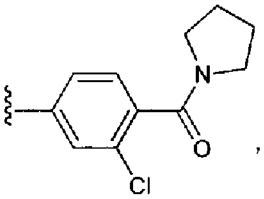
,

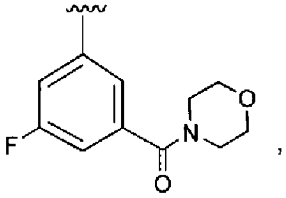
,

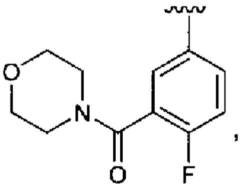
,

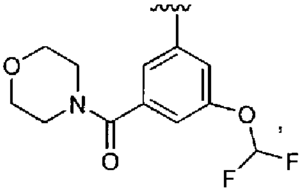
,

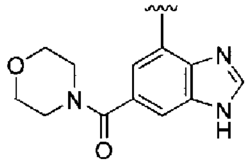
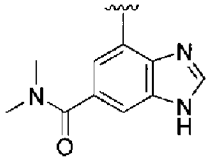
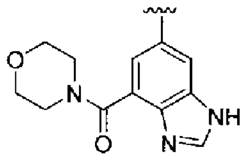
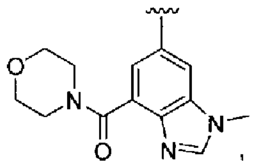
,

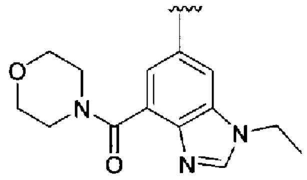
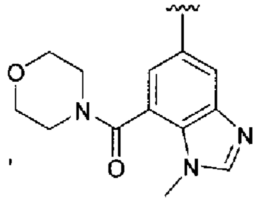
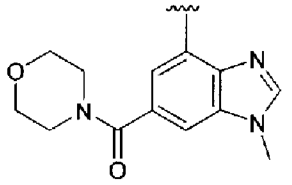
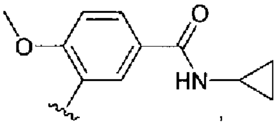
,

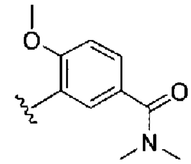
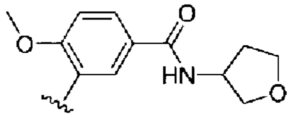
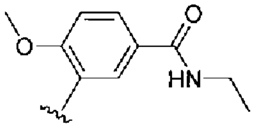
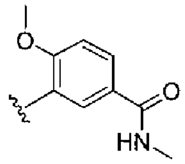
,

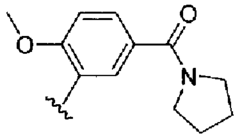
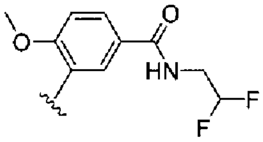
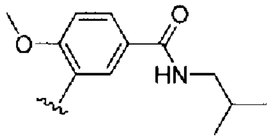
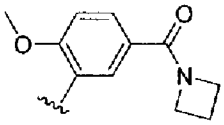
,

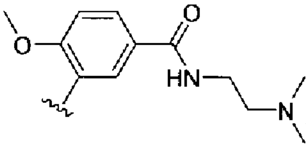
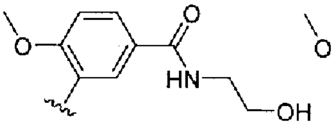
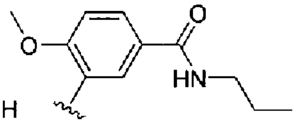
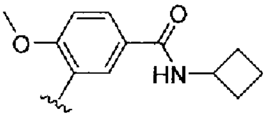


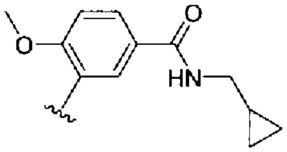
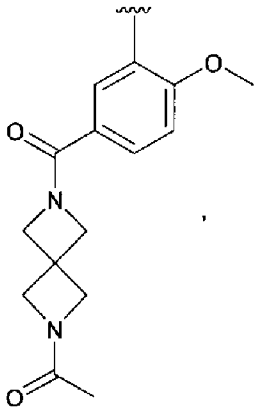
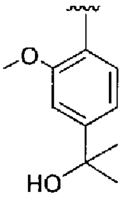
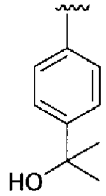
,
,
,
,

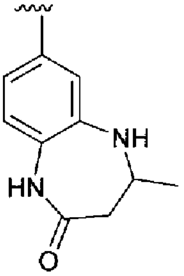
,
,
,
,

,
,
,
,

,
,
,
,

,
,
,
,

,
,
,
.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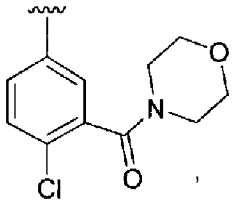
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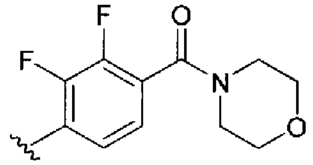
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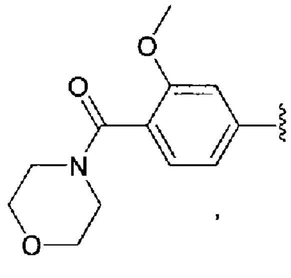
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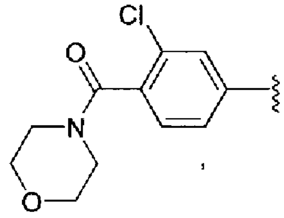
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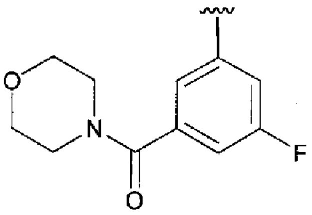
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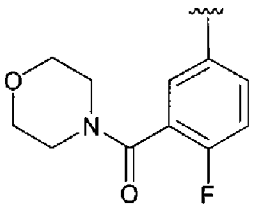
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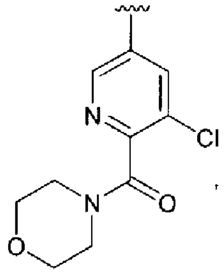
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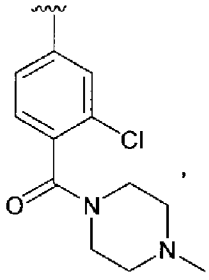
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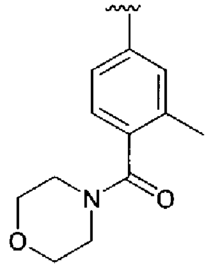
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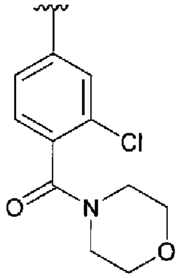
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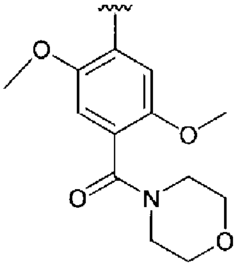
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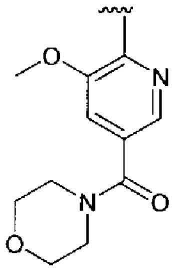
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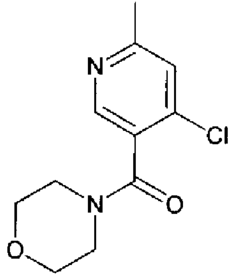
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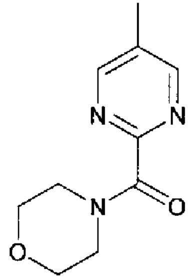
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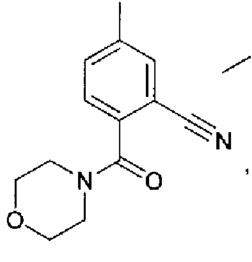
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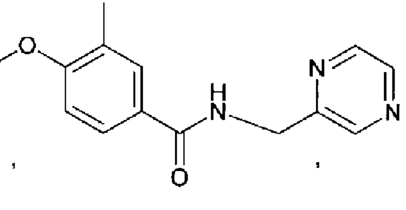
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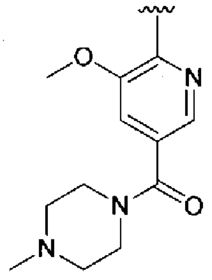
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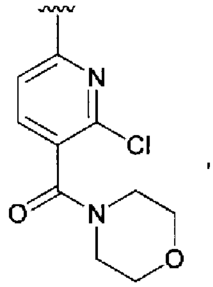
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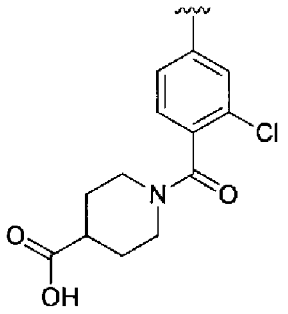
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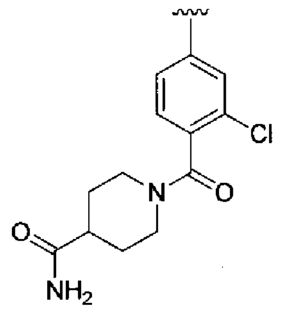
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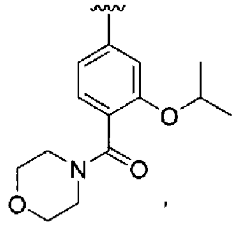
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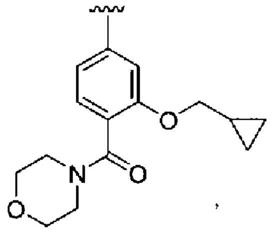
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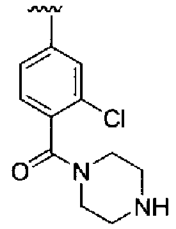
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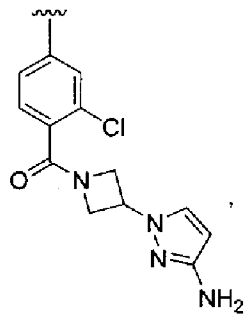
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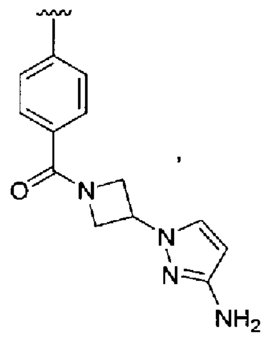
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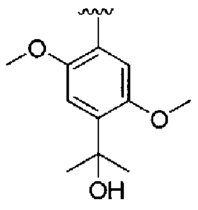

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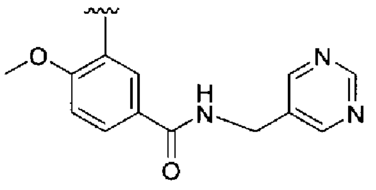


In certain embodiments the compound is selected from:

3-(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

N,N-dimethyl-3-[6-(3-methylbut-2-enyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide;

3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-(cyclopentylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-[(4-methoxyphenyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

N,N-dimethyl-3-[7-oxo-6-[(E)-pent-2-enyl]-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide;

3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-[6-(cyclohexylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-(6-isopentyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-[6-(cyclobutylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-(2-cyclohexylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

N,N-dimethyl-3-(7-oxo-6-pentyl-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide;

3-[6-(2-methoxyethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-(3-methoxypropyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-(6-isobutyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-[6-(cyclopropylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

6-but-3-enyl-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-5-fluoro-N,N-dimethylbenzamide;

4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluorobenzamide;

6-but-2-enyl-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-fluorobenzamide;

6-but-2-enyl-4-(4-tert-butylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one;

4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-methylbenzamide;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-methylbenzamide;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-cyclopropylbenzamide;

6-but-2-enyl-4-[3-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-cyclopropylbenzamide;

6-but-2-enyl-4-[4-(hydroxymethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide;

6-but-2-enyl-4-(4-isopropylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

6-but-2-enyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

N-[4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]methanesulfonamide;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-isopropylbenzamide;

4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

6-but-2-enyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluorobenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluorobenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluoro-N,N-dimethylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-N,N-dimethylbenzamide;

4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-N,N-dimethylbenzamide;

4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chlorobenzamide;

6-(2-furylmethyl)-4-phenyl-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile;

3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzonitrile;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-tetrahydrofuran-3-ylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-ethyl-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-methylbenzamide;

6-[(E)-but-2-enyl]-4-[2-methoxy-5-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2,2-difluoroethyl)-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-isobutyl-4-methoxybenzamide;

4-[5-(azetidine-1-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-[2-(dimethylamino)ethyl]-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2-hydroxyethyl)-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-propylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclobutyl-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(cyclopropylmethyl)-4-methoxybenzamide;

4-[5-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

4-[5-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)-2-methoxy-phenyl]-6-butyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-butyl-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-butyl-4-(4-(2-hydroxypropan-2-yl)phenyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one;

6-(2-cyclopropylethyl)-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-(2-cyclopropylethyl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-N,N-dimethylbenzamide;

3-[6-(2-cyclopropylethyl)-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethylbenzamide; and

7-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one;

and salts thereof.

In certain embodiments the compound is selected from:

6-but-3-enyl-4-[3,4-difluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-fluoro-5-(3-methylmorpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-(morpholine-4-carbonyl)benzonitrile

6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-(difluoromethoxy)-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[6-(morpholine-4-carbonyl)-1H-benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one ;

7-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-3H-benzimidazole-5-carboxamide;

6-but-3-enyl-4-[7-(morpholine-4-carbonyl)-3H-benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-ethyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[1-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[1-methyl-6-(morpholine-4-carbonyl)benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[4-chloro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-2-methyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one ;

6-[(E)-but-2-enyl]-2-methyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[2,3-difluoro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one ;

6-[(E)-but-2-enyl]-4-[3-methoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one ;

6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[5-chloro-6-(morpholine-4-carbonyl)-3-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(4-methylpiperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-2-methyl-4-[3-methyl-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-allyl-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-allyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-2-methyl-4-[2-(morpholine-4-carbonyl)pyrimidin-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

5-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-(morpholine-4-carbonyl)benzonitrile;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

6-[(E)-but-2-enyl]-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrazin-2-ylmethyl)benzamide

6-but-2-enyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[6-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

1-[4-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxylic acid;

1-[4-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxamide;

6-[(E)-but-2-enyl]-4-[3-isopropoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-(cyclopropylmethoxy)-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(piperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]-3-chloro-phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2,5-dimethoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrimidin-5-ylmethyl)benzamide;

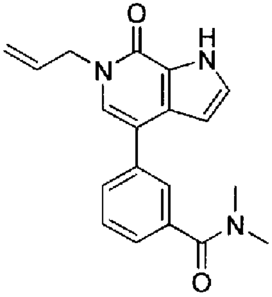
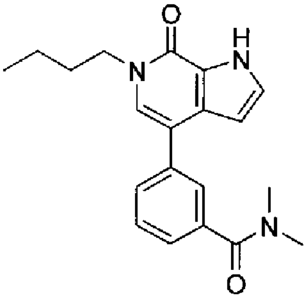
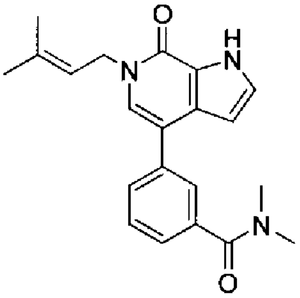
6-butyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

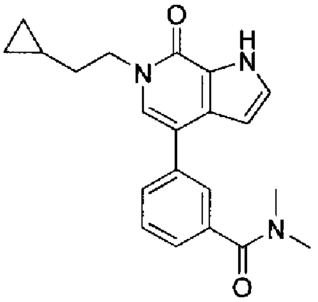
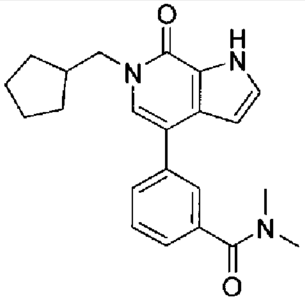
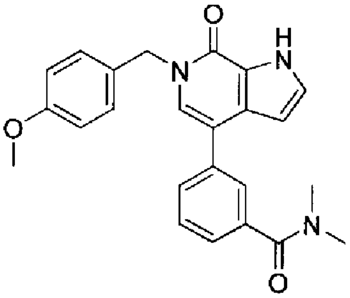
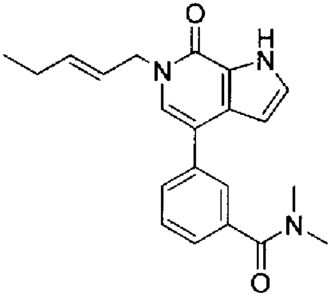
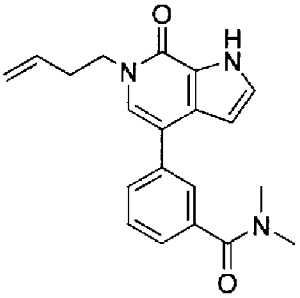
6-butyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one; and

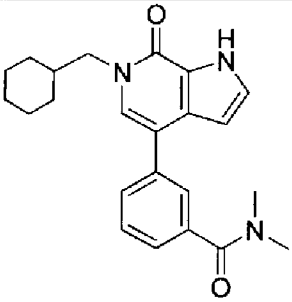
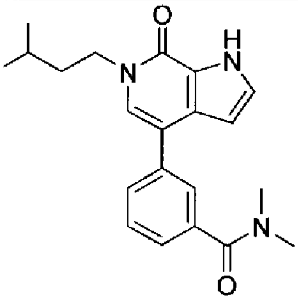
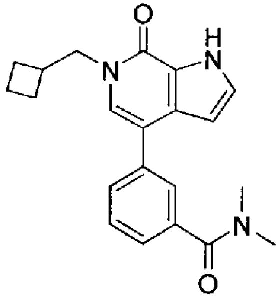
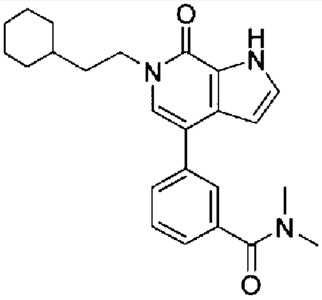
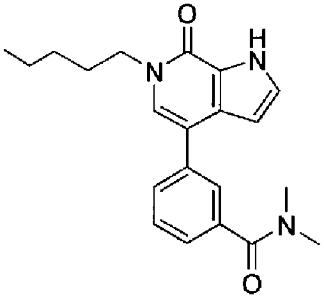
6-butyl-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

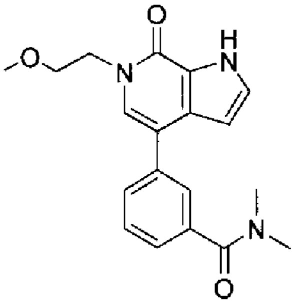
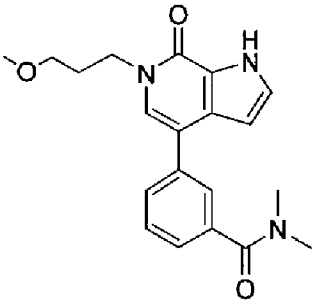
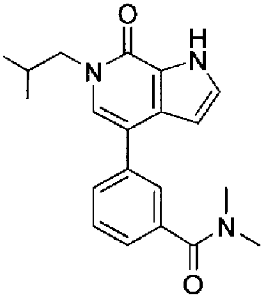
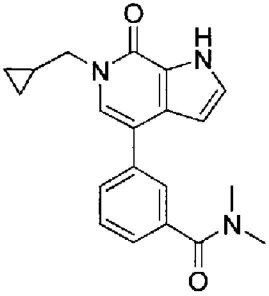
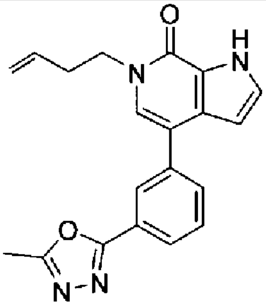
and salts thereof.

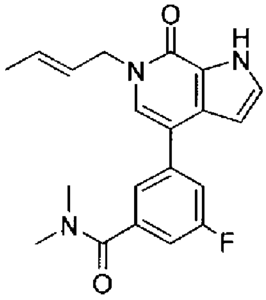
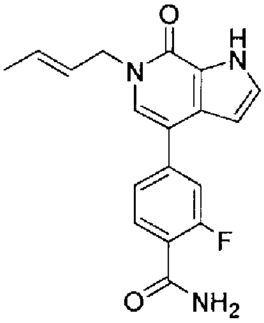
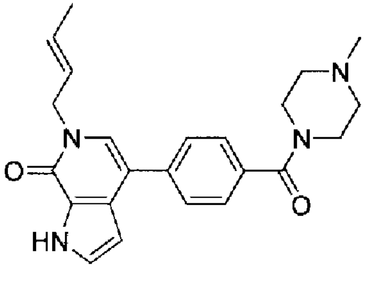
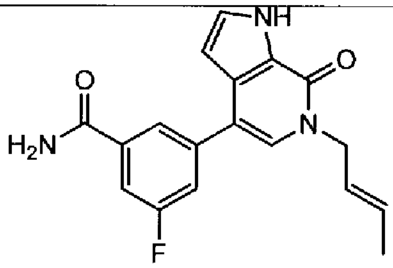
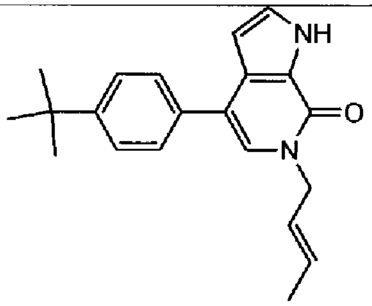
In certain embodiments the compound is selected from:

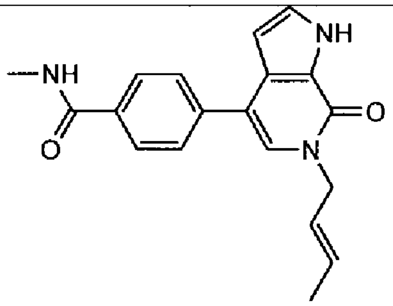
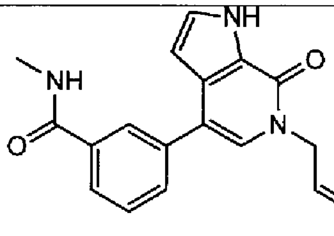
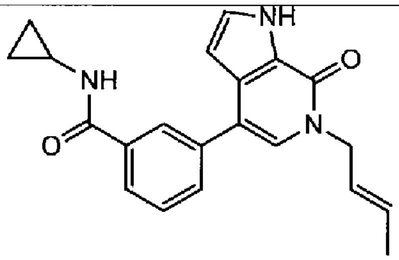
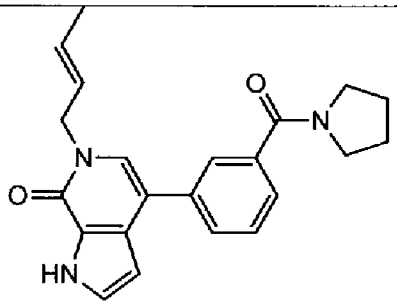
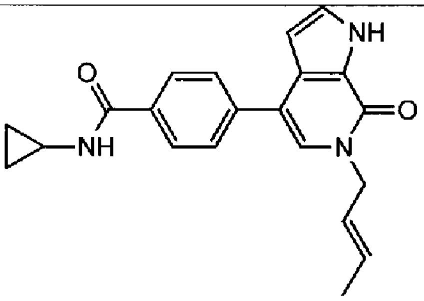
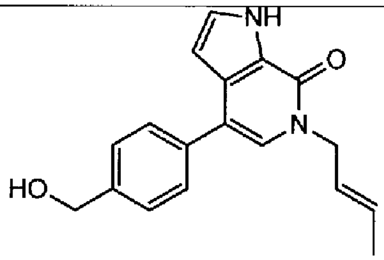
Structure	Name
	3-(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide
	3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide
	N,N-dimethyl-3-[6-(3-methylbut-2-enyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide

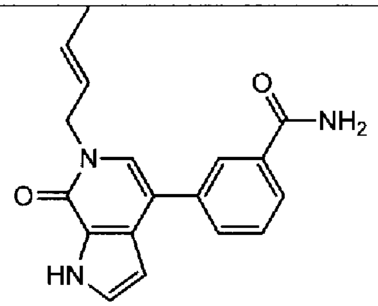
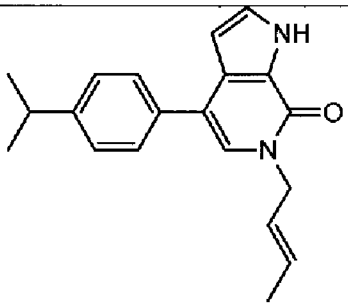
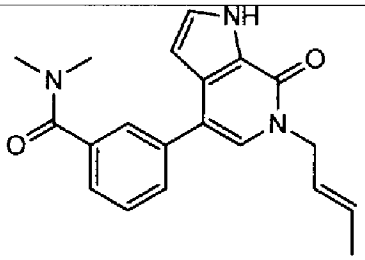
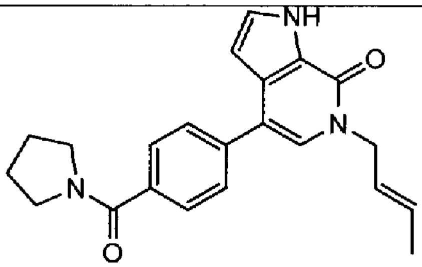
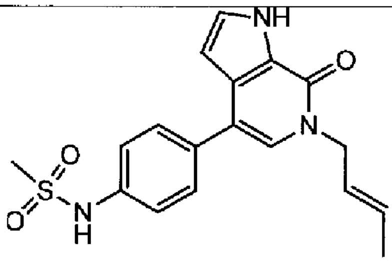
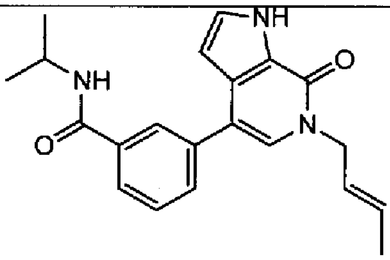
	3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-[6-(cyclopentylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-[6-[(4-methoxyphenyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	N,N-dimethyl-3-[7-oxo-6-[(E)-pent-2-enyl]-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide
	3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide

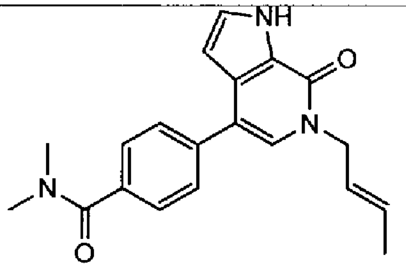
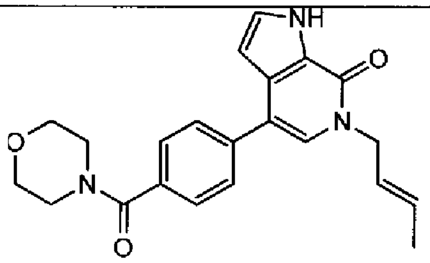
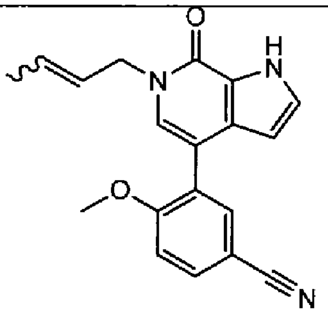
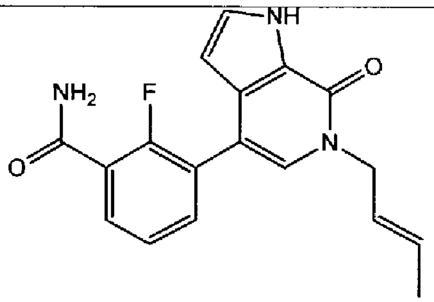
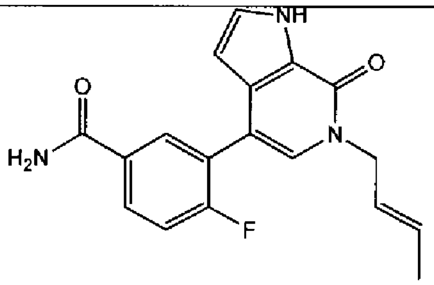
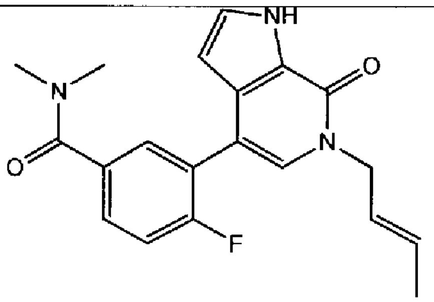
	3-[6-(cyclohexylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-(6-isopentyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide
	3-[6-(cyclobutylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-[6-(2-cyclohexylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	N,N-dimethyl-3-(7-oxo-6-pentyl-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide

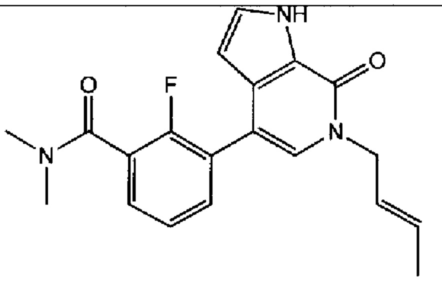
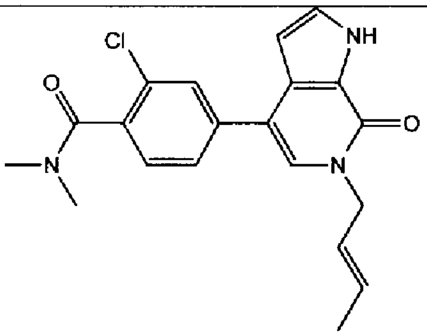
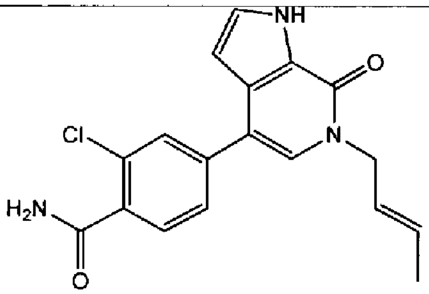
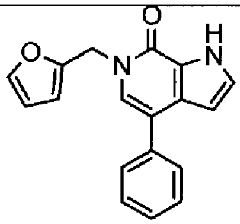
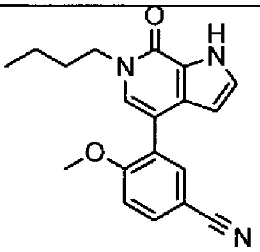
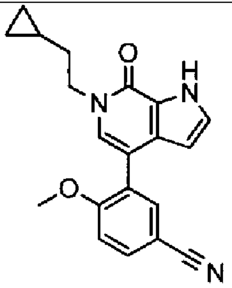
	3-[6-(2-methoxyethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-[6-(3-methoxypropyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-(6-isobutyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide
	3-[6-(cyclopropylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	6-but-3-enyl-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

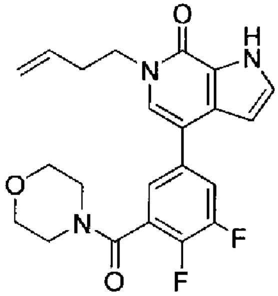
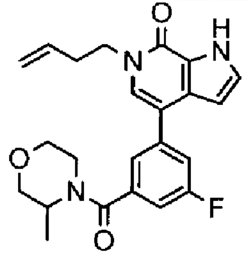
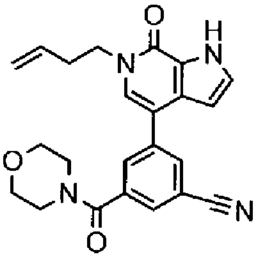
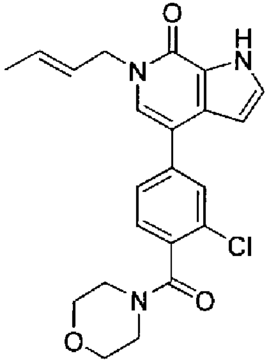
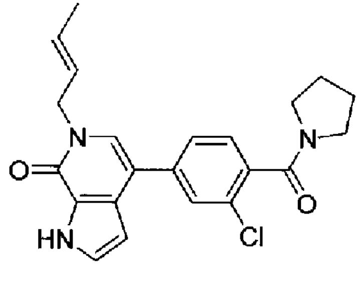
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-5-fluoro-N,N-dimethyl-benzamide
	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-benzamide
	6-[(E)-but-2-enyl]-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-5-fluoro-benzamide
	6-[(E)-but-2-enyl]-4-(4-tert-butylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one

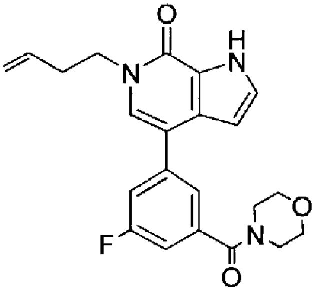
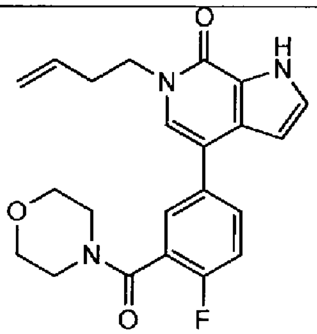
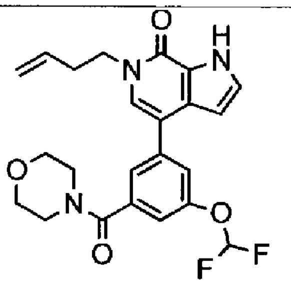
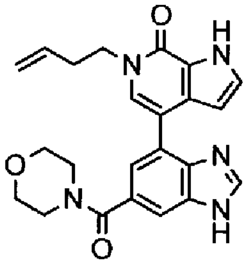
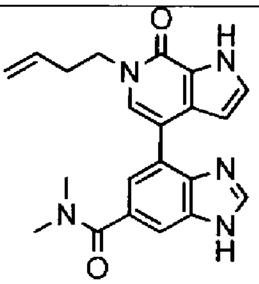
	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-methyl-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-methyl-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-benzamide
	6-[(E)-but-2-enyl]-4-[3-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-benzamide
	6-[(E)-but-2-enyl]-4-[4-(hydroxymethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

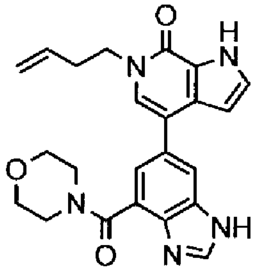
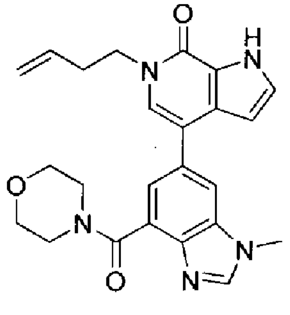
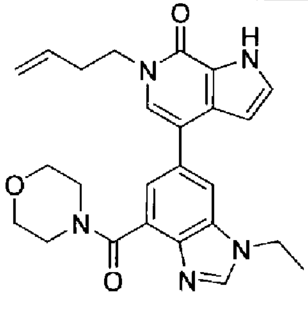
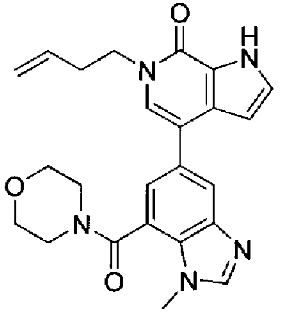
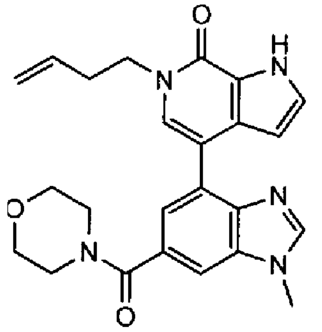
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide
	6-[(E)-but-2-enyl]-4-(4-isopropylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	6-[(E)-but-2-enyl]-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	N-[4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]phenyl]methanesulfonamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-isopropyl-benzamide

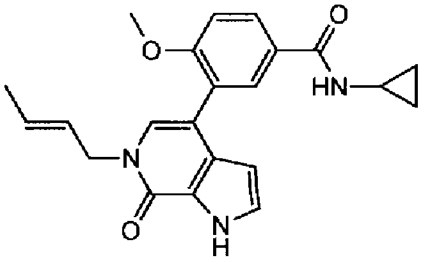
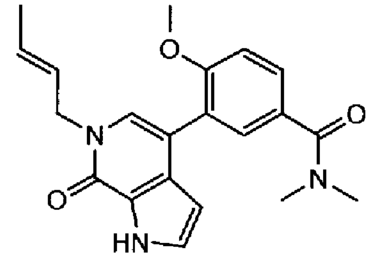
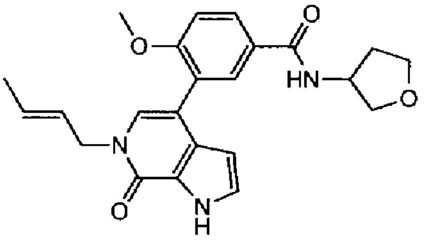
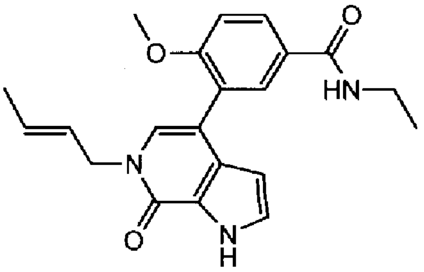
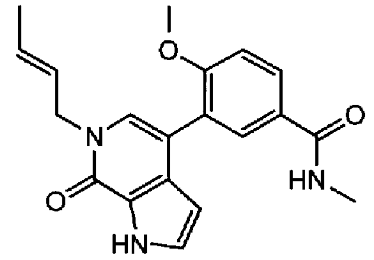
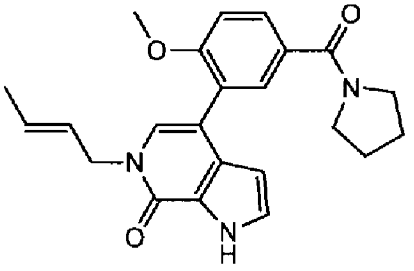
	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	6-[(E)-but-2-enyl]-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzonitrile
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluoro-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluoro-N,N-dimethyl-benzamide

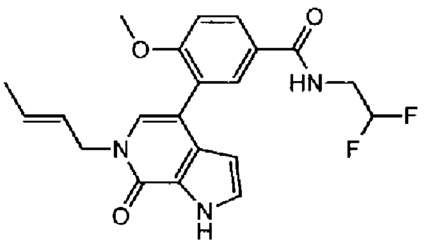
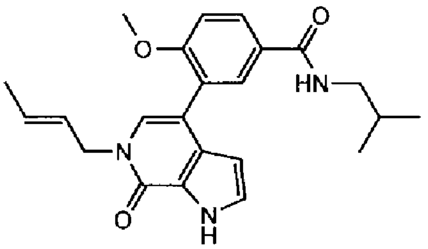
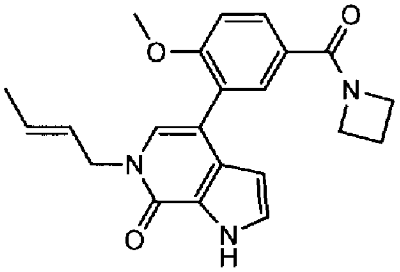
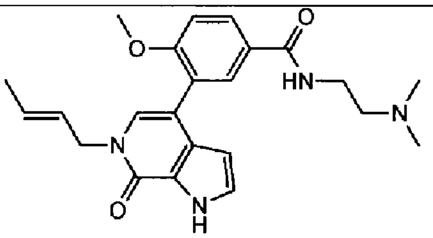
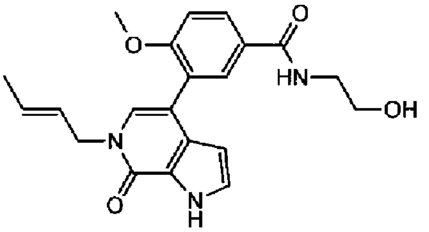
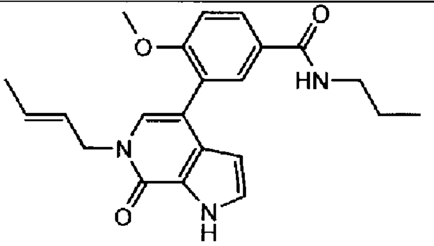
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-N,N-dimethyl-benzamide
	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-N,N-dimethyl-benzamide
	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzamide
	6-(2-furylmethyl)-4-phenyl-1H-pyrrolo[2,3-c]pyridin-7-one
	3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile
	3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzonitrile

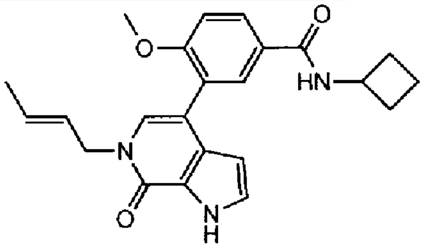
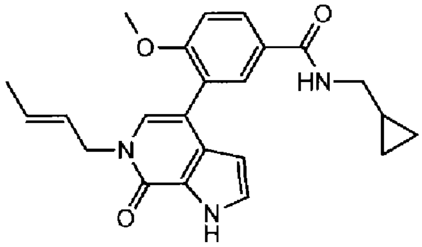
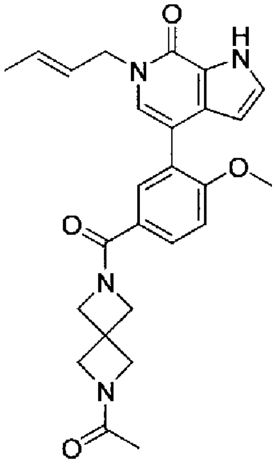
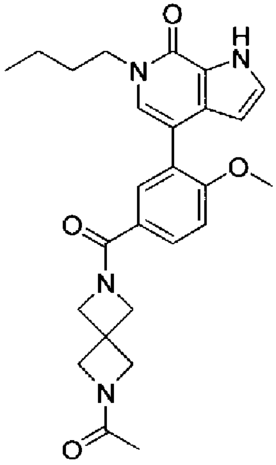
	6-but-3-enyl-4-[3,4-difluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[3-fluoro-5-(3-methylmorpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-(morpholine-4-carbonyl)benzonitrile
	6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

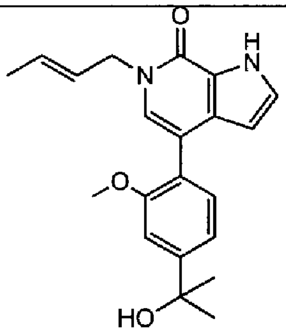
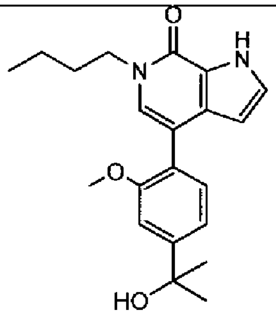
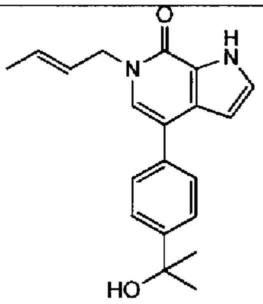
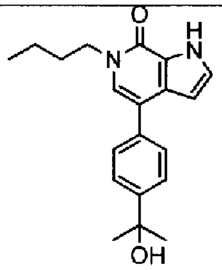
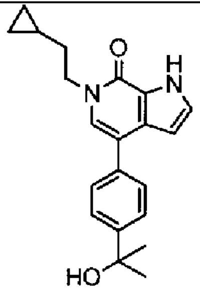
	6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[3-(difluoromethoxy)-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[6-(morpholine-4-carbonyl)-1H-benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one
	7-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-3H-benzimidazole-5-carboxamide

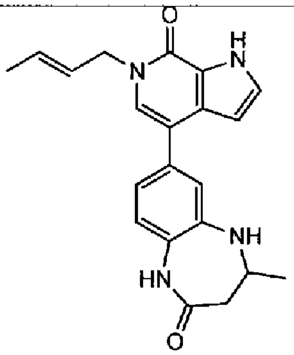
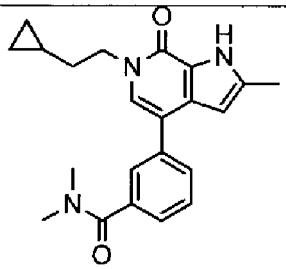
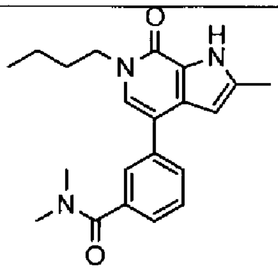
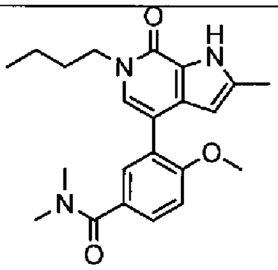
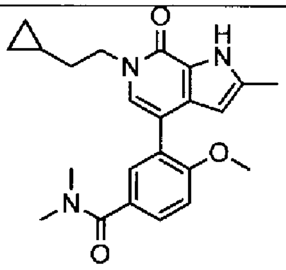
	6-but-3-enyl-4-[7-(morpholine-4-carbonyl)-3H-benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[3-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[3-ethyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[1-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[1-methyl-6-(morpholine-4-carbonyl)benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one

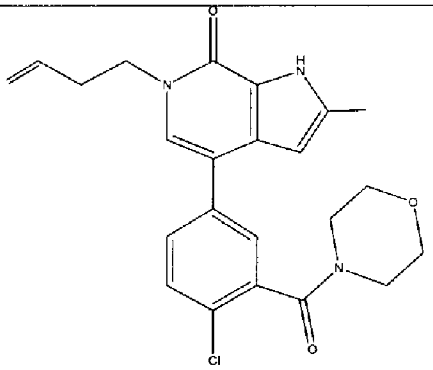
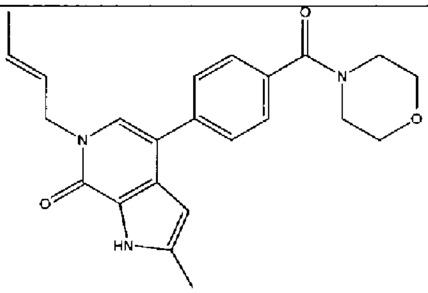
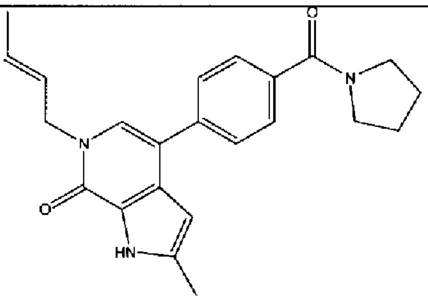
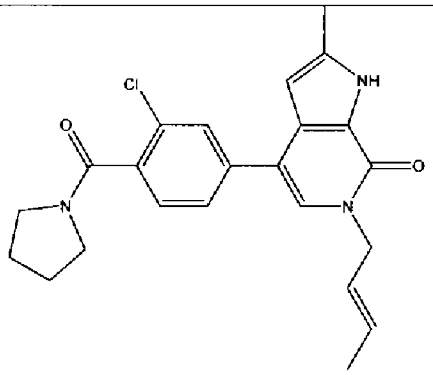
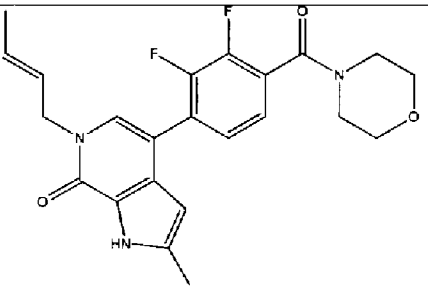
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-4-methoxy-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethyl-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-tetrahydrofuran-3-yl-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-ethyl-4-methoxy-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-methyl-benzamide
	6-[(E)-but-2-enyl]-4-[2-methoxy-5-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

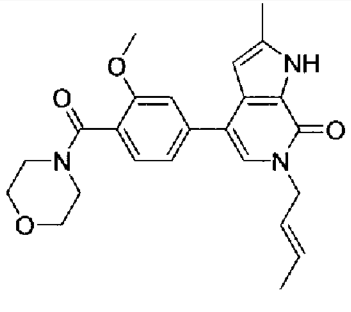
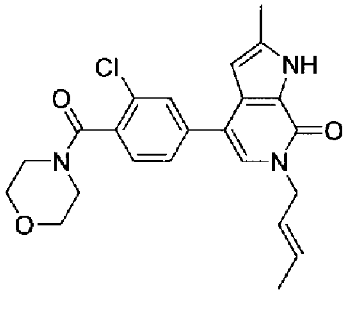
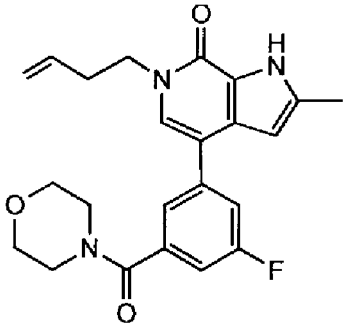
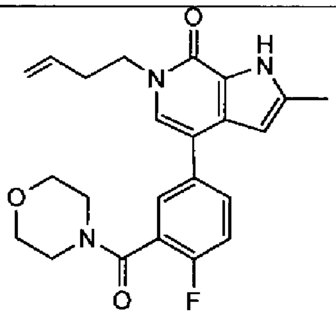
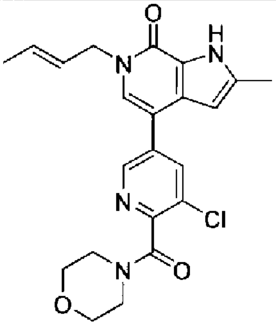
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2,2-difluoroethyl)-4-methoxy-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-isobutyl-4-methoxy-benzamide
	4-[5-(azetidine-1-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-[2-(dimethylamino)ethyl]-4-methoxy-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2-hydroxyethyl)-4-methoxy-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-propyl-benzamide

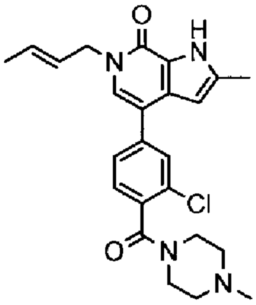
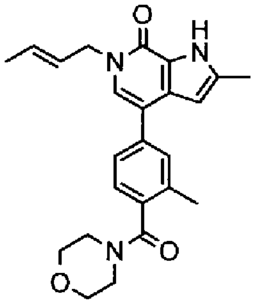
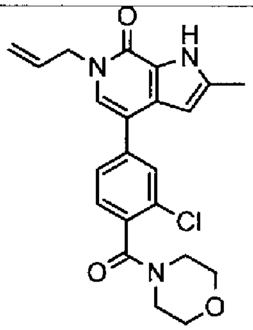
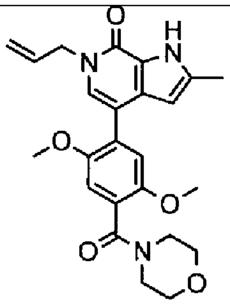
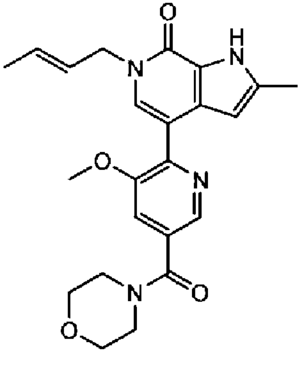
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclobutyl-4-methoxy-benzamide
	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(cyclopropylmethyl)-4-methoxy-benzamide
	4-[5-(2-acetyl-2,6-diazaspiro[3.3]heptane-6-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	4-[5-(2-acetyl-2,6-diazaspiro[3.3]heptane-6-carbonyl)-2-methoxy-phenyl]-6-butyl-1H-pyrrolo[2,3-c]pyridin-7-one

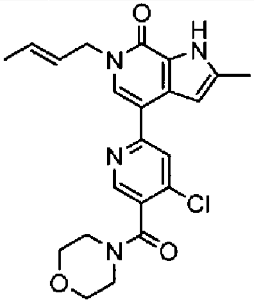
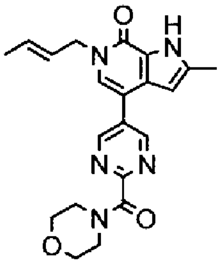
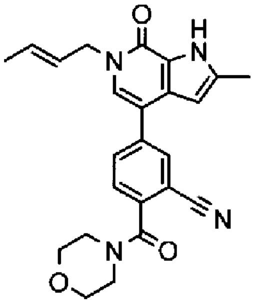
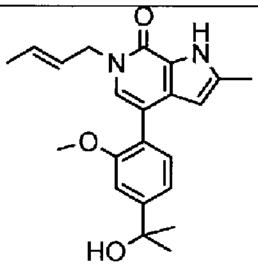
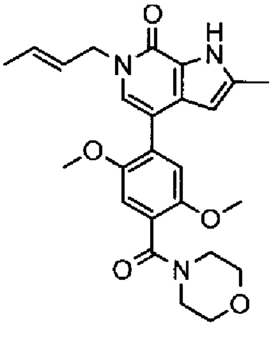
	6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-butyl-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-butyl-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-(2-cyclopropylethyl)-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

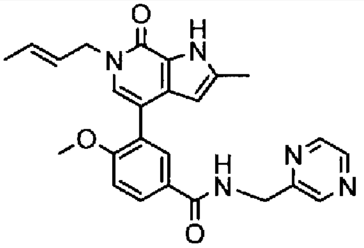
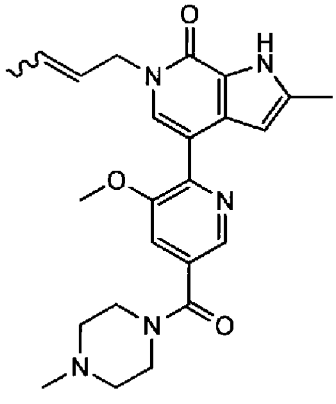
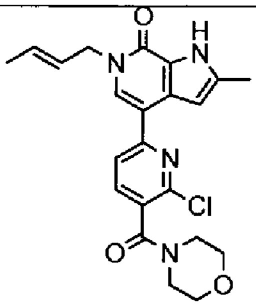
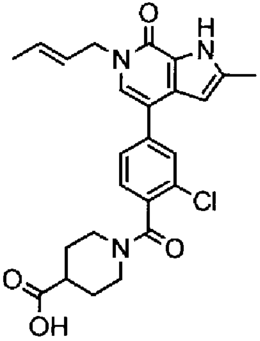
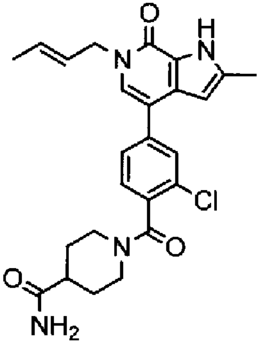
	7-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one
	3-[6-(2-cyclopropylethyl)-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide
	3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide
	3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-N,N-dimethyl-benzamide
	3-[6-(2-cyclopropylethyl)-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethyl-benzamide

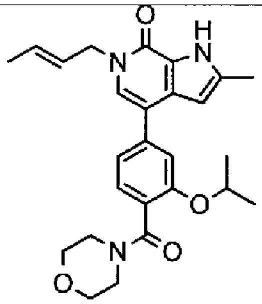
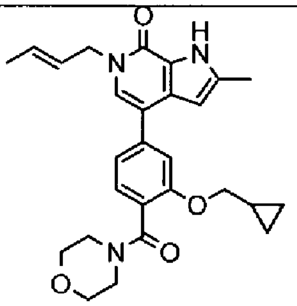
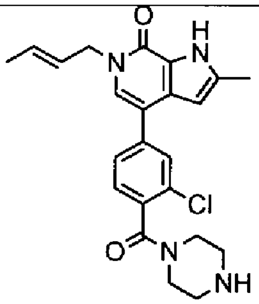
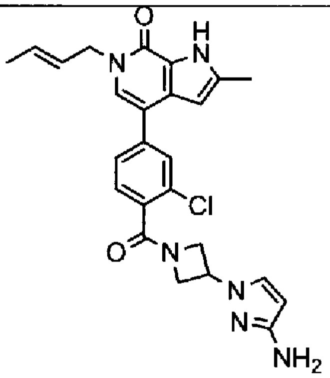
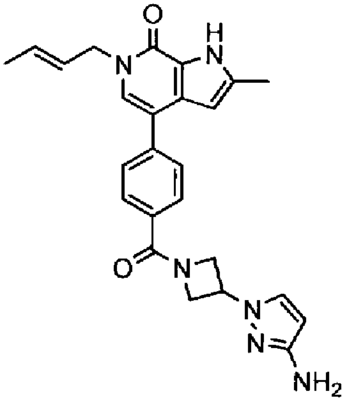
	6-but-3-enyl-4-[4-chloro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-2-methyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-2-methyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[2,3-difluoro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

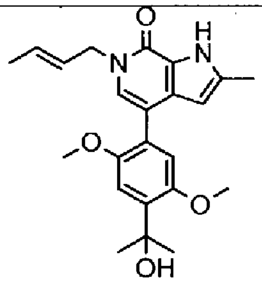
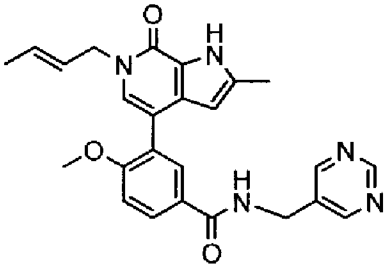
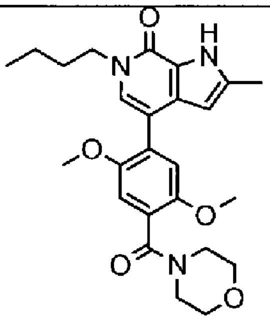
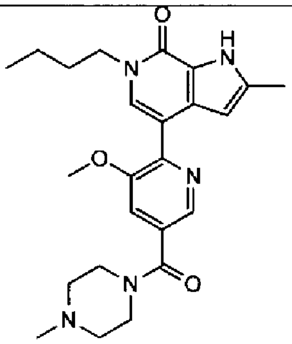
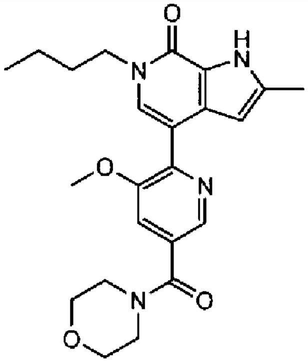
	6-[(E)-but-2-enyl]-4-[3-methoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[5-chloro-6-(morpholine-4-carbonyl)-3-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

	6-[(E)-but-2-enyl]-4-[3-chloro-4-(4-methylpiperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-2-methyl-4-[3-methyl-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one
	6-allyl-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-allyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

	6-[(E)-but-2-enyl]-4-[4-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-2-methyl-4-[2-(morpholine-4-carbonyl)pyrimidin-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one
	5-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-(morpholine-4-carbonyl)benzonitrile
	6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

	3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrazin-2-ylmethyl)benzamide
	6-[(E)-but-2-enyl]-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[6-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	1-[4-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxylic acid
	1-[4-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxamide

	6-[(E)-but-2-enyl]-4-[3-isopropoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[3-(cyclopropylmethoxy)-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-[(E)-but-2-enyl]-4-[3-chloro-4-(piperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]-3-chloro-phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

	6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2,5-dimethoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrimidin-5-ylmethyl)benzamide
	6-butyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-butyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one
	6-butyl-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

and salts thereof.

In certain embodiments the invention provides compound **1000** as described in Examples 124and 126, 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 126.

In certain embodiments the invention provides compound **1001** as described in Examples 125 and 126, 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 126.

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, Waldenstrom'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; 5αreductases 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 $\gamma 1I$ and calicheamicin $\omega I1$ (*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 λ 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 drugs with 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-l (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, SIPl 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-1, 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-l (e.g., a NIK, IKK, p38 or MAP kinase inhibitor), an IL-l 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-lRI, siL-lRII, 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-Rl, 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-l), or a caspase inhibitor (e.g. a IL-l converting enzyme inhibitor or IL-lra).

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.

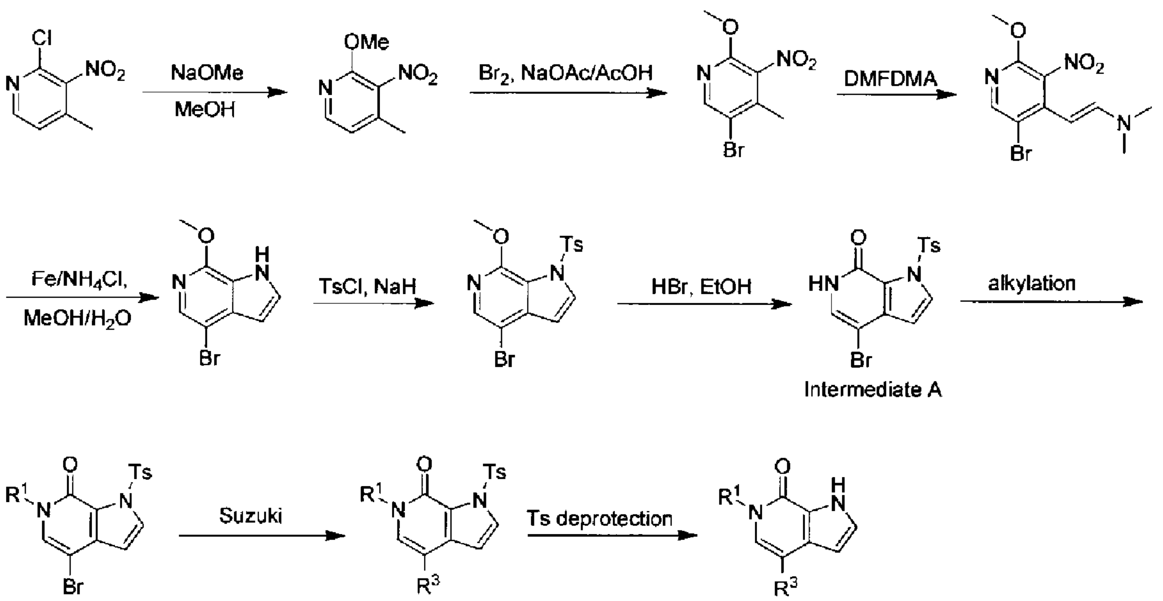
In certain embodiments of any of the methods, the cytotoxic agent is radiotherapy.

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.

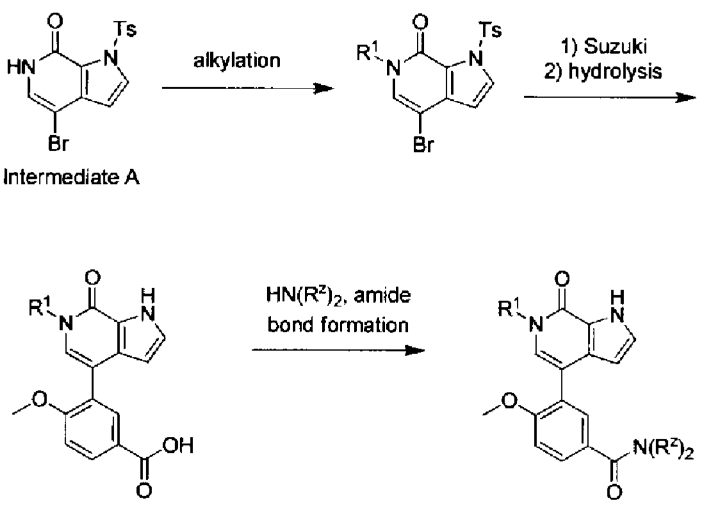
Generic Scheme A



Representative compounds of formula (I) were prepared according to the scheme shown above.

Intermediate A (prepared as described in the general synthesis of intermediates) was treated with an alkylating agent and a base in a solvent such as DMF or acetonitrile at elevated temperature to provide the corresponding N-R^1 substituted derivatives. Those products were coupled with substituted aryl boronic acids under Pd-catalyzed conditions to form biaryl intermediates from which the tosyl group was removed under hydrolytic conditions to yield compounds of formula (I).

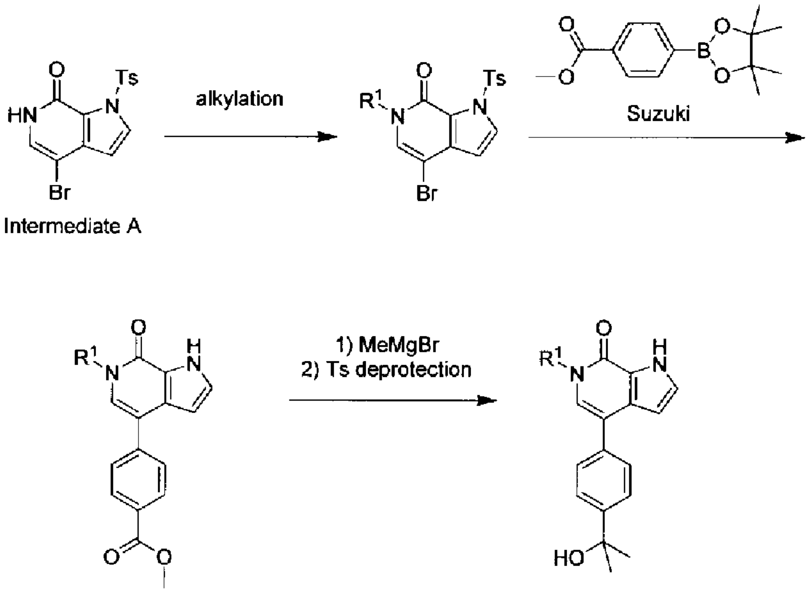
Generic Scheme B



Representative compounds of formula (I) were prepared according to the scheme shown above.

Intermediate A (prepared as described in the general synthesis of intermediates) was treated with an alkylating agent and a base in a solvent such as DMF or acetonitrile at elevated temperature to provide the corresponding N-R^1 substituted derivatives. Those products were coupled with 3-borono-4-methoxybenzoic acid under Pd-catalyzed conditions to form the corresponding biaryl carboxylate. Those intermediates were coupled with various amines to yield compounds of formula (I).

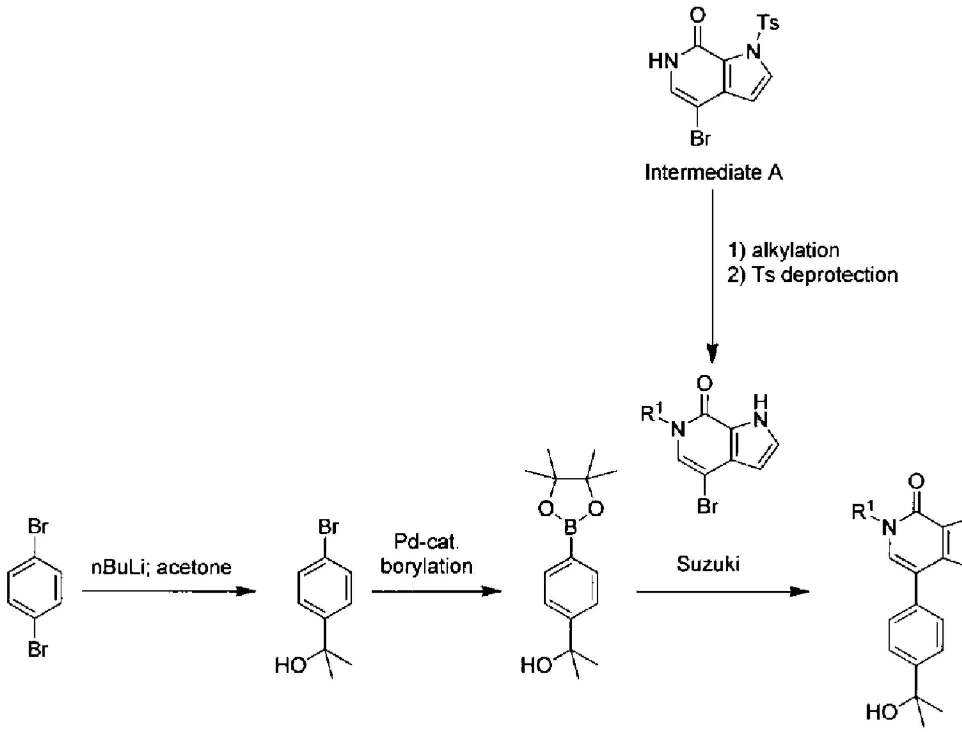
Generic Scheme C



Representative compounds of formula (I) were prepared according to the scheme shown above.

Intermediate A (prepared as described in the general synthesis of intermediates) was treated with an alkylating agent and a base in a solvent such as DMF or acetonitrile at elevated temperature to provide the corresponding N-R^1 substituted derivatives. Those products were coupled with (4-(methoxycarbonyl)phenyl)boronic acid under Pd-catalyzed conditions to form the corresponding biaryl esters. Addition of methylmagnesium bromide, followed by hydrolytic removal of the tosyl group, yielded compounds of formula (I).

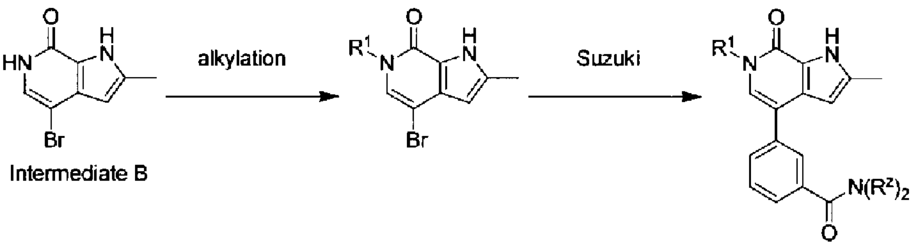
Generic Scheme D



Representative compounds of formula (I) were prepared according to the scheme shown above.

Intermediate A (prepared as described in the general synthesis of intermediates) was treated with an alkylating agent and a base in a solvent such as DMF or acetonitrile at elevated temperature to provide the corresponding N-R^1 substituted bromides. Those products were deprotected under hydrolytic conditions before being coupled with 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-ol (prepared from 1,4-dibromobenze treated with butyl lithium and quenched with acetone, followed by subsequent borylation) to form compounds of formula (I)

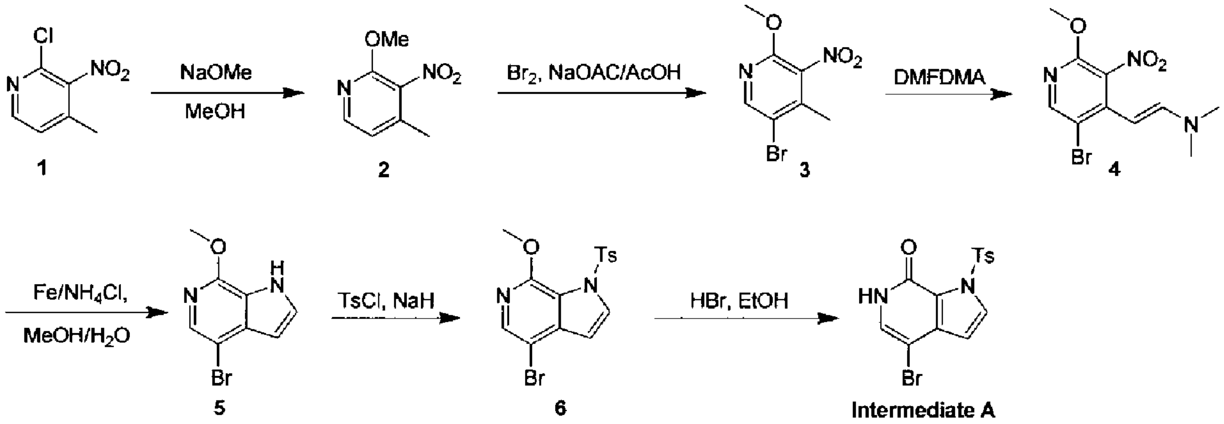
Generic Scheme E



Representative compounds of formula (I) were prepared according to the scheme shown above.

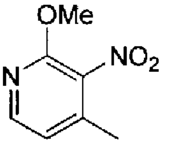
Intermediate B (prepared as described in the general synthesis of intermediates) was treated with an alkylating agent and a base in a solvent such as DMF or acetonitrile at elevated temperature to provide the corresponding N-R^1 substituted derivatives. Those products were coupled (3-(dimethylcarbamoyl)phenyl)boronic acid under Pd-catalyzed conditions to yield compounds of formula (I).

General procedure for the preparation of Intermediate A



Step 1:

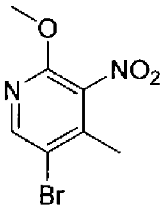
2-methoxy-4-methyl-3-nitropyridine



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. ^1H 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:

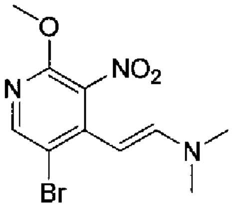
5-bromo-2-methoxy-4-methyl-3-nitropyridine



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 sodium sulfate (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:

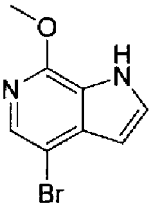
(E)-2-(5-bromo-2-methoxy-3-nitro-4-pyridyl)-N,N-dimethyl-ethenamine



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. 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:

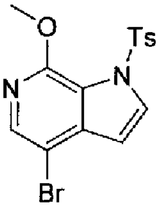
4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine



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 filtrates were concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography (petroleum ether : ethyl acetate=5:1) to yield 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:

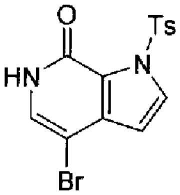
4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine



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 sodium sulfate 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.

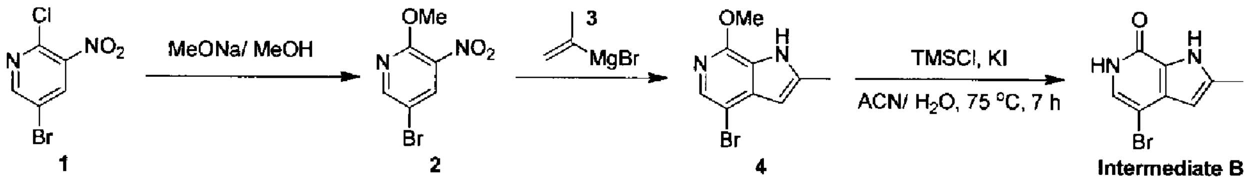
Step 6:

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



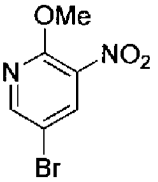
HBr (40% aqueous, 1.1 L) was added to a solution of 4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine (102.5 g, 0.27 mol) in ethanol (200 mL). After addition, the mixture was heated at 90 °C for 2h, at which time TLC indicated that the reaction had gone to completion. The mixture was cooled 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).

General procedure for the preparation of Intermediate B



Step 1:

5-bromo-2-methoxy-3-nitropyridine

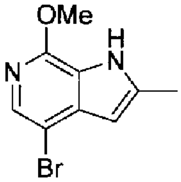


Sodium methoxide (17.2 g, 318.4 mmol) was added to a stirred solution of 5-bromo-2-chloro-3-nitropyridine (15.0 g, 64.2 mmol) in methanol (125 mL). After addition, the reaction mixture was heated at reflux for 2 h. The mixture was concentrated under reduced pressure, and the residue was diluted with 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:

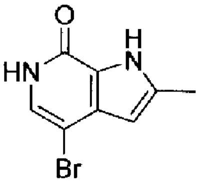
4-bromo-7-methoxy-2-methyl-1H-pyrrolo[2,3-c]pyridine



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) 240.1, 242.1.

Step 3:

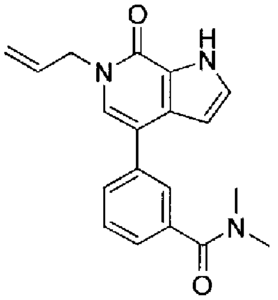
4-bromo-2-methyl-1,6-dihydropyrrolo[2,3-c]pyridin-7-one



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 (**Intermediate B**, 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) 226.8, 228.8

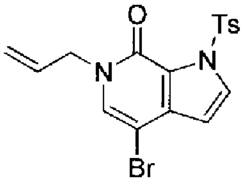
Example 1

3-(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide



Step 1

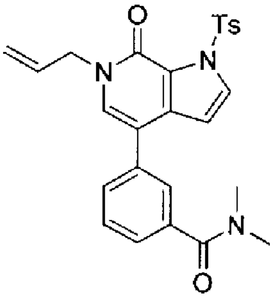
6-allyl-4-bromo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



To a cooled (0°C) solution of 4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one **(intermediate A)** (300 mg, 0.8 mmol) in DMF (4 mL) was added sodium hydride (60% in mineral oil, 50 mg, 1.0 mmol) The mixture was stirred for 15 min and then 3-bromoprop-1-ene (100 mg, 1.0 mmol) was added. The reaction mixture was allowed to warm to room temperature and stirring was continued for 2 h. The reaction was quenched with water (20 mL) and then extracted with ethyl acetate (3 x 20 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 (350 mg, 100% yield) as a yellow solid. This crude material was used in the next step without further purification. LCMS M/Z (M+H) 409.3.

Step 2

3-[6-allyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide

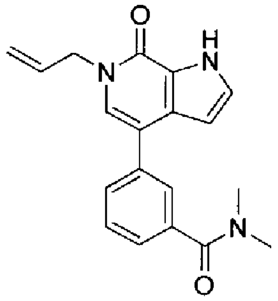


To a mixture of 3-[6-allyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide (Step 1, 350 mg, 0.86 mmol) and [3-(dimethylcarbamoyl)phenyl]boronic acid (220 mg, 1.1 mmol) in acetonitrile (2 mL) and 1 M potassium carbonate in water (2 mL) was added [1,1'-

bis(diphenylphosphino)ferrocene]palladium(ii) dichloride (63 mg, 0.086 mmol). The reaction mixture was subjected to microwave irradiation at 100 °C for 10 minutes. The mixture was filtered through a pad of Celite, using ethyl acetate (30 mL) to rinse. The filtrate was washed with brine (10 mL), dried over sodium sulfate and concentrated under reduced pressure to yield the title compound (300 mg, 70% yield) as a yellow solid. This crude material was used in the next step without further purification. LCMS M/Z (M+H) 476.4.

Step 3

3-(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide



A mixture of 3-[6-allyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide (Step 2, 35 mg, 0.074 mmol) in methanol (1 mL) and 10 M potassium hydroxide in water (0.8 mL) was stirred at 50 °C for 1h. After cooling, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in water (5 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (25-35%ACN/0.1%NH4OH in H2O) to give the title compound (13 mg, 65% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.66 (m, *J* = 7.7, 1.4 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.41 – 7.31 (m, 3H), 6.44 (d, *J* = 2.7 Hz, 1H), 6.02 (m, *J* = 17.2, 10.7, 5.5 Hz, 1H), 5.21 – 5.08 (m, 2H), 4.68 (m, *J* = 5.5, 1.6 Hz, 2H), 2.99 (m, *J* = 11.6 Hz, 6H). LCMS M/Z (M+H) 322.2.

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

Examples 2-54

Example	IUPAC Name	NMR	m/z
2	3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.11 (s, 1H), 7.67 (dt, J = 7.8, 1.4 Hz, 1H), 7.57 (t, J = 1.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.41 (s, 1H), 7.35 (dt, J = 7.7, 1.6 Hz, 2H), 6.43 (d, J = 2.8 Hz, 1H), 4.04 (t, J = 7.3 Hz, 2H), 2.99 (m, J = 11.1 Hz, 6H), 1.83 – 1.62 (m, 2H), 1.33 (h, J = 7.4 Hz, 2H), 0.92 (t, J = 7.4 Hz, 3H).	338.2
3	N,N-dimethyl-3-[6-(3-methylbut-2-enyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.13 (s, 1H), 7.65 (dt, J = 7.8, 1.5 Hz, 1H), 7.56 (t, J = 1.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.39 – 7.36 (m, 2H), 7.34 (d, J = 4.9 Hz, 1H), 6.42 (dd, J = 2.9, 1.6 Hz, 1H), 5.46 – 5.25 (m, 1H), 4.65 (d, J = 6.9 Hz, 2H), 2.99 (m, J = 10.6 Hz, 6H), 1.80 (d, J = 1.3 Hz, 3H), 1.70 (d, J = 1.3 Hz, 3H).	350.2
4	3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.12 (s, 1H), 7.48 (dd, J = 7.5, 1.9 Hz, 1H), 7.41 (dd, J = 7.7, 1.6 Hz, 1H), 7.37 (s, 1H), 7.35 – 7.24 (m, 3H), 6.19 (d, J = 2.8 Hz, 1H), 3.53 (m, J = 3.8 Hz, 6H), 2.88 (d, J = 11.2 Hz, 2H), 2.83 (s, 3H), 2.24 (s, 1H), 2.06 (d, J = 8.3 Hz, 2H), 1.89 – 1.74 (m, 2H), 1.62 (d, J = 11.7 Hz, 2H).	350.2
5	3-[6-(cyclopentylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.11 (s, 1H), 7.67 (dt, J = 7.8, 1.4 Hz, 1H), 7.57 (t, J = 1.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.41 (s, 1H), 7.39 – 7.32 (m, 2H), 6.43 (dd, J = 2.9, 1.6 Hz, 1H), 4.00 (d, J = 7.6 Hz, 2H), 3.06 – 2.93 (m, 6H), 2.46 – 2.35 (m, 1H), 1.62 (m, J = 15.2, 10.9, 9.9, 5.5 Hz, 4H), 1.51 (m, J = 9.6, 5.1 Hz, 2H), 1.39 – 1.25 (m, 2H).	364.2

6	3-[6-[(4-methoxyphenyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6 δ 12.17 (s, 1H), 7.63 (dt, J = 7.9, 1.4 Hz, 1H), 7.56 – 7.47 (m, 3H), 7.41 – 7.30 (m, 4H), 6.91 – 6.85 (m, 2H), 6.43 (d, J = 2.8 Hz, 1H), 5.20 (s, 2H), 3.70 (s, 2H), 2.98 (m, J = 14.1 Hz, 6H).	402.2
7	N,N-dimethyl-3-[7-oxo-6-[(E)-pent-2-enyl]-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide	^{1}H NMR (400 MHz, DMSO-d6 δ 12.17 (s, 1H), 7.66 (dt, J = 7.8, 1.5 Hz, 1H), 7.60 – 7.46 (m, 2H), 7.41 – 7.30 (m, 3H), 6.43 (q, J = 2.4 Hz, 1H), 5.83 – 5.51 (m, 2H), 4.75 – 4.56 (m, 2H), 2.99 (d, J = 13.5 Hz, 6H), 2.01 (ddd, J = 7.6, 6.1, 1.4 Hz, 2H), 0.96 (dt, J = 23.0, 7.4 Hz, 3H).	350.2
8	3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.14 (s, 1H), 7.67 (dt, J = 7.8, 1.4 Hz, 1H), 7.57 (t, J = 1.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.42 (s, 1H), 7.38 – 7.32 (m, 2H), 6.43 (d, J = 2.8 Hz, 1H), 5.99 – 5.75 (m, 1H), 5.17 – 4.94 (m, 2H), 4.12 (m, J = 7.3 Hz, 2H), 2.99 (d, J = 13.3 Hz, 6H).	336.1
9	3-[6-(cyclohexylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6)) δ 12.12 (s, 1H), 7.72 – 7.60 (m, 1H), 7.58 – 7.46 (m, 2H), 7.40 – 7.28 (m, 3H), 6.43 (t, J = 2.2 Hz, 1H), 3.90 (d, J = 7.3 Hz, 2H), 2.99 (d, J = 13.0 Hz, 6H), 1.84 (t, J = 3.5 Hz, 1H), 1.76 – 1.48 (m, 5H), 1.27 – 0.93 (m, 5H).	378.2
10	3-(6-isopentyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6)) δ 7.67 (dd, J = 8.1, 1.7 Hz, 1H), 7.57 (d, J = 1.8 Hz, 1H), 7.56 – 7.45 (m, 1H), 7.42 (s, 1H), 7.38 – 7.32 (m, 2H), 6.43 (t, J = 2.3 Hz, 1H), 4.03 (t, J = 7.4 Hz, 2H), 2.99 (d, J = 13.2 Hz, 6H), 1.70 (q, J = 7.2 Hz, 2H), 1.32 (q, J = 9.3, 8.1 Hz, 4H), 0.87 (t, J = 6.9 Hz, 3H).	352.2

11	3-[6-(cyclobutylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 7.66 (dt, J = 7.8, 1.4 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.41 (s, 1H), 7.38 – 7.32 (m, 2H), 6.43 (d, J = 2.8 Hz, 1H), 4.09 (d, J = 7.3 Hz, 2H), 2.99 (d, J = 13.3 Hz, 6H), 2.78 (p, J = 7.3 Hz, 1H), 1.94 (s, 6H).	350.2
12	3-[6-(2-cyclohexylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.12 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.53 (dd, *J* = 17.7, 10.1 Hz,3H), 7.43 – 7.32 (m, 3H), 6.42 (d, J = 2.5 Hz, 1H), 4.07 (m, J = 13.4, 5.5 Hz, 2H), 3.10 – 2.79 (m, 6H), 1.78 (d, J = 12.8 Hz, 4H), 1.67 (m, 3H), 1.29 (m, 3H), 0.95 (m, J = 11.7 Hz, 4H).	392.2
13	N,N-dimethyl-3-(7-oxo-6-pentyl-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.12 (s, 1H), 7.70 – 7.66 (m, 1H), 7.58 (t, J = 1.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.41 (s, 1H), 7.38 – 7.34 (m, 2H), 6.43 (d, J = 2.8 Hz, 1H), 4.06 (m, J = 7.0 Hz, 2H), 2.99 (m, J = 13.6 Hz, 6H), 1.71 – 1.50 (m, 3H), 0.94 (m, J = 6.1 Hz, 5H).	352.2
14	3-[6-(2-methoxyethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6)) δ 12.17 (s, 1H), 7.66 (m, J = 7.8, 1.5 Hz, 1H), 7.60 – 7.49 (m, 2H), 7.43 – 7.31 (m, 3H), 6.44 (d, J = 2.8 Hz, 1H), 4.22 (m, J = 5.6 Hz, 2H), 3.64 (m, J = 5.5 Hz, 2H), 3.26 (s, 3H), 2.99 (d, J = 13.1 Hz, 6H).	340.2
15	3-[6-(3-methoxypropyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 7.68 (dt, J = 7.7, 1.5 Hz, 1H), 7.60 – 7.47 (m, 2H), 7.41 – 7.30 (m, 3H), 6.43 (d, J = 2.8 Hz, 1H), 4.09 (t, J = 7.2 Hz, 2H), 3.38 (t, J = 6.2 Hz, 2H), 3.24 (d, J = 1.2 Hz, 3H), 3.09 – 2.87 (m, 6H), 1.95 (t, J = 7.0 Hz, 2H).	354.2
16	3-(6-isobutyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6)) δ 12.14 (s, 1H), 7.69 – 7.65 (m, 1H), 7.56 (t, *J* = 1.8 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 5.7 Hz, 2H), 6.44 (d, *J* = 2.7 Hz, 1H), 3.88 (d, *J* = 7.4 Hz, 2H), 3.07 – 2.92 (m, 6H), 2.33 – 1.79 (m, 1H), 0.90 (m, *J* = 6.7 Hz, 6H).	338

17	3-[6-(cyclopropylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 7.68 (m, J = 7.8, 1.4 Hz, 1H), 7.58 (t, J = 1.8 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.47 (s, 1H), 7.40 – 7.33 (m, 2H), 6.44 (m, J = 2.8, 1.4 Hz, 1H), 3.92 (d, J = 7.1 Hz, 2H), 3.09 – 2.92 (m, 6H), 1.30 (m, J = 12.6, 7.6, 5.1 Hz, 1H), 0.57 – 0.36 (m, 4H).	336.2
18	6-but-3-enyl-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d6)) δ 12.17 (s, 1H), 8.17 (t, J = 1.8 Hz, 1H), 7.93 (m, J = 7.7, 1.4 Hz, 1H), 7.84 (m, J = 7.9, 1.4 Hz, 1H), 7.68 (t, J = 7.8 Hz, 1H), 7.51 (s, 1H), 7.39 (d, J = 2.8 Hz, 1H), 6.47 (d, J = 2.8 Hz, 1H), 5.96 – 5.79 (m, 1H), 5.13 – 4.98 (m, 2H), 4.14 (m, J = 7.2 Hz, 2H), 2.61 (s, 3H).	347.2
19	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-5-fluoro-N,N-dimethyl-benzamide	1H NMR (400 MHz, DMSO-d6) δ 12.19 (s, 1H), 7.50 – 7.35 (m, 4H), 7.22 (ddd, J = 8.9, 2.5, 1.3 Hz, 1H), 6.45 (d, J = 2.7 Hz, 1H), 5.76 – 5.56 (m, 2H), 4.60 (d, J = 4.8 Hz, 2H), 2.98 (d, J = 15.3 Hz, 6H), 1.65 (d, J = 4.1 Hz, 3H).	354
20	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-benzamide	1H NMR (400 MHz, DMSO) δ 12.18 (s, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 13.9 Hz, 2H), 7.53 – 7.49 (m, 1H), 7.49 – 7.43 (m, 2H), 7.39 (d, J = 2.8 Hz, 1H), 6.50 (d, J = 2.8 Hz, 1H), 5.74 – 5.57 (m, 2H), 4.64 – 4.56 (m, 2H), 1.69 – 1.60 (m, 3H).	326
21	6-but-2-enyl-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.69 – 7.62 (m, 2H), 7.51 – 7.44 (m, 2H), 7.40 – 7.32 (m, 2H), 6.48 (d, *J* = 2.8 Hz, 1H), 5.75 – 5.60 (m, 2H), 4.65 – 4.57 (m, 2H), 3.30 (s, 3H), 2.43 – 2.24 (m, 5H), 2.21 (s, 3H), 1.67 – 1.61 (m, 3H).	392
22	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-fluoro-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (s, 1H), 8.10 (s, 1H), 7.93 (t, *J* = 1.5 Hz, 1H), 7.65 – 7.57 (m, 1H), 7.57 – 7.51 (m, 2H), 7.44 (s, 1H), 7.39 (t, *J* = 2.7 Hz, 1H), 6.50 – 6.44 (m, 1H), 5.71 – 5.60 (m, 2H), 4.60 (d, *J* = 4.5 Hz, 2H), 1.69 – 1.62 (m, 3H).	326

23	6-but-2-enyl-4-(4-tert-butylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 7.54 – 7.44 (m, 4H), 7.34 (t, J = 2.8 Hz, 1H), 7.21 (s, 1H), 6.47 – 6.42 (m, 1H), 5.74 – 5.59 (m, 2H), 4.64 – 4.55 (m, 2H), 1.68 – 1.62 (m, 3H), 1.32 (s, 9H).	321
24	4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-methyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 8.44 (q, J = 4.5 Hz, 1H), 7.98 – 7.89 (m, 2H), 7.70 – 7.62 (m, 2H), 7.41 – 7.34 (m, 2H), 6.51 – 6.44 (m, 1H), 5.72 – 5.60 (m, 2H), 4.61 (d, J = 4.3 Hz, 2H), 2.81 (d, J = 4.5 Hz, 3H), 1.65 (d, J = 4.2 Hz, 3H).	322
25	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-methyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.46 (d, J = 4.8 Hz, 1H), 8.01 – 7.99 (m, 1H), 7.80 – 7.75 (m, 1H), 7.73 – 7.68 (m, 1H), 7.58 – 7.51 (m, 1H), 7.37 (t, J = 2.8 Hz, 1H), 7.33 (s, 1H), 6.48 – 6.42 (m, 1H), 5.70 – 5.63 (m, 2H), 4.65 – 4.57 (m, 2H), 2.81 (d, J = 4.5 Hz, 3H), 1.69 – 1.61 (m, 3H).	322
26	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-cyclopropyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.46 (d, J = 4.2 Hz, 1H), 7.97 (t, J = 1.7 Hz, 1H), 7.79 – 7.73 (m, 1H), 7.73 – 7.68 (m, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.37 (t, J = 2.8 Hz, 1H), 7.32 (s, 1H), 6.46 – 6.41 (m, 1H), 5.73 – 5.57 (m, 2H), 4.61 (d, J = 4.1 Hz, 2H), 2.93 – 2.80 (m, 1H), 1.69 – 1.62 (m, 3H), 0.76 – 0.65 (m, 2H), 0.62 – 0.52 (m, 2H).	348
27	6-but-2-enyl-4-[3-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.70 – 7.63 (m, 2H), 7.56 – 7.49 (m, 1H), 7.49 – 7.43 (m, 1H), 7.37 (t, J = 2.8 Hz, 1H), 7.34 (d, J = 4.0 Hz, 1H), 6.46 – 6.40 (m, 1H), 5.71 – 5.62 (m, 2H), 4.60 (d, J = 4.2 Hz, 2H), 3.49 (t, J = 6.8 Hz, 2H), 3.43 (t, J = 6.4 Hz, 2H), 1.94 – 1.75 (m, 5H), 1.69 – 1.61 (m, 2H).	362

28	4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-cyclopropyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 8.43 (d, *J* = 4.2 Hz, 1H), 7.94 – 7.87 (m, 2H), 7.68 – 7.62 (m, 2H), 7.40 – 7.36 (m, 2H), 6.49 – 6.44 (m, 1H), 5.69 – 5.64 (m, 2H), 4.63 – 4.58 (m, 2H), 2.93 – 2.80 (m, 1H), 1.68 – 1.62 (m, 3H), 0.75 – 0.65 (m, 2H), 0.64 – 0.53 (m, 2H).	348
29	6-but-2-enyl-4-[4-(hydroxymethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.57 – 7.48 (m, 2H), 7.42 – 7.37 (m, 2H), 7.35 (t, *J* = 2.8 Hz, 1H), 7.24 (s, 1H), 6.46 – 6.39 (m, 1H), 5.72 – 5.61 (m, 2H), 5.18 (t, *J* = 5.7 Hz, 1H), 4.64 – 4.57 (m, 2H), 4.54 (d, *J* = 5.7 Hz, 2H), 1.70 – 1.59 (m, 3H).	295
30	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.11 – 7.98 (m, 2H), 7.84 – 7.80 (m, 1H), 7.76 – 7.69 (m, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.38 (q, *J* = 3.3, 2.8 Hz, 2H), 7.34 (s, 1H), 6.50 – 6.41 (m, 1H), 5.66 (t, *J* = 4.1 Hz, 2H), 4.61 (d, *J* = 4.0 Hz, 2H), 1.70 – 1.61 (m, 3H).	308
31	6-but-2-enyl-4-(4-isopropylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 7.54 – 7.46 (m, 2H), 7.38 – 7.28 (m, 3H), 7.21 (s, 1H), 6.48 – 6.39 (m, 1H), 5.76 – 5.57 (m, 2H), 4.59 (d, *J* = 5.4 Hz, 2H), 3.00 – 2.87 (m, 1H), 1.69 – 1.62 (m, 3H), 1.24 (d, *J* = 6.9 Hz, 6H).	307
32	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.70 – 7.63 (m, 1H), 7.58 – 7.46 (m, 2H), 7.40 – 7.31 (m, 3H), 6.45 – 6.39 (m, 1H), 5.67 (d, *J* = 4.8 Hz, 1H), 4.64 – 4.56 (m, 2H), 2.99 (d, *J* = 10.1 Hz, 7H), 1.68 – 1.61 (m, 3H).	336
33	6-but-2-enyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.62 (d, *J* = 4.9 Hz, 3H), 7.49 – 7.27 (m, 2H), 6.57 – 6.37 (m, 1H), 5.74 – 5.61 (m, 1H), 4.61 (d, *J* = 5.1 Hz, 2H), 3.53 – 3.41 (m, 5H), 1.95 – 1.73 (m, 5H), 1.73 – 1.46 (m, 3H).	362

34	N-[4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]methanesulfonamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 9.77 (s, 1H), 7.58 – 7.51 (m, 2H), 7.35 (t, *J* = 2.8 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.22 (s, 1H), 6.47 – 6.42 (m, 1H), 5.69 – 5.63 (m, 2H), 4.58 (d, *J* = 4.7 Hz, 2H), 3.01 (s, 3H), 1.70 – 1.61 (m, 3H).	358
35	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-isopropyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.25 (d, *J* = 7.7 Hz, 1H), 7.99 (t, *J* = 1.8 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.73 – 7.67 (m, 1H), 7.62 – 7.50 (m, 1H), 7.37 (t, *J* = 2.7 Hz, 1H), 7.32 (s, 1H), 6.47 – 6.37 (m, 1H), 5.67 (d, *J* = 4.5 Hz, 1H), 4.61 (d, *J* = 4.1 Hz, 2H), 4.21 – 4.03 (m, 1H), 1.68 – 1.61 (m, 2H), 1.24 – 1.15 (m, 8H).	350
36	4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.68 – 7.61 (m, 1H), 7.53 – 7.47 (m, 2H), 7.38 – 7.35 (m, 1H), 7.35 (s, 1H), 6.62 – 6.32 (m, 1H), 5.83 – 5.58 (m, 2H), 4.68 – 4.44 (m, 2H), 2.99 (s, 7H), 1.68 – 1.63 (m, 3H).	336
37	6-but-2-enyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.70 – 7.61 (m, 2H), 7.52 – 7.48 (m, 2H), 7.41 – 7.33 (m, 2H), 6.50 – 6.44 (m, 1H), 5.74 – 5.60 (m, 1H), 4.60 (d, *J* = 5.1 Hz, 2H), 3.62 (s, 5H), 3.29 (d, *J* = 1.5 Hz, 4H), 1.69 – 1.63 (m, 3H).	378
38	3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile	1H NMR (400 MHz, DMSO-d6) d 12.02 (br. s., 2H), 7.86 (dd, J = 2.18, 8.62 Hz, 1H), 7.70 - 7.75 (m, 1H), 7.51 - 7.67 (m, 1H), 7.25 - 7.33 (m, 3H), 7.16 - 7.24 (m, 1H), 6.04 (t, J = 2.29 Hz, 1H), 5.50 - 5.75 (m, 3H), 4.67 (d, J = 6.86 Hz, 1H), 4.56 (d, J = 4.57 Hz, 2H), 3.82 (s, 4H), 1.77 (dd, J = 1.35, 6.75 Hz, 1H), 1.65 (d, J = 4.99 Hz, 3H)	319
39	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-benzamide		326

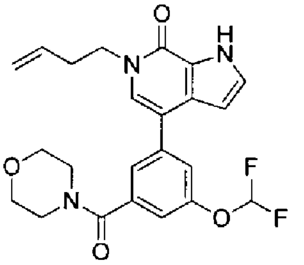
40	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluoro-benzamide	1H NMR (400 MHz, DMSO) δ 12.12 (s, 1H), 8.08 – 7.98 (m, 2H), 7.98 – 7.88 (m, 1H), 7.45 – 7.37 (m, 2H), 7.37 – 7.25 (m, 2H), 6.20 – 6.13 (m, 1H), 5.78 – 5.56 (m, 2H), 4.60 (d, J = 3.8 Hz, 2H), 1.66 (d, J = 4.9 Hz, 3H).	326
41	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluoro-N,N-dimethyl-benzamide	1H NMR (400 MHz, DMSO) δ 7.54 – 7.51 (m, 1H), 7.49 – 7.44 (m, 1H), 7.41 – 7.35 (m, 1H), 7.34 – 7.32 (m, 1H), 7.29 (d, J = 0.5 Hz, 1H), 6.23 – 6.12 (m, 1H), 5.77 – 5.56 (m, 2H), 4.67 – 4.51 (m, 2H), 2.98 (s, 6H), 1.65 (d, J = 4.8 Hz, 3H).	354
42	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-N,N-dimethyl-benzamide		354
43	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-N,N-dimethyl-benzamide	1H NMR (400 MHz, DMSO) δ 7.54 – 7.51 (m, 1H), 7.49 – 7.44 (m, 1H), 7.41 – 7.35 (m, 1H), 7.34 – 7.32 (m, 1H), 7.29 (d, J = 0.5 Hz, 1H), 6.23 – 6.12 (m, 1H), 5.77 – 5.56 (m, 2H), 4.67 – 4.51 (m, 2H), 2.98 (s, 6H), 1.65 (d, J = 4.8 Hz, 3H).	370
44	4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzamide	1H NMR (400 MHz, DMSO) δ 12.12 (s, 1H), 7.56 – 7.50 (m, 1H), 7.50 – 7.44 (m, 1H), 7.43 – 7.35 (m, 1H), 7.34 – 7.32 (m, 1H), 7.30 – 7.27 (m, 1H), 6.17 (t, J = 2.6 Hz, 1H), 5.76 – 5.59 (m, 2H), 4.59 (d, J = 4.6 Hz, 2H), 2.98 (s, 6H), 1.65 (d, J = 4.8 Hz, 3H).	342
45	6-(2-furylmethyl)-4-phenyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, CDCl3): δ 10.20 (s, 1 H), 7.57-7.54 (m, 2 H), 7.47-7.44 (m, 2 H), 7.38-7.35 (m, 2 H), 7.29-7.26 (m, 1 H), 7.13 (s, 1 H), 6.55-6.54 (m, 1 H), 6.43-6.43 (m, 1 H), 6.35-6.33 (m, 1 H), 5.31 (s, 2 H).	290

46	3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile	^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.98 (s, 1 H), 7.86-7.84 (m, 1 H), 7.74 (d, *J* = 2.4 Hz, 1 H), 7.30-7.25 (m, 3 H), 6.04 (t, *J* = 2.4 Hz, 1 H), 3.99 (t, *J* = 7.2 Hz, 2 H) , 3.82 (s, 3 H), 1.69-1.65 (m, 2 H), 1.35-1.30 (m, 2 H), 0.93-0.90 (t, *J* = 7.2, 3 H).	321
47	3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzonitrile	^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.99 (s, 1 H), 7.86-7.84 (m, 1 H), 7.73 (s, 1 H), 7.30-7.25 (m, 3 H), 6.03-6.02 (m, 1 H), 4.07-4.04 (m, 2 H), 3.81 (s, 3 H), 1.61-1.56 (m, 2 H), 0.74-0.67 (m, 1 H), 0.41-0.39 (m, 2 H), 0.09-0.01 (m, 2 H).	333
48	6-but-3-enyl-4-[3,4-difluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 12.18 (s, 1H), 7.72 (ddd, J = 11.7, 7.5, 2.2 Hz, 1H), 7.48 (s, 1H), 7.45 – 7.36 (m, 2H), 6.45 (d, J = 2.8 Hz, 1H), 5.86 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.14 – 4.99 (m, 2H), 4.10 (t, J = 7.3 Hz, 2H), 3.68 (m, 4H), 3.57 (m, J = 4.8 Hz, 2H), 3.35 (m, J = 4.7 Hz, 2H).	414
49	6-but-3-enyl-4-[3-fluoro-5-(3-methylmorpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, CD_3OD) δ 7.48-7.43 (m, 2 H), 7.43 (d, *J* = 3.2 Hz, 1 H), 7.38 (s, 1 H), 7.39-7.17 (m, 1 H), 6.55 (d, *J* = 3.2 Hz, 1 H), 5.95-5.88 (m, 1 H), 5.12-5.05 (m, 2 H), 4.22 (t, *J* = 7.2 Hz, 2 H), 3.92-3.90 (m, 1 H), 3.72-3.71 (m, 2 H), 3.36-3.32 (m, 4 H), 2.62-2.57 (m, 2 H), 1.42 (d, *J* = 6.8 Hz, 3 H).	410
50	3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-(morpholine-4-carbonyl)benzonitrile	^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.21 (s, 1 H), 8.09 (s, 1 H), 7.90 (s, 1 H), 7.83 (s, 1H), 7.58 (s,1 H), 7.38 (s, 1 H), 6.46 (s, 1 H), 5.85-5.81 (m, 1 H), 5.08-4.99 (m,2 H), 4.11-4.08 (m, 2 H), 3.63-3.53 (m, 4 H), 3.36-3.26 (m, 4 H), 2.48-2.46 (m, 2 H).	403.3
51	6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 12.22 (s, 1H), 7.70 (d, J = 1.7 Hz, 1H), 7.65 (dd, J = 7.9, 1.7 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.39 (d, J = 2.8 Hz, 1H), 6.48 (d, J = 2.8 Hz, 1H), 5.74 – 5.59 (m, 2H), 4.60 (d, J = 4.9 Hz, 2H), 3.75 – 3.62 (m, 4H), 3.61 – 3.53 (m, 2H), 3.24 – 3.16 (m, 2H), 1.68 – 1.60 (m, 3H).	412

52	6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 12.18 (s, 1H), 7.68 (d, J = 1.7 Hz, 1H), 7.63 (dd, J = 7.9, 1.7 Hz, 1H), 7.47 (s, 1H), 7.44 (d, J = 6.1 Hz, 1H), 7.39 (d, J = 2.8 Hz, 1H), 6.47 (d, J = 2.8 Hz, 1H), 5.74 – 5.60 (m, 2H), 4.60 (d, J = 4.9 Hz, 2H), 3.57 – 3.42 (m, 2H), 3.24 – 3.10 (m, 3H), 1.97 – 1.74 (m, 5H), 1.70 – 1.58 (m, 3H).	396
53	6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 12.18 (s, 1H), 7.52 (s, 1H), 7.45 (t, J = 1.5 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.23 (m, J = 8.8, 2.5, 1.3 Hz, 1H), 6.45 (d, J = 2.8 Hz, 1H), 6.00 – 5.75 (m, 1H), 5.21 – 4.92 (m, 2H), 4.12 (t, J = 7.3 Hz, 2H), 3.62 (m, 8H).	396
54	6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 12.14 (s, 1H), 7.71 (m, J = 8.6, 5.1, 2.4 Hz, 1H), 7.58 (m, J = 6.4, 2.4 Hz, 1H), 7.47 – 7.33 (m, 3H), 6.41 (d, J = 2.9 Hz, 1H), 5.95 – 5.78 (m, 1H), 5.15 – 4.96 (m, 2H), 4.20 – 4.02 (m, 2H), 3.67 (m, 4H), 3.56 (m, J = 5.1 Hz, 4H), 2.49 (m, J = 4.7 Hz, 2H).	396

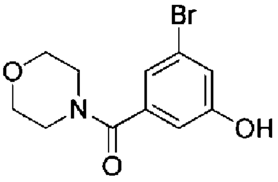
Example 55

6-(but-3-en-1-yl)-4-(3-(difluoromethoxy)-5-(morpholine-4-carbonyl)phenyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



Step 1:

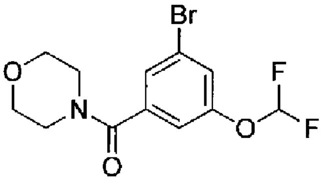
(3-bromo-5-hydroxyphenyl)(morpholino)methanone



To a solution of 3-bromo-5-hydroxybenzoic acid (2.00 g, 9.2 mmol) in DMF (20 mL) was added HATU (3.89 g, 10.2 mmol), DIPEA (1.32 g, 10.2 mmol) and morpholine (887 mg, 10.2 mmol). The reaction mixture was stirred at room temperature for 10 h, at which time LCMS showed the completion of the reaction. The mixture was poured into water (40 mL) and extracted with ethyl acetate (50 mL x 3). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography (Petroleum ether/ethyl acetate = 1:2) to give the title compound (900 mg, 31% yield) as a white solid.

Step 2:

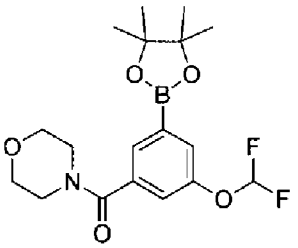
(3-bromo-5-(difluoromethoxy)phenyl)(morpholino)methanone



To a solution of (3-bromo-5-hydroxyphenyl)(morpholino)methanone (900 mg, 3.2 mmol) in DMF (20 mL)/H_2O (5 mL) was added K_2CO_3 (877 mg, 6.3 mmol) and sodium 2-chloro-2,2-difluoroacetate (966 mg, 6.3 mmol). The reaction mixture was heated at 100 °C for 2 h, at which time LCMS showed the completion of the reaction. After cooled, the mixture was poured into water (600 mL) and the resulting mixture was extracted with ethyl acetate (50 mL x 3). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography (Petroleum ether/ethyl acetate = 1:1) to give the title compound (400 mg, 38% yield) as a yellow solid.

Step 3:

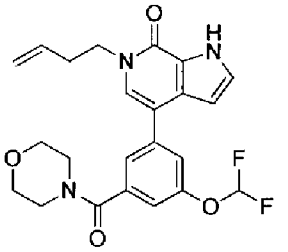
(3-(difluoromethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)(morpholino)methanone



A mixture of (3-bromo-5-(difluoromethoxy)phenyl)(morpholino)methanone (400 mg, 1.19 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (455 mg, 1.79 mmol), potassium acetate (175 mg, 1.79 mmol) and Pd(dppf)Cl_2 (73 mg, 0.1 mmol) in dioxane (25 mL) was heated at 120 °C under N_2 for 5 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (60 mL) and washed with water (30 mL x 2). The separated organic layer was concentrated under reduced pressure. The crude product was purified by flash chromatography (Petroleum ether/ethyl acetate = 1:1) to give the title compound (300 mg, 66% yield) as a yellow oil.

Step 4:

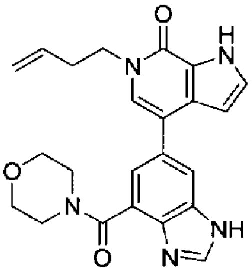
6-(but-3-en-1-yl)-4-(3-(difluoromethoxy)-5-(morpholine-4-carbonyl)phenyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



In a similar procedure as shown in Example A06, the title compound was prepared in 13.8% yield from (3-(difluoromethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl)phenyl)(morpholino)methanone and 4-bromobut-1-ene. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.18 (s, 1 H), 7.55-7.36 (m, 3 H), 7.18-7.15 (m, 1 H), 6.42 (s, 1 H), 5.87-5.80 (m, 1 H), 5.07-4.99 (m,2 H), 4.11-4.08 (m, 2 H), 3.63-3.53 (m, 4 H), 3.36-3.26 (m, 4 H), 2.48-2.46 (m, 2 H). LCMS M/Z (M+H) 444.

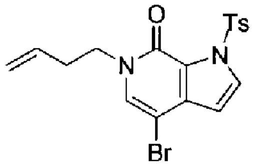
Example 56

6-but-3-enyl-4-[7-(morpholine-4-carbonyl)-3H-benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one



Step 1

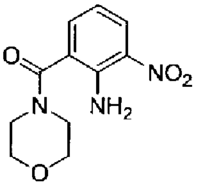
4-bromo-6-(but-3-en-1-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one



To a solution of 4-bromo-1-(p-tolylsulfonyl)-6*H*-pyrrolo[2,3-*c*]pyridin-7-one (10.0 g, 27.23 mmol) (**Intermediate A**) in DMF (150 mL) were added cesium carbonate (17.8 g, 54.46 mmol) and 4-bromobut-1-ene (4.8 g, 35.40 mmol). After addition, the mixture was stirred at ambient temperature for 16 h, at which time LCMS indicated the reaction had gone to completion. The solid was removed by filtration and the filtrate was concentrated under reduce pressure. The residue was dissolved in H_2O (100 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic layers were concentrated under reduced pressure and the crude product was purified by silica gel chromatography column (Hexanes/ethyl acetate = 5:1) to give title compound (6.0 g, 52% yield) as a colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.05-8.04 (m, 1 H), 7.94-7.89 (m, 1 H), 7.76 (s, 1 H), 7.45-7.35 (m, 2 H), 6.58-6.57 (m, 1 H), 5.73-5.66 (m, 1 H), 4.92-4.84 (m, 2 H), 3.93-3.89 (m, 2 H), 2.39 (s, 3 H), 2.36-2.27(m, 2 H).

Step 2

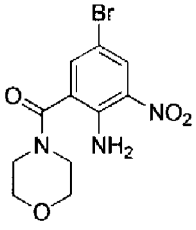
(2-amino-3-nitrophenyl)(morpholino)methanone



To a solution of morpholine (2.4 g, 27.45 mmol) in DMF (80 mL) was added 2-amino-3-nitrobenzoic acid (5.0 g, 27.45 mmol), HATU (12.5 g, 32.94 mmol) and *N*-ethyl-*N*-isopropylpropan-2-amine (10 mL). The reaction mixture was stirred at ambient temperature for 15 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 (100 mL) and washed with water (2 x 50 mL). The organic solution was concentrated under reduced pressure and the residue was purified by silica gel chromatography (Hexanes/ethyl acetate = 3:1) to give the title compound (5.0 g, 73% yield) as a yellow solid.

Step 3

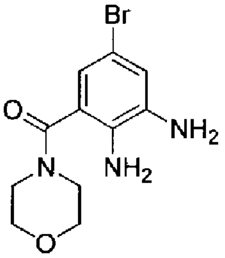
(2-amino-5-bromo-3-nitrophenyl)(morpholino)methanone



To a solution of (2-amino-3-nitrophenyl)(morpholino)methanone (5.0 g, 19.90 mmol) in acetic acid (50 mL) was added Br_2 (3.82 g, 23.88 mmol). The reaction mixture was stirred at 0 °C for 30 min, at which time LCMS indicated that the reaction had gone to completion. The reaction mixture was poured into ice-cold water (30 mL). The resulting precipitate was collected by filtration and dried under reduced pressure to give the title compound (5.0 g, 76% yield) as yellow solid.

Step 4

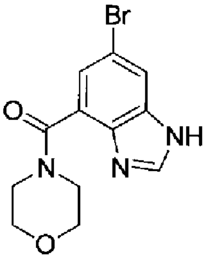
(2,3-diamino-5-bromophenyl)(morpholino)methanone



To a solution of (2-amino-5-bromo-3-nitrophenyl)(morpholino)methanone (5.0 g, 15.15 mmol) in EtOH/H_2O (5:1, 100 mL) was added NH_4Cl (4.1 g, 75.73 mmol) and Fe (4.2 g, 75.73 mmol). The reaction mixture was heated at reflux for 15 h, at which time LCMS indicated that the reaction had gone to completion. The solid was removed by filtration and the filtrate concentrated under reduced pressure. The residue was dissolved in ethyl acetate (100 mL) and washed with brine (2 x 40 mL). The separated organic layer was concentrated to give the crude title compound (4.2 g, 92% yield) as a yellow oil.

Step 5

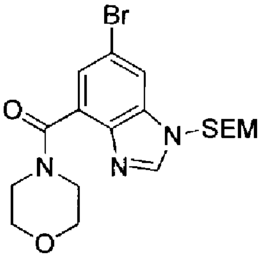
(6-bromo-1*H*-benzo[*d*]imidazol-4-yl)(morpholino)methanone



To a solution of (2-amino-5-bromo-3-nitrophenyl)(morpholino)methanone (4.2 g, 12.72 mmol) in DMF (40 mL) was added triethoxymethane (2.8 g, 19.08 mmol) and 4-methylbenzenesulfonic acid (220 mg, 1.27 mmol). After addition, the reaction mixture was stirred at ambient temperature for 15 h, at which time LCMS indicated that the reaction had gone to completion. The solvent was evaporated under reduced pressure, and the residue was diluted with water (40 mL). The mixture was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were concentrated under reduced pressure. The crude product was purified by silica gel chromatography (dichloromethane/ methanol = 10:1) to give the title compound (3.0 g, 76% yield) as a brown solid.

Step 6

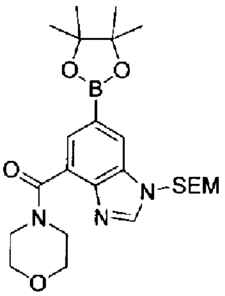
(6-bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-benzo[*d*]imidazol-4-yl)(morpholino)methanone



To a solution of (6-bromo-1*H*-benzo[d]imidazol-4-yl)(morpholino)methanone (3.0 g, 9.67 mmol) in DMF (50 mL) was slowly added sodium hydride (60%, 464 mg, 11.61 mmol) at 0 °C. After addition, the mixture was stirred at 0 °C for 1 h, and then (2-(chloromethoxy)ethyl)trimethylsilane (1.9 g, 11.61 mmol) was added dropwise. The resulting mixture was stirred at ambient temperature for another 2 h, at which time LCMS indicated that the reaction had gone to completion. The reaction was quenched by addition of saturated aqueous ammonium chloride (50 mL), and then extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were concentrated under reduced pressure. The crude product was purified by silica gel chromatography (Hexanes/ethyl acetate = 1:1) to give the title compound (3.0 g, 70% yield) as a yellow solid.

Step 7

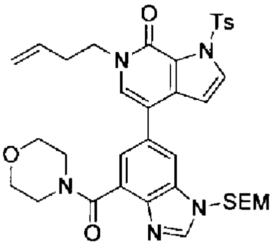
Morpholino(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-benzo[*d*]imidazol-4-yl)methanone



A mixture of (6-bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-benzo[d]imidazol -4-yl)(morpholino)methanone (3.0 g, 6.81 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'- bi(1,3,2-dioxaborolane) (3.6 g, 13.62 mmol), potassium acetate (1.7 g, 17.64 mmol) and Pd(dppf)Cl_2 (0.5 g, 0.68 mmol) in dioxane (45 mL) was heated at 110 °C under microwave conditions for 45 min, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (80 mL), washed with water (2 x 50 mL), and concentrated to give the crude title compound (1.35 g, 41% yield) as a brown oil.

Step 8

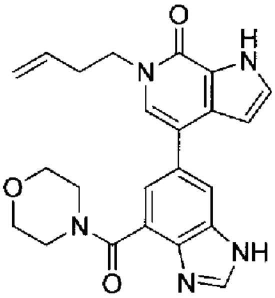
6-(but-3-en-1-yl)-4-(4-(morpholine-4-carbonyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-benzo[*d*]imidazol-6-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one



A mixture of morpholino(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-benzo[*d*]imidazol-4-yl)methanone (450 mg, 0.92 mmol), 4-bromo-6-(but-3-en-1-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one (389 mg, 0.92 mmol), Pd(dppf)Cl_2 (66 mg, 0.09 mmol) and cesium carbonate (601 mg, 1.85 mmol) in dioxane/H_2O (10 mL, 4:1) was heated at 110 °C under microwave conditions for 45 min, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (30 mL), washed with water (2 x 20 mL), concentrated under reduced pressure. The residue was purified by silica gel chromatography (Hexanes/ethyl acetate = 2:1) to give the title compound (500 mg, 77% yield) as a yellow solid.

Step 9

6-but-3-enyl-4-[7-(morpholine-4-carbonyl)-3H-benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one

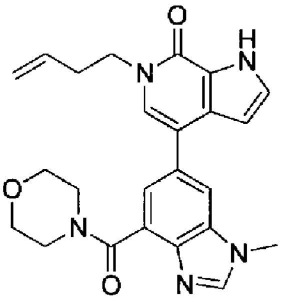


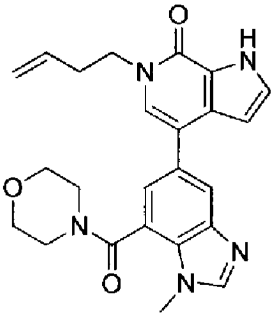
To a solution of 6-(but-3-en-1-yl)-4-(4-(morpholine-4-carbonyl)-1-((2-(trimethylsilyl) ethoxy)methyl)-1*H*-benzo[*d*]imidazol-6-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one (500 mg, 0.71 mmol) in dioxane/H_2O (10 mL, 1:1) was added sodium hydroxide (57 mg, 1.42 mmol). The reaction mixture was heated at 80 °C for 3 h, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure. The residue was diluted with ethyl acetate (30 mL), washed with water (2 x 20 mL), and concentrated under reduced pressure to give the crude 6-(but-3-en-1-yl)-4-(4-(morpholine-4-carbonyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-benzo[*d*]imidazol-6-yl)-1H-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one (350 mg, 90% yield).

To a solution of the above crude in dichloromethane (15 mL) was added trifluoroacetic acid (15 mL). After addition, the reaction mixture was stirred at ambient temperature for 3 h, at which time LCMS indicated that the reaction had gone to completion. The reaction mixture was concentrated under reduced pressure. The crude was purified by reverse phase chromatography (acetonitrile 13-33% / 0.1% HCl in water) to give the title compound (11 mg, 5% yield). ^{1}H NMR (400 MHz, CD_3OD): δ 9.58 (s, 1 H), 8.16 (s, 1 H), 7.91 (s, 1 H), 7.48 (s, 2 H), 6.57 (s, 1 H), 5.97-5.88 (m, 1 H), 5.09 (t, *J* = 10.4 Hz, 2 H), 4.26 (t, *J* = 7.2 Hz, 2 H), 4.02 -3.48 (m, 8 H), 2.65-2.57 (m, 2 H); LCMS M/Z (M+H) 418.

Example 57 and 58

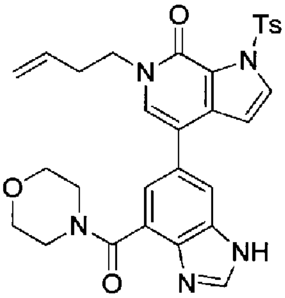
6-but-3-enyl-4-[3-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one and 6-but-3-enyl-4-[1-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one





Step 1

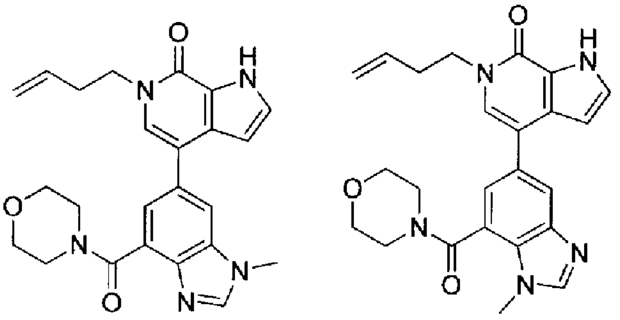
6-(but-3-en-1-yl)-4-(4-(morpholine-4-carbonyl)-1*H*-benzo[*d*]imidazol-6-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one



To a solution of 6-(but-3-en-1-yl)-4-(4-(morpholine-4-carbonyl)-1-((2-(trimethylsilyl) ethoxy)methyl)-1*H*-benzo[*d*]imidazol-6-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one (500 mg, 0.71 mmol) in dichloromethane (10 mL) was added trifluoroacetic acid (10 mL). After addition, the reaction mixture was stirred at ambient temperature for 3 h, at which time LCMS indicated that the reaction had gone to completion. The reaction mixture was concentrated under reduced pressure to give the crude title compound (400 mg, 98% yield) as a yellow oil.

Step 2

6-but-3-enyl-4-[3-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one and 6-but-3-enyl-4-[1-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one



To a stirred and cooled (0 °C) solution of (6-bromo-1*H*-benzo[d]imidazol-4-yl) (morpholino)methanone (500 mg, 0.87 mmol) in DMF (10mL) was slowly added sodium hydride (60%, 42 mg, 0.92 mmol). After addition, the mixture was stirred at 0°C for 1 h, and then iodomethane (149 mg, 0.92 mmol) was added. The resulting mixture was stirred at ambient temperature for 2 h, at which time LCMS indicated that the reaction had gone to completion. The reaction was quenched by addition of saturated aqueous ammonium chloride (10 mL), and then extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were concentrated under reduced pressure. The residue was purified by silica gel chromatography (Hexanes/ethyl acetate = 1:1) to give the mixture of the methylated regio-isomers (250 mg, 49% yield) as a brown solid.

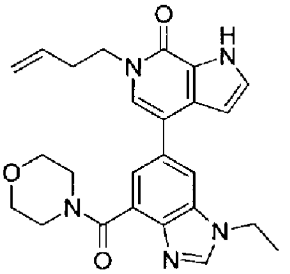
To a solution of the above regio-isomers (250 mg, 0.43 mmol) in dioxane/H_2O (10 mL, 1:1) was added sodium hydroxide (34 mg, 0.86 mmol). The reaction mixture was heated at 80 °C for 3 h, at which time LCMS indicated the reaction had gone to completion. The reaction mixture was concentrated under reduced pressure and partitioned between dichloromethane (40 mL) and water (30 mL). The separated organic layer was concentrated under reduced pressure, and the residue was purified by reverse phase chromatography (acetonitrile 18-48% / 0.1% NH_4OH in water) to the title compounds as white solids.

Example 57 (6.3 mg, 3% yield). ^{1}H NMR (400 MHz, CD_3OD): δ 9.59 (s, 1 H), 8.26 (s, 1 H), 7.95 (s, 1 H), 7.53-7.49 (m, 2 H), 7.62 (d, *J* = 2.8 Hz, 1 H), 5.98-5.89 (m, 1 H), 5.13-5.06 (m, 2 H), 4.29-4.26 (m, 4 H), 4.02 -3.46 (m, 8 H), 2.66-2.61 (m, 2 H). LCMS M/Z (M+H) 432.

Example 58 (11 mg, 6% yield). ^{1}H NMR (400 MHz, CD_3OD): δ 9.54 (s, 1 H), 8.14 (s, 1 H), 7.87 (s, 1 H), 7.48 (s, 2 H), 6.55 (d, *J* = 2.8 Hz, 1 H), 5.96-5.90 (m, 1 H), 5.13-5.06 (m, 2 H), 4.27-4.24 (m, 2 H), 4.14 (s, 3 H), 4.04-3.54 (m, 8 H), 2.64-2.59 (m, 2 H). LCMS M/Z (M+H) 432.

Example 59

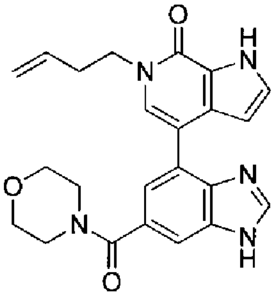
6-but-3-enyl-4-[3-ethyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1*H*-pyrrolo[2,3-*c*]pyridin-7-one



In a similar procedure as shown in Example 02, the title compound was prepared in 4% yield from iodoethane. ^{1}H NMR (400 MHz, CD_3OD): δ 8.32 (s, 1 H), 7.87 (s, 1 H), 7.54 (s, 1 H), 7.40 (s, 1 H), 7.35 (s, 1 H), 6.58 (s, 1 H), 5.93-5.87 (m, 1 H), 5.10-5.02 (m, 2 H), 4.43-4.38 (m, 2 H), 4.21 (t, J = 7.2 Hz, 2 H), 3.88-3.81 (m, 4 H), 3.62-3.56 (m, 2 H), 3.42-3.35 (m, 2 H), 2.61-2.56 (m, 2 H), 1.55 (t, J = 7.2 Hz, 3 H). LCMS M/Z (M+H) 446.

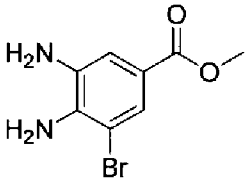
Example 60

6-but-3-enyl-4-[6-(morpholine-4-carbonyl)-1H-benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one



Step 1

Methyl 3,4-diamino-5-bromobenzoate

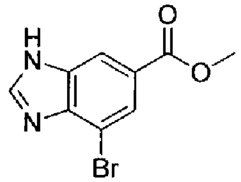


A mixture of methyl 4-amino-3-bromo-5-nitrobenzoate (1.0 g, 3.64 mmol) and $SnCl_2.2H_2O$ (1.6 g, 7.27 mmol) in ethyl acetate (30 mL) was heated at 90°C for 18 h, at which time LCMS indicated the reaction had gone to completion. After cooled, the mixture was diluted with water (30 mL), and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were concentrated under reduced pressure to give the crude title compound (850 mg, 95%

yield) as yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.74 (d, *J* = 1.6 Hz, 1 H), 7.35 (s, 1 H), 4.25 (br., s, 2 H), 3.86 (s, 3 H), 3.50 (br., s, 2 H).

Step 2

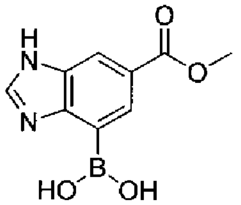
Methyl 4-bromo-1*H*-benzo[*d*]imidazole-6-carboxylate



To a solution of methyl 3,4-diamino-5-bromobenzoate (850 mg, 3.47 mmol) in THF (30 mL) were added triethoxymethane (1.04 g, 7.0 mmol) and TsOH.H$_2$O (66 mg, 0.35 mmol). The resulting mixture was stirred at room temperature for 5 h, at which time LCMS indicated that the reaction had gone to completion. The solvent was evaporated under reduced pressure. The residue was diluted with water (30 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were concentrated under reduced pressure to give the crude title compound (820 mg, 93% yield) as pale white solid. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.40 (s, 1 H), 8.22 (s, 2 H), 3.97 (s, 3 H).

Step 3

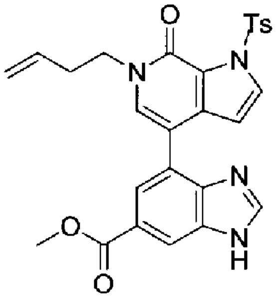
(6-(methoxycarbonyl)-1*H*-benzo[*d*]imidazol-4-yl)boronic acid



A mixture of methyl 4-bromo-1H-benzo[d]imidazole-6-carboxylate (820 mg, 3.21 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.15 g, 4.51 mmol), Pd(dppf)Cl$_2$ (234mg, 0.32 mmol) and potassium acetate (631 mg, 6.44 mmol) in dioxane (30 mL) was heated at 120°C under N$_2$ atmosphere for 16 h, at which time LCMS indicated that the reaction had gone to completion. After cooled, the mixture was filtered through a short celite pad and rinsed with dioxane (20 mL). The filtrate was concentrated under reduced pressure. The residue was diluted with water (50 mL), extracted with ethyl acetate (3 x 50 mL). The combined organic layers were concentrated under reduced pressure to give the crude product as a brown solid (650 mg, 92% yield). LCMS M/Z (M+H) 220.8.

Step 4

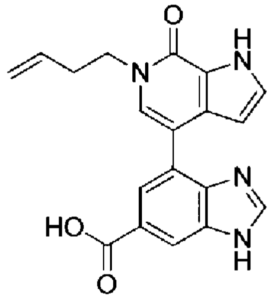
Methyl 4-(6-(but-3-en-1-yl)-7-oxo-1-tosyl-6,7-dihydro-1*H*-pyrrolo[2,3-c]pyridin-4-yl)-1*H*-benzo[*d*]imidazole-6-carboxylate



A mixture of 4-bromo-6-(but-3-en-1-yl)-1-tosyl-1*H*-pyrrolo[2,3-c]pyridin-7(6*H*)-one (421 mg, 1.00 mmol), (6-(methoxycarbonyl)-1*H*-benzo[*d*]imidazol-4-yl)boronic acid (330 mg, 1.5 mmol), cesium carbonate (652 mg, 2.0 mmol) and Pd(dppf)Cl_2 (73 mg, 0.10 mmol) in dioxane/H_2O (5/1, 30 mL) were heated at 100°C under N_2 for 3 h, at which time LCMS indicated that the reaction had gone to completion. The solvent was evaporated under reduced pressure. The residue was diluted with water (30 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by silica gel chromatography (DCM/Methanol = 99:1 to 16:1) to give the title compound as a white solid (400 mg, 77% yield). LCMS M/Z (M+H) 516.

Step 5

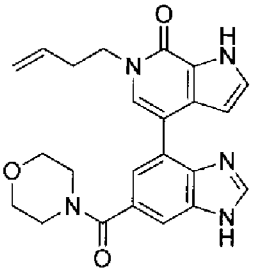
4-(6-(but-3-en-1-yl)-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridin-4-yl)-1*H*-benzo[*d*]imidazole-6-carboxylic acid



To a solution of methyl 4-(6-(but-3-en-1-yl)-7-oxo-1-tosyl-6,7-dihydro-1*H*-pyrrolo [2,3-*c*]pyridin-4-yl)-1*H*-benzo[*d*]imidazole-6-carboxylate (400 mg, 0.77 mmol) in methanol (10 mL) was added a solution of sodium hydroxide (1 N in water, 2.0 mL, 2.0 mmol) at room temperature. The resulting mixture was heated at 100°C for 2 h, at which time LCMS indicated that the reaction had gone to completion. After cooled, the mixture was adjusted to pH = 3-4 by additional of 1 N aqueous HCl. The resulting mixture was extracted with ethyl acetate (3 x 30 mL). The combined organic layers were concentrated under reduced pressure to give the crude title compound (200 mg, 74% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.94 (br. s, 1 H), 12.16 (s, 1 H), 8.84 (s, 1 H), 8.19 (s, 1 H), 8.06 (s, 1 H), 7.67 (s, 1 H), 7.45 (d, *J* = 8.0 Hz, 0.5 H), 7.34 (s, 1 H), 7.07 (d, *J* = 7.6 Hz, 0.5 H), 6.24 (s, 1 H), 5.87-5.80 (m, 1 H), 5.08-4.97 (m, 2 H), 4.13-4.09 (m, 2 H), 2.50-2.48 (m, 1 H), 2.25 (s, 1 H).

Step 6

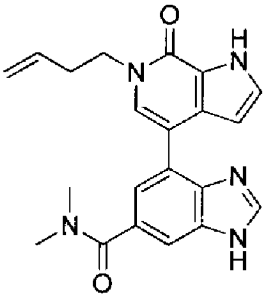
6-but-3-enyl-4-[6-(morpholine-4-carbonyl)-1H-benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one



A mixture of 4-(6-(but-3-en-1-yl)-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-4-yl) -1H-benzo[*d*]imidazole-6-carboxylic acid (100 mg, 0.28 mmol), morpholine (73 mg, 0.84 mmol), HATU (141 mg, 0.37 mmol) and *N*-ethyl-*N*-isopropylpropan-2-amine (72 mg, 0.56 mmol) in DMF (10 mL) was heated at 60°C for 8 h, at which time LCMS indicated that the reaction had gone to completion. The solvent was evaporated under reduced pressure. The residue was dissolved in dichloromethane (50 mL), washed with brine (2 x 20 mL), and concentrated under reduced pressure. The crude product was purified by reverse phase chromatography (acetonitrile10-40% / 0.1% HCl in water) to give the title compound as a white solid (25 mg, 21% yield). ^{1}H NMR (400 MHz, CD$_3$OD): δ 9.56 (s, 1 H), 7.97 (d, *J* = 4.0 Hz, 1 H), 7.78 (s, 1 H), 7.58 (s, 1 H), 7.45 (d, *J* = 2.8 Hz, 1 H), 6.28 (d, *J* = 2.8 Hz, 1 H), 5.94-5.88 (m, 1 H), 5.15-5.05 (m, 2 H), 4.27 (t, *J* = 7.2 Hz, 2 H), 3.93-3.47 (m, 8 H), 2.65-2.59 (m, 2 H). LCMS M/Z (M+H) 418.

Example 61

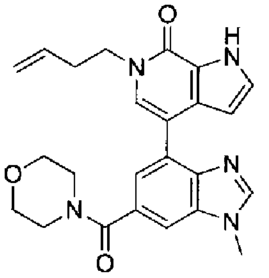
4-(6-(but-3-en-1-yl)-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridin-4-yl)-*N*,*N*-dimethyl-1*H*-benzo[*d*]imidazole-6-carboxamide



In a similar procedure as shown in Example 04, the title compound was prepared in 33% yield from dimethylamine hydrochloride. ^{1}H NMR (400 MHz, CD_3OD): δ 9.54 (s, 1 H), 7.96 (d, J = 1.6 Hz, 1 H), 7.78 (d, J = 1.6 Hz, 1 H), 7.55 (s, 1 H), 7.44 (d, J = 2.8 Hz, 1 H), 6.29 (d, J = 2.8 Hz, 1 H), 5.95-5.88 (m, 1 H), 5.14-5.04 (m, 2 H), 4.26 (t, J = 7.2 Hz, 2 H), 3.20 (s, 3 H), 3.12 (s, 3 H), 2.65-2.59 (m, 2 H). LCMS M/Z (M+H) 376.

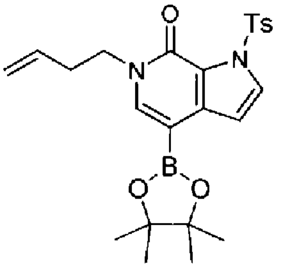
Example 62

6-but-3-enyl-4-[1-methyl-6-(morpholine-4-carbonyl)benzimidazol-4-yl]-1*H*-pyrrolo[2,3-c]pyridin-7-one



Step 1

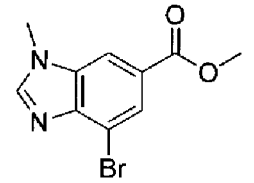
6-(but-3-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one



A mixture of 4-bromo-6-(but-3-en-1-yl)-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one (5.0 g, 11.87 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (7.5 g, 29.67 mmol), potassium acetate (2.3 g, 23.74 mmol) and Pd(dppf)Cl_2 (870 mg, 1.19 mmol) in dioxane (50 mL) was heated at 120°C under microwave conditions for 1 h, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure. The residue was diluted with H_2O (20 mL), extracted with ethyl acetate (3 x 20 mL). The combined organic layers were concentrated under reduced pressure and the crude product was purified by silica gel chromatography column (Hexanes/ethyl acetate = 2:1) to give the title compound (3.5 g, 44% yield) as a pale yellow oil.

Step 2

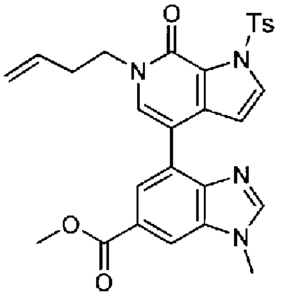
Methyl 4-bromo-1-methyl-1*H*-benzo[*d*]imidazole-6-carboxylate



To a solution of methyl 4-bromo-1*H*-benzo[*d*]imidazole-6-carboxylate (3.8 g, 14.9 mmol) in DMF (80 mL) was added potassium carbonate (6.2 g, 44.69 mmol) and CH_3I (6.3 g, 44.69 mmol). After addition, the reaction mixture was stirred at 30°C for 6 h, at which time LCMS indicated the reaction had gone to completion. The solvent was removed by concentration under reduced pressure. The residue was diluted with H_2O (30 mL), extracted with ethyl acetate (3 x 30 mL). The combined organic layers were concentrated to give the title compound (1.8 g, 45% yield) as a yellow solid.

Step 3

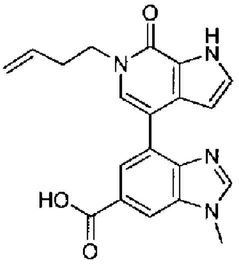
Methyl 4-(6-(but-3-en-1-yl)-7-oxo-1-tosyl-6,7-dihydro-*1H*-pyrrolo[2,3-*c*]pyridin-4-yl)-1-methyl-1*H*-benzo[*d*]imidazole-6-carboxylate



A mixture of methyl 4-bromo-1-methyl-1*H*-benzo[*d*]imidazole-6-carboxylate (500 mg, 1.86 mmol), 6-(but-3-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) -1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridin-7(6*H*)-one (1.04 g, 2.23 mmol), cesium carbonate (908 mg, 2.79 mmol) and Pd(dppf)Cl_2 (136 mg, 0.19 mmol) in dioxane/H_2O (5:1, 18 mL) was heated at 120°C under microwave conditions for 40 min, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure. The residue was diluted with H_2O (50 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by silica gel chromatography column (Hexanes/ethyl acetate = 1:2) to give the title compound (350 mg, 36% yield) as a yellow solid.

Step 4

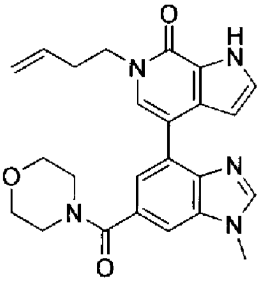
4-(6-(but-3-en-1-yl)-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridin-4-yl)-1-methyl-1*H*-benzo[*d*]imidazole-6-carboxylic acid



To a solution of methyl 4-(6-(but-3-en-1-yl)-7-oxo-1-tosyl-6,7-dihydro-1*H*-pyrrolo [2,3-*c*]pyridin-4-yl)-1-methyl-1*H*-benzo[d]imidazole-6-carboxylate (350 mg, 0.66 mmol) in Methanol/H_2O (15/3 mL) was added sodium hydroxide (132 mg, 3.30 mmol). The mixture was heated at 80°C for 16 h, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure and the residue was diluted with H_2O (8 mL). The solution was adjusted to pH = 5-6 by addition of 2 N aqueous HCl. The resulting precipitate was collected by filtration, washed with water and dried under reduced pressure to give the title compound (220 mg, 92% yield) as a yellow solid.

Step 5:

6-but-3-enyl-4-[1-methyl-6-(morpholine-4-carbonyl)benzimidazol-4-yl]-1*H*-pyrrolo[2,3-*c*]pyridin-7-one

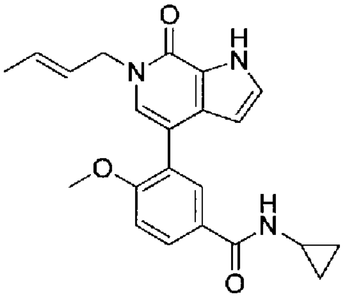


To a solution of 4-(6-(but-3-en-1-yl)-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridin-4-yl) -1-methyl-1*H*-benzo[*d*]imidazole-6-carboxylic acid (220 mg, 0.61 mmol) in DMF (5 mL) was added triethylamine (123 mg, 1.21 mmol), HATU (460 mg, 1.21 mmol) and morpholine (106 mg, 1.21 mmol). The resulting mixture was stirred at 30°C for 16 h, at which time LCMS indicated the reaction had gone to completion. The reaction mixture was concentrated under reduced pressure and the crude product was purified by reverse phase chromatography (acetonitrile 19% / 0.1% NH4OH in water) to give the title compound (86 mg, 33% yield) as a white solid. ^1H NMR (400 MHz, DMSO-d_6): δ 12.09 (s, 1 H), 8.33 (s, 1 H), 7.84 (s, 1 H), 7.64 (s, 1 H), 7.46 (s, 1 H), 7.35-7.34 (m, 1 H), 6.37 (s, 1 H), 5.93-5.84 (m, 1 H), 5.12-5.07

(m, 2 H), 5.03-5.00 (m, 1 H), 4.15-4.11 (m, 2 H), 4.08 (s, 3 H), 3.63-3.57 (m, 8 H), 2.46-2.44 (m, 2 H). LCMS M/Z (M+H) 432.

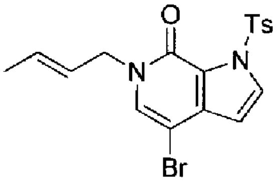
Example 63

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-4-methoxy-benzamide



Step 1:

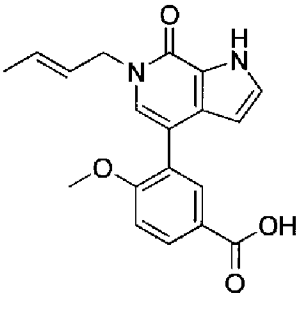
4-bromo-6-[(E)-but-2-enyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



Title compound was prepared in the same manner as described in Example 1, Step 1.

Step 2:

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzoic acid

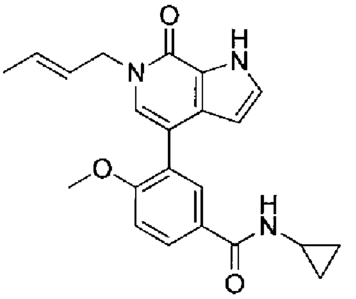


Bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II) (0.05 equiv., 0.24 mmol) was added to a mixture of 4-bromo-6-[(E)-but-2-enyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one (4.75 mmol) and 3-borono-4-methoxy-benzoic acid (1.25 equiv., 5.9 mmol) in 1,4-dioxane (14 mL) and potassium phosphate tribasic (2M in water, 3 equiv., 14.24 mmol). The reaction was heated at 90 °C for 2 h. After cooling, the reaction was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (30-70% ethyl acetate/heptanes) to afford the expected tosyl intermediate.

The intermediate was taken up in methanol (10 mL) and 10 M potassium hydroxide in water (1 mL) was added. The reaction was heated to 45°C for 2 h and then the methanol was removed under reduced pressure. The residue was dissolved in water 10 mL and the aqueous layer was extracted with diethyl ether. The aqueous solution was adjusted to pH 2 using 1 M hydrochloric acid and the resulting precipitate was collected by filtration. The crude product was triturated with hot isopropanol, to afford the desired product (1.01 g, 63%) as a 9:1 mixture of trans:cis diastereomers. LCMS M/Z (M+H) 339.

Step 3:

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-4-methoxy-benzamide



A mixture of 3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzoic acid (42 mg, 0.125 mmol), cyclopropylamine (14 mg, 0.250 mmol), triethylamine (0.053 mL, 0.38 mmol), and HATU (53 mg, 0.14 mmol) in N,N-dimethylformamide (1 mL) was heated at 45 °C overnight. The reaction was filtered using ethyl acetate to rinse and the filtrate was concentrated under reduced pressure. The residue was purified by preparative HPLC (5-85%ACN/0.1%NH4OH in H2O) to yield 3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-4-methoxy-benzamide. (29.9 mg, 63%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 8.28 (d, J = 4.2 Hz, 1H), 7.85 (dd, J = 8.6, 2.4 Hz, 1H), 7.79 (d, J = 2.3 Hz, 1H), 7.30 – 7.21 (m, 1H), 7.21 – 7.07 (m, 2H), 6.07 – 5.94 (m, 1H), 5.78 – 5.52 (m, 2H), 4.57 (dd, J = 4.7, 1.8 Hz, 2H), 3.77 (s, 3H), 2.89 – 2.70 (m, 1H), 1.72 – 1.59 (m, 2H), 0.75 – 0.61 (m, 2H), 0.61 – 0.50 (m, 2H). LCMS M/Z (M+H) 378.

The following compounds were prepared in a similar fashion to Example 63

Examples 64-78

Example	IUPAC Name	NMR	m/z
64	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 7.43 (dd, J = 8.4, 2.2 Hz, 1H), 7.35 (d, J = 2.2 Hz, 1H), 7.26 (t, J = 2.7 Hz, 1H), 7.20 – 7.08 (m, 2H), 6.04 (dd, J = 2.7, 1.8 Hz, 1H), 5.78 – 5.54 (m, 2H), 4.56 (dd, J = 5.0, 1.6 Hz, 2H), 3.77 (s, 3H), 2.98 (s, 5H), 1.72 – 1.51 (m, 3H).	366
65	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-tetrahydrofuran-3-yl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 8.38 (d, J = 6.5 Hz, 1H), 7.91 (dd, J = 8.6, 2.3 Hz, 1H), 7.85 (d, J = 2.4 Hz, 1H), 7.26 (t, J = 2.8 Hz, 1H), 7.21 – 7.13 (m, 1H), 7.12 (s, 1H), 6.01 (dd, J = 2.8, 2.0 Hz, 1H), 5.81 – 5.53 (m, 2H), 4.57 (d, J = 5.3 Hz, 2H), 4.52 – 4.36 (m, 1H), 3.83 (td, J = 8.6, 6.7 Hz, 2H), 3.78 (s, 3H), 3.70 (td, J = 8.0, 5.9 Hz, 1H), 3.56 (dd, J = 8.9, 4.4 Hz, 1H), 2.13 (dtd, J = 12.6, 7.9, 6.7 Hz, 1H), 1.97 – 1.83 (m, 1H), 1.72 – 1.61 (m, 3H).	408
66	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-ethyl-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.32 (t, J = 5.6 Hz, 1H), 7.87 (dd, J = 8.6, 2.4 Hz, 1H), 7.81 (d, J = 2.3 Hz, 1H), 7.26 (t, J = 2.7 Hz, 1H), 7.16 (d, J = 8.7 Hz, 1H), 7.12 (s, 1H), 6.02 (dd, J = 2.8, 1.9 Hz, 1H), 5.84 – 5.50 (m, 2H), 4.57 (d, J = 5.3 Hz, 2H), 3.78 (s, 3H), 3.33 – 3.21 (m, 22H), 1.69 – 1.63 (m, 3H), 1.11 (t, J = 7.2 Hz, 3H).	364

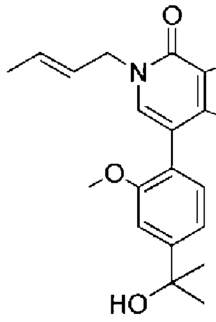
67	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-methyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.36 – 8.22 (m, 1H), 7.91 – 7.83 (m, 1H), 7.81 (d, *J* = 2.3 Hz, 1H), 7.26 (t, *J* = 2.8 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 1H), 7.15 – 7.08 (m, 1H), 6.03 (dd, *J* = 2.8, 2.0 Hz, 1H), 5.75 – 5.54 (m, 2H), 4.57 (d, *J* = 5.5 Hz, 2H), 3.78 (s, 3H), 2.76 (d, *J* = 4.4 Hz, 3H), 1.74 – 1.61 (m, 3H).	352
68	6-[(E)-but-2-enyl]-4-[2-methoxy-5-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 7.60 – 7.51 (m, 1H), 7.46 (d, *J* = 2.2 Hz, 1H), 7.26 (dd, *J* = 3.2, 2.3 Hz, 1H), 7.17 – 7.09 (m, 2H), 6.04 (dd, *J* = 2.8, 1.9 Hz, 1H), 5.75 – 5.52 (m, 2H), 4.62 – 4.50 (m, 2H), 3.76 (d, *J* = 8.0 Hz, 3H), 3.47 (s, 3H), 1.84 (d, *J* = 8.7 Hz, 4H), 1.72 – 1.61 (m, 3H).	392
69	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2,2-difluoroethyl)-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 8.72 (t, *J* = 5.6 Hz, 1H), 7.98 – 7.90 (m, 1H), 7.86 (d, *J* = 2.4 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.25 – 7.17 (m, 1H), 7.13 (s, 1H), 6.31 – 5.88 (m, 2H), 5.76 – 5.56 (m, 2H), 4.57 (d, *J* = 5.1 Hz, 2H), 3.78 (s, 3H), 3.73 – 3.57 (m, 3H), 1.71 – 1.59 (m, 3H).	402
70	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-isobutyl-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.32 (t, *J* = 5.8 Hz, 1H), 7.88 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.82 (d, *J* = 2.3 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.17 (d, *J* = 8.7 Hz, 1H), 7.13 (s, 1H), 6.02 (dd, *J* = 2.8, 2.0 Hz, 1H), 5.75 – 5.57 (m, 2H), 4.57 (d, *J* = 5.2 Hz, 2H), 3.78 (s, 3H), 3.14 – 3.00 (m, 2H), 1.94 – 1.73 (m, 1H), 1.73 – 1.57 (m, 3H), 0.88 (d, *J* = 6.7 Hz, 6H).	394

71	4-[5-(azetidine-1-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 7.64 (dd, J = 8.6, 2.3 Hz, 1H), 7.57 (d, J = 2.3 Hz, 1H), 7.33 – 7.21 (m, 1H), 7.20 – 7.10 (m, 2H), 6.05 (d, J = 2.7 Hz, 1H), 5.78 – 5.52 (m, 2H), 4.57 (d, J = 5.1 Hz, 2H), 4.34 (s, 2H), 4.04 (s, 2H), 2.32 – 2.20 (m, 2H), 1.71 – 1.59 (m, 3H).	378
72	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-[2-(dimethylamino)ethyl]-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.25 (t, J = 5.7 Hz, 1H), 7.87 (dd, J = 8.6, 2.3 Hz, 1H), 7.81 (d, J = 2.3 Hz, 1H), 7.26 (t, J = 2.7 Hz, 1H), 7.17 (d, J = 8.7 Hz, 1H), 7.12 (s, 1H), 6.01 (dd, J = 2.8, 1.9 Hz, 1H), 5.77 – 5.54 (m, 2H), 4.57 (d, J = 5.1 Hz, 2H), 3.78 (s, 3H), 3.40 – 3.24 (m, 2H), 2.43 – 2.33 (m, 2H), 2.16 (s, 6H), 1.71 – 1.57 (m, 3H).	409
73	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2-hydroxyethyl)-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.30 (t, J = 5.6 Hz, 1H), 7.89 (dd, J = 8.6, 2.3 Hz, 1H), 7.83 (d, J = 2.3 Hz, 1H), 7.31 – 7.22 (m, 1H), 7.17 (d, J = 8.7 Hz, 1H), 7.12 (s, 1H), 6.02 (dd, J = 2.8, 1.9 Hz, 1H), 5.81 – 5.53 (m, 2H), 4.75 – 4.63 (m, 1H), 4.57 (d, J = 5.2 Hz, 2H), 3.78 (s, 3H), 3.57 – 3.42 (m, 2H), 3.39 – 3.28 (m, 2H), 1.75 – 1.55 (m, 3H).	382
74	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-propyl-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 8.39 – 8.25 (m, 1H), 7.91 – 7.83 (m, 1H), 7.82 (d, J = 2.3 Hz, 1H), 7.26 (d, J = 2.8 Hz, 1H), 7.21 – 7.09 (m, 2H), 6.02 (s, 1H), 5.82 – 5.54 (m, 2H), 4.64 – 4.52 (m, 2H), 3.76 (s, 4H), 3.19 (tt, J = 7.9, 2.7 Hz, 2H), 1.82 – 1.60 (m, 3H), 1.60 – 1.45 (m, 2H), 0.87 (t, J = 7.4, 2.7 Hz, 3H).	380

75	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclobutyl-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.46 (d, J = 7.6 Hz, 1H), 7.94 – 7.86 (m, 1H), 7.82 (d, J = 2.3 Hz, 1H), 7.31 – 7.22 (m, 1H), 7.17 (dd, J = 8.7, 3.6 Hz, 1H), 7.12 (d, J = 3.1 Hz, 1H), 6.01 (dd, J = 2.8, 1.9 Hz, 1H), 5.78 – 5.50 (m, 2H), 4.57 (d, J = 5.3 Hz, 2H), 4.50 – 4.31 (m, 1H), 3.78 (s, 3H), 2.28 – 2.13 (m, 2H), 2.13 – 1.95 (m, 2H), 1.82 – 1.48 (m, 5H).	392
76	3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(cyclopropylmethyl)-4-methoxy-benzamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.42 (t, J = 5.7 Hz, 1H), 7.89 (dd, J = 8.6, 2.3 Hz, 1H), 7.83 (d, J = 2.4 Hz, 1H), 7.32 – 7.22 (m, 1H), 7.17 (d, J = 8.6 Hz, 1H), 7.13 (s, 1H), 6.01 (dd, J = 2.8, 1.9 Hz, 1H), 5.82 – 5.59 (m, 2H), 4.68 – 4.54 (m, 2H), 3.78 (s, 3H), 3.13 (dd, J = 6.7, 5.7 Hz, 2H), 1.76 – 1.57 (m, 2H), 1.10 – 0.93 (m, 1H), 0.51 – 0.33 (m, 2H), 0.29 – 0.14 (m, 2H).	392
77	4-[5-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO) δ 11.97 (s, 1H), 7.65 (dd, J = 8.6, 2.3 Hz, 1H), 7.56 (d, J = 2.2 Hz, 1H), 7.27 (t, J = 2.8 Hz, 1H), 7.24 – 7.14 (m, 1H), 7.13 (d, J = 9.6 Hz, 1H), 6.10 – 6.01 (m, 1H), 5.77 – 5.55 (m, 2H), 4.57 (d, J = 4.4 Hz, 2H), 4.57 – 4.44 (m, 2H), 4.25 (s, 2H), 4.18 (s, 2H), 3.98 (s, 2H), 3.79 (s, 3H), 1.72 (s, 3H), 1.66 (d, J = 5.0 Hz, 3H).	461
78	4-[5-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)-2-methoxy-phenyl]-6-butyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO) δ 11.93 (s, 1H), 7.65 (dd, J = 8.6, 2.3 Hz, 1H), 7.58 (d, J = 2.2 Hz, 1H), 7.26 (t, J = 2.7 Hz, 1H), 7.17 (t, J = 4.3 Hz, 2H), 6.09 – 6.01 (m, 1H), 4.49 (s, 2H), 4.26 (s, 2H), 4.18 (s, 2H), 4.05 – 3.95 (m, 4H), 3.79 (s, 3H), 2.53 – 2.47 (m, 3H), 1.72 (s, 2H), 1.71 – 1.65 (m, 2H), 1.39 – 1.28 (m, 2H), 0.97 – 0.88 (m, 3H).	463

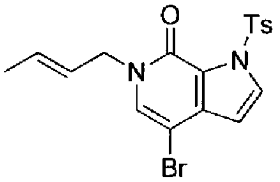
Example 79

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one



Step 1:

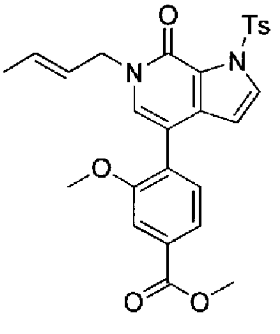
4-bromo-6-[(E)-but-2-enyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



Title compound was prepared in the same manner as described in Example 1, Step 1.

Step 2:

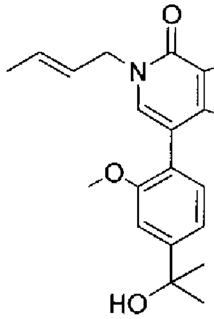
methyl 4-[6-[(E)-but-2-enyl]-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-4-yl]-3-methoxy-benzoate



Bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II) (141 mg, 0.2 mmol) was added to a mixture of 4-bromo-6-[(E)-but-2-enyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one (Step 1, 1.52 g, 3.6 mmol) and methyl 3-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (1.56 g, 5.3 mmol) in 1,4-dioxane (10 mL) and 2 M potassium phosphate tribasic in water (3 equiv., 10.7 mmol). The reaction was heated to 90 °C for 2 h. The reaction was cooled to room temperature, diluted with ethyl acetate, and washed with water. The organic solution was dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (10-35% ethyl acetate : heptanes) to yield title compound (470 mg, 26%). LCMS M/Z (M+H) 507.

Step 3:

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one



Methyl magnesium bromide, (3.0 M in diethyl ether, 0.47 mL, 1.4 mmol) was added dropwise to a cooled (0 °C) solution of methyl 4-[6-[(E)-but-2-enyl]-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-4-yl]-3-methoxy-benzoate (233 mg, 0.46 mmol) in tetrahydrofuran (8 mL). The reaction was allowed to gradually warm to room temperature and then quenched with 1 N HCl until the solution was pH 3. The mixture was diluted with water (100 mL) and then 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 taken up in methanol (1 mL) and 10 M potassium hydroxide in water (0.25 mL) was added. The reaction was heated to 45°C for 2 h and then concentrated under reduced pressure. The residue was taken up in water (50 mL) and extracted with dichloromethane (3 x 30 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by preparative HPLC (5-50%ACN/0.1%NH4OH in H2O) yielding 6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one (104 mg, 64%). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 11.91 (s, 1H), 7.29 – 7.14 (m, 3H), 7.10 – 7.02 (m, 2H), 6.12 – 5.98 (m, 1H), 5.77 – 5.53 (m, 2H), 5.03 (s, 1H), 4.55 (d, *J* = 5.4 Hz, 2H), 3.73 (s, 3H), 1.72 – 1.61 (m, 2H), 1.47 (s, 5H). LCMS M/Z (M+H) 353.

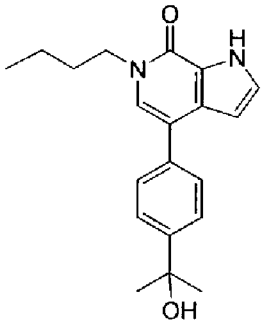
The following compounds were prepared in a similar fashion to Example 79:

Examples 80-81

Example	IUPAC Name	NMR	m/z
80	6-butyl-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO) δ 11.88 (s, 1H), 7.27 – 7.17 (m, 3H), 7.11 (s, 1H), 7.07 (dd, J = 7.8, 1.7 Hz, 1H), 6.08 – 6.02 (m, 1H), 5.04 (s, 1H), 3.99 (t, J = 7.2 Hz, 2H), 3.73 (s, 3H), 1.73 – 1.61 (m, 2H), 1.48 (s, 6H), 1.39 – 1.26 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H).	355
81	6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO) δ 12.09 (s, 1H), 7.61 – 7.42 (m, 4H), 7.34 (s, 1H), 7.23 (d, J = 3.5 Hz, 1H), 6.44 (d, J = 2.5 Hz, 1H), 5.75 – 5.53 (m, 2H), 5.00 (d, J = 4.1 Hz, 1H), 4.71 (d, J = 6.5 Hz, 1H), 4.59 (d, J = 4.8 Hz, 2H), 1.79 (d, J = 6.8 Hz, 1H), 1.74 – 1.58 (m, 3H), 1.46 (d, J = 4.1 Hz, 6H).	323

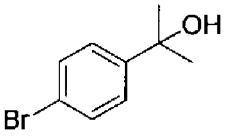
Example 82

6-butyl-4-(4-(2-hydroxypropan-2-yl)phenyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



Step 1:

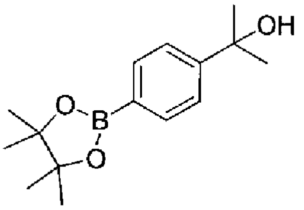
2-(4-bromophenyl)propan-2-ol



n-Butyl lithium (2.5 M in hexanes, 6.8 mL, 17.0 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of 1,4-dibromobenzene (4.0 g, 16.9 mmol) in THF (50 mL). After addition, stirring at -78 °C was continued for 1 h, and acetone (3.0 g, 51.7 mmol) was added dropwise. The resulting mixture was warmed to 0 °C and stirred for another 3 h before being quenched by addition of saturated aqueous ammonium chloride (40 mL). The mixture was extracted with 75% ethyl acetate/petroleum ether (3 x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over sodium sulfate and concentrated under reduced pressure to give title compound (1.8 g, 50%) as a colorless oil. LCMS M/Z [M-OH$^+$] 197.

Step 2:

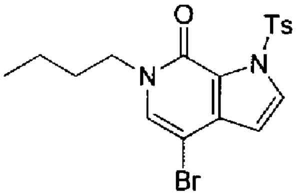
2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-ol



A mixture of potassium acetate (1.4 g, 13.9 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (2.2 g, 8.4 mmol), 2-(4-bromophenyl)propan-2-ol (1.5 g, 7.0 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]palladium(ii) dichloride (0.15 g, 0.2 mmol) in dioxane (15 mL) was degassed for 30 min and then heated at 80 °C for 12 h under nitrogen. After cooling, the reaction mixture was filtered through a pad of Celite using ethyl acetate to rinse. The filtrate was evaporated and the residue was purified by silica gel chromatography (petroleum ether : ethyl acetate 1:1) to give the title compound (1.1 g, 69%) as a colorless oil.

Step 3:

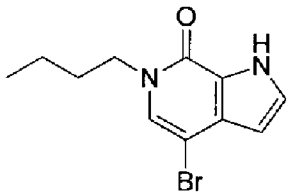
4-bromo-6-butyl-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



Title compound was prepared in the same manner as described in Example 1, Step 1.

Step 4:

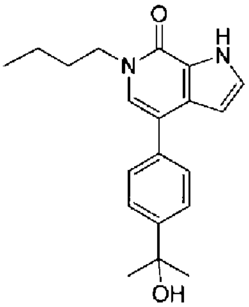
4-bromo-6-butyl-1H-pyrrolo[2,3-c]pyridin-7-one



Sodium hydroxide (0.5 g, 12.5 mmol) in water (2 mL) was added slowly to a solution of 4-bromo-6-butyl-1H-pyrrolo[2,3-c]pyridin-7-one (1.0 g, 2.4 mmol) in methanol (20 mL) and water (2 mL). The resulting mixture was heated at 80 °C for 2 h. After cooling, the mixture was concentrated under reduced pressure and the aqueous residue was diluted with water (30 mL). The resulting precipitated was collected by filtration, washed with water (2 x 30 mL) and concentrated under reduced pressure to give the title compound (0.5 g, 78%) as a white solid. LCMS M/Z (M+1) 270.

Step 5:

6-butyl-4-(4-(2-hydroxypropan-2-yl)phenyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



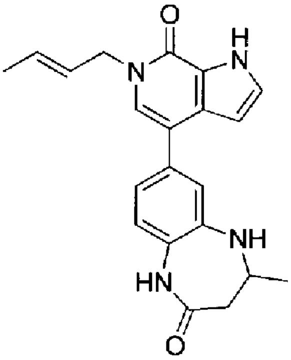
A mixture of 4-bromo-6-butyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (190 mg, 0.7 mmol), 2-(4-(4,4, 5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-ol (210 mg, 0.8 mmol), cesium carbonate (456 mg, 1.4 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]palladium(ii) dichloride (51 mg, 0.07 mmol) in dioxane (5 mL) and water (1 mL) was heated at 90 °C for 3 h under nitrogen protection. After cooling, the mixture was filtered through a small pad of Celite using ethyl acetate to rinse. The filtrate was concentrated under reduced pressure and the residue was purified by preparative HPLC, acetonitrile : water (10nM ammonia bicarbonate), 55%-85%, to give the title compound (38 mg, 17%) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.07 (s, 1 H), 7.55-7.50 (m, 4 H), 7.34-7.33 (t, *J* = 2.6 Hz,1 H), 7.30 (s, 1 H), 6.44 (t, *J* = 2.2 Hz, 1 H), 5.01 (d, *J* = 3.6 Hz, 1 H) , 4.02 (t, *J* = 7.2 Hz, 2 H), 1.70-1.66 (m, 2 H), 1.46 (s, 6 H), 1.35-1.30 (m, 2 H), 0.93-0.90 (t, *J* =7.2, 3 H). LCMS M/Z (M+H) 329.

Example 83 was prepared in a similar fashion to Example 82:

Example	IUPAC Name	NMR	m/z
83	6-(2-cyclopropylethyl)-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6): δ 12.05 (s, 1 H), 7.55-7.50 (m, 4 H), 7.34-7.32 (m, 2 H), 6.44-6.42 (m, 1 H), 5.02 (s, 1 H), 4.12-4.07 (m, 2 H), 1.62-1.57 (m, 2 H), 1.41 (s, 6 H), 0.73-0.68 (m, 1 H), 0.41-0.39 (m, 2 H), 0.09-0.05 (m, 2 H).	336

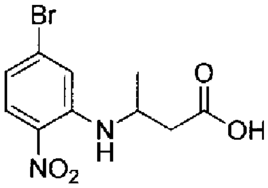
Example 84

7-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one



Step 1:

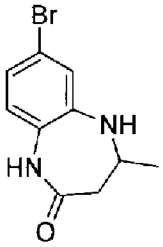
3-(5-bromo-2-nitro-anilino)butanoic acid



A round bottomed flask was charged with 4-bromo-2-fluoro-1-nitrobenzene (0.511 g, 2.321 mmol), (R)-3-aminobutanoic acid, HCl (0.216 g, 1.548 mmol), potassium carbonate (0.428 g, 3.10 mmol) and DMSO (7.5 mL). The flask was heated to 100°C and stirred 18 h. After cooling, the mixture was poured into 1 M HCl and washed with ethyl acetate (3X). The combined organic layers were washed with brine and concentrated under reduced pressure. The crude was purified by silica gel chromatography (eluting with dichloromethane/ methanol) to yield 3-((5-bromo-2-nitrophenyl)amino)butanoic acid, which was used in the subsequent reduction. LCMS M/Z (M+H) 303/305.

Step 2:

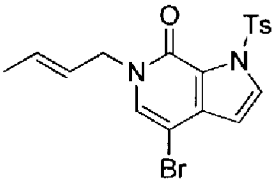
7-bromo-4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one



A disposable reaction tube was charged with (R)-3-(5-bromo-2-nitrophenylamino)butanoic acid (0.283 g, 0.934 mmol), ethanol (6 mL) and acetic acid (1.069 ml, 18.67 mmol). Iron (0.417 g, 7.47 mmol) was added, and the suspension was stirred at 110°C 18 h. After cooling, the mixture was filtered through celite and concentrated under reduced pressure to a residue that was purified by silica gel chromatography (eluting with hexanes / ethyl acetate) to yield the title compound. LCMS M/Z (M+H) 255/257.

Step 3:

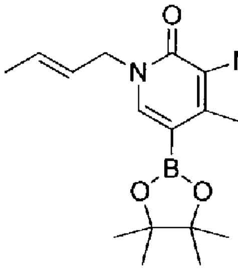
4-bromo-6-[(E)-but-2-enyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



A disposable tube was charged with 4-bromo-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (**Intermediate A**) (500 mg, 1.362 mmol), (E)-1-chlorobut-2-ene (265 µl, 2.72 mmol), cesium carbonate (665 mg, 2.042 mmol), and 1,4-dioxane (10 mL), and the mixture was stirred at room temperature overnight. The reaction was quenched with water, and the product was extracted three times with ethyl acetate before the organic layers were combined, dried with sodium sulfate and concentrated under reduced pressure to yield (E)-4-bromo-6-(but-2-en-1-yl)-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one, which was used without purification in the subsequent step.

Step 4:

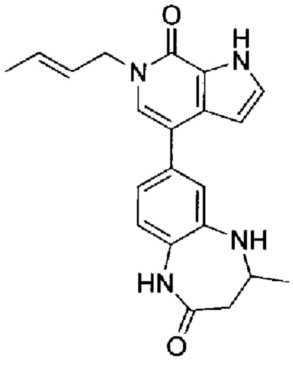
6-[(E)-but-2-enyl]-1-(p-tolylsulfonyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolo[2,3-c]pyridin-7-one



A disposable reaction vial was charged with (E)-4-bromo-6-(but-2-enyl)-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (150 mg, 0.36 mmol), triethylamine (149 µl, 1.068 mmol), bis(acetonitrile)dichloropalladium(II) (9.2 mg, 0.036 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (14.6 mg, 0.036 mmol), and 1,4-dioxane (2 mL). 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (103 µl, 0.712 mmol) was added, and the mixture was stirred at room temperature while gas was evolved from the reaction. After 15 min, the mixture was heated to 100 °C and stirred 2h before being cooled, diluted with ethyl acetate, stripped with 1,4-dioxane twice, and concentrated to yield (E)-6-(but-2-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one as a yellow oil that was used without purification in the next step.

Step 5:

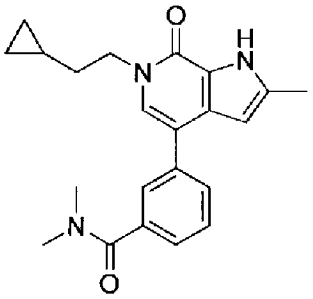
7-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one



A disposable reaction tube was charged with (E)-6-(but-2-enyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (167 mg, 0.357 mmol), 7-bromo-4-methyl-4,5-dihydro-1H-benzo[b][1,4]diazepin-2(3H)-one (76 mg, 0.297 mmol), tetrakis(triphenylphosphine)palladium(0) (34.3 mg, 0.030 mmol), potassium phosphate (82 mg, 0.594 mmol). 1,4-dioxane (3.8 mL)/ water (0.2 mL) was added, and the mixture was degassed before being stirred at 100°C 2 h. The reaction was cooled, quenched with 2 M sodium hydroxide and methanol, and stirred at room temperature 2 h. Ammonium hydroxide (sat., aq.) was added, and the product was extracted 4x with ethyl acetate. The organic layers were combined and concentrated under reduced pressure to yield a residue that was purified by silica gel chromatography (eluting with Hexanes and ethyl acetate) to provide the title compound as a white amorphous solid (31 mg). ^{1}H NMR (400MHz, DMSO-d6) □ = 12.10 (br. s., 1 H), 9.51 (s, 1 H), 7.35 (t, J = 2.7 Hz, 1 H), 7.17 (s, 1 H), 7.11 (s, 1 H), 6.92 (dd, J = 8.0, 13.0 Hz, 2 H), 6.47 (t, J = 2.4 Hz, 1 H), 5.67 - 5.62 (m, 2 H), 5.48 (br. s., 1 H), 4.58 (d, J = 3.5 Hz, 2 H), 3.92 - 3.78 (m, 1 H), 2.47 (d, J = 3.7 Hz, 1 H), 2.27 (dd, J = 7.5, 13.5 Hz, 1 H), 1.65 (d, J = 4.4 Hz, 3 H), 1.21 (d, J = 6.2 Hz, 3 H). LCMS M/Z (M+H) 363.

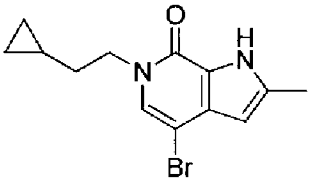
Example 85

3-(6-(2-cyclopropylethyl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide



Step 1:

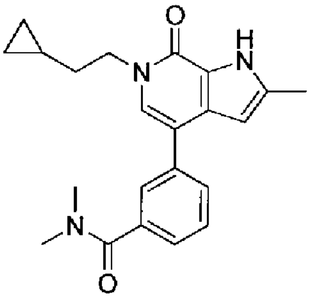
4-bromo-6-(2-cyclopropylethyl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



Sodium hydride (60% oil dispersion, 70.5 mg, 1.76 mmol) was added to cooled (0 °C) solution of 4-bromo-2-methyl-1,6-dihydropyrrolo[2,3-c]pyridin-7-one (**Intermediate B**) (400 mg, 1.76 mmol) in THF (7 mL). After addition, the reaction mixture was stirred for 0.5 h, and then a solution of (2-iodoethyl) cyclopropane (345 mg, 1.76 mmol) in THF (1 mL) was added. The mixture was warmed to room temperature and stirred for 2 h, at which time LCMS indicated that the reaction had gone to completion. The reaction was quenched by the addition of saturated aqueous ammonium chloride (0.5 mL), and then concentrated under reduced pressure. The residue was dissolved in ethyl acetate (50 mL), washed with water (2 x 15 mL), and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether:ethyl acetate 1:1) to give the title compound (150 mg, 29% yield) as a light brown solid. ^{1}H NMR (400 MHz, CD_3OD): δ 7.35 (s, 1 H), 6.08 (s, 1 H), 4.15-4.04 (m, 2 H), 2.54-2.24 (m, 3 H), 1.70-1.54 (m, 2 H), 0.77-0.60 (m, 1 H), 0.48-0.35 (m, 2 H), 0.08-0.04 (m, 2 H). LCMS M/Z (M+H) 295.

Step 2:

3-(6-(2-cyclopropylethyl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide



A mixture of 4-bromo-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (79 mg, 0.27 mmol), (3-(dimethylcarbamoyl)phenyl)boronic acid (51.7 mg, 0.27 mmol), cesium carbonate (174 mg, 0.54 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]palladium(ii) dichloride (10 mg, 0.01 mmol) in dioxane (3 mL) and water (0.5 mL) was subjected to microwave irradiation at 110 °C for 0.5 h. After cooling, the mixture was filtered through a small pad of Celite using ethyl acetate to rinse. The filtrate was concentrated under reduced pressure and the residue was purified by preparative HPLC, acetonitrile : water (0.3% formic acid), 46%-76%, to give the title compound (30.5 mg, 31%) as a white solid. ^{1}H NMR (400 MHz, CD_3OD): δ 7.72 (d, J = 8.0 Hz, 1 H), 7.65 (s, 1 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.42 (d, J = 7.6 Hz, 1 H), 7.33 (s, 1 H), 6.28 (s, 1 H), 4.23 (t, J = 7.0 Hz, 2 H), 3.15 (s, 3 H), 3.09 (s, 3 H), 2.45 (s, 3 H), 1.75-1.69 (m, 2 H), 0.79-0.77 (m, 1 H), 0.48-0.43 (m, 2 H), 0.09-0.05 (m, 2 H). LCMS M/Z (M+H) 364.

The following compounds were prepared in a similar fashion to Example 85:

Examples 86-103

Example	IUPAC Name	NMR	m/z
86	3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-benzamide	1H NMR (400 MHz, CD3OD): δ 7.70 (d, J = 7.6 Hz, 1 H), 7.62 (s, 1 H), 7.53-7.57 (m, 1 H), 7.40 (d, J = 7.2 Hz, 1 H), 7.27 (s, 1 H), 6.26 (s, 1 H), 4.12 (t, J = 7.4 Hz, 2 H), 3.13 (s, 3 H), 3.07 (s, 3 H), 2.43 (s, 3 H), 1.83-1.75 (m, 2 H), 1.47-1.38 (m, 2 H), 0.97 (t, J = 7.4 Hz, 3 H).	352
87	3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, CD$_3$OD): δ 7.50-7.45 (m, 2 H), 7.19-7.17 (t, *J* = 4.4 Hz, 1 H), 5.94 (s, 1 H), 4.11 (t, *J* = 7.4 Hz, 2 H), 3.86 (s, 3 H), 3.12 (s, 6 H), 2.41 (s, 3 H), 1.83-1.76 (m, 2 H), 1.49-1.40 (m, 2 H), 1.01 (t, *J* = 7.2 Hz, 3 H).	382
88	3-[6-(2-cyclopropylethyl)-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethyl-benzamide	^{1}H NMR (400 MHz, CD$_3$OD): δ 7.52 7.47 (m, 2 H), 7.28 (s, 1 H), 7.19 (d, *J* = 8.4 Hz, 1 H), 4.24 (t, *J* = 7.0 Hz, 2 H), 3.85 (s, 3 H), 3.13 (s, 6 H), 2.43 (s, 3 H), 1.72 (m, 2 H), 0.77-0.74 (m, 1 H), 0.48-0.44 (m, 2 H), 0.09-0.05 (m, 2 H).	394
89	6-but-3-enyl-4-[4-chloro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.92 (s, 1H), 7.65 (dd, J = 8.5, 2.2 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.42 (s, 1H), 6.15 (dd, J = 1.9, 1.0 Hz, 1H), 5.85 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.19 – 4.96 (m, 2H), 4.09 (t, J = 7.3 Hz, 2H), 3.82 – 3.50 (m, 6H), 3.21 (m, J = 5.1 Hz, 2H), 2.47 (m, J = 6.6 Hz, 2H), 2.34 (s, 3H).	426

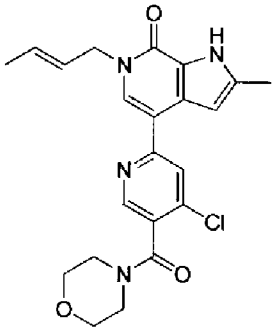
90	6-[(E)-but-2-enyl]-2-methyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.91 (s, 1H), 7.67 – 7.56 (m, 2H), 7.55 – 7.41 (m, 2H), 7.30 (d, J = 2.8 Hz, 1H), 6.25 – 6.14 (m, 1H), 5.71 – 5.49 (m, 2H), 4.70 (d, J = 6.7 Hz, 1H), 4.64 – 4.50 (m, 2H), 3.57 (d, J = 38.6 Hz, 7H), 2.34 (d, J = 0.8 Hz, 3H), 1.82 – 1.73 (m, 1H), 1.69 – 1.58 (m, 2H).	391
91	6-[(E)-but-2-enyl]-2-methyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.91 (s, 1H), 7.65 – 7.55 (m, 4H), 7.31 (d, J = 2.9 Hz, 1H), 6.21 (dd, J = 2.0, 1.0 Hz, 1H), 5.71 – 5.60 (m, 2H), 4.59 (d, J = 4.1 Hz, 2H), 3.47 (dt, J = 13.8, 6.4 Hz, 4H), 3.37 – 3.24 (m, 19H), 2.34 (d, J = 0.8 Hz, 3H), 1.93 – 1.75 (m, 5H), 1.68 – 1.61 (m, 2H).	376
92	6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.95 (s, 1H), 7.69 – 7.57 (m, 2H), 7.48 – 7.37 (m, 2H), 6.20 (dd, J = 2.0, 1.1 Hz, 1H), 5.72 – 5.57 (m, 2H), 4.58 (d, J = 4.1 Hz, 2H), 3.49 (t, J = 6.7 Hz, 2H), 3.16 (t, J = 6.5 Hz, 2H), 2.35 (d, J = 0.8 Hz, 3H), 1.96 – 1.75 (m, 5H), 1.68 – 1.61 (m, 2H).	410
93	6-[(E)-but-2-enyl]-4-[2,3-difluoro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.93 (s, 1H), 7.44 – 7.35 (m, 1H), 7.34 – 7.25 (m, 2H), 6.00 (s, 1H), 5.70 – 5.60 (m, 2H), 4.60 – 4.54 (m, 2H), 3.67 (s, 4H), 3.60 – 3.53 (m, 2H), 3.32 – 3.25 (m, 4H), 2.32 (d, J = 0.8 Hz, 3H), 1.65 (dt, J = 5.0, 1.1 Hz, 2H).	428
94	6-[(E)-but-2-enyl]-4-[3-methoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.89 (s, 1H), 7.35 – 7.22 (m, 2H), 7.22 – 7.14 (m, 2H), 6.25 (dd, J = 2.1, 1.1 Hz, 1H), 5.69 – 5.61 (m, 2H), 4.58 (dd, J = 4.1, 2.1 Hz, 2H), 3.88 (s, 3H), 3.66 – 3.61 (m, 4H), 3.57 – 3.46 (m, 2H), 3.21 – 3.16 (m, 2H), 2.34 (s, 3H), 1.68 – 1.61 (m, 2H).	422

95	6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.95 (s, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.62 (dd, J = 7.9, 1.7 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.39 (d, J = 4.0 Hz, 1H), 6.21 (d, J = 1.7 Hz, 1H), 5.75 – 5.51 (m, 2H), 4.62 – 4.46 (m, 2H), 3.74 – 3.61 (m, 4H), 3.60 – 3.54 (m, 2H), 3.23 – 3.17 (m, 2H), 2.34 (s, 3H), 1.67 – 1.62 (m, 2H).	425
96	6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.93 (s, 1H), 7.56 – 7.38 (m, 3H), 7.21 (ddd, J = 8.8, 2.5, 1.3 Hz, 1H), 6.18 (dd, J = 2.0, 1.0 Hz, 1H), 5.85 (m, J = 17.0, 10.2, 6.7 Hz, 1H), 5.16 – 4.96 (m, 2H), 4.09 (t, J = 7.3 Hz, 2H), 3.62 (m, 8H), 2.47 (m, J = 1.3 Hz, 2H), 2.35 (s, 3H).	396
97	6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	1H NMR (400 MHz, DMSO-d6) δ 11.90 (s, 1H), 7.68 (m, J = 8.6, 5.1, 2.4 Hz, 1H), 7.56 (dd, J = 6.4, 2.4 Hz, 1H), 7.42 – 7.33 (m, 2H), 6.13 (dd, J = 2.1, 1.0 Hz, 1H), 5.94 – 5.79 (m, 1H), 5.14 – 4.97 (m, 2H), 4.09 (t, J = 7.3 Hz, 2H), 3.67 (m, 4H), 3.57 (m,2H), 2.47 (m, J = 6.7 Hz, 2H), 2.34 (s, 3H).	410
98	6-[(E)-but-2-enyl]-4-[5-chloro-6-(morpholine-4-carbonyl)-3-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400MHz, CD$_3$OD) δ 8.80 (d, *J* = 1.8 Hz, 1 H), 8.23 (d, *J* = 1.8 Hz, 1 H), 7.44 (s, 1 H), 6.31 (s, 1 H), 5.85-5.57 (m, 2 H), 4.84 (d, *J* = 7.0 Hz, 0.55 H), 4.70 (d, *J* = 5.5 Hz, 1.45 H), 3.90-3.78 (m, 4 H), 3.73-3.66 (m, 2 H), 2.47 (s, 3 H), 1.86 (d, *J* = 5.3 Hz, 0.56 H), 1.73 (dd, *J* = 0.9, 6.1 Hz, 2.4 H).	427
99	6-[(E)-but-2-enyl]-4-[3-chloro-4-(4-methylpiperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, CD$_3$OD) δ 7.69 (d, *J* = 1.2 Hz, 1 H), 7.65-7.63 (m, 1 H), 7.44 (d, *J* = 8.0 Hz, 1 H), 7.27 (s, 1 H), 6.26 (s, 1 H), 5.78-5.64 (m, 2 H), 4.67 (d, *J* = 6.0 Hz, 2 H), 3.84-3.82 (m, 2 H), 3.38-3.34 (m, 2 H), 2.57-2.55 (m, 2 H), 2.49-2.47 (m, 1 H), 2.44 (s, 3 H), 2.34 (s, 3 H), 1.71 (d, *J* = 6.0 Hz, 3 H).	439

100	6-[(E)-but-2-enyl]-2-methyl-4-[3-methyl-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR(400MHz, CD_3OD) δ 12.00 (s, 1 H), 7.42 (d, *J* = 5.1 Hz, 2 H), 7.25 (d, *J* = 8.3 Hz, 1 H), 6.93-7.02 (m, 1 H), 6.22 (s, 1 H), 5.67-5.74 (m, 1 H), 4.71 (d, *J* = 2.9 Hz, 2 H), 3.78-3.91 (m, 4 H), 3.63 (s, 2 H), 3.35 (s, 2 H), 2.49 (s, 3 H), 2.40 (s, 3 H), 1.84 (d, *J* = 6.9 Hz, 1 H), 1.72 (d, *J* = 4.4 Hz, 2 H).	406
101	6-allyl-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400MHz, DMSO-d_6) δ 12.03 (br. s, 1 H), 7.67 (s, 1 H), 7.63 (dd, *J* = 1.4, 7.8 Hz, 1 H), 7.46 (d, *J* = 7.9 Hz, 1 H), 7.41 (s, 1 H), 6.23 (s, 1 H), 6.09-5.93 (m, 1 H), 5.20-5.04 (m, 2 H), 4.66 (d, J = 5.1 Hz, 2 H), 3.73-3.61 (m, 4 H), 3.59-3.53 (m, 2 H), 3.20 (d, *J* = 4.6 Hz, 2 H), 2.35 (s, 3 H).	412
102	6-allyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400MHz, $CDCl_3$) d 10.49 (br. s, 1H), 7.03 (s, 1 H), 6.98 (s, 1 H), 6.94 (s, 1 H), 5.94-6.09 (m, 2 H), 5.17-5.27 (m, 2 H), 4.75 (d, *J* = 5.3 Hz, 2 H), 3.73-3.86 (m, 10 H), 3.70 (br. s, 1 H), 3.65 (br. s, 1 H), 3.41 (br. s, 1 H), 2.45 (s, 3 H).	438
103	6-[(E)-but-2-enyl]-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (4:1 E/Z mixture) (400 MHz, DMSO-d6) d 11.77 (br. s., 1H), 8.26 (d, *J* = 1.22 Hz, 1H), 7.63 (s, 1H), 7.54 (d, *J* = 1.46 Hz, 1H), 6.24 - 6.26 (m, 1H), 5.65 (dd, *J* = 5.13, 7.32 Hz, 2H), 4.58 (d, *J* = 4.64 Hz, 2H), 3.82 - 3.90 (m, 3H), 3.40 - 3.76 (m, 8H), 2.31 (s, 3H), 1.67 (d, *J* = 5.37 Hz, 3H).	423

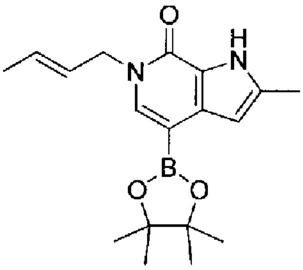
Example 104

6-[(E)-but-2-enyl]-4-[4-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one



Step 1:

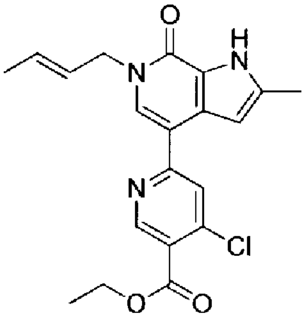
(E)-6-(but-2-en-1-yl)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



To a mixture of 4-bromo-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one (3.00 g, 10.7 mmol) and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.83 g, 53.3 mmol) in 1,4-dioxane (50 mL) was added triethylamine (3.24 g, 32.01 mmol), SPhos (2.19 g, 5.34 mmol) and bis(acetonitrile)dichloropalladium(II) (277.0 mg, 1.07 mmol). The reaction was then stirred at 80°C for 16 hrs under N_2 atmosphere. The mixture was then concentrated under reduced pressure, and the residue then purified by silica gel chromatography (Petroleum ether/ ethyl acetate = 5/1) to give 6-[(E)-but-2-enyl]-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-c]pyridin-7-one (4.00 g, crude) as a yellow solid.

Step 2:

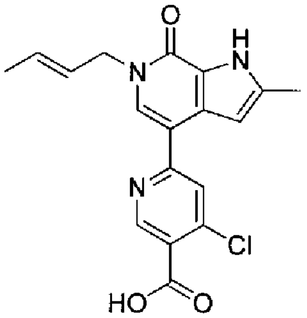
(E)-ethyl 6-(6-(but-2-en-1-yl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-chloronicotinate



This compound was prepared in a similar procedure to Example 62, step 3.

Step 3:

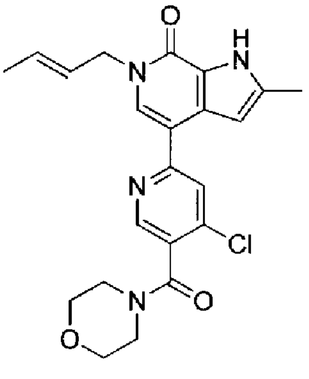
(E)-6-(6-(but-2-en-1-yl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-chloronicotinic acid



This compound was prepared in a similar procedure to Example 60, step 5.

Step 4:

(E)-6-(but-2-en-1-yl)-4-(4-chloro-5-(morpholine-4-carbonyl)pyridin-2-yl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (5)



Example 103 was prepared in a similar procedure to Example 60, step 6. ^{1}H NMR (400MHz, CD_3OD) δ 8.69 (s, 1 H), 8.10 (s, 1 H), 7.88-7.80 (m, 1 H), 5.84-5.72 (m, 1 H), 5.71-5.61 (m, 1 H), 4.68 (d, *J* = 5.6 Hz, 2 H), 3.87-3.73 (m, 4 H), 3.71-3.63 (m, 2 H), 3.46-3.36 (m, 2 H), 2.45 (s, 3 H), 1.87-1.79 (m, 0.8 H), 1.70 (d, *J* = 6.1 Hz, 2.2 H). LCMS (M + H^+) m/z: 427.

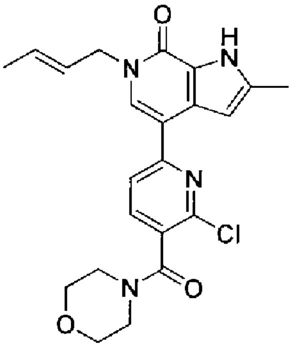
The following compounds were prepared in a similar fashion to Example 104: Examples 105-110

Example	IUPAC Name	NMR	m/z
105	6-[(E)-but-2-enyl]-2-methyl-4-[2-(morpholine-4-carbonyl)pyrimidin-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400MHz, CD_3OD) δd9.10 (s, 2 H), 7.45 (d, *J* = 2.0 Hz, 1 H), 6.31 (s, 0.4 H), 5.78-5.56 (m, 2 H), 4.68-4.66 (m, 2 H), 3.80 (d, *J* = 2.0 Hz, 4 H), 3.69-3.66 (m, 2 H), 3.47-3.45 (m, 2 H), 2.43 (s, 3 H), 1.82 (dd, *J* = 0.6 Hz, 0.6 H), 1.69 (d, *J* = 3.6 Hz, 2.6 H).	394
106	5-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-(morpholine-4-carbonyl)benzonitrile	^{1}H NMR (400 MHz, $CDCl_3$) δ 11.39-11.28 (m, 1 H), 7.91 (s, 1 H), 7.88-7.85 (m, 1 H), 7.55 (d, *J* = 8.0 Hz, 1 H), 7.02 (s, 1 H), 6.19 (s, 1 H), 5.80-5.59 (m, 2 H), 4.85-4.71 (m, 2 H), 3.87 (d, *J* = 6.0 Hz, 4 H), 3.75 (s, 2 H), 3.43 (s, 2 H), 2.51 (s, 3 H), 1.74 (d, *J* = 6.0Hz, 3 H).	417
107	6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, $CDCl_3$) d 7.34 (d, *J* = 7.78 Hz, 1 H), 7.22 (s, 1 H), 7.08 (d, *J* = 8.03 Hz, 1 H), 7.00-7.03 (m, 1 H), 5.98 (s, 1 H), 5.65-5.70 (m, 1 H), 4.65 (d, *J* = 4.77 Hz, 2 H), 3.84 (s, 3 H), 2.42 (s, 3 H), 1.84 (s, 1 H), 1.81 (d, *J* = 7.28 Hz, 1 H), 1.71 (d, *J* = 4.77 Hz, 2 H), 1.65 (s, 6 H).	367
108	6-[(E)-but-2-enyl]-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 1 H), 6.97 (d, *J* = 13.2 Hz, 1 H), 6.55 (s, 2 H), 6.48 (t, *J* = 9.4 Hz, 1 H), 6.18-5.68 (m, 2 H), 4.95-4.83 (m, 2 H), 3.90-3.66 (m, 10 H), 3.37 (d, *J* = 28 Hz, 2 H), 2.57 (s, 3 H) , 1.85 (d, *J* = 6.0 Hz, 0.6 H), 1.75 (d, *J* = 4.4 Hz, 2.3 H).	452

109	3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrazin-2-ylmethyl)benzamide	^{1}H NMR (400MHz, CD_3OD) d 8.69 (s, 1 H), 8.64 (s, 1 H), 8.53 (s, 1 H),7.96-7.91 (m, 2 H) , 7.23-7.17 (m, 2 H), 5.76-5.59 (m, 2 H), 4.81-4.66 (m, 4 H), 3.84 (s, 3 H), 2.40 (s, 3 H), 1.81-1.68 (m, 3 H).	444
110	6-but-2-enyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (4:1 E/Z mixture) (400 MHz, DMSO-d6) d 11.76 (br. s, 1H), 8.23 (d, *J* = 1.71 Hz, 1H), 7.62 (s, 1H), 7.50 (d, *J* = 1.71 Hz, 1H), 6.25 (dd, *J* = 0.98, 2.20 Hz, 1H), 5.57 - 5.73 (m, 2H), 4.58 (d, *J* = 5.13 Hz, 2H), 3.85 (s, 3H), 3.54 - 3.73 (m, 2H), 3.39 - 3.53 (m, 2H), 2.32 - 2.47 (m, 4H), 2.31 (s, 3H), 2.21 (s, 3H), 1.67 (d, *J* = 5.13 Hz, 3H).	436

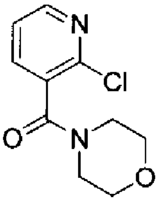
Example 111

6-[(*E*)-but-2-enyl]-4-[6-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one



Step 1:

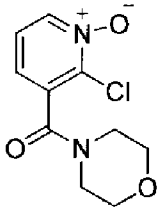
(2-chloropyridin-3-yl)(morpholino)methanone



This compound was prepared in a similar procedure to Example 55, step 1.

Step 2:

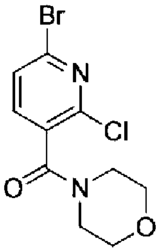
2-chloro-3-(morpholine-4-carbonyl)pyridine 1-oxide



To a mixture of (2-chloro-3-pyridyl)-morpholino-methanone (3.00 g, 13.24 mmol) in trifluoroacetic acid (15 mL) was added hydrogen peroxide (5.90 g, 52.04 mmol) in one portion under N_2. The mixture was stirred at 65°C for 16 hrs. The mixture was concentrated under reduced pressure and the residue was adjusted to pH 8 with saturated $NaHCO_3$ solution. The mixture was extracted with DCM. The combined organics were dried with anhydrous sodium sulfate and concentrated under reduced pressure to afford (2-chloro-1-oxido-pyridin-1-ium-3-yl)-morpholino-methanone (2.40 g, crude) as a yellow solid.

Step 3:

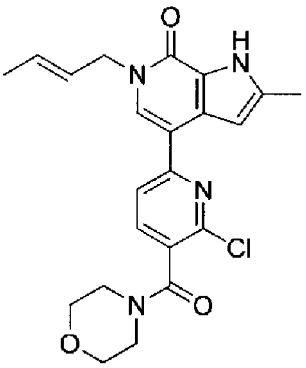
(6-bromo-2-chloropyridin-3-yl)(morpholino)methanone



A solution of (2-chloro-1-oxido-pyridin-1-ium-3-yl)-morpholino-methanone (2.00 g, 8.24 mmol) and $POBr_3$ (9.45 g, 32.96 mmol) in CH_3CN (80 mL) was stirred at 70°C for 16 hrs. The mixture was concentrated under reduced pressure and quenched with water (20 mL). The aqueous layer was extracted with DCM, and the combined organic layers were washed with saturated sodium bicarbonate and brine (30 mL), then dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (Petroleum ether/ ethyl acetate = 30/1, 20/1) to afford (6-bromo-2-chloro-3-pyridyl)-morpholino-methanone (300 mg, 0.87 mmol, 11%) as a yellow oil.

Step 4:

(E)-6-(but-2-en-1-yl)-4-(6-chloro-5-(morpholine-4-carbonyl)pyridin-2-yl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one

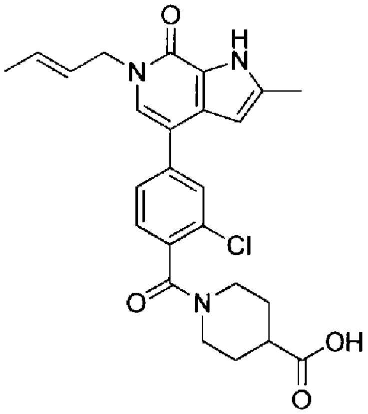


Example 111 was prepared in a similar procedure to Example 85, step 2.

^{1}H NMR (400MHz, CD_3OD) δ 7.88-7.82 (m, 3 H), 6.68 (s, 1 H), 5.78-5.66 (m, 2 H), 4.69-4.68 (m, 2 H), 3.79 (s, 4 H), 3.71-3.64 (m, 2 H), 3.39-3.34 (m, 2 H), 2.45 (s, 3 H), 1.71 (d, J = 6.0 Hz, 3 H). LCMS (M + H$^+$) m/z: 427.

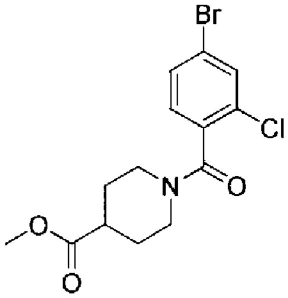
Example 112

1-[4-[6-[(*E*)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxylic acid



Step 1:

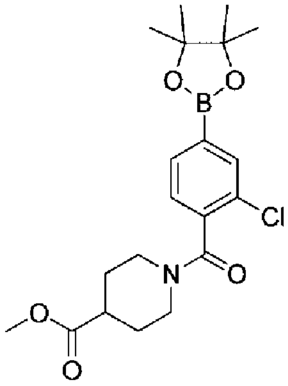
methyl 1-(4-bromo-2-chlorobenzoyl)piperidine-4-carboxylate



This compound was prepared in a similar procedure to Example 55, step 1.

Step 2:

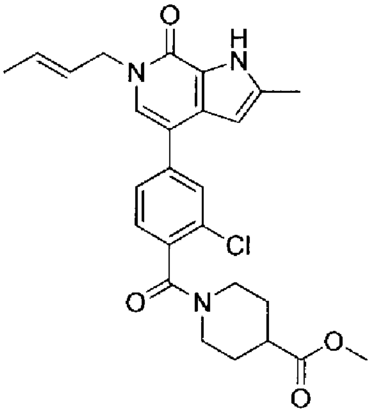
methyl 1-(2-chloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoyl)piperidine-4-carboxylate



This compound was prepared in a similar procedure to Example 55, step 3.

Step 3:

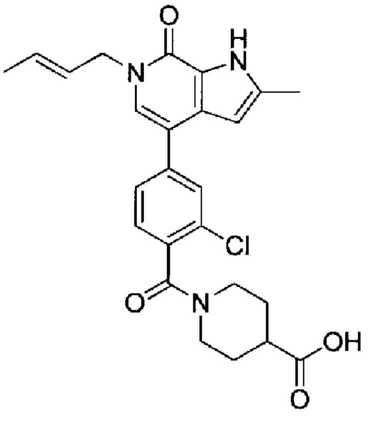
(E)-methyl1-(4-(6-(but-2-en-1-yl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-2-chlorobenzoyl)piperidine-4-carboxylate



This compound was prepared in a similar procedure to Example 1.

Step 4:

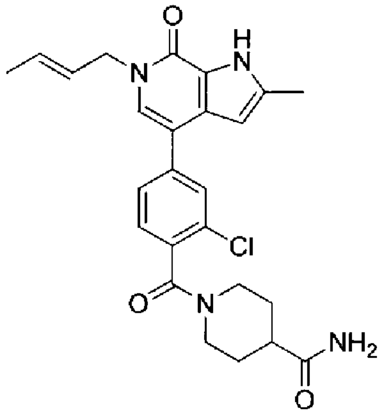
(E)-1-(4-(6-(but-2-en-1-yl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-2-chlorobenzoyl)piperidine-4-carboxylic acid



Example 112 was prepared in a similar procedure to Example 60, step 5. ^{1}H NMR (400MHz, CD_3OD) δ 7.69 (d, J = 6.0 Hz, 1 H), 7.65-7.61 (m, 1 H), 7.45-7.43 (m, 1 H), 7.28 (s, 1H), 6.25 (s, 1 H), 5.77-5.67 (m, 2 H), 4.66-4.65 (m, 2 H), 4.54-4.51 (m, 1 H), 3.52-3.48 (m, 1 H), 3.19-3.01 (m, 2 H), 2.66-2.64 (m, 1 H), 2.43 (s, 3 H), 2.09-2.06 (m, 1 H), 1.92-1.89 (m, 1 H), 1.84-1.69 (m, 5 H). LCMS (M + H$^+$) m/z: 468.

Example 113

(E)-1-(4-(6-(but-2-en-1-yl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-2-chlorobenzoyl)piperidine-4-carboxamide

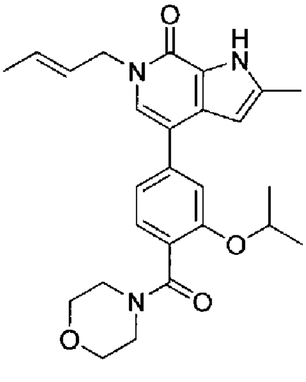


Example 113 was prepared in a similar procedure to Example 60, step 6.

^{1}H NMR (400MHz, CD_3OD) δ 7.71 (d, J = 6.8 Hz, 2 H), 7.67-7.63 (m, 1 H), 7.51-7.39 (m, 1 H), 7.30 (s, 1 H), 6.28 (s, 1 H), 5.80-5.66 (m, 2 H), 4.83-4.82 (m, 1 H), 4.73-4.68 (m, 3 H), 3.56 (s, 1 H), 3.24-3.14 (m, 1 H), 3.02-2.96 (m, 1 H), 2.59-2.56 (m, 2 H), 2.46 (s, 3 H), 2.00-1.98 (m, 1 H), 1.87-1.63 (m, 6 H). LCMS (M + H$^+$) m/z: 467.

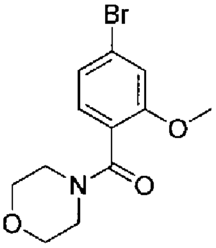
Example 114

6-[(E)-but-2-enyl]-4-[3-isopropoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one



Step 1:

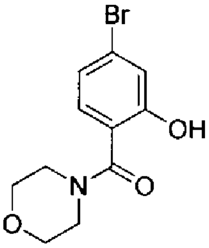
(4-bromo-2-methoxy-phenyl)-morpholino-methanone



This compound was prepared in a similar procedure to Example 55, Step 1.

Step 2:

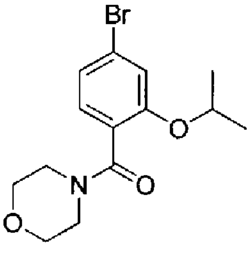
(4-bromo-2-hydroxy-phenyl)-morpholino-methanone



To a mixture of (4-bromo-2-methoxy-phenyl)-morpholino-methanone (500 mg, 1.67 mmol) in dichloromethane (10 mL) was added BBr_3 (835mg, 3.33 mmol) at 0 °C under N_2. The mixture was stirred at 80°C for 16 hrs. The mixture was poured into H_2O (50 mL) and extracted with DCM. The combined organic layers were dried with sodium sulfate and concentrated under reduced pressure to give (4-bromo-2-hydroxy-phenyl)-morpholino-methanone (400 mg, crude) as a white solid.

Step 3:

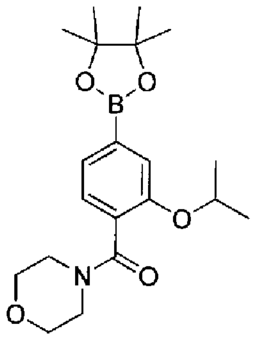
(4-bromo-2-isopropoxy-phenyl)-morpholino-methanone



To a mixture of (4-bromo-2-hydroxy-phenyl)-morpholino-methanone (300 mg, 1.05 mmol) and 2-bromopropane (155 mg, 1.26 mmol) in DMF (8 mL) was added potassium carbonate (435 mg, 3.15 mmol). The mixture was stirred at 80°C for 16 hrs. TLC showed the reaction was completed. The mixture was poured into H_2O (80 mL), then extracted with ethyl acetate. The combined organic layers were dried with sodium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (Petroleum ether/ ethyl acetate = 4/1) to give (4-bromo-2-isopropoxy-phenyl)-morpholino-methanone (344 mg, 1.05 mmol, 100%) as a white solid.

Step 4:

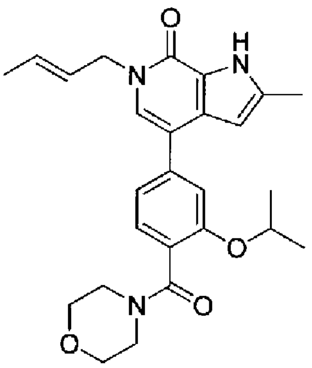
[2-isopropoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-morpholino-methanone



This compound was prepared in a similar procedure to Example 55, Step 3.

Step 5:

6-[(E)-but-2-enyl]-4-[3-isopropoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one



This compound was prepared in a similar procedure to Example 85, Step 3. ^1H NMR (400MHz, $CDCl_3$) δ 10.90-10.77 (m, 1 H), 7.34 (d, J = 8.0 Hz, 1 H), 7.17-7.14 (m, 1 H), 7.08

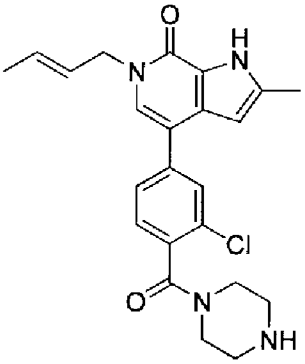
(s, 1 H), 6.97 (s, 1 H), 6.19 (d, *J* = 1.2 Hz, 1 H), 5.80-5.58 (m, 2 H), 4.81 (d, *J* = 6.8 Hz, 0.36 H), 4.69 (d, *J* = 4.0 Hz, 1.40 H), 4.66-4.60 (m, 1 H), 3.89-3.86 (m, 1 H), 3.78-3.72 (m, 4 H), 3.62-3.61 (m, 1 H), 3.44-3.27 (m, 2 H), 2.48 (s, 3 H), 1.84-1.83 (m, 0.53 H), 1.72 (d, *J* = 5.2 Hz, 2.36 H), 1.37 (dd, *J* = 10.8, 6 H). LCMS (M + H^+) m/z: 450.

Example 115 was prepared in a similar procedure to Example 114.

Example	IUPAC Name	NMR	m/z
115	6-[(E)-but-2-enyl]-4-[3-(cyclopropylmethoxy)-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1 H), 7.35 (d, *J* = 7.6 Hz, 1 H), 7.16 (t, *J* = 3.8 Hz, 1 H), 7.03-6.96 (m, 2 H), 6.20 (s, 1 H), 5.75-5.63 (m, 2 H), 4.79 (d, *J* = 7.2 Hz, 0.5 H), 4.67 (d, *J* = 4.4 Hz, 1.5 H), 3.93-3.33(m, 11 H), 2.47 (s, 3 H) , 1.83 (d, *J* = 6.0 Hz, 0.6 H), 1.71 (d, *J* = 5.2 Hz, 2.2 H), 1.28 (t, *J* = 6.0 Hz, 1 H), 0.65 (d, *J* = 7.6 Hz, 2 H), 0.36 (s, 2 H).	462

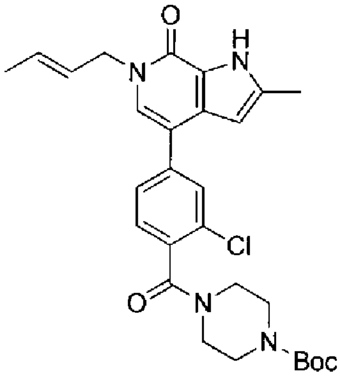
Example 116

(E)-6-(but-2-en-1-yl)-4-(3-chloro-4-(piperazine-1-carbonyl)phenyl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



Step 1:

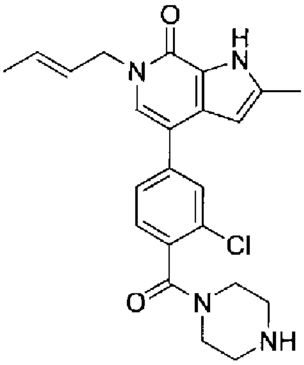
(E)-tert-butyl 4-(4-(6-(but-2-en-1-yl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-2-chlorobenzoyl)piperazine-1-carboxylate



This compound was prepared in a similar procedure to Example 85, Step 2.

Step 2:

(E)-6-(but-2-en-1-yl)-4-(3-chloro-4-(piperazine-1-carbonyl)phenyl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one

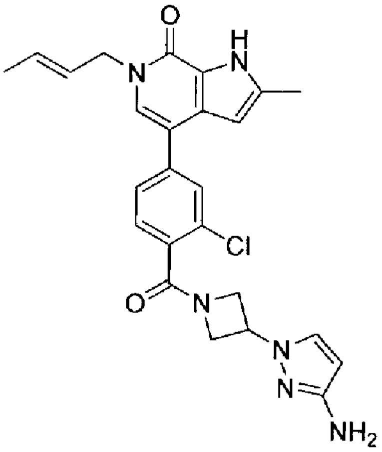


To a mixture of tert-butyl 4-[4-[6-[(*E*)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperazine-1-carboxylate (200 mg, 380.9 umol) in methanol (4 mL) was added HCl/methanol (4 M, 1.00 mL) solution in one portion under N_2. The mixture was stirred at 20°C for 4 hrs. The mixture was then concentrated under reduced pressure. The residue was purified by Prep-HPLC (Column : Waters Xbridge C18 150*20mm*5um. Mobile phase A: water with 0.5 % (v/v) $NH_3.H_2O$. Mobile phase B: MeOH, Gradient : 40-70%. Flow rate: 25ml/min) to afford 6-[(*E*)-but-2-enyl]-4-[3-chloro-4-(piperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one (66 mg, 150 umol, 40%) as a white solid. ^{1}H NMR (400 MHz, CD_3OD): δ 7.70 (s, 1 H), 7.65-7.63 (m, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 7.28 (s, 1 H), 6.26 (s, 1 H), 5.78-5.68 (m, 2 H), 4.67 (d, J = 6.4 Hz, 2 H), 3.79-

3.77 (m, 2 H), 2.94-2.76 (m, 5 H), 2.44 (s, 3 H), 1.72 (d, *J* = 5.6 Hz, 3 H). LCMS (M + H^+) m/z: 425.

Example 117

(E)-4-(4-(3-(3-amino-1H-pyrazol-1-yl)azetidine-1-carbonyl)-3-chlorophenyl)-6-(but-2-en-1-yl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



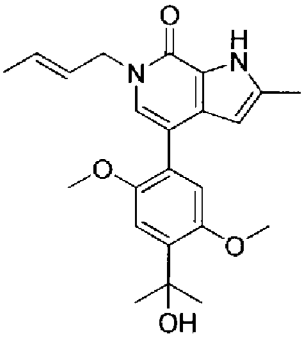
Example 117 was prepared in a similar procedure to Example 60, Step 6.
^{1}H NMR (400 MHz, CD_3OD) δ 7.69 (s, 1 H), 7.64-7.62 (m, 1 H), 7.58 (d, *J* = 8.0 Hz, 1 H), 7.40 (d, *J* = 6.4 Hz, 1 H), 7.27 (s, 1 H), 6.24 (s, 1 H), 5.73-5.67 (m, 2 H), 5.63 (d, *J* = 2.4 Hz, 1 H), 5.10-5.09 (m, 1 H), 4.60-4.55 (m, 3 H), 4.49-4.48 (m, 1 H), 4.40-4.38 (m, 2 H), 2.43 (s, 3 H), 1.70 (d, *J* = 5.6 Hz, 3 H). LCMS (M + H^+) m/z: 477.

Example 118 was prepared in a similar procedure to Example 117.

Example	IUPAC Name	NMR	m/z
118	4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400MHz, D_2O) δ 7.62 (d, *J* = 2.4 Hz, 1 H), 7.42-7.28 (m, 2 H), 7.18-7.08 (m, 2 H), 6.83-6.73 (m, 1 H), 6.21-6.11 (m, 1 H), 5.94-5.84 (m, 1 H), 5.39-5.26 (m, 2 H), 5.15-5.03 (m, 2 H), 4.54-4.43 (m, 2 H), 4.42-4.29 (m, 2 H), 4.25 (br. s, 1 H), 2.16 (s, 3 H), 1.50 (d, *J* = 6.4 Hz, 0.74 H), 1.41 (d, *J* = 3.4 Hz, 2.36 H).	443

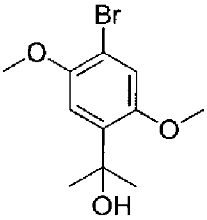
Example 119

(E)-6-(but-2-en-1-yl)-4-(4-(2-hydroxypropan-2-yl)-2,5-dimethoxyphenyl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



Step 1:

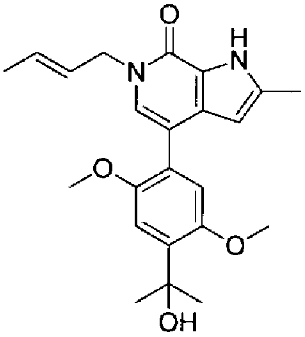
2-(4-bromo-2,5-dimethoxyphenyl)propan-2-ol



To a solution of 1-(4-bromo-2,5-dimethoxy-phenyl)ethanone (500 mg, 1.93 mmol) in tetrahydrofuran (10 mL) was added dropwise methylmagnesium bromide (3 M, 2.00 mL) at -78°C. The mixture was stirred at -78°C for 1hr, then the mixture was warmed to 0°C and stirred for 1hr. The mixture was quenched with saturated NH_4Cl solution and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine (50 mL), dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (Petroleum ether/ ethyl acetate = 20/1, 10/1) to give 2-(4-bromo-2,5-dimethoxy-phenyl)propan-2-ol (300 mg, 0.98 mmol, 51% yield) as a yellow oil.

Step 2:

(E)-6-(but-2-en-1-yl)-4-(4-(2-hydroxypropan-2-yl)-2,5-dimethoxyphenyl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one

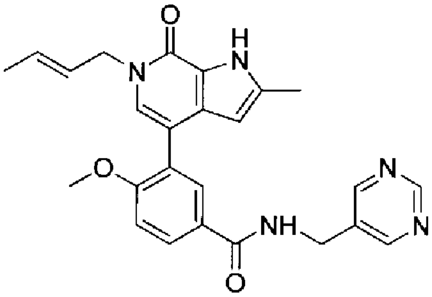


Example 119 was prepared in a similar procedure to Example 85, Step 2.

^{1}H NMR (400 MHz, CD_3OD) δ 7.32 (s, 1 H), 7.13-7.11 (m, 1 H), 6.95 (s, 1 H), 5.96 (s, 1 H), 5.75-5.66 (m, 2 H), 4.62 (d, J = 5.2 Hz, 2 H), 3.82 (s, 3 H), 3.72 (s, 3 H), 2.39 (s, 3 H), 1.71 (d, J = 5.6 Hz, 3 H), 1.61 (s, 6 H). LCMS (M + H^+) m/z: 397.

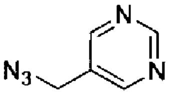
Example 120

3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrimidin-5-ylmethyl)benzamide



Step 1:

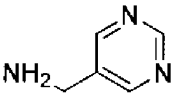
5-(azidomethyl)pyrimidine



To a mixture of pyrimidin-5-ylmethanol (800 mg, 7.27 mmol) in DCM (30 mL) and toluene (25 mL) was added DBU (2.21 g, 14.5 mmol) and DPPA (4.00 g, 14.5 mmol). The mixture was stirred at 25°C for 16 hrs. The mixture was then concentrated under reduced pressure. The residue was purified by silica gel chromatography (Petroleum ether/ ethyl acetate = 4/1) to give 5-(azidomethyl)pyrimidine (1.20 g, crude) as a colorless oil.

Step 2:

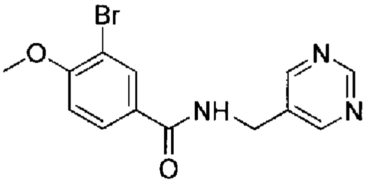
pyrimidin-5-ylmethanamine



To a mixture of 5-(azidomethyl)pyrimidine (600.0 mg, 4.44 mmol) in THF (15 mL) was added triphenylphosphine (2.33 g, 8.88 mmol) and water (160.0 mg, 8.88 mmol). The mixture was stirred at 25°C for 16hr. The mixture was concentrated under reduced pressure, then the residue was partitioned with water and DCM. The phases were separated, and the aqueous phase was adjusted to pH=8 with sat. sodium bicarbonate. The mixture was lyophilized to give pyrimidin-5-ylmethanamine (1.10 g, crude) as a white solid.

Step 3:

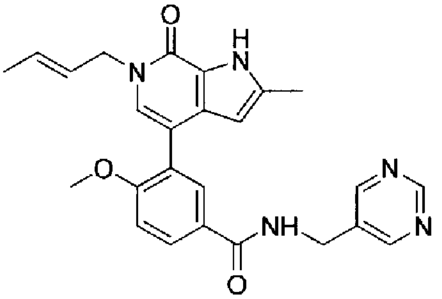
3-bromo-4-methoxy-N-(pyrimidin-5-ylmethyl)benzamide



This compound was prepared in a similar procedure to Example 55, Step 1.

Step 4:

3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrimidin-5-ylmethyl)benzamide

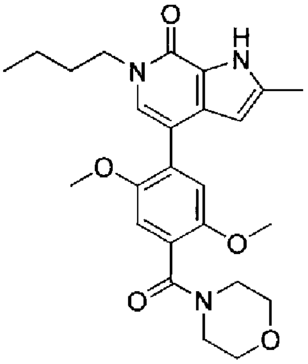


Example 120 was prepared in a similar procedure to Example 85, Step 2.

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.99 (d, J = 13.6 Hz, 1 H), 9.12 (s, 1 H), 8.90 (s, 2 H), 8.28 (s, 1 H), 8.09-8.01 (m, 2 H), 7.35 (s, 1 H), 7.07 (d, J = 8.4 Hz, 1 H), 5.99 (s, 1 H), 5.86-5.81 (m, 1 H), 5.64-5.55 (m, 1 H), 4.79-4.62(m, 4 H), 3.82 (s, 3 H), 2.30 (d, J = 5.2 Hz, 3 H), 1.78 (d, J = 6.8 Hz, 0.6 H), 1.71 (d, J = 6.0 Hz, 2.4 H). LCMS ($M + H^+$) m/z: 444.

Example 121

6-butyl-4-[2, 5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo [2, 3-c] pyridin-7-one



To a solution of 6-[(E)-but-2-enyl]-4-[2, 5-dimethoxy-4-(morpholine-4-carbonyl) phenyl]-2-methyl-1H-pyrrolo [2, 3-c] pyridin-7-one (**Example 108**, 30.0 mg, 66.4 umol) in methanol (2 mL) was added Pd/C (7.0 mg, 6.6 umol). The mixture was degassed under vacuum and purged with H_2. The mixture was stirred under H_2 atmosphere at 80°C for 12 hr, then the mixture was filtered and the filtrate was concentrated in vacuum. The residue was purified by silica gel chromatography (Dichloromethane: Methanol=20:1) to afford the crude product.

The crude product was purified by Pre-HPLC (Column: Waters Xbridge C18 150*20mm*5um; Mobile phase A : water with 0.05% ammonia solution; Mobile phase B: CH_3CN; Gradient: 14-44% B, 10 min) to afford 6-butyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one (4.0 mg, 8.8 umol, 13% yield) as white solid. ^1H NMR (400MHz, $CDCl_3$) δ 7.05 (s, 1 H), 6.99 (s, 1 H), 6.95 (s, 1 H), 5.98 (s, 1 H), 4.09 (t, *J* = 7.3 Hz, 2H), 3.60-3.96 (m, 11 H), 3.30-3.47 (m, 1 H), 2.45 (s, 3 H), 1.77-1.86 (m, 2 H), 1.44 (d, *J* = 7.5 Hz, 2 H), 0.97 (t, *J* = 7.3 Hz, 3 H). LCMS ($M + H^+$) m/z: 454.

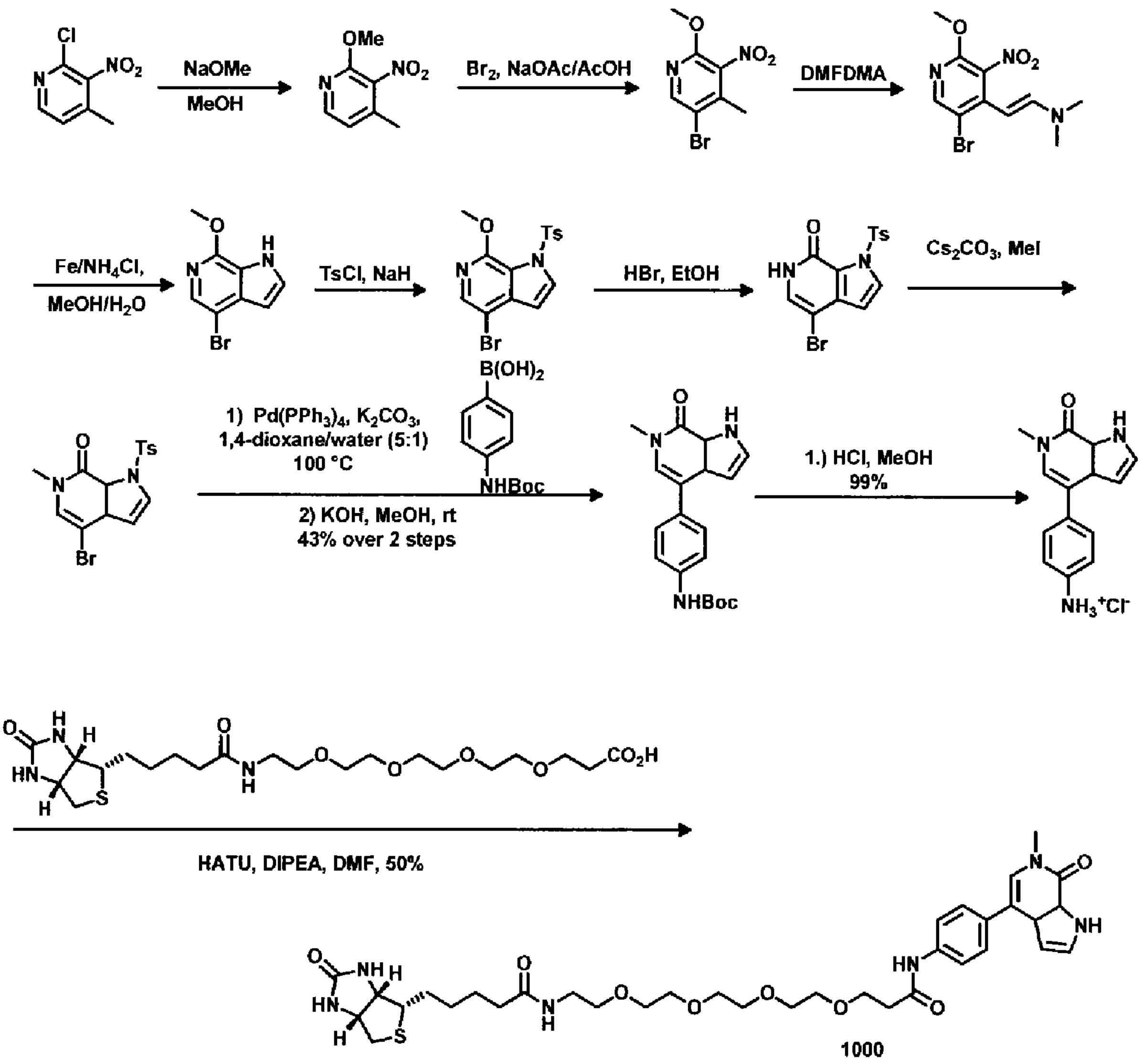
The following compounds were prepared in a similar fashion to Example 121:

Examples 122-123

Example	**IUPAC Name**	**NMR**	**m/z**
122	6-butyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^1H NMR (400 MHz, DMSO-d6) d11.72 (br. s, 1H), 8.23 (d, *J* = 1.71 Hz, 1H), 7.66 (s, 1H), 7.50 (d, *J* = 1.71 Hz, 1H), 6.24 (dd, *J* = 0.98, 2.20 Hz, 1H), 4.02 (t, *J* = 7.08 Hz, 2H), 3.86 (s, 3H), 3.57 (s, 2H), 3.38 - 3.54 (m, 2H), 2.31 - 2.45 (m, 4H), 2.31 (s, 3H), 2.22 (s, 3H), 1.67 (quin, *J* = 7.26 Hz, 2H), 1.27 - 1.38 (m, 2H), 0.92 (t, *J* = 7.32 Hz, 3H).	438
123	6-butyl-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^1H NMR (400 MHz, DMSO-d6) d 11.73 (br. s., 1H), 8.27 (d, *J* = 1.71 Hz, 1H), 7.66 (s, 1H), 7.54 (d, *J* = 1.71 Hz, 1H), 6.24 (dd, *J* = 0.85, 2.08 Hz, 1H), 4.02 (t, *J* = 6.96 Hz, 2H), 3.87 (s, 3H), 3.41 - 3.89 (m, 8H), 2.31 (s, 3H), 1.67 (quin, *J* = 7.26 Hz, 2H), 1.33 (qd, *J* = 7.49, 14.89 Hz, 2H), 0.92 (t, *J* = 7.45 Hz, 3H).	425

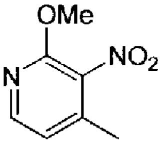
Example 124

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



Step 1:

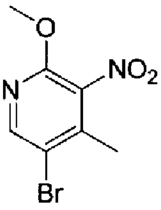
2-methoxy-4-methyl-3-nitropyridine



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:

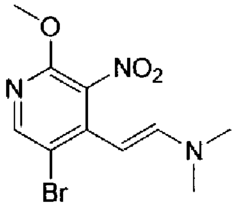
5-bromo-2-methoxy-4-methyl-3-nitropyridine



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:

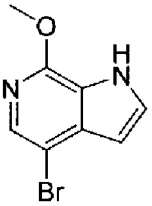
(E)-2-(5-bromo-2-methoxy-3-nitro-4-pyridyl)-N,N-dimethyl-ethenamine



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:

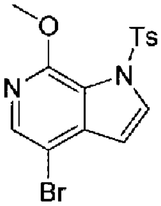
4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine



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:

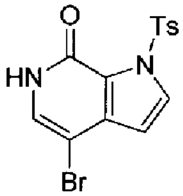
4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine



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:

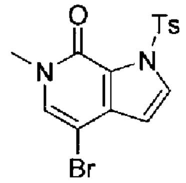
4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one



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. ^1H 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:

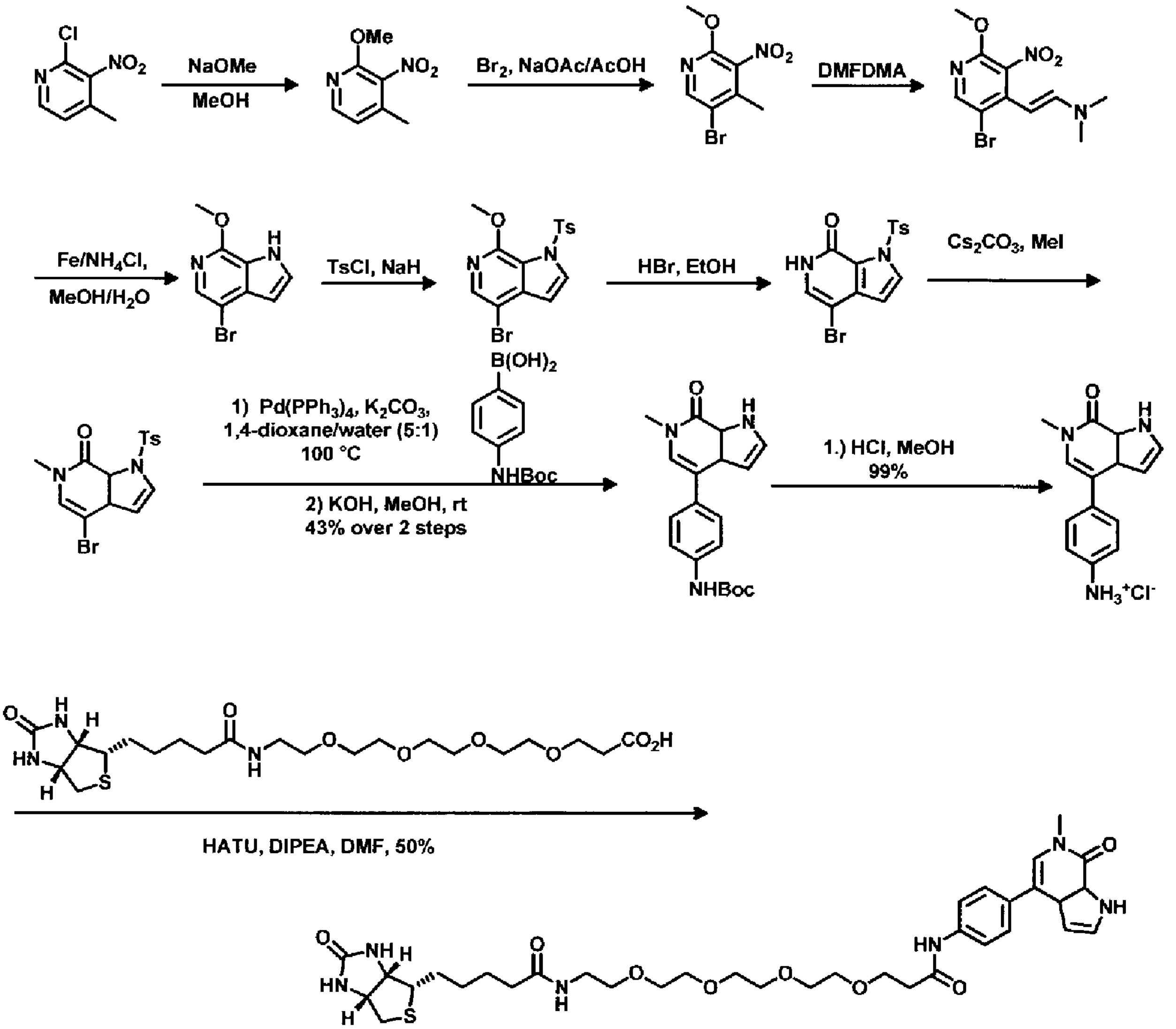
A 50 mL round bottom flask was charged with a magnetic stir bar, tert-butyl 4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenylcarbamate (350 mg, 1.031 mmol), MeOH (2.062 mL, 1.031 mmol), and HCl (1.031 mL, 4.12 mmol) (4N in dioxane). The reaction was then allowed to stir at rt for 4 h 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 125

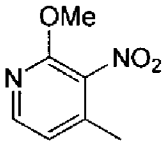
Synthesis of biotinylated probe compound (1001) for CECR2 assay described below.



1001

Step 1:

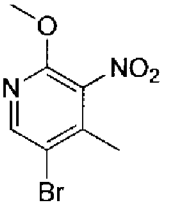
2-methoxy-4-methyl-3-nitropyridine



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:

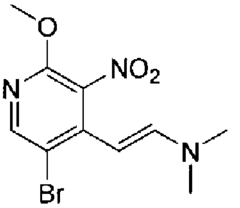
5-bromo-2-methoxy-4-methyl-3-nitropyridine



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

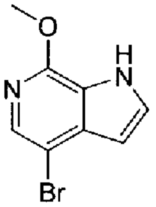


DMF-DMA (600 mL) was slowly added to a stirred and heated (80 °C) solution of 5-bromo-2-methoxy-4-methyl-3-nitropyridine (134 g, 0.54 mol) in DMF (1.1 L). After addition, the mixture was heated at 95 °C for 5 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled to 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:

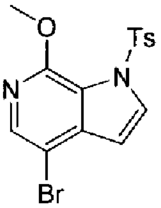
4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine



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:

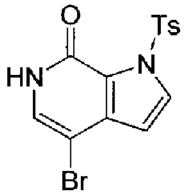
4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine



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:

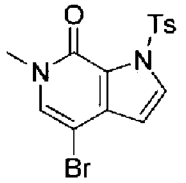
4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one



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 126

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 homogeneity. 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$_{1504\text{-}1635}$ 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 124) 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$_{424\text{-}538}$ 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 125) 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	IC50 (uM)	Assay
2	2.6	BRD4
4	2.1	BRD4
5	6.4	BRD4
7	2.7	BRD4
9	15	BRD4
11	3.6	BRD4
12	12	BRD4
13	4.5	BRD4
16	8.0	BRD4
20	0.89	BRD4
22	3.0	BRD4
23	2.1	BRD4
26	0.83	BRD4
28	0.51	BRD4
31	1.6	BRD4
32	0.33	BRD4
35	0.72	BRD4
38	1.4	BRD4
39	1.2	BRD4
40	1.8	BRD4
45	8.4	BRD4
63	0.98	BRD4
65	1.6	BRD4
69	0.32	BRD4
75	1.3	BRD4
76	1.2	BRD4
86	2.3	BRD4
84	1.9	BRD4
10	0.32	BRD9
19	0.094	BRD9
24	0.029	BRD9
27	0.039	BRD9
30	0.51	BRD9
34	0.022	BRD9
37	0.013	BRD9
41	0.13	BRD9
42	0.082	BRD9
46	0.046	BRD9
51	0.013	BRD9
52	0.046	BRD9
64	0.056	BRD9
66	0.028	BRD9
67	0.035	BRD9
68	0.039	BRD9
70	0.028	BRD9
72	0.023	BRD9
73	0.035	BRD9
74	0.027	BRD9
78	0.065	BRD9
79	0.020	BRD9
80	0.073	BRD9
81	0.017	BRD9
82	0.043	BRD9
83	0.28	BRD9
87	0.066	BRD9
88	0.30	BRD9
90	0.013	BRD9

91	0.013	BRD9
92	0.010	BRD9
93	0.034	BRD9
94	0.003	BRD9
95	0.005	BRD9
98	0.032	BRD9
99	0.009	BRD9
100	0.011	BRD9
101	0.012	BRD9
102	0.009	BRD9
103	0.046	BRD9
104	0.022	BRD9
105	0.083	BRD9
106	0.006	BRD9
107	0.10	BRD9
108	0.004	BRD9
109	0.006	BRD9
110	0.039	BRD9
111	0.069	BRD9
112	0.008	BRD9
113	0.003	BRD9
114	0.003	BRD9
115	0.005	BRD9
116	0.004	BRD9
117	0.005	BRD9
118	0.009	BRD9
119	0.006	BRD9
120	0.003	BRD9
121	0.017	BRD9
122	0.18	BRD9
123	0.21	BRD9
1	0.39	CECR2
21	3.3	CECR2
33	3.5	CECR2
36	5.7	CECR2
3	5.2	TAF-1
8	0.11	TAF-1
14	2.0	TAF-1
15	9.3	TAF-1
17	5.6	TAF-1
18	0.095	TAF-1
25	0.64	TAF-1
29	4.5	TAF-1
43	2.0	TAF-1
44	1.6	TAF-1
47	3.4	TAF-1
48	0.017	TAF-1
49	0.019	TAF-1
50	0.021	TAF-1
53	0.02	TAF-1
54	0.011	TAF-1
55	0.010	TAF-1
56	0.021	TAF-1
57	0.011	TAF-1
58	0.011	TAF-1
59	0.014	TAF-1
60	0.012	TAF-1
61	0.020	TAF-1
62	0.011	TAF-1
71	1.8	TAF-1

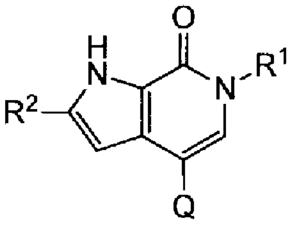
77	0.90	TAF-1
85	0.48	TAF-1
89	0.012	TAF-1
96	0.014	TAF-1
97	0.011	TAF-1

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 methyl, ethyl, C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl, or heterocyclyl, wherein any methyl of R^1 is substituted with one or more groups R^m, wherein any ethyl of R^1 is substituted with one or more groups R^n, and wherein any C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl 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, or C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b;

Q is carbocyclyl or heterocyclyl, which carbocyclyl or heterocyclyl is optionally substituted with one or more groups R^c;

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 $-N(R^v)-S(O)_2-N(R^v)_2$;

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

each R^m is independently selected from oxo, carbocyclyl, heterocyclyl, -F, -NO_2, -CN, -C(O)-$N(R^v)_2$, -S(O)-$N(R^v)_2$, -$S(O)_2$-$N(R^v)_2$, -C(O)-R^v, -C(O)-O-R^v, -S(O)-R^v, and -$S(O)_2$-R^v, wherein carbocyclyl is optionally substituted with one or more -O-R^v;

each R^n is independently selected from oxo, 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 -$N(R^v)$-$S(O)_2$-$N(R^v)_2$;

each R^u 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -$N(R^{ua})_2$, 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^u 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, C_{1-3}alkyl and heteroaryl wherein C_{1-3}alkyl is optionally substituted with one or more groups independently selected from oxo, hydroxyl, -$N(R^{ua})_2$ and halo and heteroaryl is optionally substituted with one or more -$N(R^{ua})_2$;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -$N(R^{va})_2$, 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^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;

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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-N(R^{wa})_2$, 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;

each R^{ua} is independently selected from hydrogen and C_{1-6}alkyl;

each R^{va} is independently selected from hydrogen and C_{1-6}alkyl; and

each R^{wa} is independently selected from hydrogen and C_{1-6}alkyl.

2. The compound of claim 1 wherein R^1 is methyl that is substituted with one or more groups R^m.

3. The compound of claim 1 wherein R^1 is ethyl that is substituted with one or more groups R^n.

4. The compound of claim 1 wherein R^1 is C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl, wherein any C_{3-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, carbocyclyl or heterocyclyl of R^1 is optionally substituted with one or more groups R^a.

5. The compound of claim 1 wherein R^1 is C_{3-6}alkyl or C_{3-6}alkenyl, wherein each C_{3-6}alkyl and C_{3-6}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 $-C(O)-O-R^v$.

6. The compound of claim 1 wherein R^1 is C_{3-6}alkyl or C_{3-6}alkenyl, wherein each C_{3-6}alkyl and C_{3-6}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 $-C(O)-O-R^v$.

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

8. The compound of claim 1 wherein R^1 is butyl, 2-cyclopropylethyl, cyclopentylmethyl, 2-penten-1-yl, cyclohexylmethyl, cyclobutylmethyl, 2-cyclohexylethyl, pentyl, 2-methylpropyl, 2-buten-1-yl, butyl, 2-furylmethyl, 3-methylbut-1-yl, 2-propenyl, 3-methyl-2-buten-1-yl, 3-buten-1-yl, 2-methoxyethyl, 3-methoxypropyl, or 4-methoxybenzyl.

9. The compound of any one of claims 1-8 wherein R^2 is H.

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

11. The compound of any one of claims 1-8 wherein R^2 is methyl.

12. The compound of any one of claims 1-11 wherein Q is carbocyclyl that is optionally substituted with one or more groups R^c.

13. The compound of any one of claims 1-11 wherein Q is heterocyclyl that is optionally substituted with one or more groups R^c.

14. The compound of any one of claims 1-11 wherein Q is C_3-C_8cycloalkyl that is optionally substituted with one or more groups R^c.

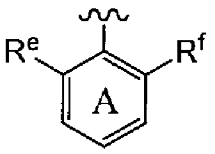
15. The compound of any one of claims 1-11 wherein Q is aryl that is optionally substituted with one or more groups R^c.

16. The compound of any one of claims 1-11 wherein Q is phenyl that is optionally substituted with one or more groups R^c.

17. The compound of any one of claims 1-11 wherein Q is C_3-C_8heterocycloalkyl that is optionally substituted with one or more groups R^c.

18. The compound of any one of claims 1-11 wherein Q is heteroaryl that is optionally substituted with one or more groups R^c.

19. The compound of any one of claims 1-11 wherein Q is:



wherein:

ring A is optionally substituted with one or more groups R^g, or ring A is optionally fused with a carbocyclyl or a heterocyclyl to form a polycyclyl that is optionally substituted with one or more groups R^g;

R^e is hydrogen, -F, -Cl, -Br, -I, -CN, $-O-R^x$, C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^x)_2$, -CN, $-C(O)-N(R^x)_2$, $-S(O)-N(R^x)_2$, $-S(O)_2-N(R^x)_2$, $-O-R^x$, $-S-R^x$, $-O-C(O)-R^x$, $-C(O)-R^x$, $-C(O)-O-R^x$, $-S(O)-R^x$, $-S(O)_2-R^x$, $-N(R^x)-C(O)-R^x$, $-N(R^x)-S(O)-R^x$, and$-N(R^x)-S(O)_2-R^x$,;

R^f is hydrogen, -F, -Cl, -Br, -I, -CN, $-O-R^y$, C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^y)_2$, -CN, $-C(O)-N(R^y)_2$, $-S(O)-N(R^y)_2$, $-S(O)_2-N(R^y)_2$, $-O-R^y$, $-S-R^y$, $-O-C(O)-R^y$, $-C(O)-R^y$, $-C(O)-O-R^y$, $-S(O)-R^y$, $-S(O)_2-R^y$, $-N(R^y)-C(O)-R^y$, $-N(R^y)-S(O)-R^y$ and $-N(R^y)-S(O)_2-R^y$;

each R^g 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, $-NO_2$, $-N(R^z)_2$, -CN, $-C(O)-N(R^z)_2$, $-S(O)-N(R^z)_2$, $-S(O)_2-N(R^z)_2$, $-O-R^z$, $-S-R^z$, $-O-C(O)-R^z$, $-O-C(O)-O-R^z$, $-C(O)-R^z$, $-C(O)-O-R^z$, $-S(O)-R^z$, $-S(O)_2-R^z$, $-O-C(O)-N(R^z)_2$, $-N(R^z)-C(O)-OR^z$, $-N(R^z)-C(O)-N(R^z)_2$, $-N(R^z)-C(O)-R^z$, $-N(R^z)-S(O)-R^z$, $-N(R^z)-S(O)_2-R^z$, $-N(R^z)-S(O)-N(R^z)_2$, and $-N(R^z)-S(O)_2-N(R^z)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^z)_2$, -CN, $-C(O)-N(R^z)_2$, $-S(O)-N(R^z)_2$, $-S(O)_2-N(R^z)_2$, $-O-R^z$, $-S-R^z$, $-O-C(O)-R^z$, $-C(O)-R^z$, $-C(O)-O-R^z$, $-S(O)-R^z$, $-S(O)_2-R^z$, $-N(R^z)-C(O)-R^z$, $-N(R^z)-S(O)-R^z$, $-N(R^z)-S(O)_2-R^z$ and C_{1-6}alkyl and heteroaryl wherein C_{1-3}alkyl is optionally substituted with one or more groups independently selected from oxo, hydroxyl, $-N(R^{ua})_2$ and halo and heteroaryl is optionally substituted with one or more $-N(R^{ua})_2$;

each R^x is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl;

each R^y is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl, wherein each C_{1-6}alkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl; and

each R^z 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, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, heterocyclyl, carbocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^z 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.

20. The compound of claim 19 wherein R^e is hydrogen.

21. The compound of claim 19 wherein R^f is hydrogen.

22. The compound of any one of claims 19-21 wherein ring A is optionally substituted with one or more groups R^g.

23. The compound of any one of claims 1-18, wherein each R^c 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, $-N(R^u)_2$, -CN, $-C(O)-N(R^u)_2$, $-O-R^u$, and $-N(R^u)-S(O)_2-R^u$, - wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^u)_2$, -CN, $-C(O)-N(R^u)_2$, $-S(O)-N(R^u)_2$, $-S(O)_2-N(R^u)_2$, $-O-R^u$, $-S-R^u$, $-O-C(O)-R^u$, $-C(O)-R^u$, $-C(O)-O-R^u$, $-S(O)-R^u$, $-S(O)_2-R^u$, $-N(R^u)-C(O)-R^u$, $-N(R^u)-S(O)-R^u$, $-N(R^u)-S(O)_2-R^u$ and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

24. The compound of any one of claims 1-18, wherein each R^c is independently selected from oxo, C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, $-C(O)-N(R^u)_2$, $-O-R^u$, and $-N(R^u)-S(O)_2-R^u$,

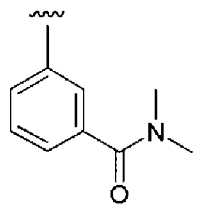
wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO_2, -$N(R^u)_2$, -CN, -C(O)-$N(R^u)_2$, -S(O)-$N(R^u)_2$, -$S(O)_2$-$N(R^u)_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -$S(O)_2$-R^u, -$N(R^u)$-C(O)-R^u, -$N(R^u)$-S(O)-R^u, -$N(R^u)$-$S(O)_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

25. The compound of any one of claims 1-18, wherein each R^c is independently selected from oxo, C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-$N(R^u)_2$, -O-R^u, and -$N(R^u)$-$S(O)_2$-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from -O-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

26. The compound of any one of claims 1-18, wherein Q is substituted with one -C(O)-$N(R^u)_2$ group and optionally substituted with one or more R^c groups independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -$N(R^u)_2$, -CN, -C(O)-$N(R^u)_2$, -O-R^u, and -$N(R^u)$-$S(O)_2$-R^u, - wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO_2, -$N(R^u)_2$, -CN, -C(O)-$N(R^u)_2$, -S(O)-$N(R^u)_2$, -$S(O)_2$-$N(R^u)_2$, -O-R^u, -S-R^u, -O-C(O)-R^u, -C(O)-R^u, -C(O)-O-R^u, -S(O)-R^u, -$S(O)_2$-R^u, -$N(R^u)$-C(O)-R^u, -$N(R^u)$-S(O)-R^u, -$N(R^u)$-$S(O)_2$-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

27. The compound of any one of claims 1-11 wherein Q is phenyl that is substituted with a group -C(O)-$N(R^u)_2$, and that is optionally substituted with one or more groups R^c, wherein each R^c is independently selected from C_{1-6}alkyl, heterocyclyl, -F, -Cl, -CN, -C(O)-$N(R^u)_2$, and -O-R^u, wherein any C_{1-6}alkyl or heterocyclyl is optionally substituted with one or more groups independently selected from -O-R^u and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

28. The compound of any one of claims 1-11 wherein Q is selected from: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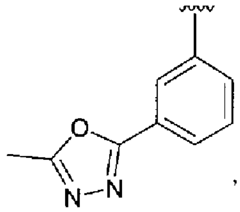
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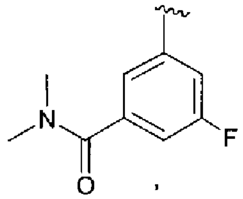
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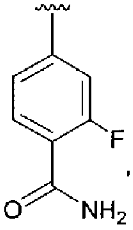
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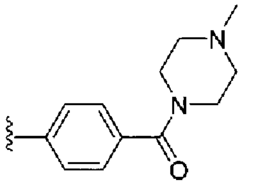
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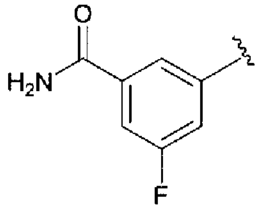
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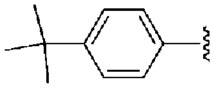
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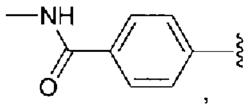
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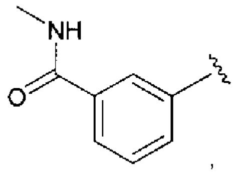
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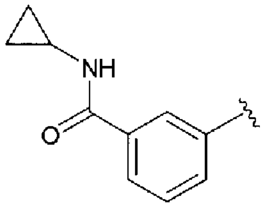
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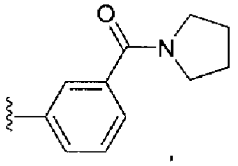
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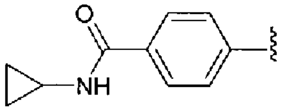
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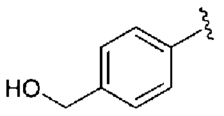
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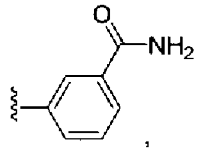
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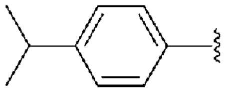
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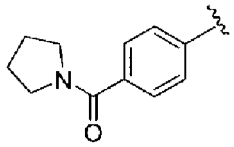
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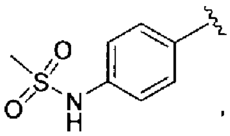
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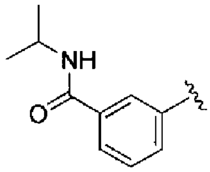
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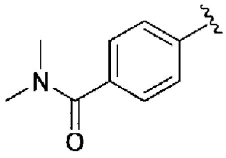
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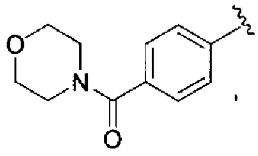
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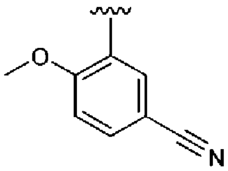
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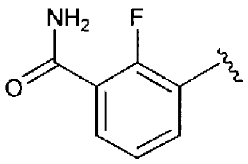
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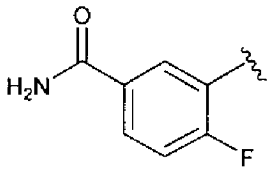
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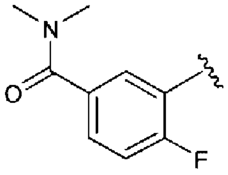
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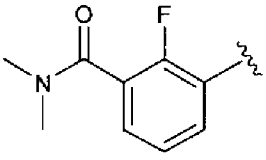
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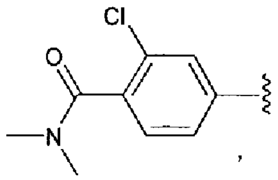
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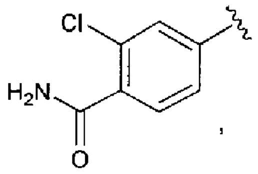
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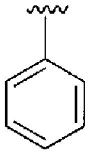
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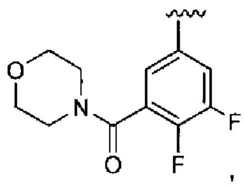
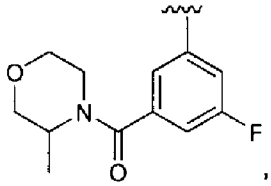
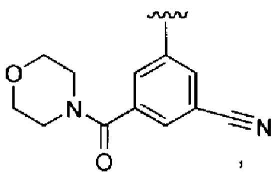
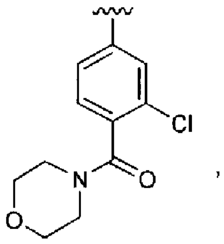

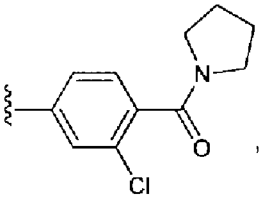
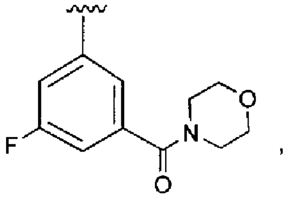
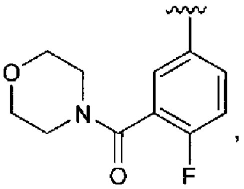
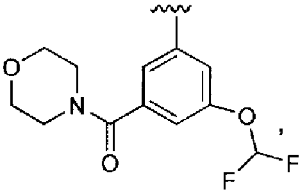

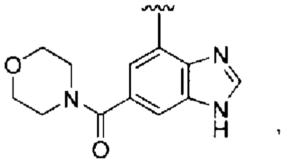
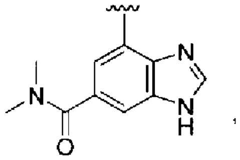
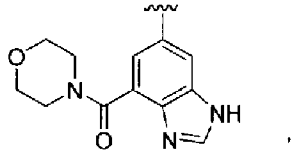
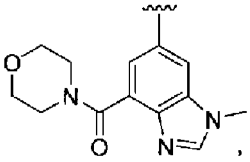

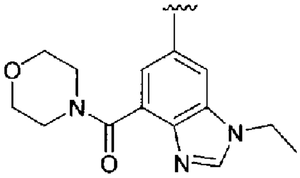
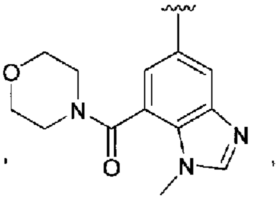
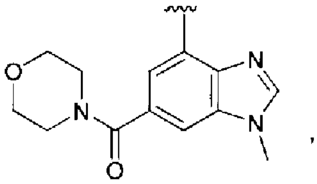
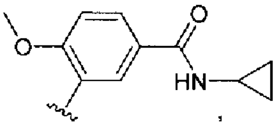

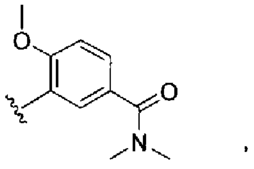
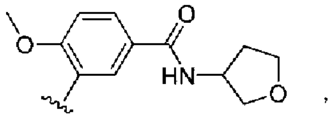
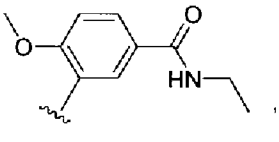
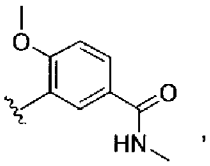

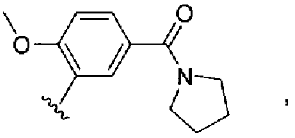
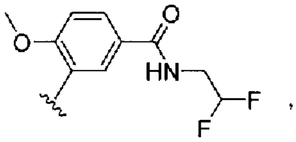
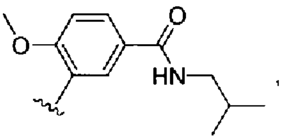
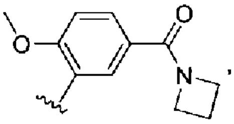

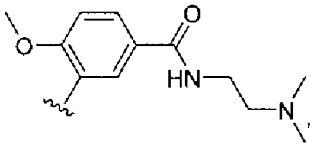

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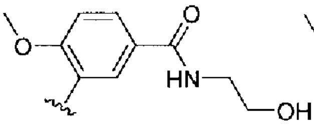

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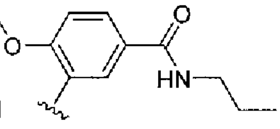

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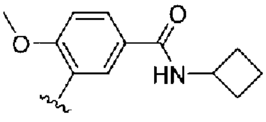

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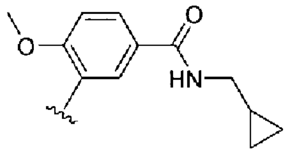

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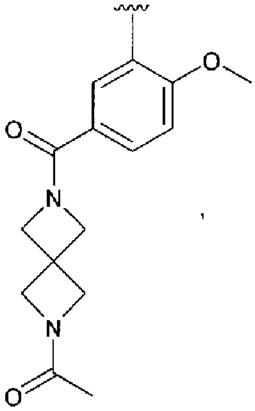

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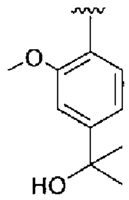

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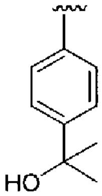

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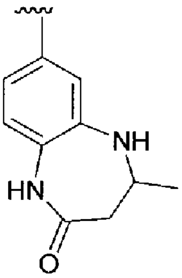

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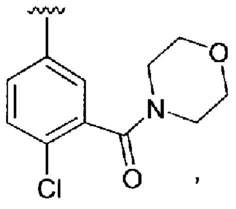

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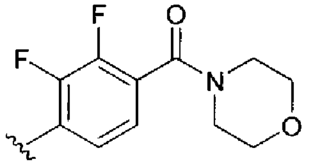

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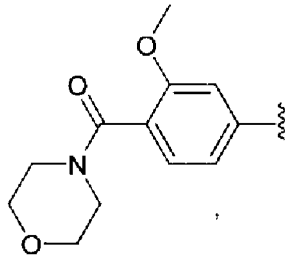

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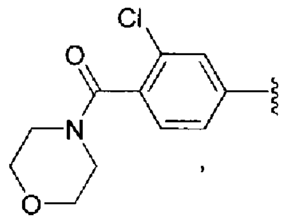

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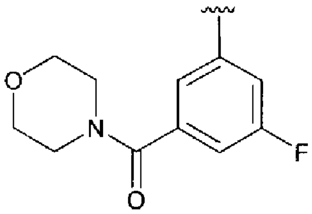

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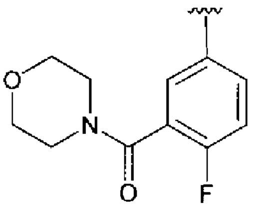

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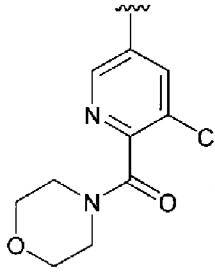

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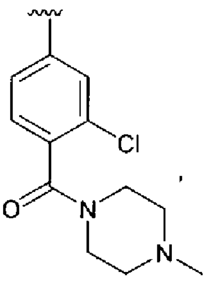

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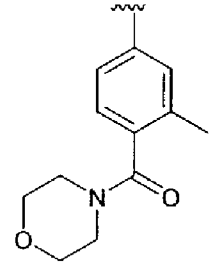

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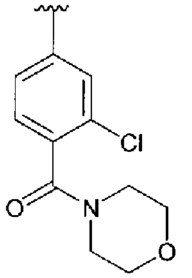

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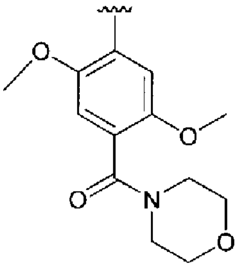

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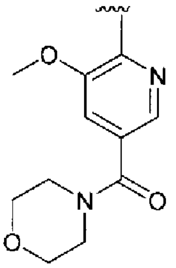

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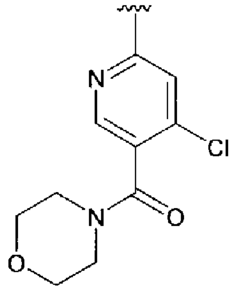
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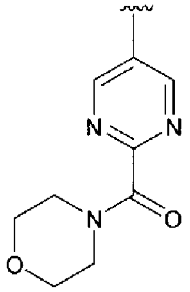
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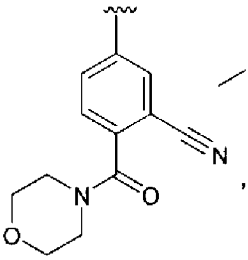
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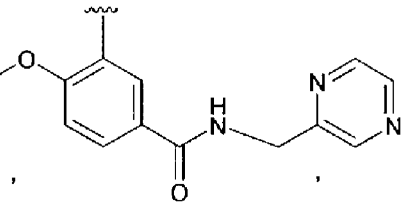
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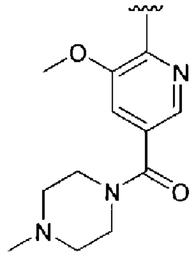
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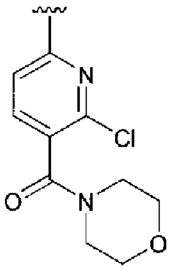
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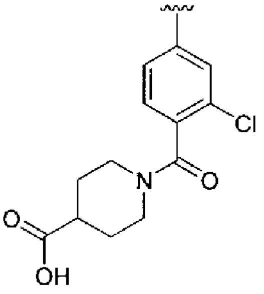
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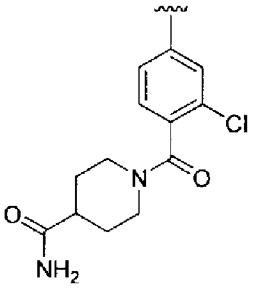
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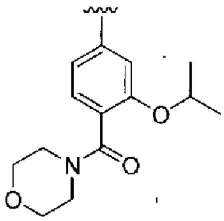
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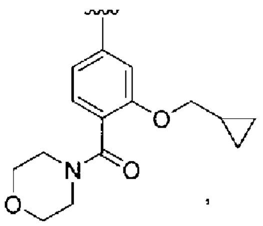
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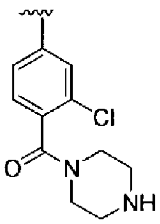
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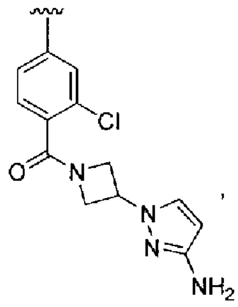
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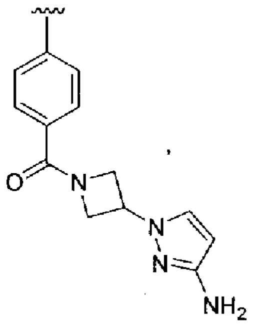
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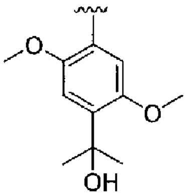
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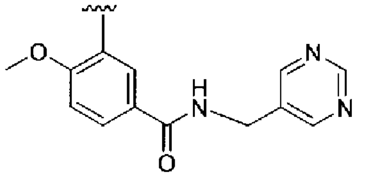
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29. The compound of claim 1 that is selected from:

3-(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

N,N-dimethyl-3-[6-(3-methylbut-2-enyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide;

3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-(cyclopentylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-[(4-methoxyphenyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

N,N-dimethyl-3-[7-oxo-6-[(E)-pent-2-enyl]-1H-pyrrolo[2,3-c]pyridin-4-yl]benzamide;

3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-[6-(cyclohexylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-(6-isopentyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-[6-(cyclobutylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-(2-cyclohexylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

N,N-dimethyl-3-(7-oxo-6-pentyl-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide;

3-[6-(2-methoxyethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-[6-(3-methoxypropyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

3-(6-isobutyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-[6-(cyclopropylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N,N-dimethylbenzamide;

6-but-3-enyl-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-5-fluoro-N,N-dimethylbenzamide;

4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluorobenzamide;

6-but-2-enyl-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-fluorobenzamide;

6-but-2-enyl-4-(4-tert-butylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one;

4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-methylbenzamide;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-methylbenzamide;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-cyclopropylbenzamide;

6-but-2-enyl-4-[3-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-cyclopropylbenzamide;

6-but-2-enyl-4-[4-(hydroxymethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)benzamide;

6-but-2-enyl-4-(4-isopropylphenyl)-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

6-but-2-enyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

N-[4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]methanesulfonamide;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N-isopropylbenzamide;

4-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

6-but-2-enyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluorobenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluorobenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-fluoro-N,N-dimethylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-fluoro-N,N-dimethylbenzamide;

4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-N,N-dimethylbenzamide;

4-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chlorobenzamide;

6-(2-furylmethyl)-4-phenyl-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-benzonitrile;

3-[6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-benzonitrile;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclopropyl-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-tetrahydrofuran-3-ylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-ethyl-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-methylbenzamide;

6-[(E)-but-2-enyl]-4-[2-methoxy-5-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2,2-difluoroethyl)-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-isobutyl-4-methoxybenzamide;

4-[5-(azetidine-1-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-[2-(dimethylamino)ethyl]-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(2-hydroxyethyl)-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-propylbenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-cyclobutyl-4-methoxybenzamide;

3-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-N-(cyclopropylmethyl)-4-methoxybenzamide;

4-[5-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)-2-methoxy-phenyl]-6-[(E)-but-2-enyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

4-[5-(6-acetyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)-2-methoxy-phenyl]-6-butyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-butyl-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-butyl-4-(4-(2-hydroxypropan-2-yl)phenyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one;

6-(2-cyclopropylethyl)-4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-(2-cyclopropylethyl)-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethylbenzamide;

3-(6-butyl-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-4-methoxy-N,N-dimethylbenzamide;

3-[6-(2-cyclopropylethyl)-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N,N-dimethylbenzamide;

7-[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one;

6-but-3-enyl-4-[3,4-difluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-fluoro-5-(3-methylmorpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

3-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-5-(morpholine-4-carbonyl)benzonitrile

6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-(difluoromethoxy)-5-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[6-(morpholine-4-carbonyl)-1H-benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one ;

7-(6-but-3-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl)-N,N-dimethyl-3H-benzimidazole-5-carboxamide;

6-but-3-enyl-4-[7-(morpholine-4-carbonyl)-3H-benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-ethyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[1-methyl-7-(morpholine-4-carbonyl)benzimidazol-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[1-methyl-6-(morpholine-4-carbonyl)benzimidazol-4-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[4-chloro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-2-methyl-4-[4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one ;

6-[(E)-but-2-enyl]-2-methyl-4-[4-(pyrrolidine-1-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one

6-[(E)-but-2-enyl]-4-[3-chloro-4-(pyrrolidine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[2,3-difluoro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one ;

6-[(E)-but-2-enyl]-4-[3-methoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-but-3-enyl-4-[3-fluoro-5-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one ;

6-but-3-enyl-4-[4-fluoro-3-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[5-chloro-6-(morpholine-4-carbonyl)-3-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(4-methylpiperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-2-methyl-4-[3-methyl-4-(morpholine-4-carbonyl)phenyl]-1H-pyrrolo[2,3-c]pyridin-7-one;

6-allyl-4-[3-chloro-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-allyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-2-methyl-4-[2-(morpholine-4-carbonyl)pyrimidin-5-yl]-1H-pyrrolo[2,3-c]pyridin-7-one;

5-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-(morpholine-4-carbonyl)benzonitrile;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2-methoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

6-[(E)-but-2-enyl]-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrazin-2-ylmethyl)benzamide

6-but-2-enyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[6-chloro-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

1-[4-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxylic acid;

1-[4-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-2-chloro-benzoyl]piperidine-4-carboxamide;

6-[(E)-but-2-enyl]-4-[3-isopropoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-(cyclopropylmethoxy)-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[3-chloro-4-(piperazine-1-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]-3-chloro-phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

4-[4-[3-(3-aminopyrazol-1-yl)azetidine-1-carbonyl]phenyl]-6-[(E)-but-2-enyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-[(E)-but-2-enyl]-4-[4-(1-hydroxy-1-methyl-ethyl)-2,5-dimethoxy-phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

3-[6-[(E)-but-2-enyl]-2-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridin-4-yl]-4-methoxy-N-(pyrimidin-5-ylmethyl)benzamide;

6-butyl-4-[2,5-dimethoxy-4-(morpholine-4-carbonyl)phenyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one;

6-butyl-4-[3-methoxy-5-(4-methylpiperazine-1-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one; and

6-butyl-4-[3-methoxy-5-(morpholine-4-carbonyl)-2-pyridyl]-2-methyl-1H-pyrrolo[2,3-c]pyridin-7-one

and salts thereof.

30. A composition comprising a compound of formula (I) as described in any one of claims 1-29 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

31. The composition according to claim 30, in combination with an additional therapeutic agent.

32. The composition according to claim 31, wherein the additional therapeutic agent is a chemotherapeutic agent.

33. 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 1-29, to the animal.

34. The method of claim 33 wherein the disorder is cancer, an inflammatory disorder, or an autoimmune disease.

35. The method of claim 34 wherein the disorder is cancer and 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.

36. The method of claim 34 wherein the disorder is cancer and the cancer is selected from lung cancer, breast cancer, pancreatic cancer, colorectal cancer, and melanoma.

37. The method of claim 34 wherein the disorder is an inflammatory disorder or an autoimmune disease and 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.

38. The method of claim 33 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.

39. A compound of formula (I) or a pharmaceutically acceptable salt thereof as described in any one of claims 1-29 for use in medical therapy.

40. A compound of formula (I) or a pharmaceutically acceptable salt thereof as described in any one of claims 1-29 for the prophylactic or therapeutic treatment of a bromodomain-mediated disorder.

41. The use of a compound of formula (I) or a pharmaceutically acceptable salt thereof as described in any one of claims 1-29 to prepare a medicament for treating a bromodomain-mediated disorder in an animal.

42. 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 as described in any one of claims 1-29.

43. The method of claim 42 further comprising administering the cytotoxic agent to the animal.

44. 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 as described in any one of claims 1-29.

45. 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, as described in any one of claims 1-29, 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.

46. 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 as described in any one of claims 1-29, and (b) a cytotoxic agent.

47. The method of claim 46 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.

48. The method of claim 46 wherein the cytotoxic agent is a taxane.

49. The method of claim 48, wherein the taxane is paclitaxel or docetaxel.

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

51. The method of claim 46 wherein the cytotoxic agent is an antagonist of EGFR.

52. The method of claim 51, wherein the antagonist of EGFR is N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine or a pharmaceutically acceptable salt thereof.

53. The method of claim 46, wherein the cytotoxic agent is a RAF inhibitor.

54. The method of claim 53, wherein the RAF inhibitor is a BRAF or CRAF inhibitor.

55. The method of claim 53, wherein the RAF inhibitor is vemurafenib.

56. The method of claim 46 wherein the cytotoxic agent is a PI3K inhibitor.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
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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

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X A	US 2014/094456 A1 (BUCKMAN BRAD OWEN [US] ET AL) 3 April 2014 (2014-04-03) claims; examples 25, 26; compounds 604-609 -----	1-32,39 33-38, 40-56
X A	WO 2014/125408 A2 (AURIGENE DISCOVERY TECH LTD [IN]) 21 August 2014 (2014-08-21) page 56 - page 57; claims; examples 3, 10, 12-14 ----- -/--	1-32,39 33-38, 40-56

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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Date of the actual completion of the international search 14 December 2015	Date of mailing of the international search report 21/12/2015
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Gavriliu, Daniela

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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