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(71) Applicant *(for all designated States except US)*: **GLAXOSMITHKLINE LLC** [US/US]; One Franklin Plaza, 200 North 16th Street, Philadelphia, Pennsylvania 19102 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BANKA, Anna** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **CATALANO, John, G.** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **CHONG, Pek, Yoke** [MY/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **FANG, Jing** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **GARRIDO, Dulce, Maria** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **PEAT, Andrew, James** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **PRICE, Daniel, J.** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **SHOTWELL, John, Brad** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **TAI, Vincent** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US). **ZHANG, Huichang** [US/US]; c/o GlaxoSmithKline, Global Patents Dept., Five Moore Drive, P O Box 13398, Research Triangle Park, North Carolina 27709 (US).

(74) Agents: **LINEBERRY, Douglas, L.** et al.; DORITY & MANNING, P.A., P O Box 1449, Greenville, South Carolina 29602-1449 (US).

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(54) Title: PIPERAZINYL ANTIVIRAL AGENTS

(57) Abstract: Provided are compounds of Formula (I) and pharmaceutically acceptable salts thereof, their pharmaceutical compositions, their methods of preparation, and their use for treating viral infections mediated by a member of the Flaviviridae family of viruses such as hepatitis C virus (HCV).

PIPERAZINYL ANTIVIRAL AGENTS

CROSS REFERENCE TO RELATED PATENTS AND PATENT APPLICATIONS

[0001] This application is a Patent Cooperation Treaty application and claims the priority benefit of U.S. Provisional Patent Application No. 61/248,063, filed October 2, 2009, which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to the field of pharmaceuticals. Provided herein are compounds and compositions, methods for their preparation, and methods for their use in treating viral infections in patients mediated, at least in part, by a virus in the *Flaviviridae* family of viruses.

BACKGROUND OF THE INVENTION

[0003] Chronic infection with HCV is a major health problem associated with chronic liver disease, cirrhosis, hepatocellular carcinoma, and liver failure. HCV is a *hepacivirus* member of the *Flaviviridae* family of RNA viruses that affect animals and humans. The genome is a single ~9.6-kilobase strand of RNA, and consists of one open reading frame that encodes for a polyprotein of ~3000 amino acids flanked by untranslated regions at both 5' and 3' ends (5'- and 3'-UTR). The polyprotein serves as the precursor to at least 10 separate viral proteins critical for replication and assembly of progeny viral particles. The organization of structural and non-structural proteins in the HCV polyprotein is as follows: C-E1-E2-p7-NS2-NS3-NS4a-NS4b-NS5a-NS5b. Because the replicative cycle of HCV does not involve any DNA intermediate and the virus is not integrated into the host genome, HCV infection can theoretically be cured. While the pathology of HCV infection affects mainly the liver, the virus is found in other cell types in the body including peripheral blood lymphocytes.

[0004] HCV is major causative agent for post-transfusion and for sporadic hepatitis. Infection by HCV is insidious in a high proportion of chronically infected (and infectious) carriers who may not experience clinical symptoms for many years. An estimated 170 million chronic carriers worldwide are at risk of developing liver disease. See, for example, Szabo, *et al.*, *Pathol.Oncol.Res.* 2003, 9:215-221, and Hoofnagle JH, *Hepatology* 1997, 26:15S-20S. In the United States alone 2.7 million are chronically infected with HCV, and the number of HCV-related deaths in 2000 was estimated between 8,000 and 10,000, a number that is expected to increase significantly over the next years.

[0005] At present, the standard treatment for chronic HCV is interferon alpha (IFN-alpha) in combination with ribavirin and this requires at least six months of treatment. IFN-alpha belongs to a family of naturally occurring small proteins with characteristic biological effects such as antiviral, immunoregulatory, and antitumoral activities that are produced and secreted by most animal nucleated cells in response to several diseases, in particular viral infections. IFN-alpha is an important regulator of growth and differentiation affecting cellular communication and immunological control. Treatment of HCV with interferon has frequently been associated with adverse side effects such as fatigue, fever, chills, headache, myalgias, arthralgias, mild alopecia, psychiatric effects and associated disorders, autoimmune phenomena and associated disorders and thyroid dysfunction. Ribavirin, an inhibitor of inosine 5'-monophosphate dehydrogenase (IMPDH), enhances the efficacy of IFN-alpha in the treatment of HCV. Despite the introduction of ribavirin, more than 50% of the patients do not eliminate the virus with the current standard therapy of interferon-alpha (IFN) and ribavirin. By now, standard therapy of chronic hepatitis C has been changed to the combination of pegylated IFN-alpha plus ribavirin. However, a number of patients still have significant side effects, primarily related to ribavirin. Ribavirin causes significant hemolysis in 10-20% of patients treated at currently recommended doses, and the drug is both teratogenic and embryotoxic. Even with recent improvements, a substantial fraction of patients do not respond with a sustained reduction in viral load and there is a clear need for more effective antiviral therapy of HCV infection.

[0006] A number of approaches are being pursued to combat the virus. These include, for example, application of antisense oligonucleotides or ribozymes for inhibiting HCV replication. Furthermore, low-molecular weight compounds that directly inhibit HCV proteins and interfere with viral replication are considered as attractive strategies to control HCV infection. Among the viral targets, the NS3/4a protease/helicase and the NS5b RNA-dependent RNA polymerase are considered the most promising viral targets for new drugs. Indeed, compounds said to be useful for treating HCV infections are disclosed, for example, in WO2005/051318 (Chunduru, *et al.*) and WO2009/023179 (Schmitz, *et al.*). These references disclose methods for preparing the compounds, compositions comprising the compounds, compositions comprising the compounds and additional compounds, and methods of treating HCV.

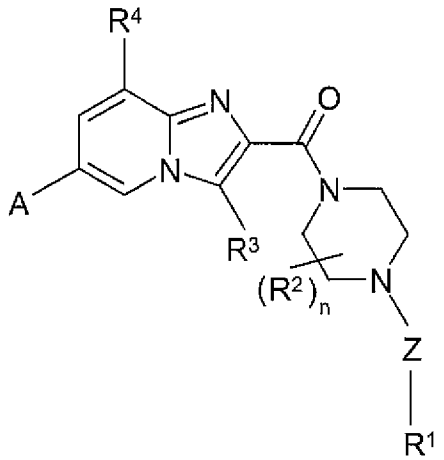
[0007] Besides targeting viral genes and their transcription and translation products, antiviral activity can also be achieved by targeting host cell proteins that are necessary for viral replication. For example, antiviral activity can be achieved by inhibiting host cell cyclophilins. Alternatively, a potent TLR7 agonist has been shown to reduce HCV plasma levels in humans.

[0008] In view of the worldwide epidemic level of HCV and other members of the *Flaviviridae* family of viruses, and further in view of the limited treatment options, there is a strong need for new effective drugs for treating infections cause by these viruses.

SUMMARY OF THE INVENTION

[0009] In accordance with one embodiment of the present invention, provided is a compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or $(C_1$-$C_3)$alkylene;

A is selected from the group consisting of hydrogen, halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkenyl, $(C_1$-$C_6)$alkynyl, $(C_3$-$C_{14})$cycloalkyl, aryl, hydroxyl, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, $-SO_2N(R^6)_2$, $-C(O)NR^6R^6$, $-OR^7$, $-R^6R^7$, $-SO_2R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$, $-alkylR^9R^6$, $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, $(C_2$-$C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O, $(C_2$-$C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{10};

R^1 is selected from the group consisting of hydrogen, halo, cyano, hydroxyl, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkenyl, $(C_1$-$C_6)$alkynyl, $-C(O)N(R^6)_2$, $-R^9R^6$, $-SO_2N(R^6)_2$, $-SO_2R^6$, $(C_3$-$C_{14})$cycloalkyl, aryl, $(C_2$-$C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2$-$C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{11};

R^2 is independently selected from the group consisting of oxo, $(C_1$-$C_6)$alkyl, $(C_3$-

C_{14})cycloalkyl, –alkylR^8, and aryl, or optionally two R^2 alkyl groups, together with any intervening atoms, form a spiro or fused (C_3-C_{14})cycloalkyl ring;

R^3 is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_3-C_{14})cycloalkyl, halo, –alkylR^8, and cyano;

R^4 is selected from the group consisting of hydrogen, hydroxyl, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, (C_3-C_{14})cycloalkyl, aryl, –$OR^6(R^5)_m$, –$R^6(R^5)_m$, –alkyl$(R^5)_mR^6$, –alkylR^9R^6, –NR^6R^6, –$NR^6C(O)NR^6R^6$, –$SO_2N(R^6)_2$, –$C(O)NR^6R^6$, –OR^7, –R^6R^7, –SO_2R^6, –$NR^6C(S)NR^6R^6$, –$NR^6S(O)_2R^6$, –alkylR^9R^6, –$NR^6C(O)OR^6$, –$NR^6C(O)R^6$, (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{10};

R^5 is halo;

R^6 is independently selected from the group consisting of hydrogen and (C_1-C_6)alkyl;

R^7 is (C_3-C_{14})cycloalkyl;

R^8 is hydroxyl;

R^9 is carboxyl;

R^{10} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, hydroxyl, oxo, carboxyl, cyano, halo, –$C(O)NH_2$, –SO_2NH_2, –SR^6, –$S(O)R^6$, –$S(O)_2R^6$, –$S(O)_2NR^6R^6$, –NR^6R^6, –$NR^6C(O)NR^6R^6$, –$NR^6C(S)NR^6R^6$, –$NR^6S(O)_2R^6$ –$NR^6C(O)OR^6$, –$NR^6C(O)R^6$, –$C(NR^6)NR^6R^6$, –$C(O)NR^6R^6$, –$C(O)OR^6$, –$C(O)R^6$, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O;

R^{11} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, hydroxyl, –$NR^6C(O)R^6$, –$OC(O)R^6$, –$OR^6(R^5)_m$, –$R^6(R^5)_m$, halo, -$C(O)N(R^6)_2$, –$SO_2N(R^6)_2$, –SO_2R^6, oxo, –alkylR^8, –alkylR^9, –alkylR^9R^6, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O; or optionally two R^{11} groups, together with any intervening atoms, form a fused (C_3-C_{14})cycloalkyl ring or a fused (C_2-C_6)heterocyclic ring having 1-3 heteroatoms selected from S, N and O; wherein said fused cycloalkyl or

heterocyclic ring is optionally substituted with one to three R^{12};

R^{12} is independently selected from the group consisting of $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, oxo, halo, hydroxyl, carboxyl, cyano, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, and $-NR^6R^6$;

m is an integer from 1 to 3; and

n is zero or an integer from 1 to 4.

[0010] Also provided is a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Formula (I) or a pharmaceutically acceptable salt or solvate thereof.

[0011] Also provided are synthetic intermediates, methods for preparing the compounds of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, and compositions thereof and for their therapeutic uses. In some embodiments, provided is a method for treating a viral infection in a patient mediated at least in part by a virus in the *Flaviviridae* family of viruses, comprising administering to said patient a composition comprising a compound Formula (I), or a pharmaceutically acceptable salt or solvate thereof. In some embodiments, the viral infection is mediated by hepatitis C virus. Those and other embodiments are further described in the text that follows.

DETAILED DESCRIPTION OF REPRESENTATIVE EMBODIMENTS

[0012] Throughout this application, references are made to various embodiments relating to compounds, compositions, and methods. The various embodiments described are meant to provide a variety of illustrative examples and should not be construed as descriptions of alternative species. Rather it should be noted that the descriptions of various embodiments provided herein may be of overlapping scope. The embodiments discussed herein are merely illustrative and are not meant to limit the scope of the present invention.

[0013] It is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the present invention. In this specification and in the claims that follow, reference will be made to a number of terms that shall be defined to have the following meanings.

[0014] "Alkyl" refers to monovalent saturated aliphatic hydrocarbyl groups having from 1 to 14 carbon atoms and, in some embodiments, from 1 to 6 carbon atoms. "$(C_x$-$C_y)$alkyl" refers to alkyl groups having from x to y carbon atoms. This term includes, by way of example, linear and branched hydrocarbyl groups such as methyl (CH_3-), ethyl (CH_3CH_2-), *n*-propyl ($CH_3CH_2CH_2$-), isopropyl ($(CH_3)_2CH$-), *n*-butyl ($CH_3CH_2CH_2CH_2$-),

isobutyl ($(CH_3)_2CHCH_2$-), *sec*-butyl ($(CH_3)(CH_3CH_2)CH$-), *t*-butyl ($(CH_3)_3C$-), *n*-pentyl ($CH_3CH_2CH_2CH_2CH_2$-), and neopentyl ($(CH_3)_3CCH_2$-).

[0015] "Alkylidene" or "alkylene" refers to divalent saturated aliphatic hydrocarbyl groups having from 1 to 10 carbon atoms and, in some embodiments, from 1 to 6 carbon atoms. "(C_{u-v})alkylene" refers to alkylene groups having from u to v carbon atoms. The alkylidene and alkylene groups include branched and straight chain hydrocarbyl groups. For example "(C_{1-6})alkylene" is meant to include methylene, ethylene, propylene, 2-methypropylene, pentylene, and so forth.

[0016] "Alkenyl" refers to a linear or branched hydrocarbyl group having from 2 to 10 carbon atoms and in some embodiments from 2 to 6 carbon atoms or 2 to 4 carbon atoms and having at least 1 site of vinyl unsaturation (>C=C<). For example, (C_x-C_y)alkenyl refers to alkenyl groups having from x to y carbon atoms and is meant to include for example, ethenyl, propenyl, isopropylene, 1,3-butadienyl, and the like.

[0017] "Alkynyl" refers to a linear monovalent hydrocarbon radical or a branched monovalent hydrocarbon radical containing at least one triple bond. The term "alkynyl" is also meant to include those hydrocarbyl groups having one triple bond and one double bond. For example, (C_2-C_6)alkynyl is meant to include ethynyl, propynyl, and the like.

[0018] "Alkoxy" refers to the group -O-alkyl wherein alkyl is defined herein. Alkoxy includes, by way of example, methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, *t*-butoxy, *sec*-butoxy, and *n*-pentoxy.

[0019] "Acyl" refers to the groups H-C(O)-, alkyl-C(O)-, alkenyl-C(O)-, alkynyl-C(O)-, cycloalkyl-C(O)-, aryl-C(O)-, heteroaryl-C(O)-, and heterocyclic-C(O)-. Acyl includes the "acetyl" group $CH_3C(O)$-.

[0020] "Acylamino" refers to the groups -NR^{20}C(O)alkyl, -NR^{20}C(O)cycloalkyl, -NR^{20}C(O)alkenyl, -NR^{20}C(O)alkynyl, -NR^{20}C(O)aryl, -NR^{20}C(O)heteroaryl, and -NR^{20}C(O)heterocyclic, wherein R^{20} is hydrogen or alkyl.

[0021] "Acyloxy" refers to the groups alkyl-C(O)O-, alkenyl-C(O)O-, alkynyl-C(O)O-, aryl-C(O)O-, cycloalkyl-C(O)O-, heteroaryl-C(O)O-, and heterocyclic-C(O)O-.

[0022] "Amino" refers to the group -$NR^{21}R^{22}$ where R^{21} and R^{22} are independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, heterocyclic, -SO_2-alkyl, -SO_2-alkenyl, -SO_2-cycloalkyl, -SO_2-aryl, -SO_2-heteroaryl, and -SO_2-heterocyclic, and wherein R^{21} and R^{22} are optionally joined together with the nitrogen bound thereto to form a heterocyclic group. When R^{21} is hydrogen and R^{22} is alkyl, the amino group is sometimes referred to herein as alkylamino. When R^{21} and R^{22} are alkyl, the amino group is sometimes referred to herein as dialkylamino. When referring to a

monosubstituted amino, it is meant that either R^{21} or R^{22} is hydrogen but not both. When referring to a disubstituted amino, it is meant that neither R^{21} nor R^{22} are hydrogen.

[0023] "Hydroxyamino" refers to the group -NHOH.

[0024] "Alkoxyamino" refers to the group -NHO-alkyl wherein alkyl is defined herein.

[0025] "Aminocarbonyl" refers to the group $-C(O)NR^{26}R^{27}$ where R^{26} and R^{27} are independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, heterocyclic, hydroxy, alkoxy, amino, and acylamino, and where R^{26} and R^{27} are optionally joined together with the nitrogen bound thereto to form a heterocyclic group.

[0026] "Aryl" or "Ar" refers to an aromatic group of from 6 to 14 carbon atoms and no ring heteroatoms and having a single ring (*e.g.*, phenyl) or multiple condensed (fused) rings (*e.g.*, naphthyl or anthryl). For multiple ring systems, including fused, bridged, and spiro ring systems having aromatic and non-aromatic rings that have no ring heteroatoms, the term "Aryl" or "Ar" applies when the point of attachment is at an aromatic carbon atom (*e.g.*, 5,6,7,8 tetrahydronaphthalene-2-yl is an aryl group as its point of attachment is at the 2-position of the aromatic phenyl ring).

[0027] "Cyano" or "carbonitrile" refers to the group -CN.

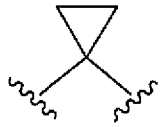
[0028] "Cycloalkyl" refers to a saturated or partially saturated cyclic group of from 3 to 14 carbon atoms and no ring heteroatoms and having a single ring or multiple rings including fused, bridged, and spiro ring systems. For multiple ring systems having aromatic and non-aromatic rings that have no ring heteroatoms, the term "cycloalkyl" applies when the point of attachment is at a non-aromatic carbon atom (e.g. 5,6,7,8,-tetrahydronaphthalene-5-yl). The term "Cycloalkyl" includes cycloalkenyl groups, such as cyclohexenyl. Examples of cycloalkyl groups include, for instance, adamantyl, cyclopropyl, cyclobutyl, cyclohexyl, cyclopentyl, cyclooctyl, cyclopentenyl, and cyclohexenyl. Examples of cycloalkyl groups that include multiple ring systems are bicyclohexyl, bicyclopentyl, bicyclooctyl, and the like. Two such cycloalkyl multiple ring structures are exemplified and named below:

 bicyclohexyl, and  bicyclohexyl.

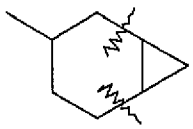
[0029] "$(C_u$-$C_v)$cycloalkyl" refers to cycloalkyl groups having u to v carbon atoms.

[0030] "Spiro cycloalkyl" refers to a 3 to 10 member cyclic substituent formed by replacement of two hydrogen atoms at a common carbon atom in a cyclic ring structure or in an alkylene group having 2 to 9 carbon atoms, as exemplified by the following structure

wherein the group shown here attached to bonds marked with wavy lines is substituted with a spiro cycloalkyl group:



[0031] "Fused cycloalkyl" refers to a 3 to 10 member cyclic substituent formed by the replacement of two hydrogen atoms at different carbon atoms in a cycloalkyl ring structure, as exemplified by the following structure wherein the cycloalkyl group shown here contains bonds marked with wavy lines which are bonded to carbon atoms that are substituted with a fused cycloalkyl group:



[0032] "Halo" or "halogen" refers to fluoro, chloro, bromo, and iodo.

[0033] "Haloalkoxy" refers to substitution of alkoxy groups with 1 to 5 (*e.g.* when the alkoxy group has at least 2 carbon atoms) or in some embodiments 1 to 3 halo groups (*e.g.* trifluoromethoxy).

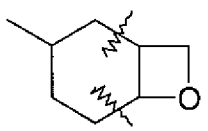
[0034] "Hydroxy" or "hydroxyl" refers to the group -OH.

[0035] "Heteroaryl" refers to an aromatic group of from 1 to 14 carbon atoms and 1 to 6 heteroatoms selected from oxygen, nitrogen, and sulfur and includes single ring (*e.g.* imidazolyl) and multiple ring systems (*e.g.* benzimidazol-2-yl and benzimidazol-6-yl). For multiple ring systems, including fused, bridged, and spiro ring systems having aromatic and non-aromatic rings, the term "heteroaryl" applies if there is at least one ring heteroatom and the point of attachment is at an atom of an aromatic ring (*e.g.* 1,2,3,4-tetrahydroquinolin-6-yl and 5,6,7,8-tetrahydroquinolin-3-yl). In some embodiments, the nitrogen and/or the sulfur ring atom(s) of the heteroaryl group are optionally oxidized to provide for the N-oxide (N→O), sulfinyl, or sulfonyl moieties. More specifically the term heteroaryl includes, but is not limited to, pyridyl, furanyl, thienyl, thiazolyl, isothiazolyl, triazolyl, imidazolyl, imidazolinyl, isoxazolyl, pyrrolyl, pyrazolyl, pyridazinyl, pyrimidinyl, purinyl, phthalazyl, naphthylpryidyl, benzofuranyl, tetrahydrobenzofuranyl, isobenzofuranyl, benzothiazolyl, benzoisothiazolyl, benzotriazolyl, indolyl, isoindolyl, indolizinyl, dihydroindolyl, indazolyl, indolinyl, benzoxazolyl, quinolyl, isoquinolyl, quinolizyl, quianazolyl, quinoxalyl, tetrahydroquinolinyl, isoquinolyl, quinazolinonyl, benzimidazolyl, benzisoxazolyl, benzothienyl, benzopyridazinyl, pteridinyl, carbazolyl, carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenoxazinyl, phenothiazinyl, and phthalimidyl.

[0036] "Heterocyclic" or "heterocycle" or "heterocycloalkyl" or "heterocyclyl" refers to a saturated or partially saturated cyclic group having from 1 to 14 carbon atoms and from 1 to 6 heteroatoms selected from nitrogen, sulfur, phosphorus or oxygen and includes single ring and multiple ring systems including fused, bridged, and spiro ring systems. For multiple ring systems having aromatic and/or non-aromatic rings, the terms "heterocyclic", "heterocycle", "heterocycloalkyl", or "heterocyclyl" apply when there is at least one ring heteroatom and the point of attachment is at an atom of a non-aromatic ring (*e.g.* 1,2,3,4-tetrahydroquinoline-3-yl, 5,6,7,8-tetrahydroquinoline-6-yl, and decahydroquinolin-6-yl). In one embodiment, the nitrogen, phosphorus and/or sulfur atom(s) of the heterocyclic group are optionally oxidized to provide for the N-oxide, phosphinane oxide, sulfinyl, sulfonyl moieties. More specifically the heterocyclyl includes, but is not limited to, tetrahydropyranyl, piperidinyl, piperazinyl, 3-pyrrolidinyl, 2-pyrrolidon-1-yl, morpholinyl, and pyrrolidinyl. A prefix indicating the number of carbon atoms (*e.g.*, C_3-C_{10}) refers to the total number of carbon atoms in the portion of the heterocyclyl group exclusive of the number of heteroatoms.

[0037] Examples of heterocycle and heteroaryl groups include, but are not limited to, azetidine, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, pyridone, indolizine, isoindole, indole, dihydroindole, indazole, purine, quinolizine, isoquinoline, quinoline, phthalazine, naphthylpyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, phenanthroline, isothiazole, phenazine, isoxazole, phenoxazine, phenothiazine, imidazolidine, imidazoline, piperidine, piperazine, indoline, phthalimide, 1,2,3,4-tetrahydroisoquinoline, 4,5,6,7-tetrahydrobenzo[b]thiophene, thiazole, thiazolidine, thiophene, benzo[b]thiophene, morpholine, thiomorpholine (also referred to as thiamorpholine), piperidine, pyrrolidine, and tetrahydrofuranyl.

[0038] "Fused heterocyclic" refers to a 3 to 10 member cyclic substituent formed by the replacement of two hydrogen atoms at different carbon atoms in a cycloalkyl ring structure, as exemplified by the following structure wherein the cycloalkyl group shown here contains bonds marked with wavy lines which are bonded to carbon atoms that are substituted with a fused heterocyclic group:



[0039] "Compound", "compounds", "chemical entity", and "chemical entities" as used herein refers to a compound encompassed by the generic formulae disclosed herein,

any subgenus of those generic formulae, and any forms of the compounds within the generic and subgeneric formulae, including the racemates, stereoisomers, and tautomers of the compound or compounds.

[0040] "Racemates" refers to a mixture of enantiomers. In an embodiment of the invention, the compounds of Formula I, or pharmaceutically acceptable salts thereof, are enantiomerically enriched with one enantiomer wherein all of the chiral carbons referred to are in one configuration. In general, reference to an enantiomerically enriched compound or salt, is meant to indicate that the specified enantiomer will comprise more than 50% by weight of the total weight of all enantiomers of the compound or salt.

[0041] "Solvate" or "solvates" of a compound refer to those compounds, as defined above, which are bound to a stoichiometric or non-stoichiometric amount of a solvent. Solvates of a compound includes solvates of all forms of the compound. In certain embodiments, solvents are volatile, non-toxic, and/or acceptable for administration to humans in trace amounts. Suitable solvates include water.

[0042] "Stereoisomer" or "stereoisomers" refer to compounds that differ in the chirality of one or more stereocenters. Stereoisomers include enantiomers and diastereomers.

[0043] "Tautomer" refer to alternate forms of a compound that differ in the position of a proton, such as enol-keto and imine-enamine tautomers, or the tautomeric forms of heteroaryl groups containing a ring atom attached to both a ring -NH- moiety and a ring =N- moiety such as pyrazoles, imidazoles, benzimidazoles, triazoles, and tetrazoles.

[0044] "Pharmaceutically acceptable salt" refers to pharmaceutically acceptable salts derived from a variety of organic and inorganic counter ions well known in the art and include, by way of example only, sodium, potassium, calcium, magnesium, ammonium, and tetraalkylammonium, and when the molecule contains a basic functionality, salts of organic or inorganic acids, such as hydrochloride, hydrobromide, tartrate, mesylate, acetate, maleate, and oxalate. Suitable salts include those described in P. Heinrich Stahl, Camille G. Wermuth (Eds.), Handbook of Pharmaceutical Salts Properties, Selection, and Use; 2002.

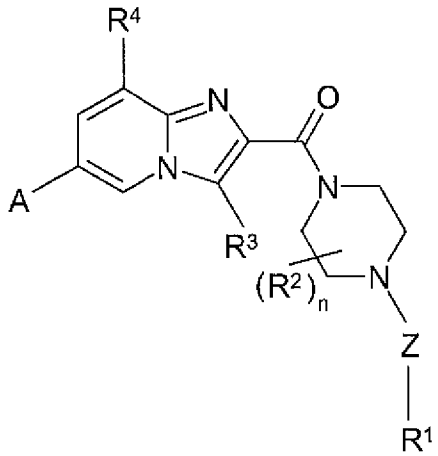
[0045] "Patient" refers to mammals and includes humans and non-human mammals.

[0046] "Treating" or "treatment" of a disease in a patient refers to 1) preventing the disease from occurring in a patient that is predisposed or does not yet display symptoms of the disease; 2) inhibiting the disease or arresting its development; or 3) ameliorating or causing regression of the disease.

[0047] Unless indicated otherwise, the nomenclature of substituents that are not explicitly defined herein are arrived at by naming the terminal portion of the functionality followed by the adjacent functionality toward the point of attachment. For example, the substituent "arylalkyloxycarbonyl" refers to the group (aryl)-(alkyl)-O-C(O)-. In a term such as "$C(R^x)_2$", it should be understood that the two R^x groups can be the same, or they can be different if R^x is defined as having more than one possible identity. In addition, certain substituents are drawn as $-R^xR^y$, where the "-" indicates a bond adjacent to the parent molecule and R^y being the terminal portion of the functionality. Similarly, it is understood that the above definitions are not intended to include impermissible substitution patterns (*e.g.*, methyl substituted with 5 fluoro groups). Such impermissible substitution patterns are well known to the skilled artisan.

[0048] In one embodiment of the invention, there is provided a compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or $(C_1\text{-}C_3)$alkylene;

A is selected from the group consisting of hydrogen, halo, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkenyl, $(C_1\text{-}C_6)$alkynyl, $(C_3\text{-}C_{14})$cycloalkyl, aryl, hydroxyl, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, $-SO_2N(R^6)_2$, $-C(O)NR^6R^6$, $-OR^7$, $-R^6R^7$, $-SO_2R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$, $-alkylR^9R^6$, $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, $(C_2\text{-}C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O, $(C_2\text{-}C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{10};

R^1 is selected from the group consisting of hydrogen, halo, cyano, hydroxyl, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkenyl, $(C_1\text{-}C_6)$alkynyl, $-C(O)N(R^6)_2$, $-R^9R^6$,

$-SO_2N(R^6)_2$, $-SO_2R^6$, (C_3-C_{14})cycloalkyl, (C_3-C_{14})cycloalkenyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{11};

R^2 is independently selected from the group consisting of oxo, (C_1-C_6)alkyl, (C_3-C_{14})cycloalkyl, $-alkylR^8$, and aryl, or optionally two R^2 alkyl groups, together with any intervening atoms, form a spiro or fused (C_3-C_{14})cycloalkyl ring;

R^3 is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_3-C_{14})cycloalkyl, halo, $-alkylR^8$, and cyano;

R^4 is selected from the group consisting of hydrogen, hydroxyl, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, (C_3-C_{14})cycloalkyl, aryl, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, $-alkyl(R^5)_mR^6$, $-alkylR^9R^6$, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-SO_2N(R^6)_2$, $-C(O)NR^6R^6$, $-OR^7$, $-R^6R^7$, $-SO_2R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$, $-alkylR^9R^6$, $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{10};

R^5 is halo;

R^6 is independently selected from the group consisting of hydrogen and (C_1-C_6)alkyl;

R^7 is (C_3-C_{14})cycloalkyl;

R^8 is hydroxyl;

R^9 is carboxyl;

R^{10} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, hydroxyl, oxo, carboxyl, cyano, halo, $-C(O)NH_2$, $-SO_2NH_2$, $-SR^6$, $-S(O)R^6$, $-S(O)_2R^6$, $-S(O)_2NR^6R^6$, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$ $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, $-C(NR^6)NR^6R^6$, $-C(O)NR^6R^6$, $-C(O)OR^6$, $-C(O)R^6$, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O;

R^{11} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, hydroxyl, $-NR^6C(O)R^6$, $-OC(O)R^6$, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, halo, $-C(O)N(R^6)_2$, $-SO_2N(R^6)_2$, $-SO_2R^6$,

oxo, –alkylR^8, –alkylR^9, –alkylR^9R^6, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O; or optionally two R^{11} groups, together with any intervening atoms, form a fused (C_3-C_{14})cycloalkyl ring or a fused (C_2-C_6)heterocyclic ring having 1-3 heteroatoms selected from S, N and O; wherein said fused cycloalkyl or heterocyclic ring is optionally substituted with one to three R^{12};

R^{12} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, oxo, halo, hydroxyl, carboxyl, cyano, $–OR^6(R^5)_m$, $–R^6(R^5)_m$, and $–NR^6R^6$;

m is an integer from 1 to 3; and

n is zero or an integer from 1 to 4.

[0049] In another embodiment of the invention, there is provided a compound of Formula (I), wherein Z is a bond.

[0050] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of (C_1-C_6)alkyl, halo, $–OR^6$, $–OR^7$, –alkoxy$(R^5)_m$, (C_3-C_{14})cycloalkyl, $-R^6$(C_3-C_{14})cycloalkyl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O.

[0051] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of hydrogen, bromo, fluoro, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, cyclopropylmethyl, cyclopropyloxy, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, thienyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl.

[0052] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of ethyl, butyl, propyl, bromo, chloro, methoxy, ethoxy, propoxy, cyclopropyl, furanyl, pyrazolyl, tetrahydrofuranyl, and difluoromethoxy.

[0053] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of isobutyl, ethyl, ethoxy, cyclopropyl, furanyl, pyrazolyl, and difluoromethoxy.

[0054] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of furanyl and cyclopropyl.

[0055] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is cyclopropyl.

[0056] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is furanyl.

[0057] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is selected from the group consisting of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_{14})$cycloalkyl, aryl, $(C_2\text{-}C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2\text{-}C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O.

[0058] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, acetate, thiazolyl, cyclopropyl, cyclobutyl, bicyclohexyl, bicyclopentyl, bicyclooctyl, cyclohexyl, cyclopentyl, cyclopentenyl, cyclohexenyl, cycloheptyl, oxabicyclohexyl, phenyl, benzyl, pyridyl, pyridinyl, pyrrolidinyl, piperidinyl, thiophenyl, pyrazolyl, octahydropentalenyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, and thienyl.

[0059] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is $(C_3\text{-}C_{14})$cycloalkyl.

[0060] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is selected from the group consisting of cyclohexyl, cyclobutyl, cyclopentyl, and bicyclohexyl.

[0061] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is substituted with one or two R^{11}.

[0062] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is substituted with one R^{11}.

[0063] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^2 is selected from the group consisting of hydrogen, oxo, and $(C_1\text{-}C_6)$alkyl.

[0064] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^2 is selected from the group consisting of hydrogen, oxo, and methyl.

[0065] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^2 is oxo.

[0066] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of $(C_1\text{-}C_6)$alkyl, halo, $-OR^6$, $-OR^7$, $-$alkoxy$(R^5)_m$, $(C_3\text{-}C_{14})$cycloalkyl, $-R^6(C_3\text{-}C_{14})$cycloalkyl, $(C_2\text{-}C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2\text{-}C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O.

[0067] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of hydrogen, bromo, fluoro, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, cyclopropylmethyl, cyclopropyloxy, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl.

[0068] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of ethyl, isobutyl, bromo, chloro, ethoxy, cyclopropyl, furanyl, and difluoromethoxy.

[0069] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of isobutyl, ethoxy, cyclopropyl, furanyl, and difluoromethoxy.

[0070] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is selected from the group consisting of furanyl and cyclopropyl.

[0071] In another embodiment of the invention, there is provided a compound of Formula (I), wherein A is cyclopropyl.

[0072] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is selected from the group consisting of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_{14})$cycloalkyl, aryl, $(C_2\text{-}C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2\text{-}C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O.

[0073] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, acetate, thiazolyl, cyclopropyl, cyclobutyl, bicyclohexyl, bicyclopentyl, bicyclooctyl, cyclohexyl, cyclopentyl, cyclopentenyl, cyclohexenyl, cycloheptyl, phenyl, benzyl, pyridyl, pyridinyl, pyrrolidinyl, piperidinyl, thiophenyl, pyrazolyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, and thienyl.

[0074] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is $(C_3\text{-}C_{14})$cycloalkyl.

[0075] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is selected from the group consisting of cyclohexyl, cyclobutyl, cyclopentyl, and bicyclohexyl.

[0076] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is substituted with one or two R^{11}.

[0077] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^1 is substituted with one R^{11}.

[0078] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^2 is selected from the group consisting of hydrogen, oxo, and (C_1-C_6)alkyl.

[0079] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^2 is selected from the group consisting of hydrogen, oxo, and methyl.

[0080] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^2 is oxo.

[0081] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^3 is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, halo, cyano, –alkylR^8, and (C_3-C_{14})cycloalkyl.

[0082] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^3 is selected from the group consisting of hydrogen, methyl, ethyl, chloro, bromo, cyano, hydroxymethyl, and cyclopropyl.

[0083] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^3 is selected from the group consisting of chloro and cyano.

[0084] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^3 is chloro.

[0085] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^4 is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkenyl, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, $-alkyl(R^5)_mR^6$.

[0086] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^4 is selected from the group consisting of trifluoromethyl, ethyl, and isopropylene.

[0087] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^4 is trifluoromethyl.

[0088] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^{11} is selected from the group consisting of hydroxyl, oxo, $-OC(O)R^6$, $-NR^6C(O)R^6$, –alkylR^8, $-R^6(R^5)_m$, halo, (C_1-C_6)alkyl, and (C_1-C_6)alkoxy.

[0089] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^{11} is selected from the group consisting of hydroxyl, oxo, hydroxymethyl, acetate, fluoro, trifluoromethyl, methoxy, and methyl.

[0090] The In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^{11} is hydroxyl.

[0091] In another embodiment of the invention, there is provided a compound of Formula (I), wherein R^{11} is absent.

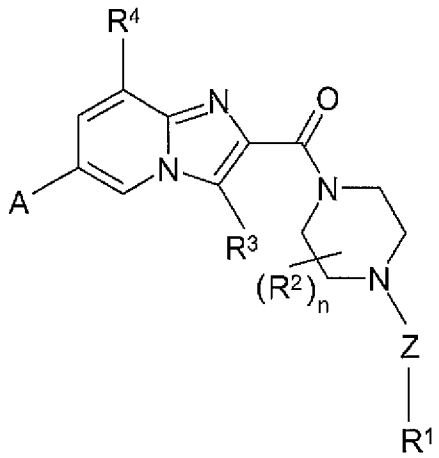
[0092] In another embodiment of the invention, there is provided a compound of Formula (I), wherein m is three.

[0093] In another embodiment of the invention, there is provided a compound of Formula (I), wherein m is two.

[0094] In another embodiment of the invention, there is provided a compound of Formula (I), wherein n is zero.

[0095] In another embodiment of the invention, there is provided a compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or methylene;

A is selected from the group consisting of hydrogen, bromo, fluoro, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, cyclopropylmethyl, cyclopropyloxy, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl;

R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, thiazolyl, cyclopropyl, cyclobutyl, bicyclohexyl, bicyclopentyl, bicyclooctyl, cyclohexyl, cyclopentyl, cycloheptyl, phenyl, benzyl, pyridyl, pyrrolidinyl, piperidinyl, thiophenyl, pyrazolyl, tetrahydrofuranyl, tetrahydropyranyl, thienyl, cyclopentenyl, and cyclohexenyl, wherein R^1 is optionally substituted with one to two R^{11};

R^2 is independently selected from the group consisting of hydrogen, oxo, methyl, ethyl, cyclopropyl, hydroxymethyl, and phenyl, or optionally two R^2 groups, together with any intervening atoms, form a spiro or fused cyclopropyl ring;

R^3 is selected from the group consisting of hydrogen, chloro, bromo, fluoro, and cyano;

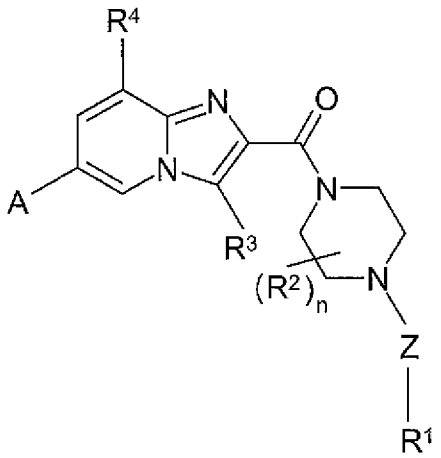
R^4 is selected from the group consisting of hydrogen, methyl, ethyl, isopropyl, dimethylamino, methylamino, methoxy, ethoxy, cyclopropyl, chloro, fluoro, bromo, difluoroethyl, and trifluoromethyl;

R^{11} is independently selected from the group consisting of methyl, methoxy, trifluoromethyl, fluoro, oxo, hydroxyl, hydroxymethyl, and acyloxy; and

n is zero or an integer from 1 to 4.

[0096] In another embodiment of the invention, there is provided a compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or (C_1-C_3)alkylene;

A is selected from the group consisting of hydrogen, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, haloalkoxy, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heteroaryl with 1-3 heteroatoms selected from S, N, and O, and (C_2-C_6)heterocyclic with 1-3 heteroatoms selected from N and O;

R^1 is selected from the group consisting of hydrogen, halo, cyano, carboxyl, hydroxy, (C_1-C_6)alkyl, (C_3-C_{14})cycloalkyl, aryl, (C_3-C_6)heterocyclic with 1-2 heteroatoms selected from S and O, and (C_3-C_6)heteroaryl with 1-2 heteroatoms selected from S, N, and O; wherein R^1 is optionally substituted with one to three R^{11};

R^2 is independently selected from the group consisting of hydrogen, oxo, methyl, and aryl;

R^3 is selected from the group consisting of hydrogen, halo, and cyano;

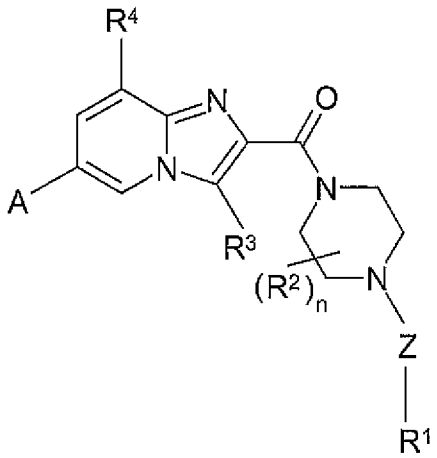
R^4 is selected from the group consisting of hydrogen and haloalkyl;

R^{11} is independently selected from the group consisting of alkyl, alkoxy, haloalkyl, halo, oxo, hydroxyl, acyloxy; and

n is zero or an integer from 1 to 4.

[0097] In another embodiment of the invention, there is provided a compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or methylene;

A is selected from the group consisting of hydrogen, bromo, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl;

R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, thiazolyl, cyclopropyl, cyclobutyl, cyclohexyl, cyclopentyl, cycloheptyl, phenyl, benzyl, pyridyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, thienyl, cyclopentenyl, and cyclohexenyl, wherein R^1 is optionally substituted with one to two R^{11};

R^2 is independently selected from the group consisting of hydrogen, oxo, methyl, and phenyl;

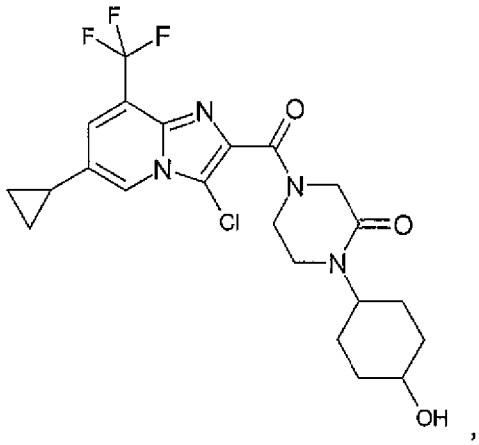
R^3 is selected from the group consisting of hydrogen, chloro, bromo, and cyano;

R^4 is selected from the group consisting of hydrogen and trifluoromethyl;

R^{11} is independently selected from the group consisting of methyl, methoxy, trifluoromethyl, fluoro, oxo, hydroxyl, and acyloxy; and

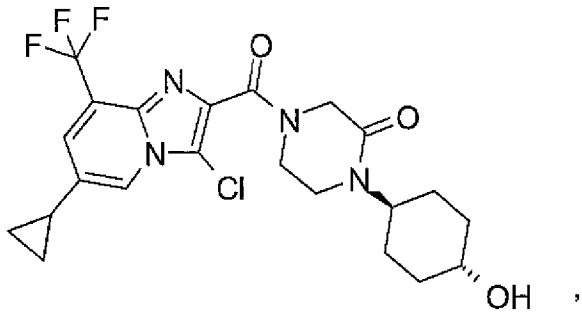
n is zero or an integer from 1 to 2.

[0098] In one embodiment of the invention, there is provided a compound having the structure:



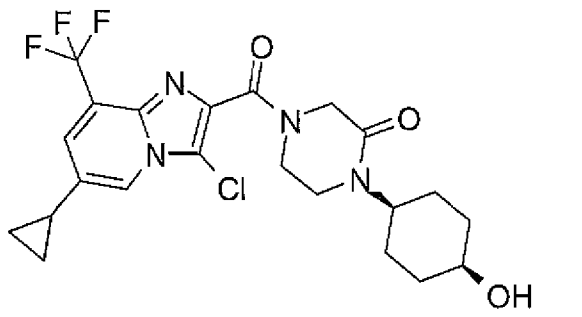
or a pharmaceutically acceptable salt thereof.

[0099] In another embodiment of the invention, there is provided a compound having the structure:



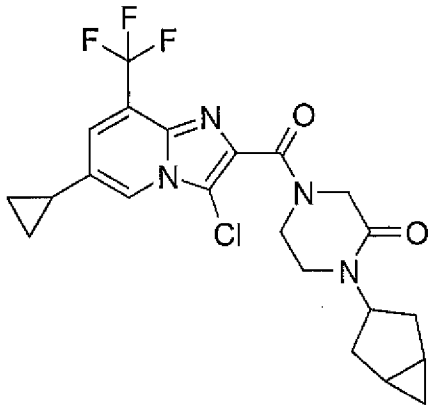
or a pharmaceutically acceptable salt thereof.

[00100] In another embodiment of the invention, there is provided a compound having the structure:



or a pharmaceutically acceptable salt thereof.

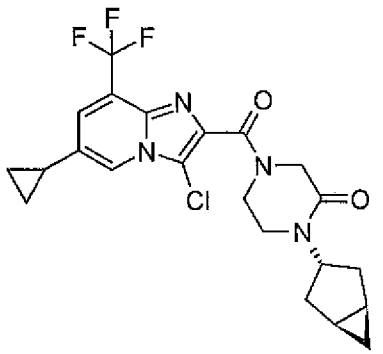
[00101] In another embodiment of the invention, there is provided a compound having the stru



,

or a pharmaceutically acceptable salt thereof.

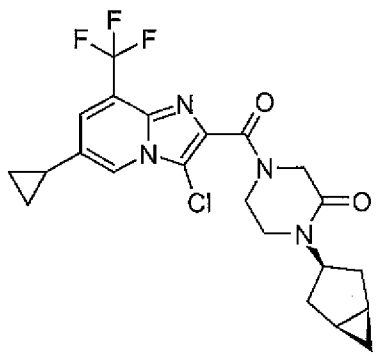
[00102] In another embodiment of the invention, there is provided a compound having the structure:



,

or a pharmaceutically acceptable salt thereof.

[00103] In another embodiment of the invention, there is provided a compound having the structure:



,

or a pharmaceutically acceptable salt thereof.

[00104] In another embodiment of the invention, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of a compound of any preceding claim.

[00105] In another embodiment of the invention, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the *Flaviviridae* family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of formula (I).

[00106] In another embodiment of the invention, said virus is a hepatitis C virus.

[00107] In another embodiment of the invention, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the *Flaviviridae* family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of formula (I) further comprising administration of a therapeutically effective amount of one or more agents active against hepatitis C virus.

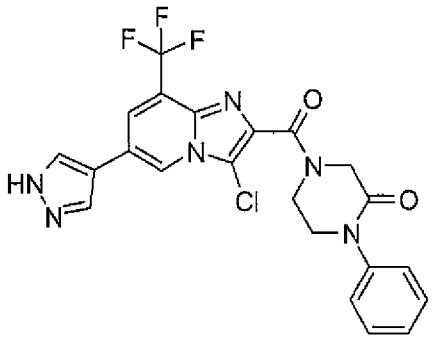
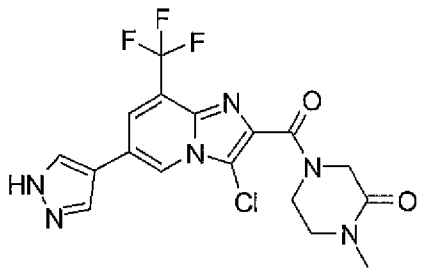
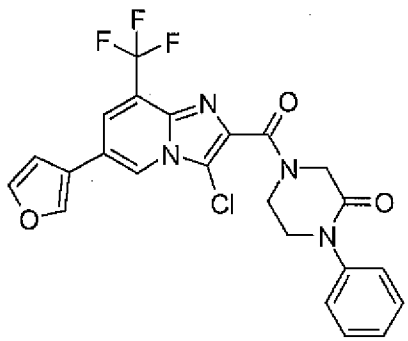
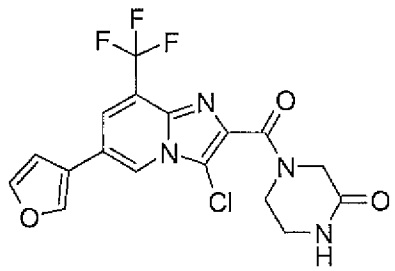
[00108] In another embodiment of the invention, said agent active against hepatitis C virus is an inhibitor of HCV protease, HCV polymerase, HCV helicase, HCV entry, HCV assembly, HCV egress, HCV replicase, HCV NS5A protein, or inosine 5'-monophosphate dehydrogenase.

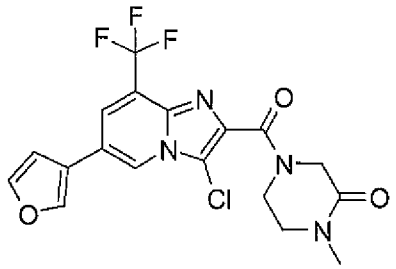
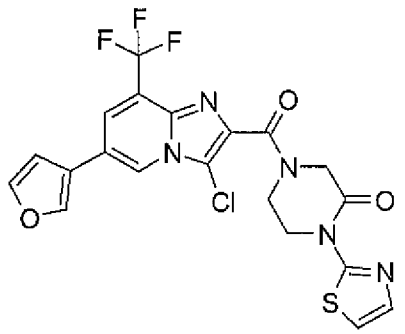
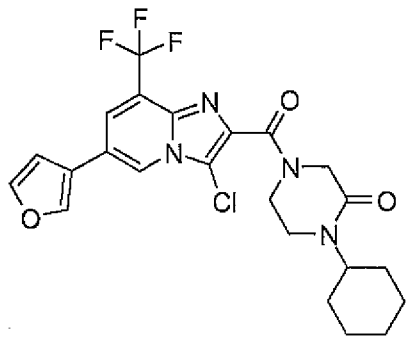
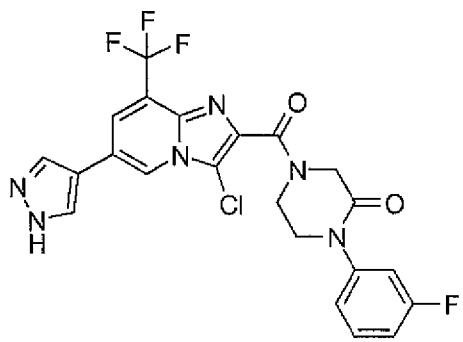
[00109] In another embodiment of the invention, said agent active against hepatitis C virus is interferon in combination with ribavirin.

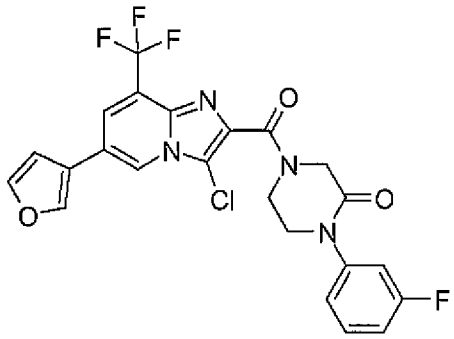
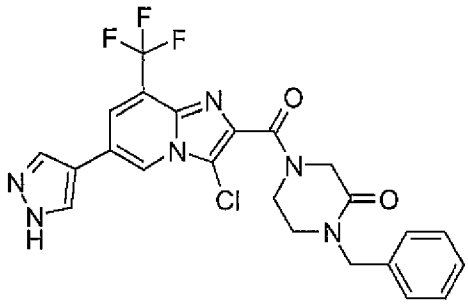
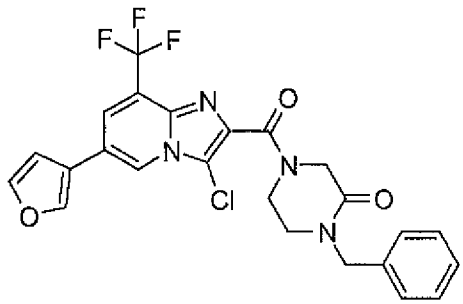
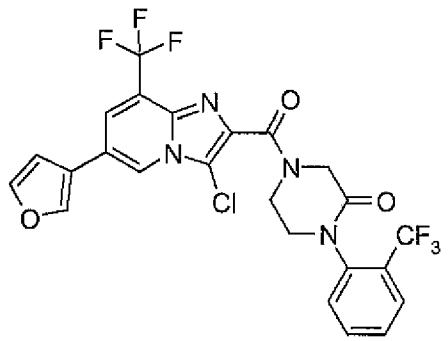
[00110] In another embodiment of the invention, said agent active against hepatitis C virus is interferon.

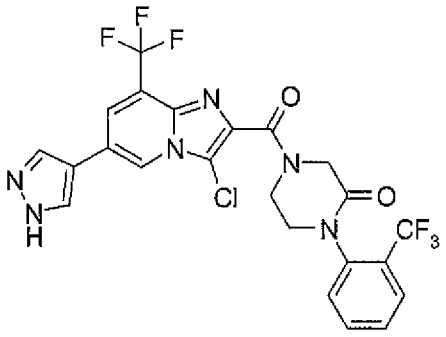
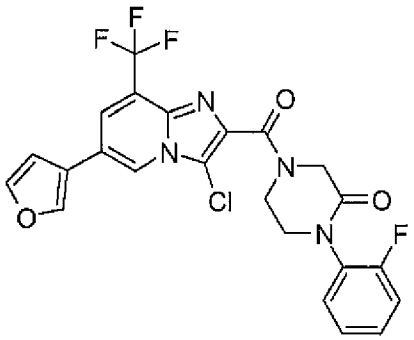
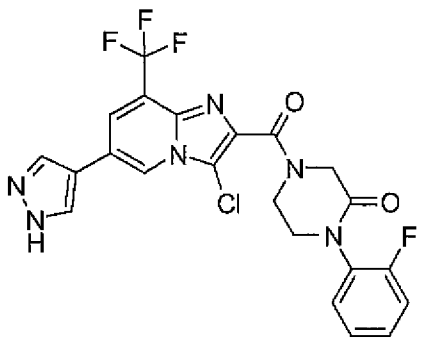
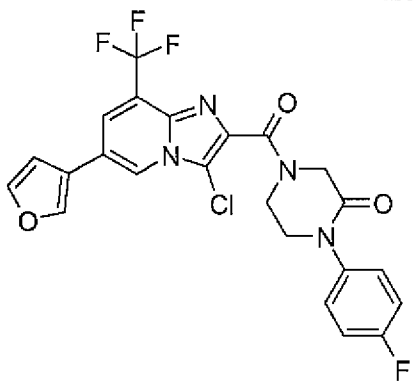
[00111] In yet further embodiments, the compound of the present invention, or a pharmaceutically acceptable salt thereof, is chosen from the compounds set forth in Table 1.

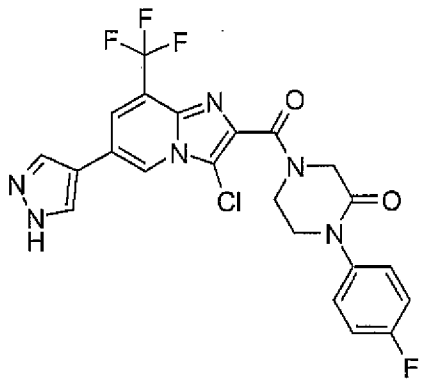
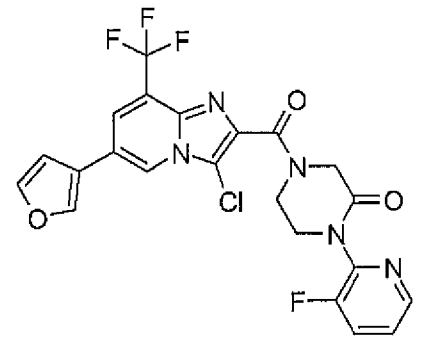
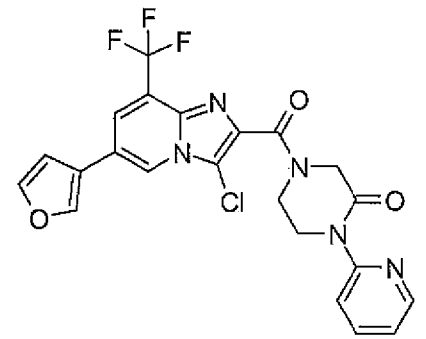
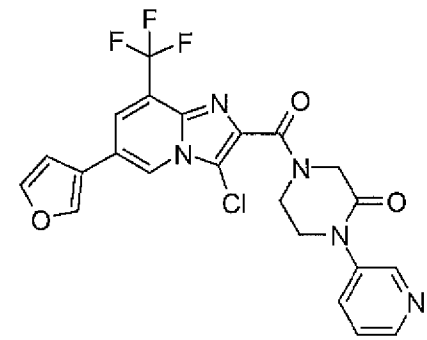
Table 1

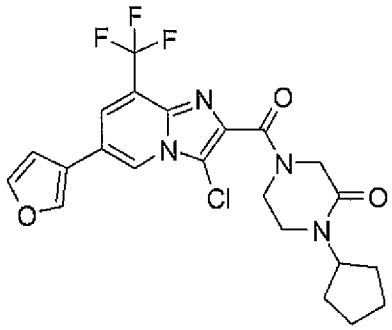
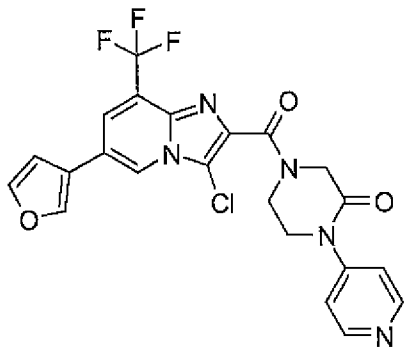
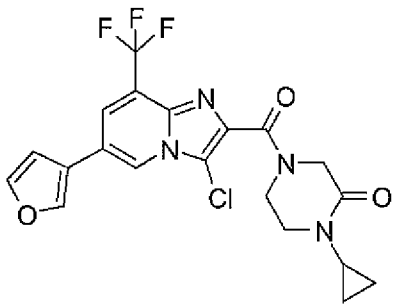
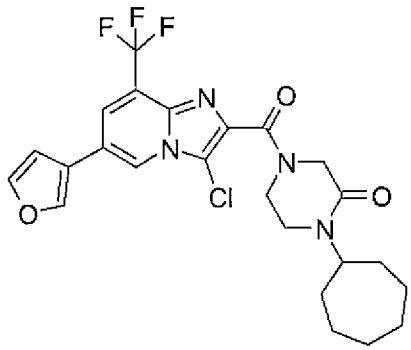
Compound Number	Structure	Name
1		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone
2		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone
3		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone
4		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

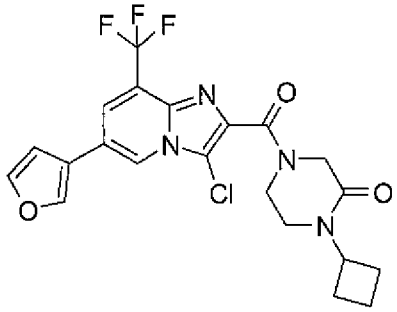
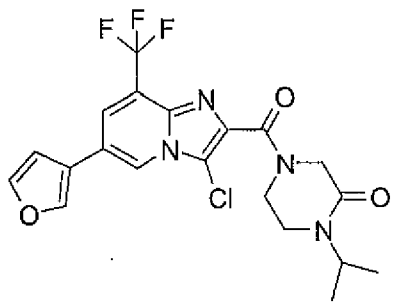
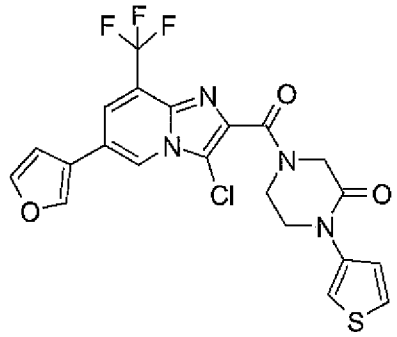
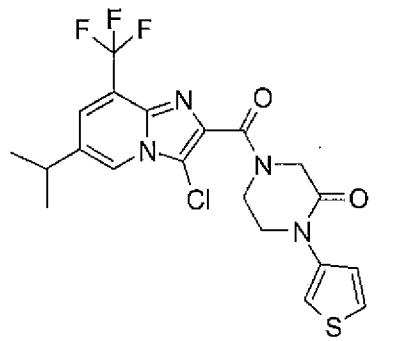
5		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone
6		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone
7		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
8		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone

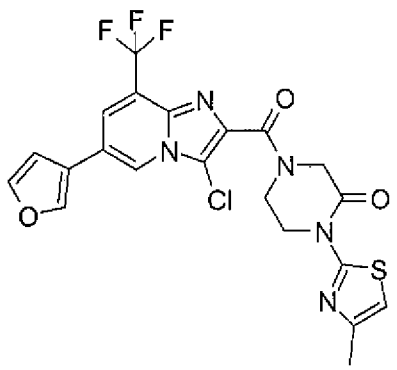
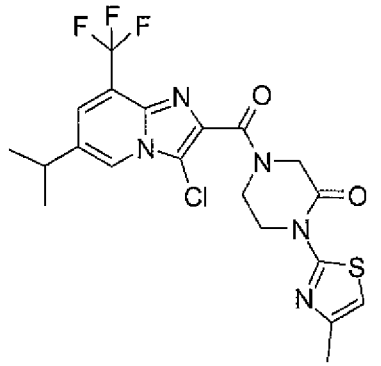
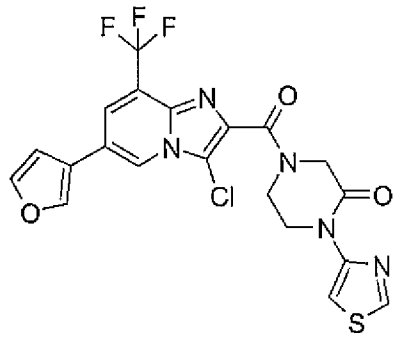
9		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone
10		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone
11		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone
12		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone

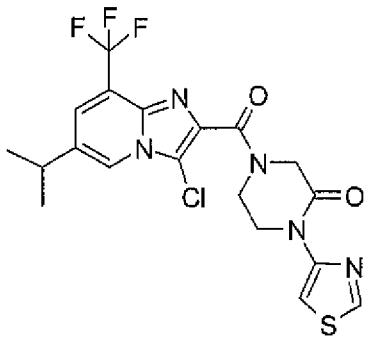
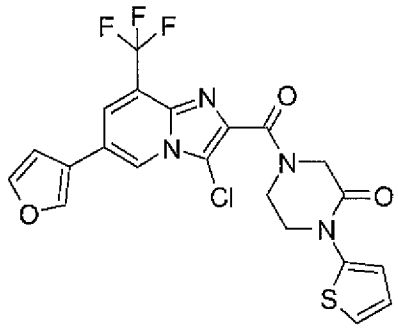
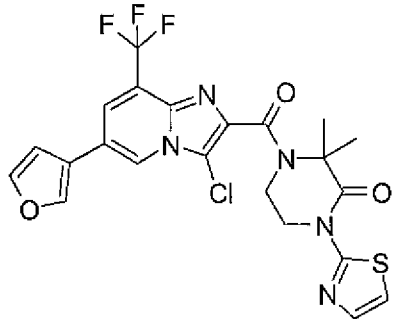
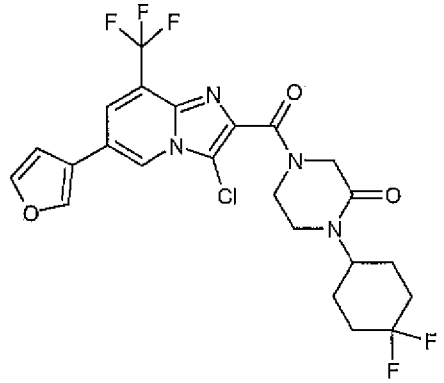
13		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone
14		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone
15		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone
16		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone

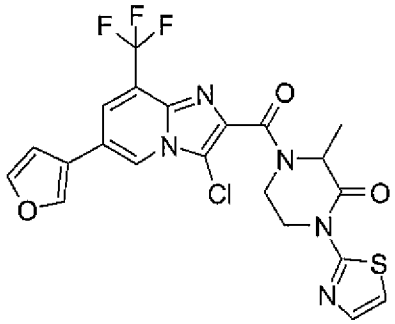
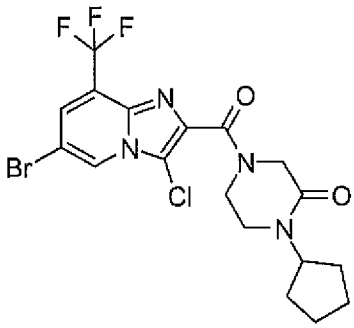
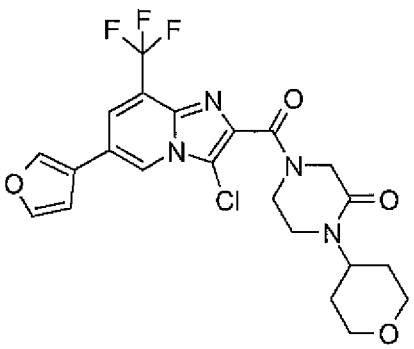
17		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone
18		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-2-pyridinyl)-2-piperazinone
19		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-pyridinyl)-2-piperazinone
20		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-pyridinyl)-2-piperazinone

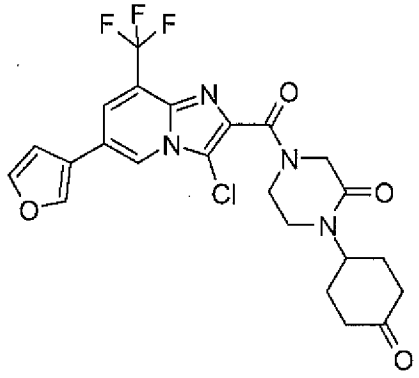
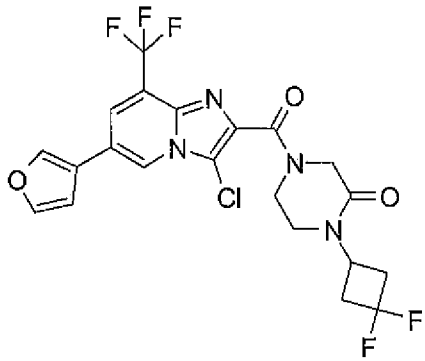
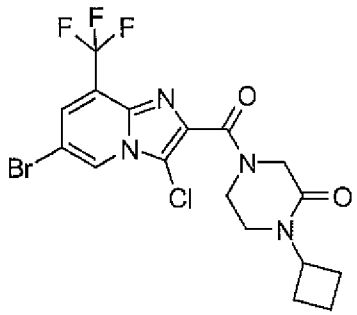
21		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
22		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-pyridinyl)-2-piperazinone
23		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopropyl-2-piperazinone
24		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cycloheptyl-2-piperazinone

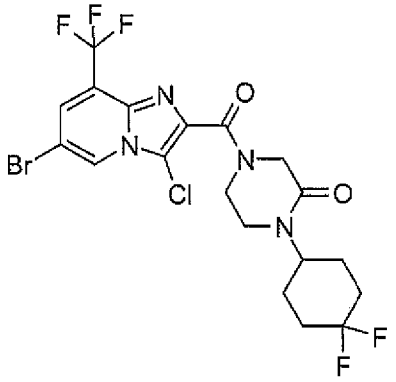
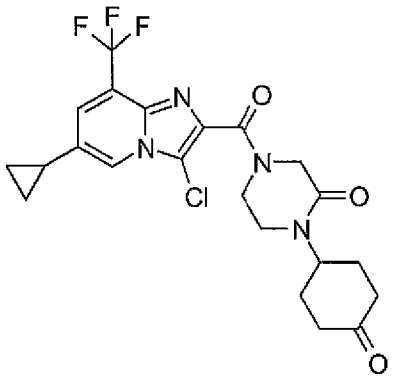
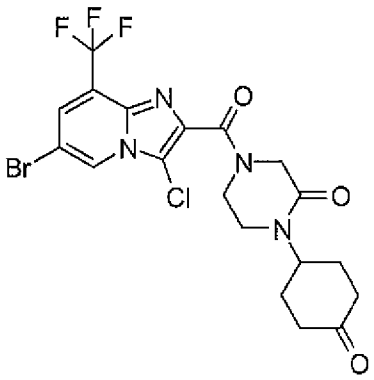
25		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
26		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylethyl)-2-piperazinone
27		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone
28		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

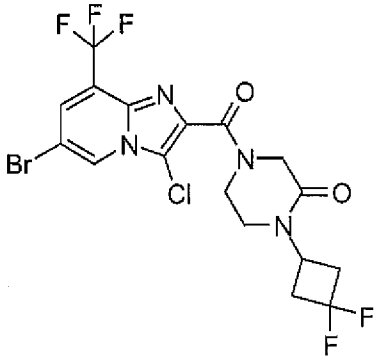
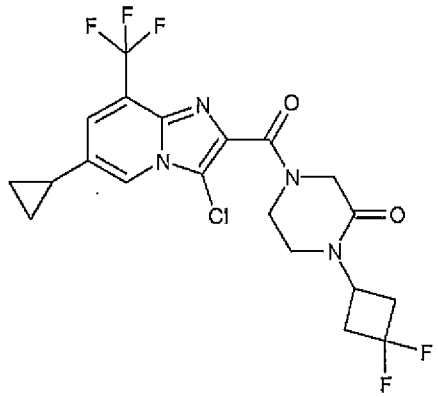
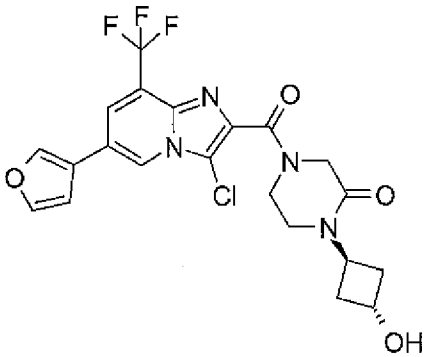
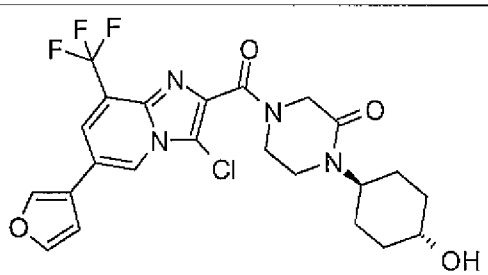
29		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone
30		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone
31		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone

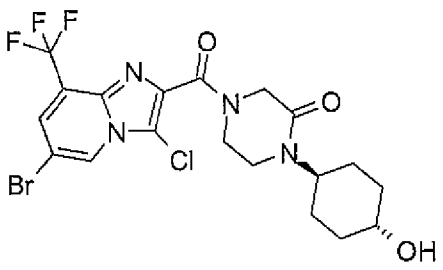
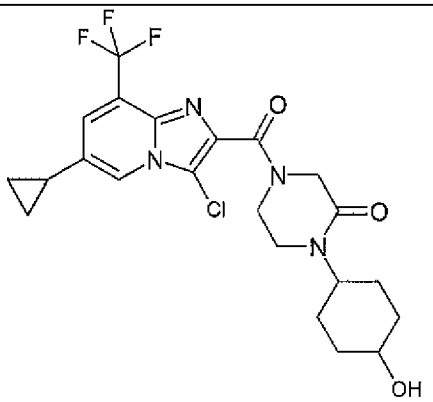
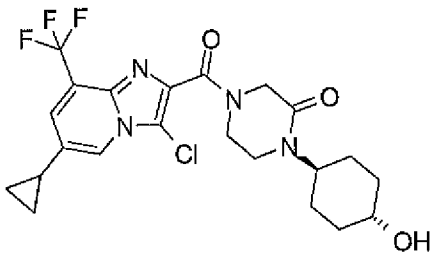
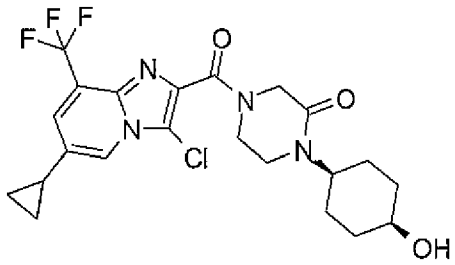
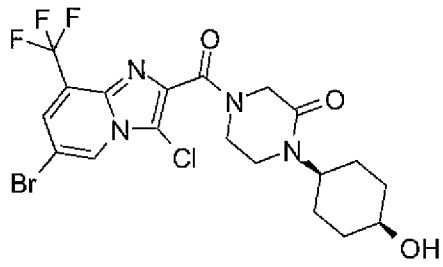
32		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone
33		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone
34		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone
35		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone

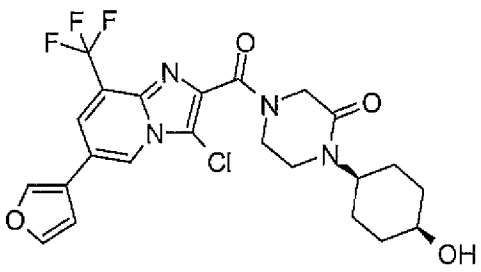
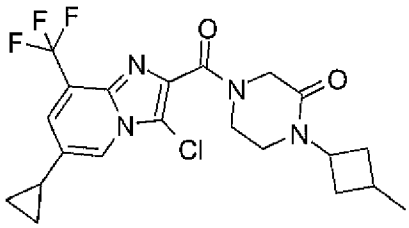
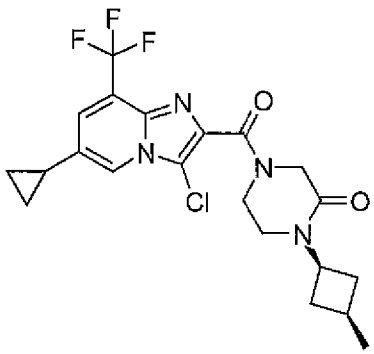
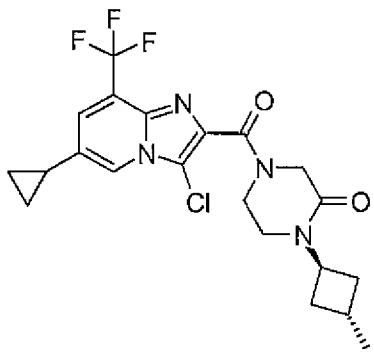
36		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone
37		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
38		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

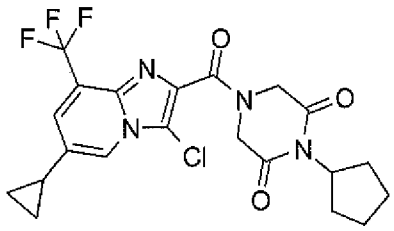
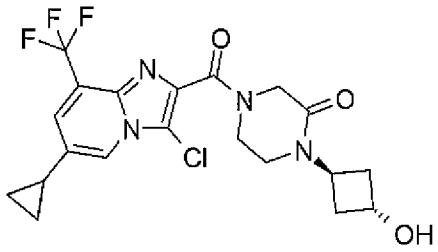
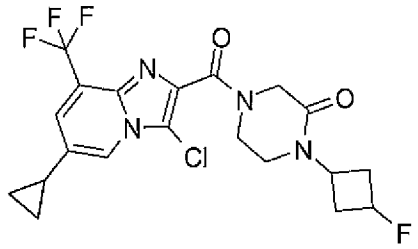
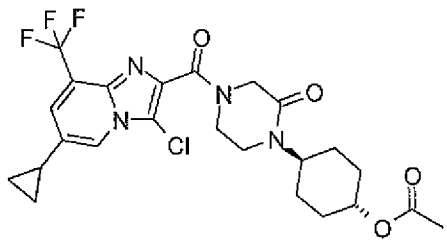
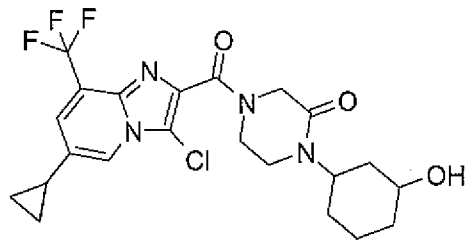
39		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone
40		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone
41		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

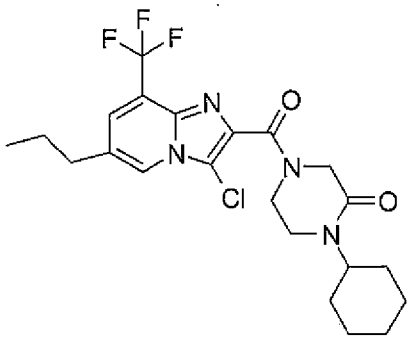
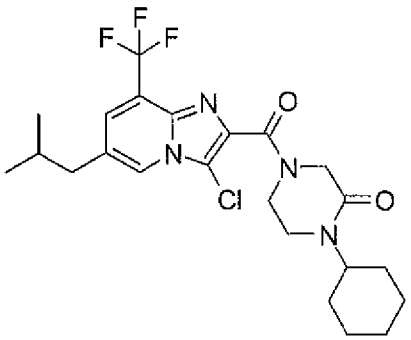
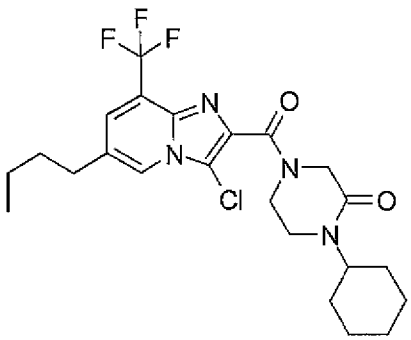
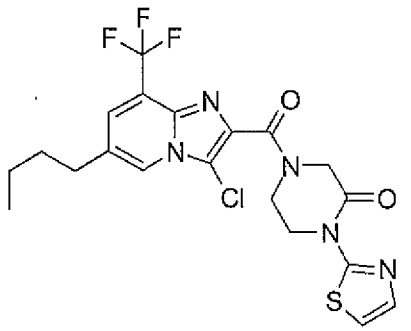
42		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone
43		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone
44		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

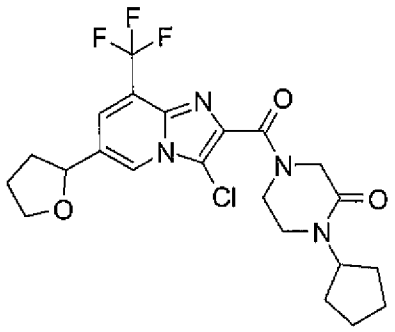
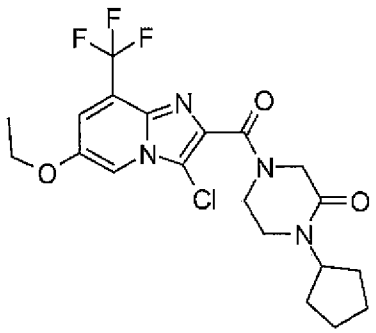
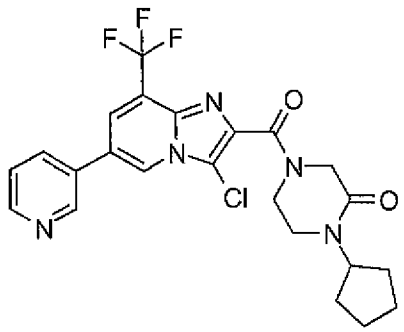
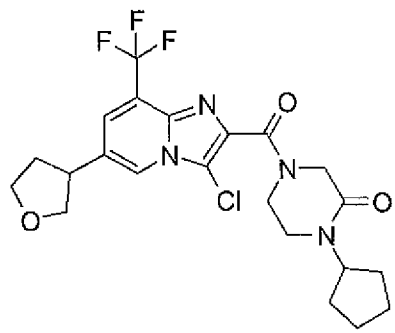
45		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone
46		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone
47		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone
48		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

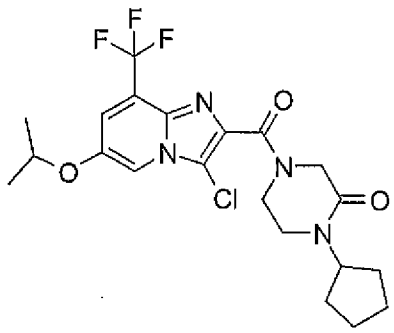
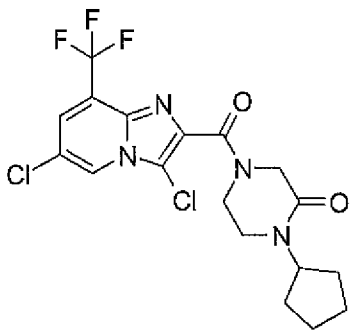
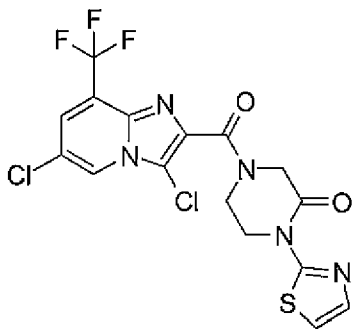
49		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone
50		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone
50(a)		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone
51		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone
52		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone

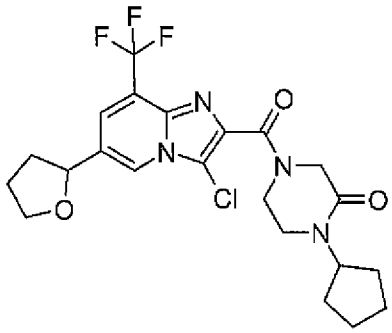
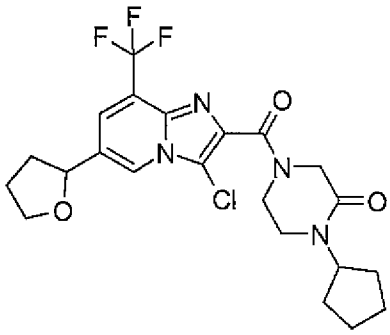
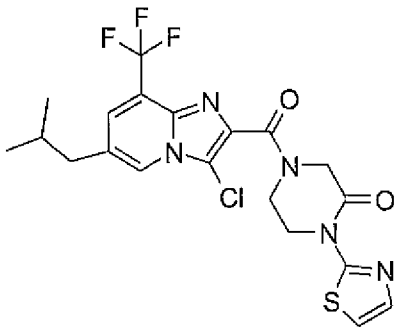
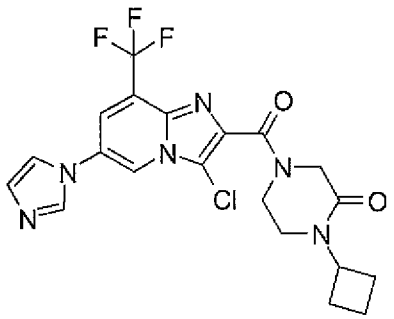
53		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone
54		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone
55		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-3-methylcyclobutyl)-2-piperazinone
56		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-methylcyclobutyl)-2-piperazinone

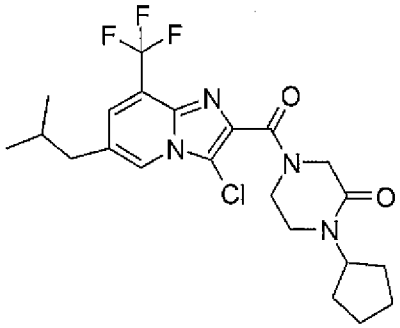
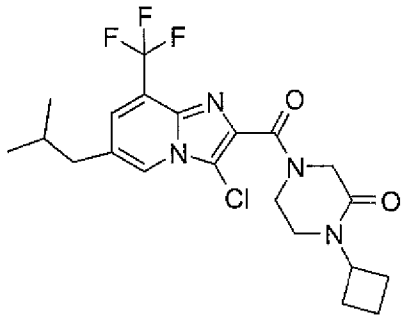
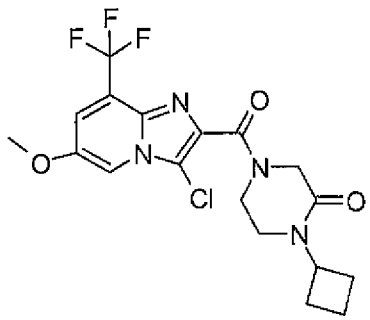
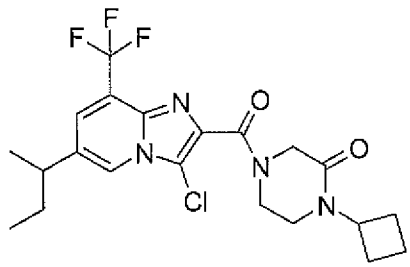
57		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2,6-piperazinedione
58		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone
59		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone
60		trans-4-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)cyclohexyl acetate
61		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxycyclohexyl)-2-piperazinone

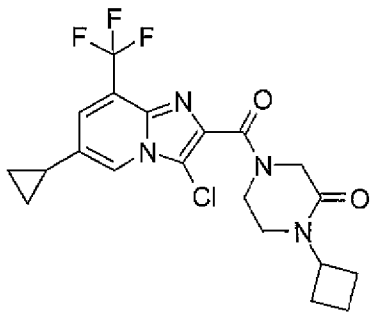
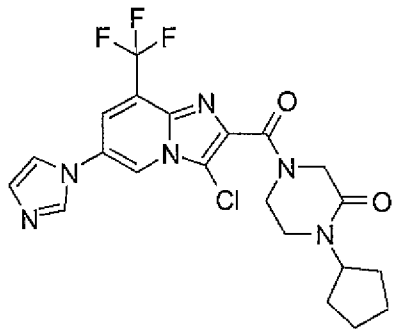
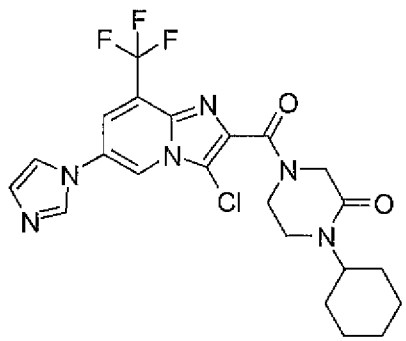
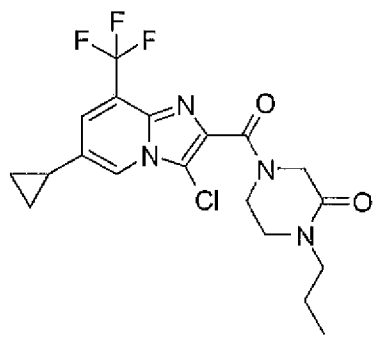
62		4-{[3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
63		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
64		4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
65		4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

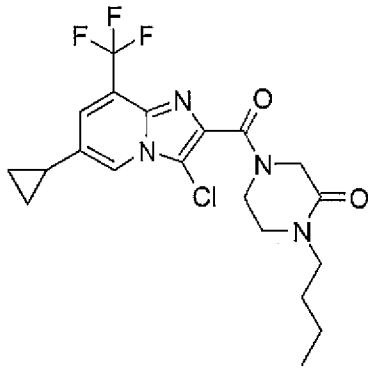
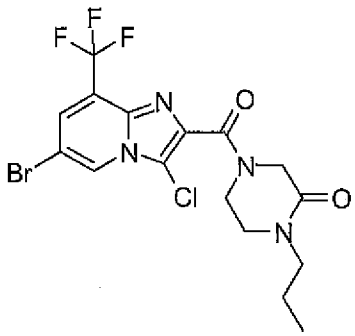
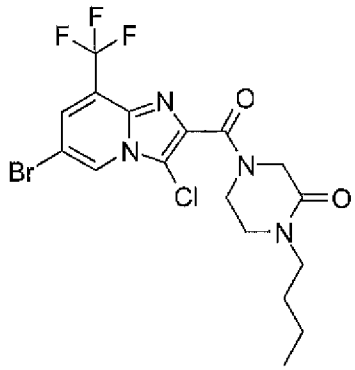
66		(+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
67		4-{[3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
68		4-{[3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
69		(+/-)-4-{[3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

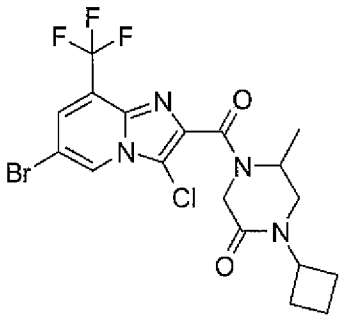
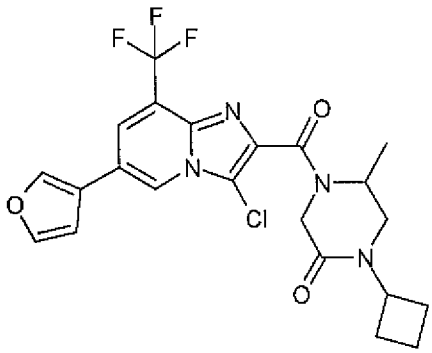
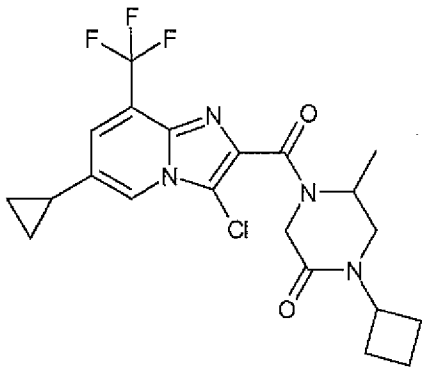
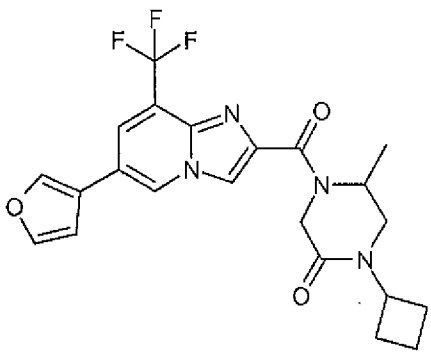
70		4-{[3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
71		1-cyclopentyl-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
72		4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

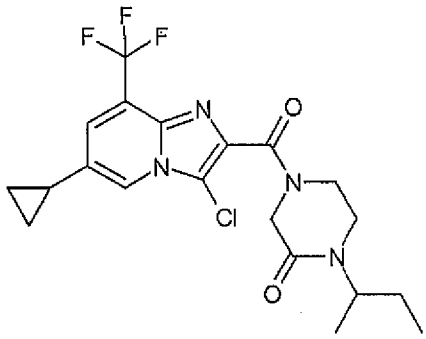
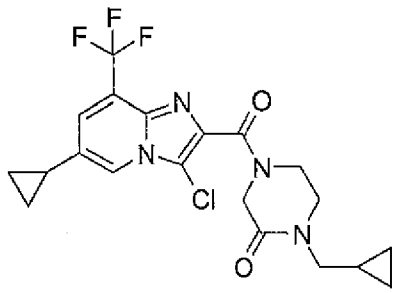
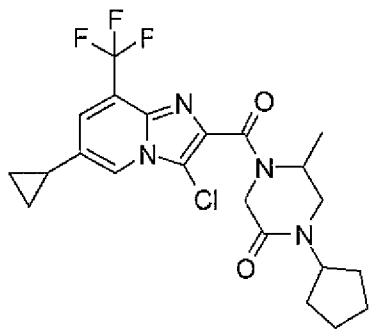
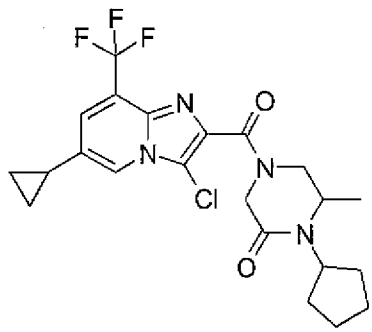
73		4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (Enantiomer 1)
74		4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (Enantiomer 2)
75		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone
76		4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

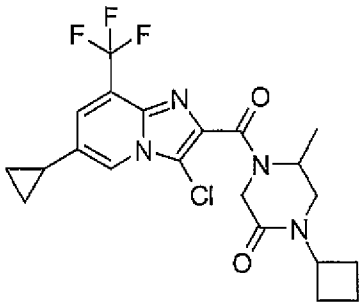
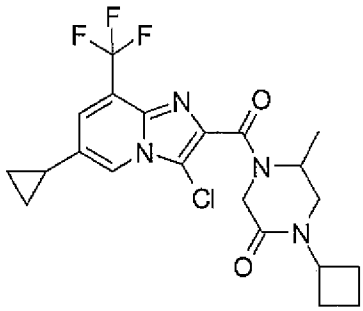
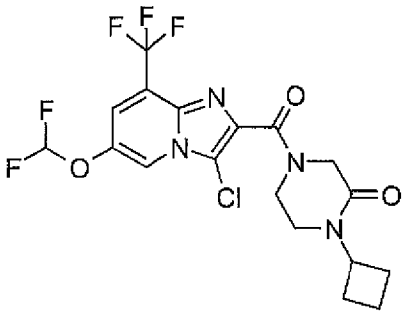
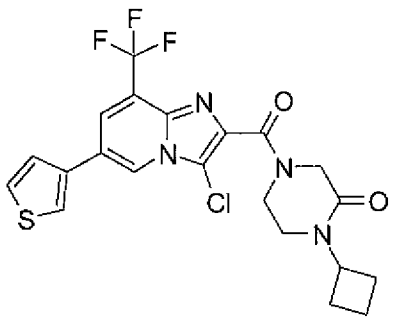
77		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
78		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
79		4-{[3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
80		(+/-)-4-{[3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

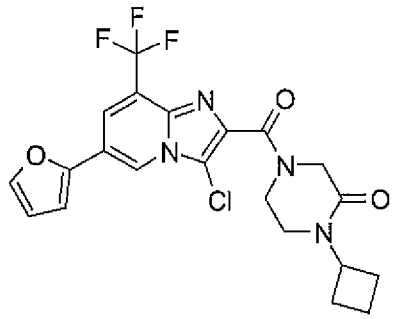
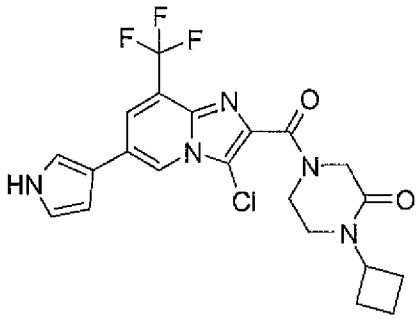
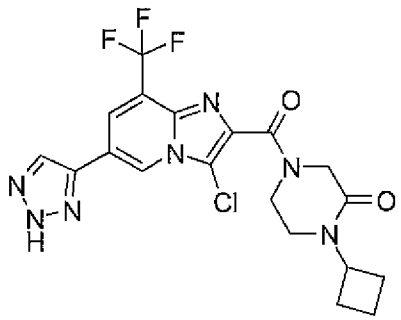
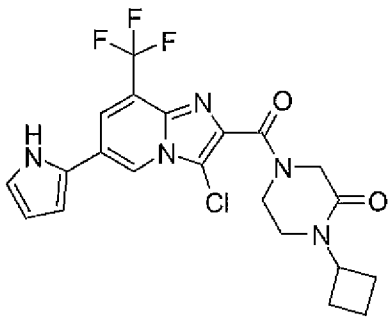
81		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
82		4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
83		4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
84		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone

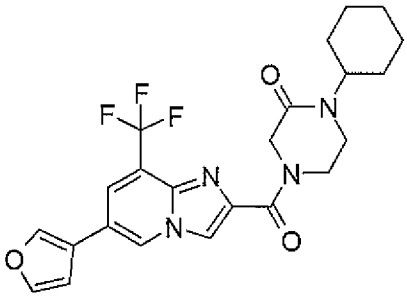
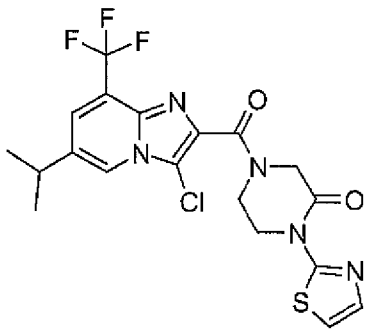
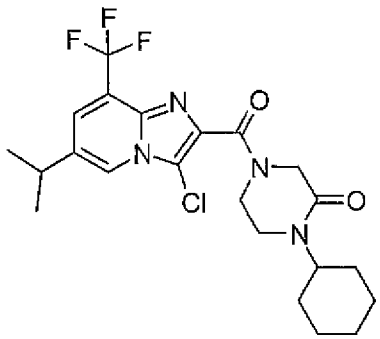
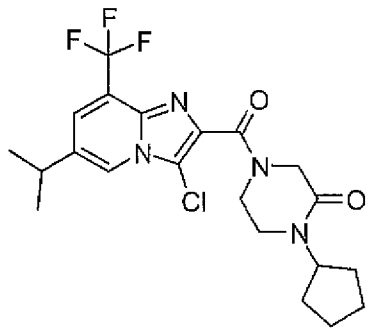
85		1-butyl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
86		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone
87		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-butyl-2-piperazinone

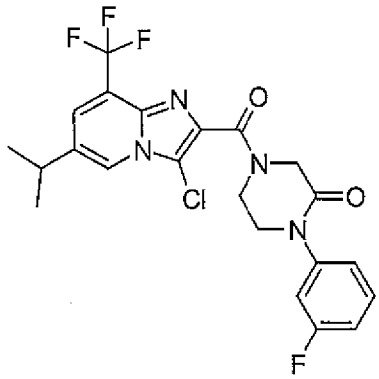
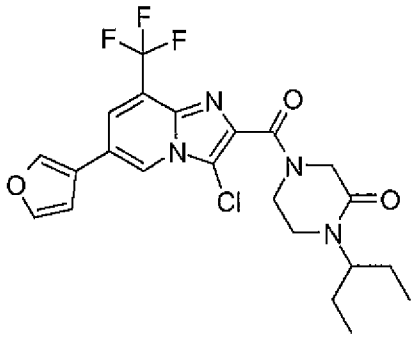
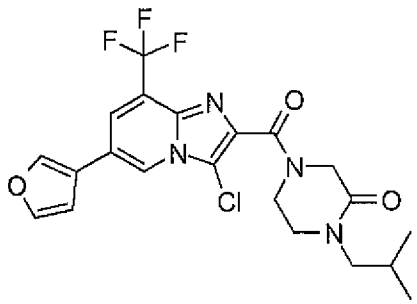
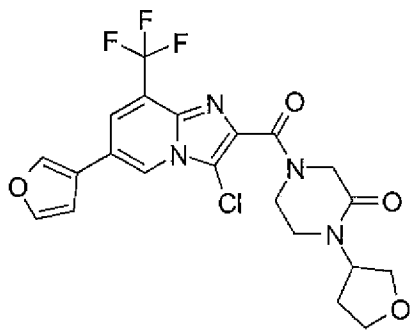
88		(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone
89		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone
90		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone
91		(+/-)-1-cyclobutyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-5-methyl-2-piperazinone

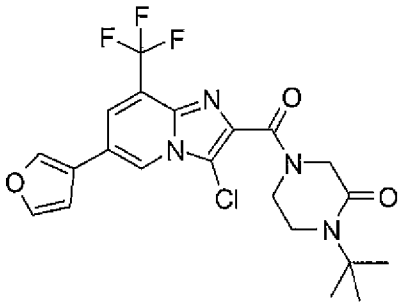
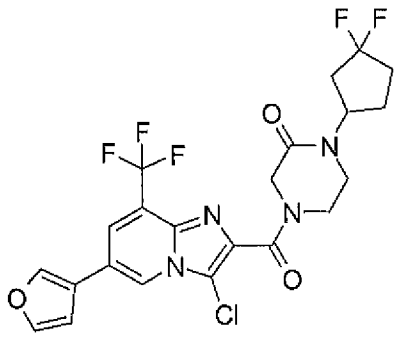
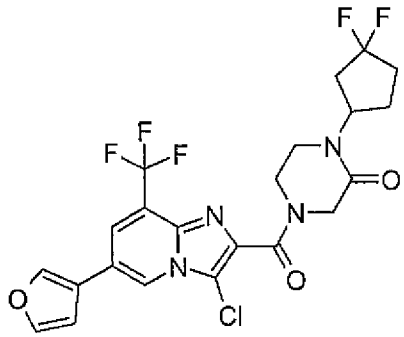
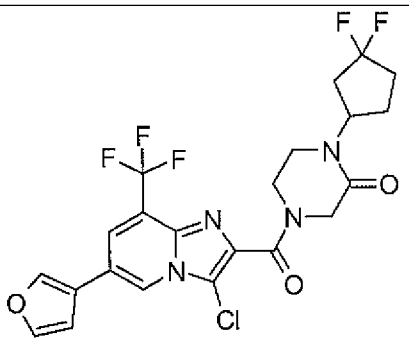
92		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylpropyl)-2-piperazinone
93		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclopropylmethyl)-2-piperazinone
94		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone
95		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone

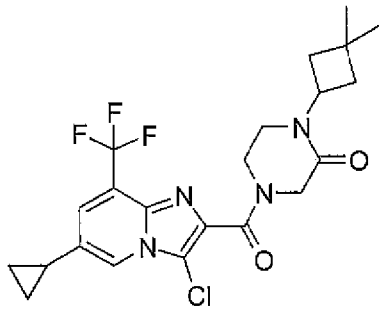
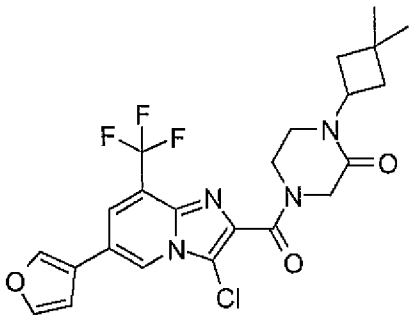
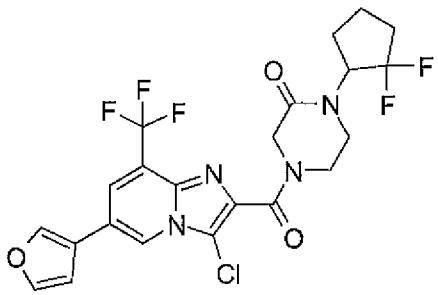
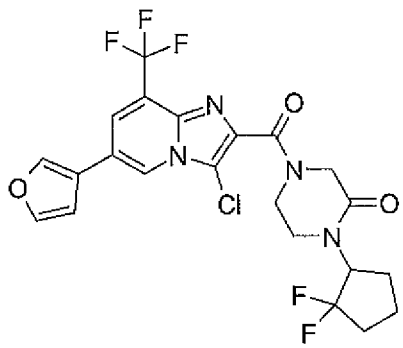
96		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone (Enantiomer 1)
97		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone (Enantiomer 2)
98		4-{[3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
99		4-{[3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

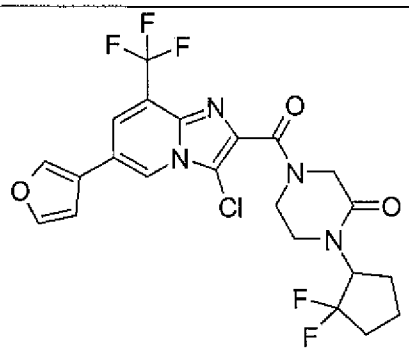
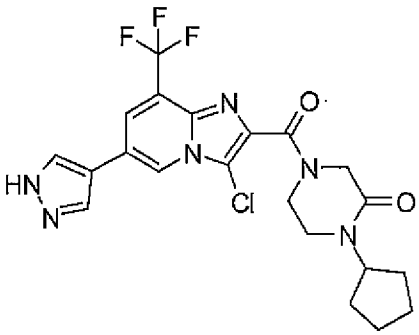
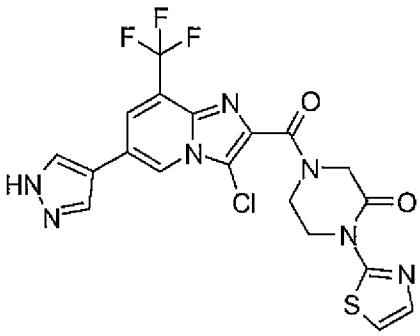
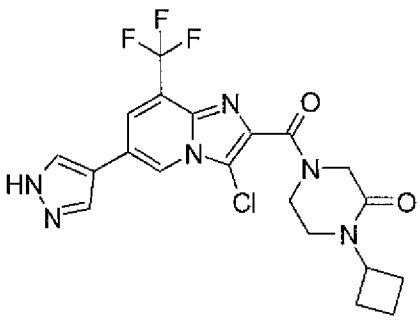
100		4-{[3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
101		4-{[3-chloro-6-(1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
102		4-{[3-chloro-6-(2H-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone
103		4-{[3-chloro-6-(1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

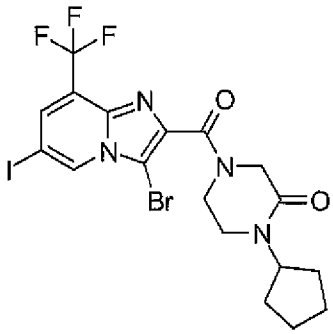
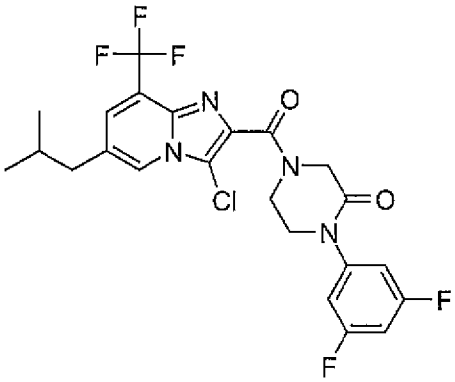
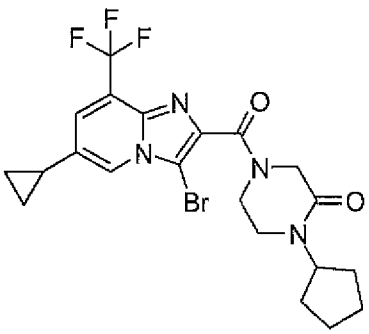
104		1-cyclohexyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
105		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone
106		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
107		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

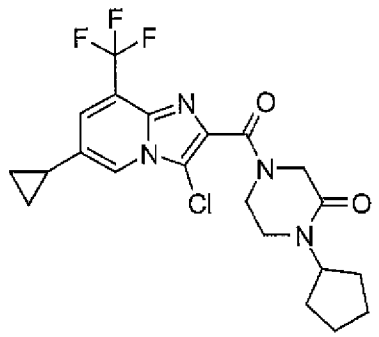
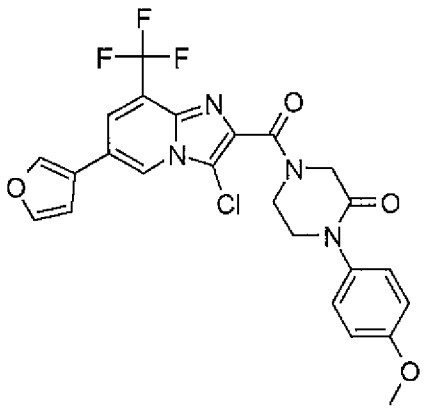
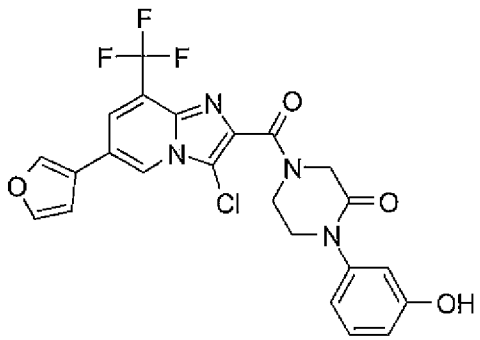
108		4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone
109		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-ethylpropyl)-2-piperazinone
110		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-methylpropyl)-2-piperazinone
111		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-3-furanyl)-2-piperazinone

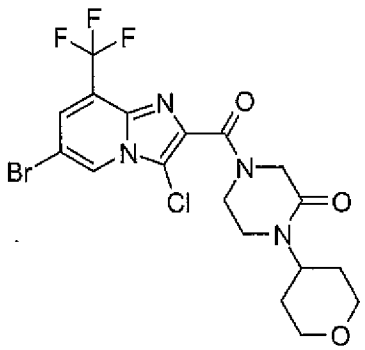
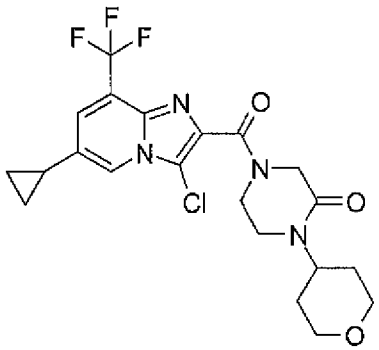
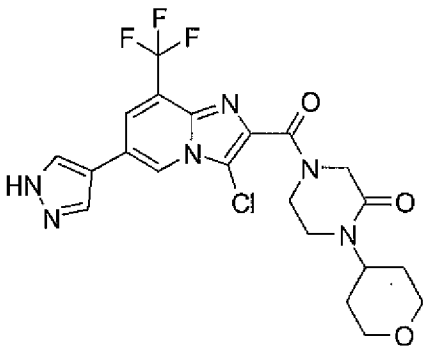
112		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dimethylethyl)-2-piperazinone
113		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone
114		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone (Enantiomer 1)
115		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone (Enantiomer 2)

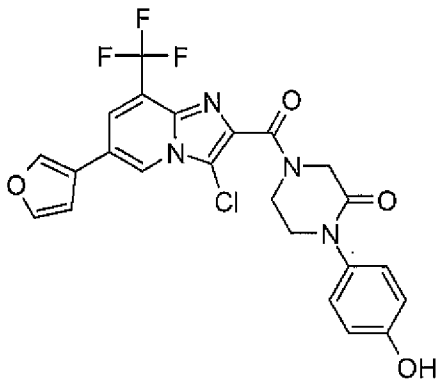
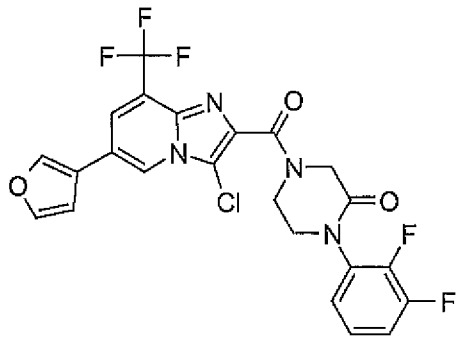
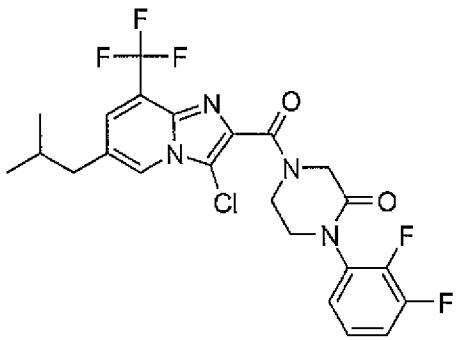
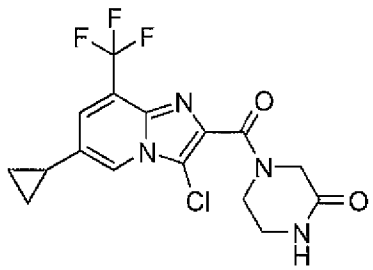
116		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone
117		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone
118		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone
119		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (Enantiomer 1)

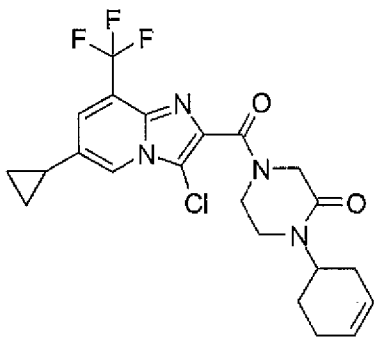
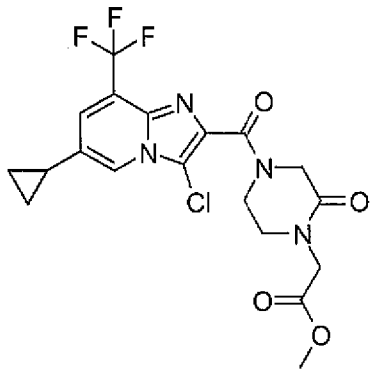
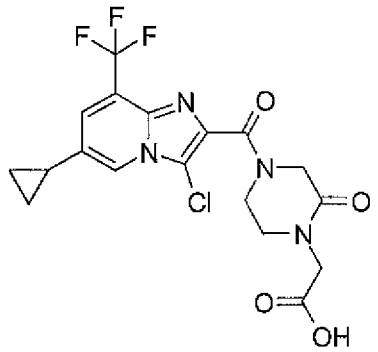
120		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (Enantiomer 2)
121		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
122		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone
123		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

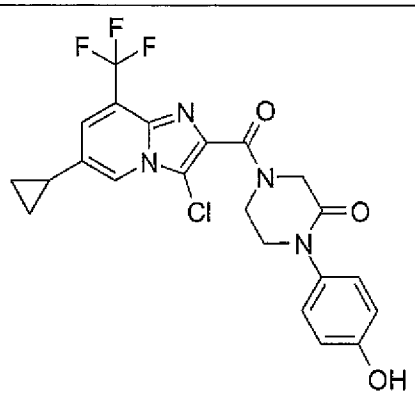
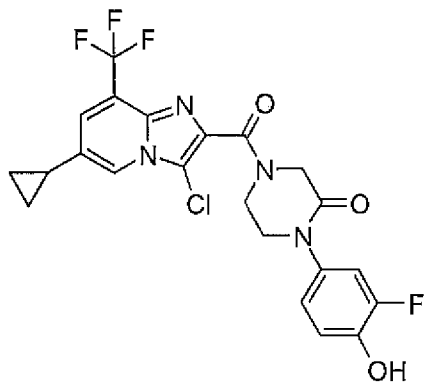
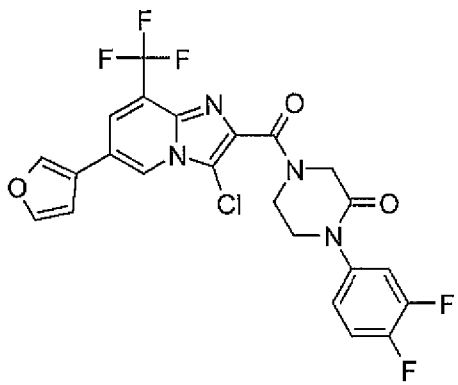
124		4-{[3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
125		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone
126		4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

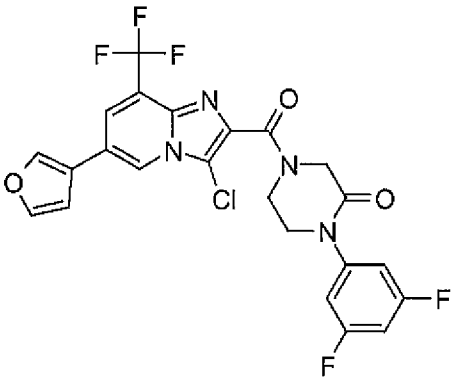
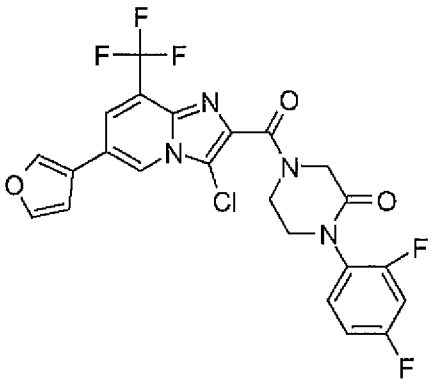
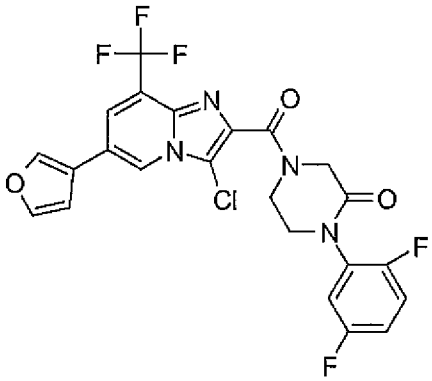
127		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
128		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methyloxy)phenyl]-2-piperazinone
129		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxyphenyl)-2-piperazinone

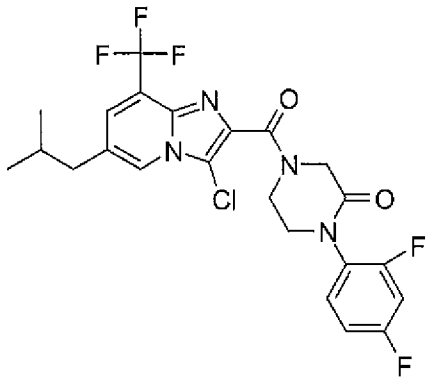
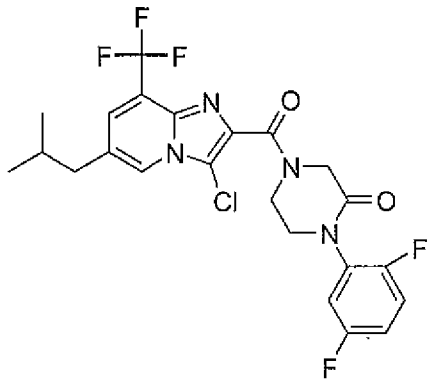
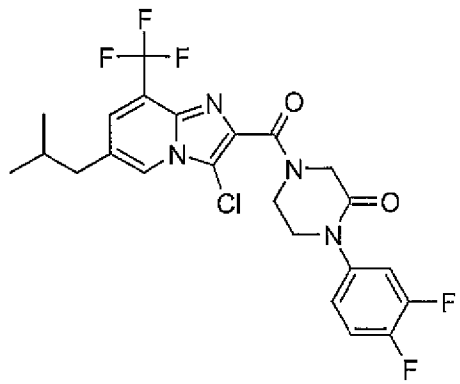
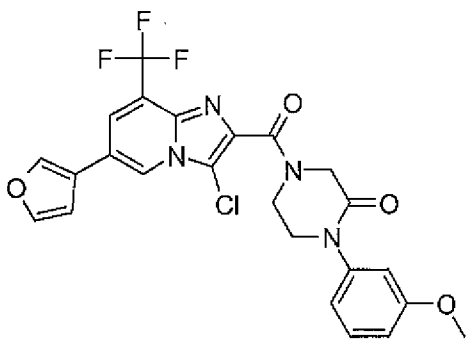
130		4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone
131		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone
132		4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

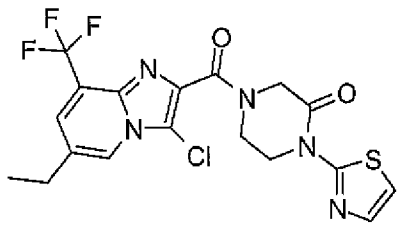
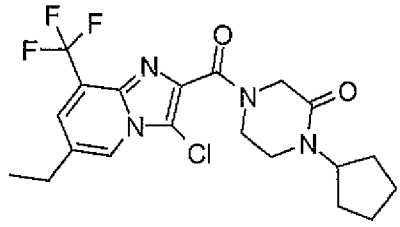
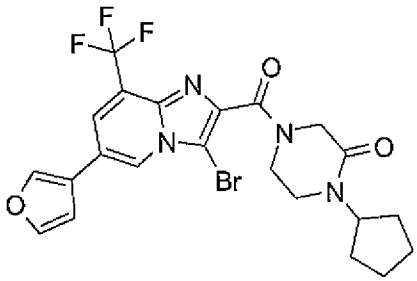
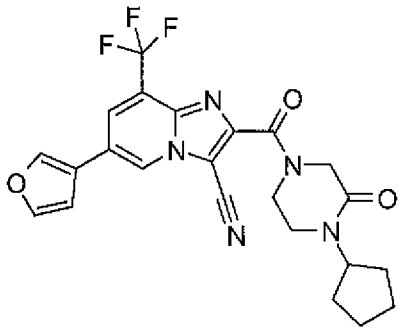
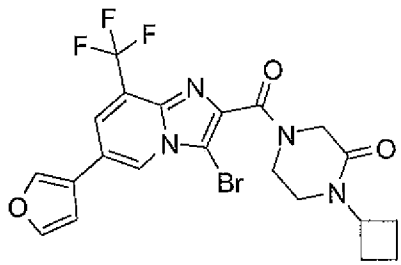
133		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone
134		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone
135		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone
136		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

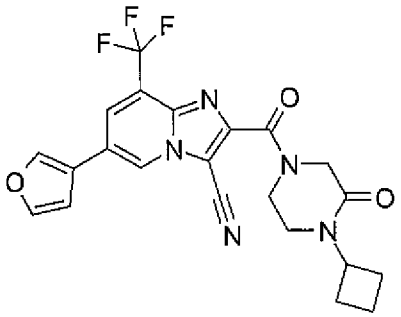
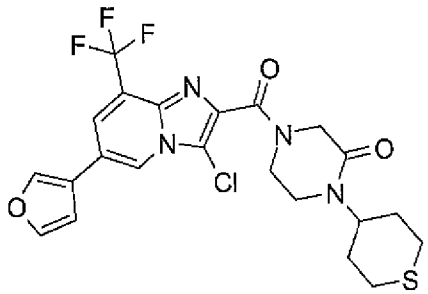
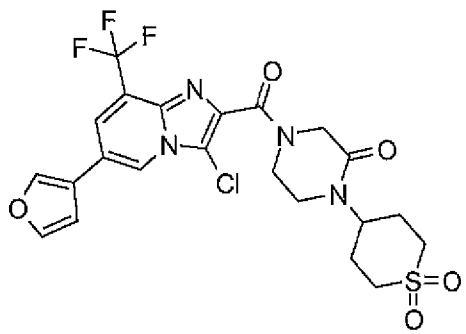
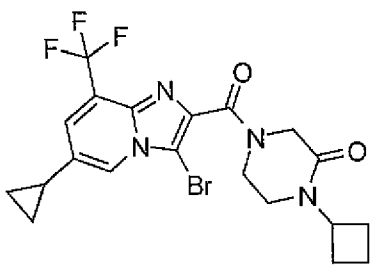
137		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclohexen-1-yl)-2-piperazinone
138		methyl (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetate
139		(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetic acid

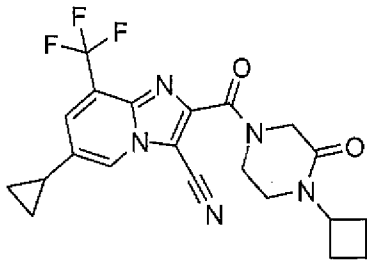
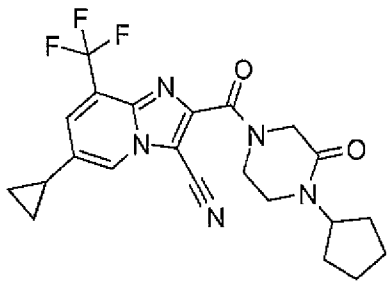
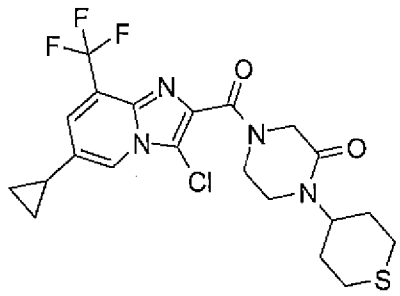
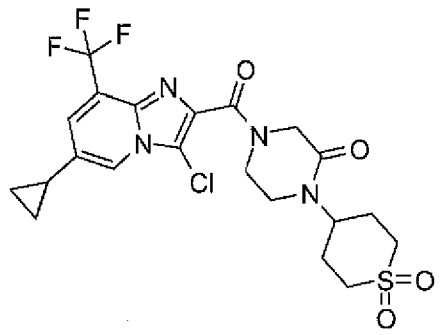
140		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone
141		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone
142		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone

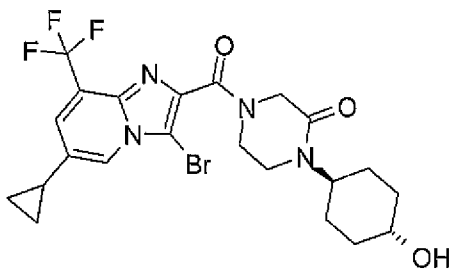
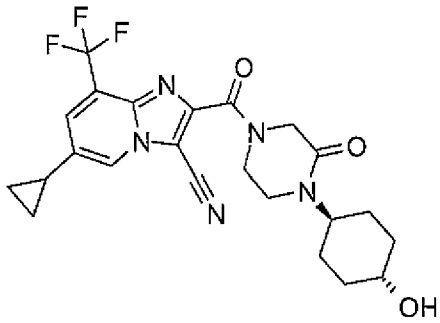
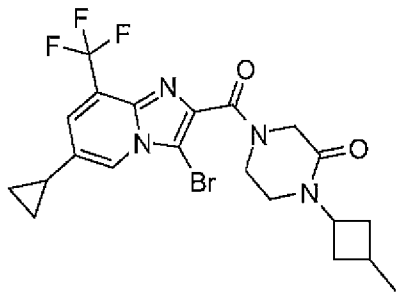
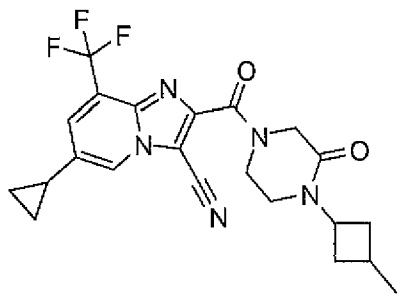
143		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone
144		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone
145		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone

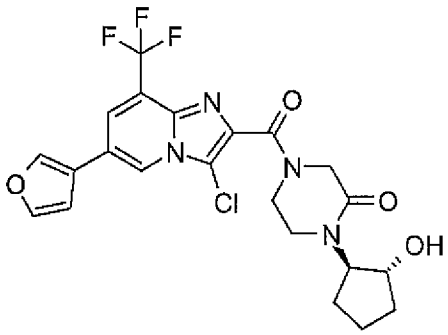
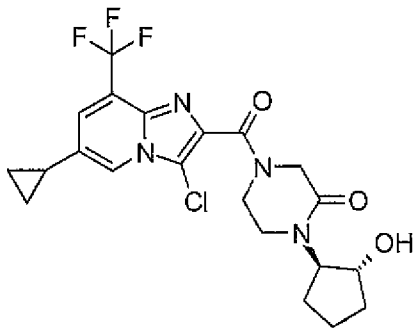
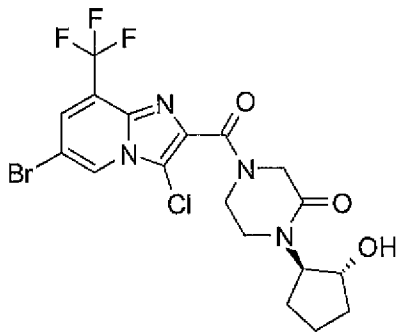
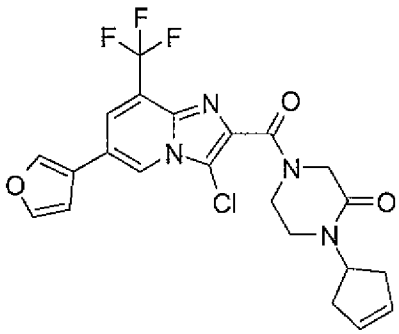
146		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone
147		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone
148		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone
149		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-(methyloxy)phenyl]-2-piperazinone

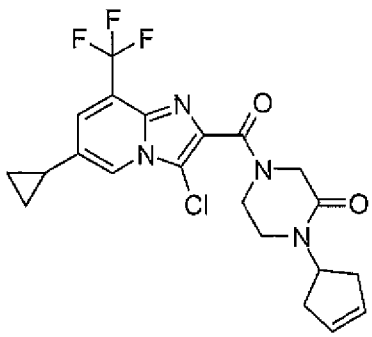
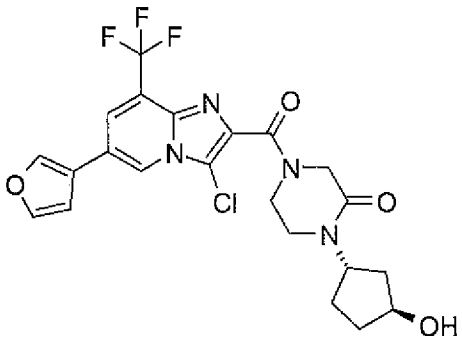
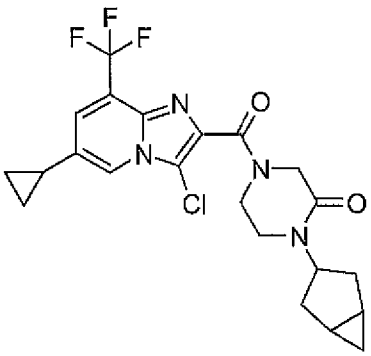
150		4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone
151		4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
152		4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone
153		2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
154		4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

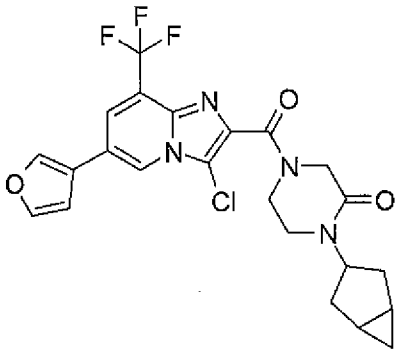
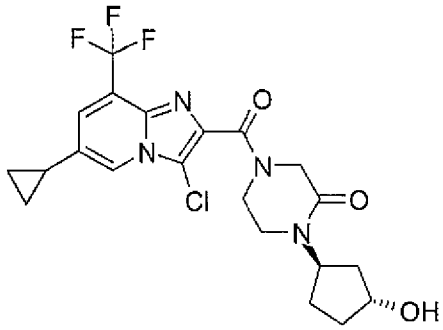
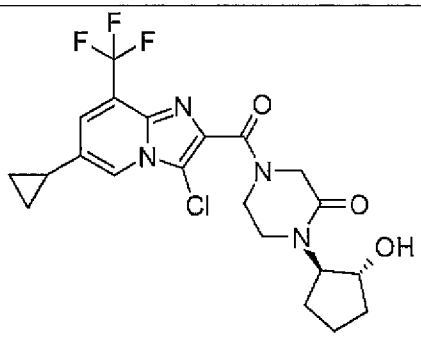
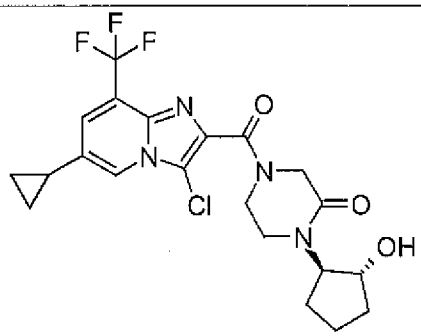
155		2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
156		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone
157		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone
158		4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

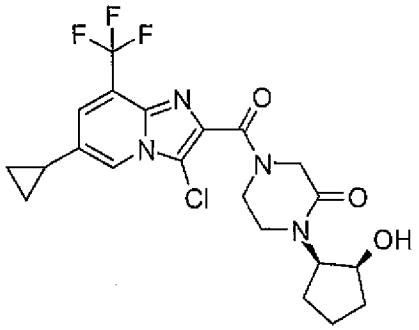
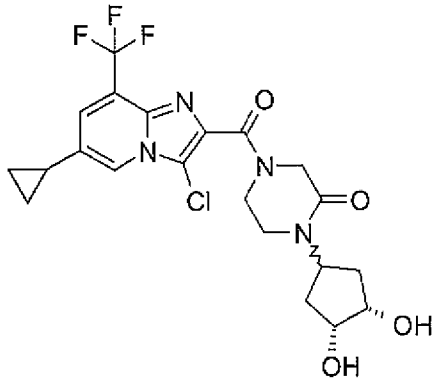
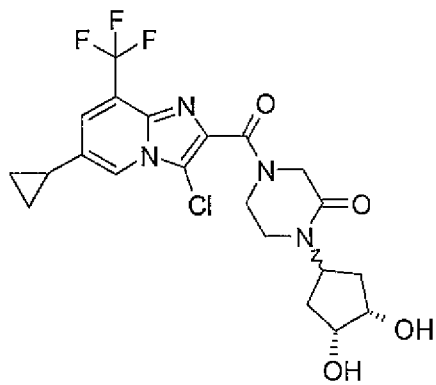
159		2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
160		2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
161		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone
162		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone

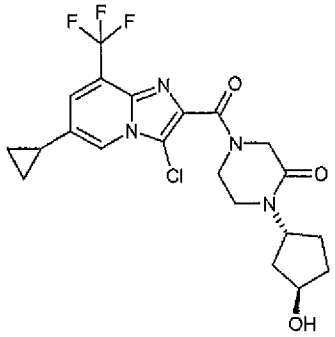
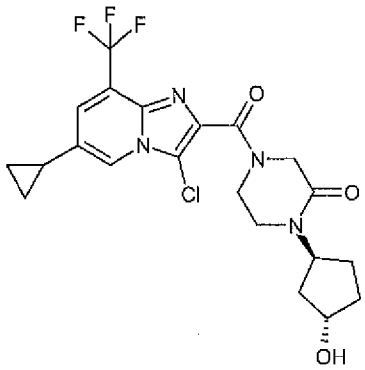
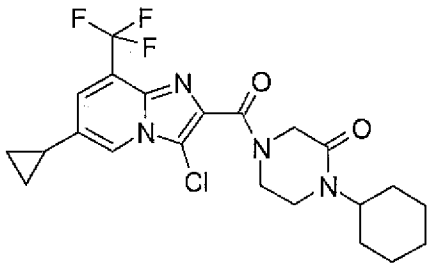
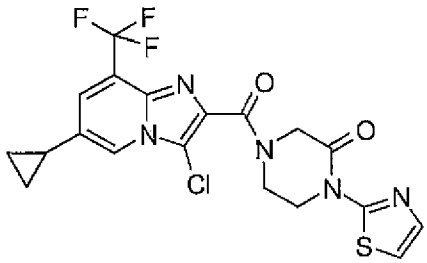
163		4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone
164		6-cyclopropyl-2-{[4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
165		4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone
166		6-cyclopropyl-2-{[4-(3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

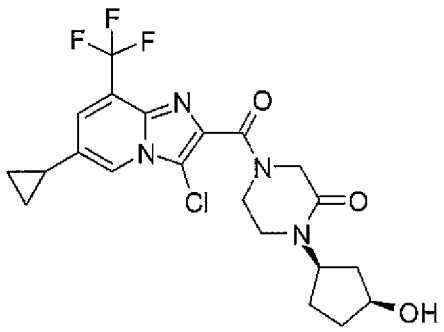
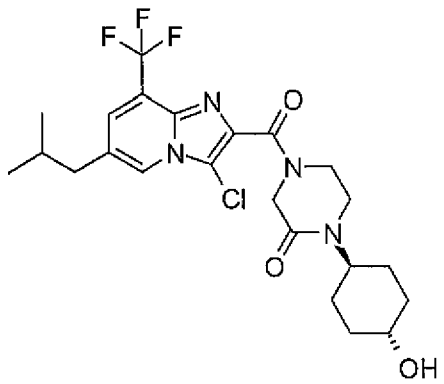
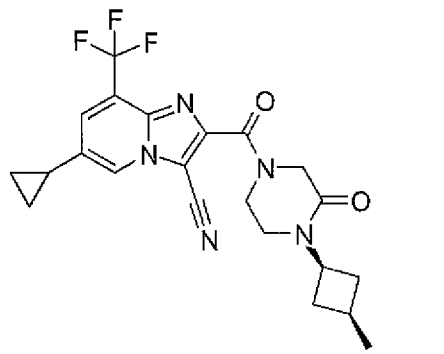
167		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone
168		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone
169		(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone
170		4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone

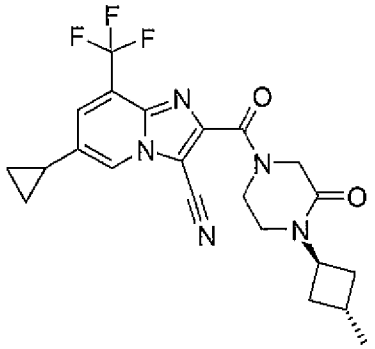
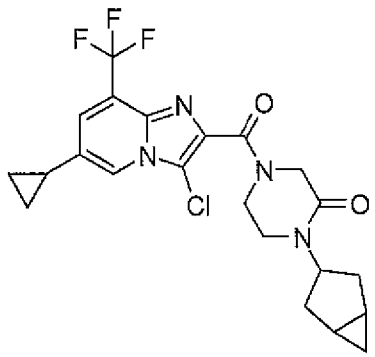
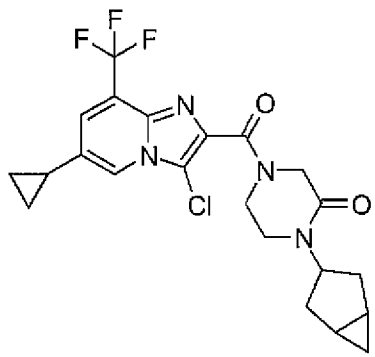
171		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone
172		(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone
173		(cis/trans mixture)-1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

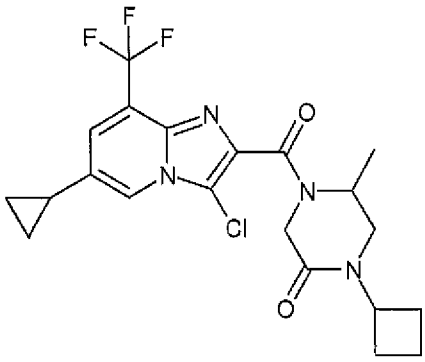
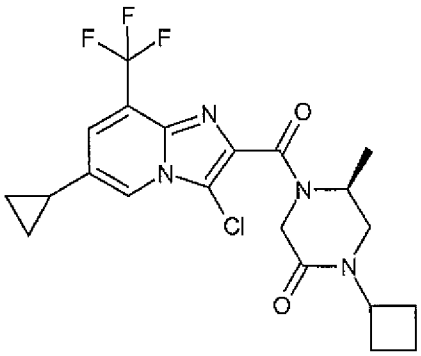
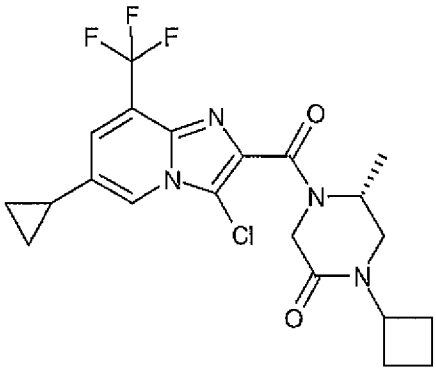
174		(cis/trans mixture)-1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
175		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone
176		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone (Enantiomer 1)
177		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone (Enantiomer 2)

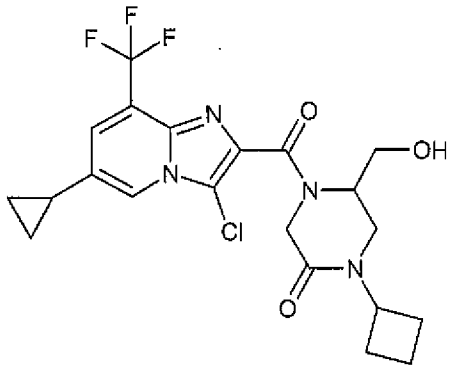
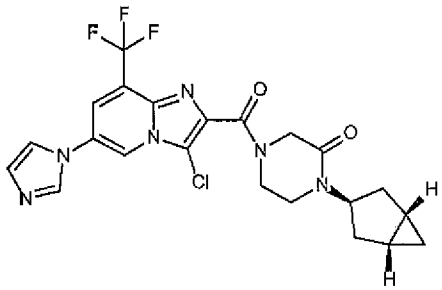
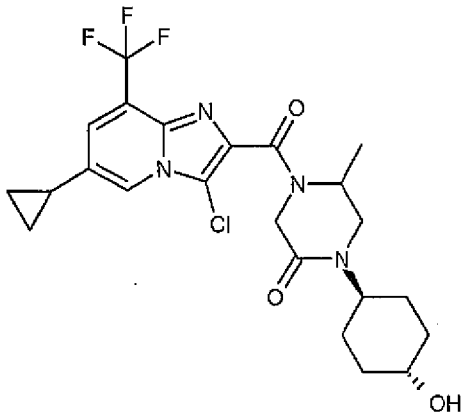
178		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone
179		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3,4-dihydroxycyclopentyl)-2-piperazinone (Isomer 1)
180		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3,4-dihydroxycyclopentyl)-2-piperazinone (Isomer 2)

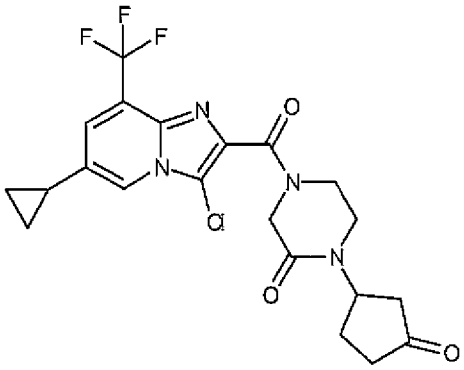
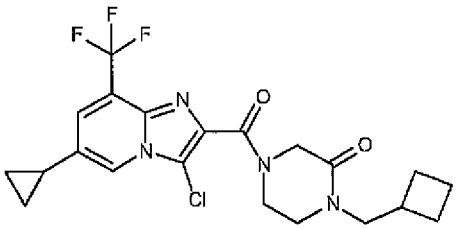
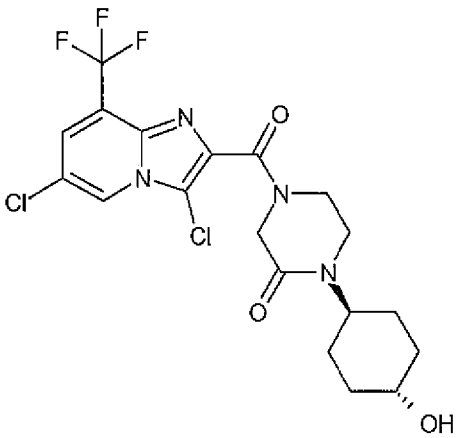
181		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-hydroxycyclopentyl]-2-piperazinone
182		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S)-3-hydroxycyclopentyl]-2-piperazinone
183		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone
184		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

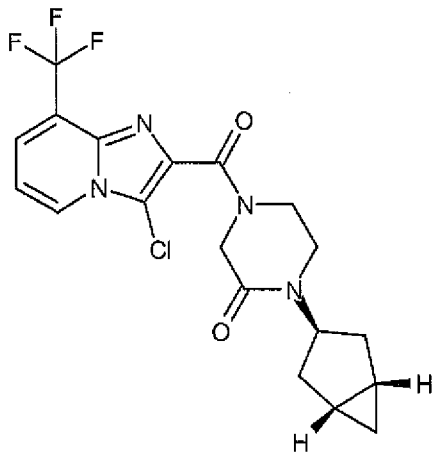
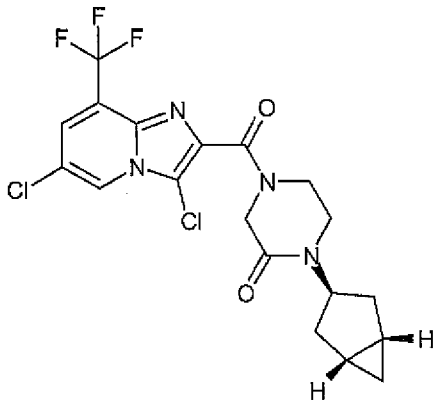
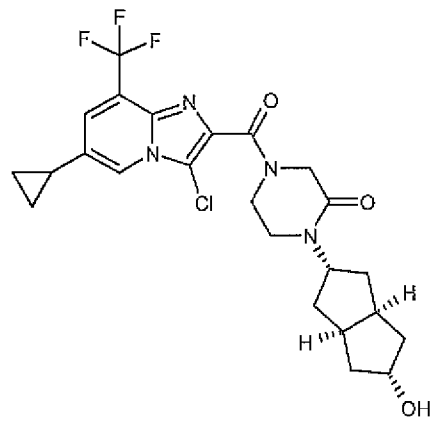
185		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone
186		4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone
187		6-cyclopropyl-2-{[4-(cis-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

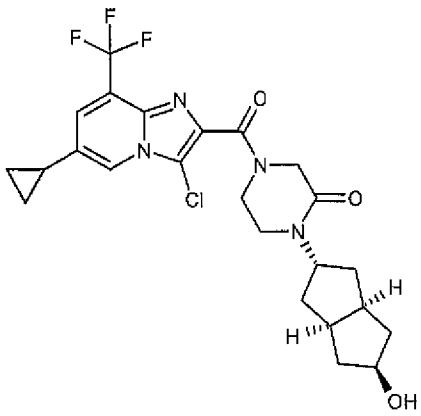
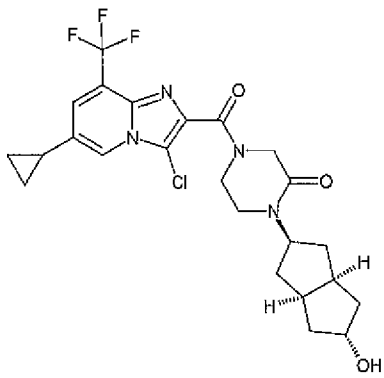
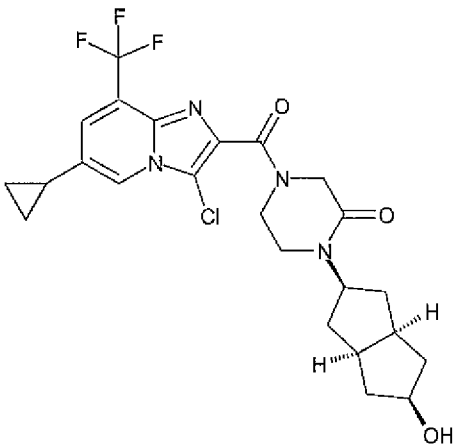
188		6-cyclopropyl-2-{[4-(trans-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
189		1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone **(Isomer 1)**
190		1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone **(Isomer 2)**

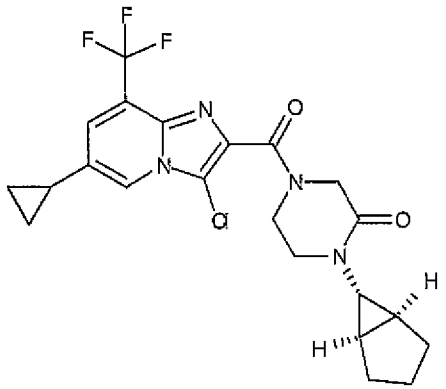
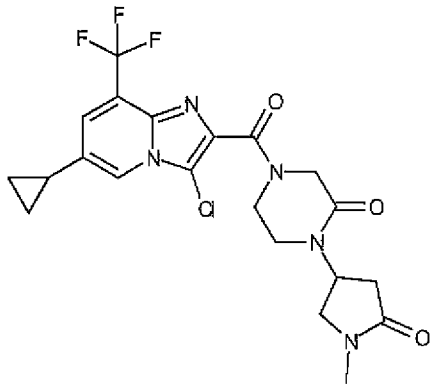
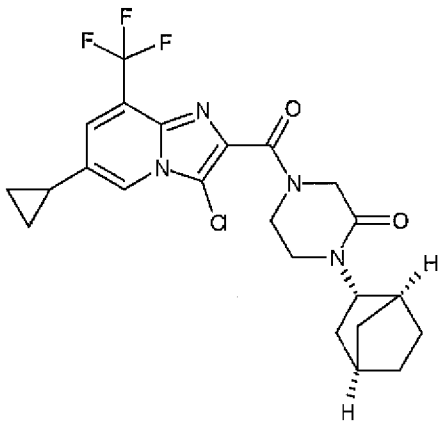
191(a)		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone
191		(5S)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone
192		(5R)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

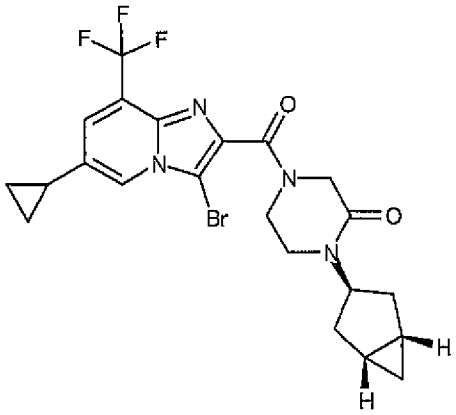
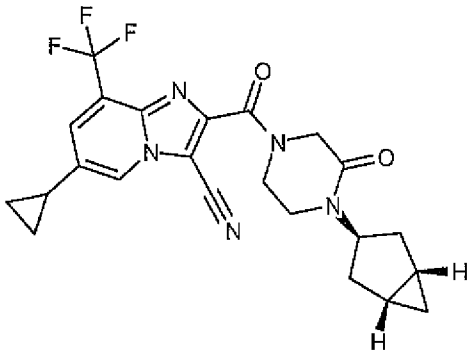
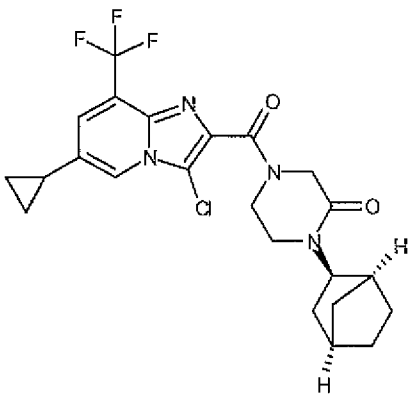
193		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-(hydroxymethyl)-2-piperazinone
194		1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
195		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-5-methyl-2-piperazinone

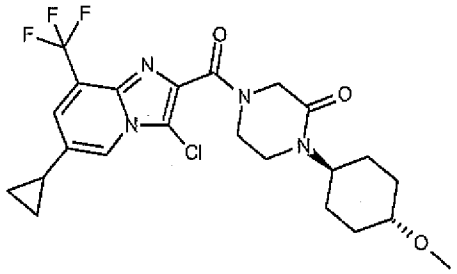
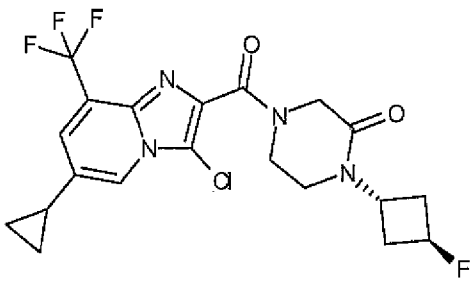
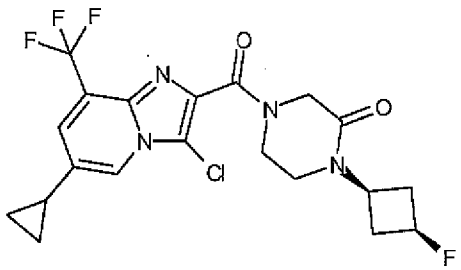
196		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxocyclopentyl)-2-piperazinone
197		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclobutylmethyl)-2-piperazinone
198		4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

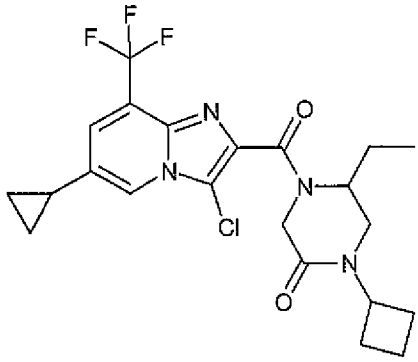
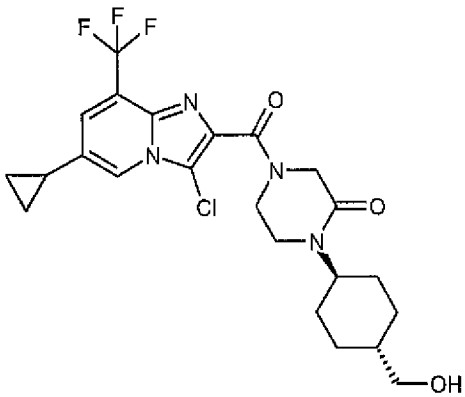
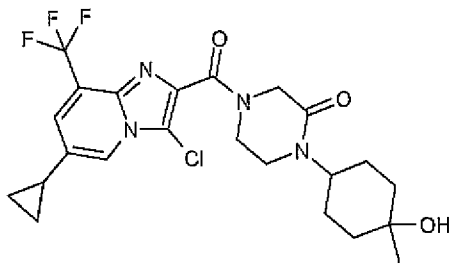
199		1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
200		1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
201		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

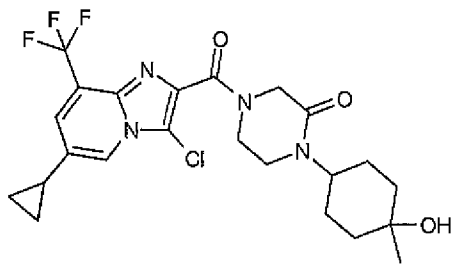
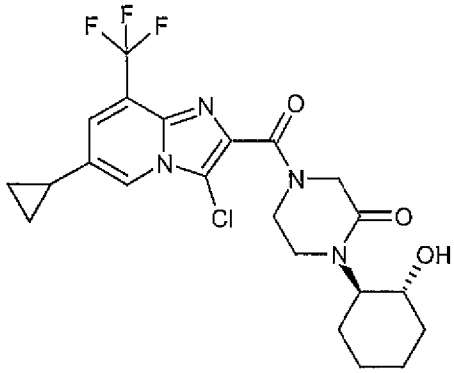
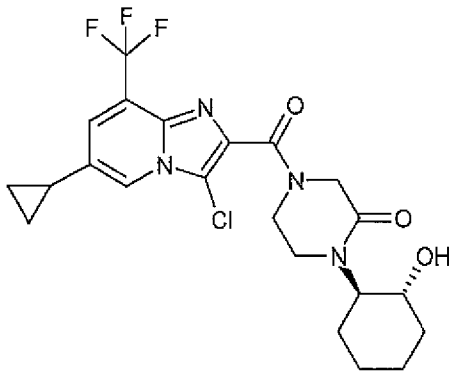
202		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-anti-hydroxy-5-methyloctahydro-2-pentalenyl]-2-piperazinone
203		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-anti-hydroxyoctahydro-2-pentalenyl]-2-piperazinone
204		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

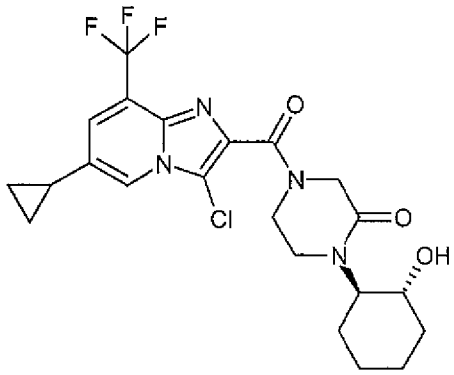
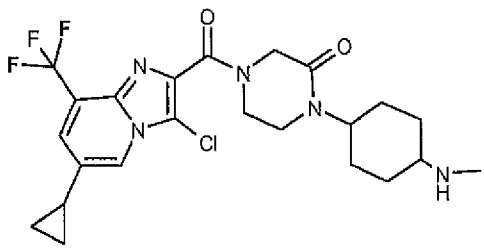
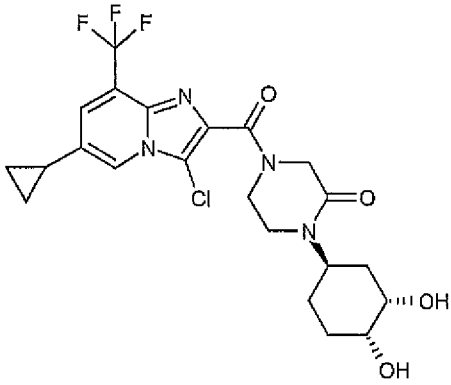
205		1-[(1R,5S,6r)-bicyclo[3.1.0]hex-6-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
206		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone
207		1-[(endo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

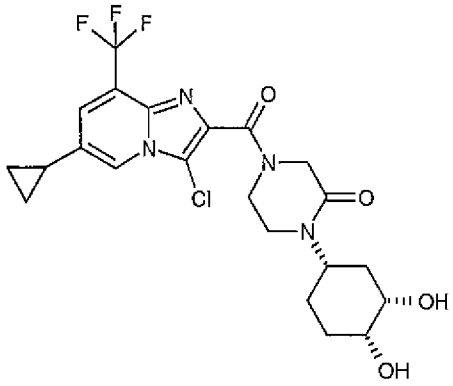
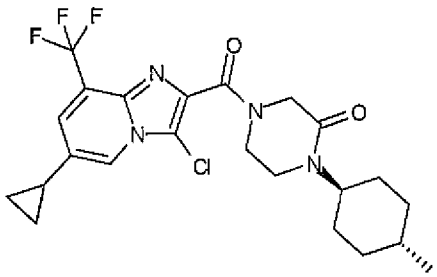
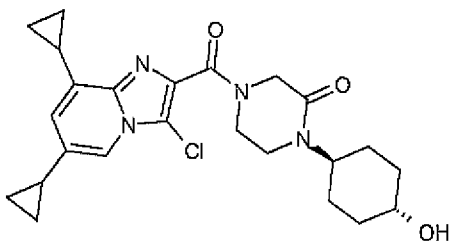
208		1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
209		2-({4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinyl}carbonyl)-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile
210		1-[(exo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

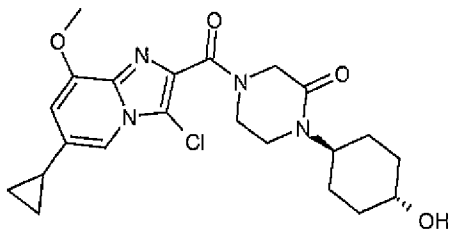
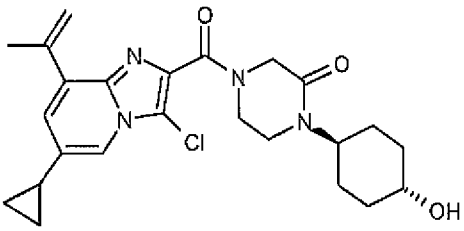
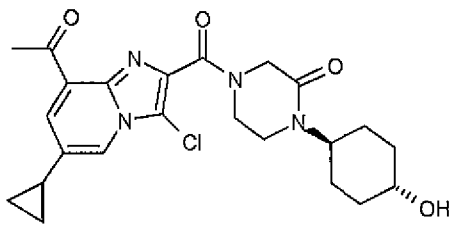
211		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(methyloxy)cyclohexyl]-2-piperazinone
212		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone
213		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone

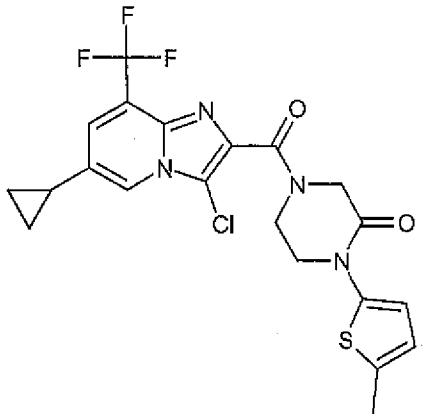
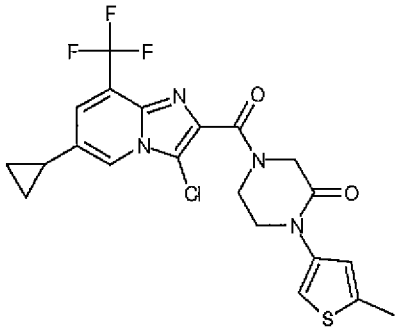
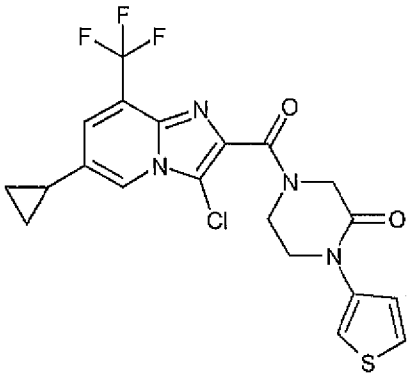
214		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-ethyl-2-piperazinone
215		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(hydroxymethyl)cyclohexyl]-2-piperazinone
216		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone (Isomer 1)

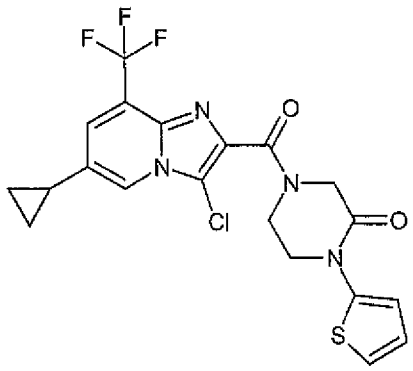
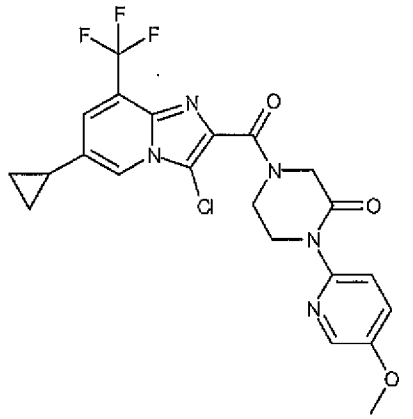
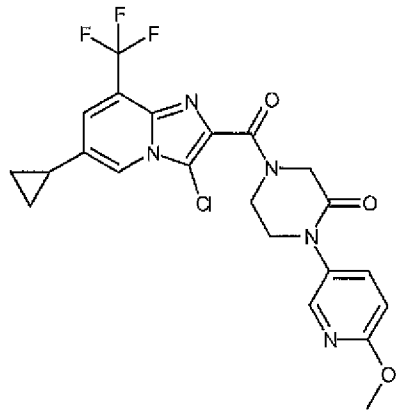
217		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone (Isomer 2)
218		(+/-)-trans-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxycyclohexyl)-2-piperazinone (racemic)
219		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone Enantiomer 1

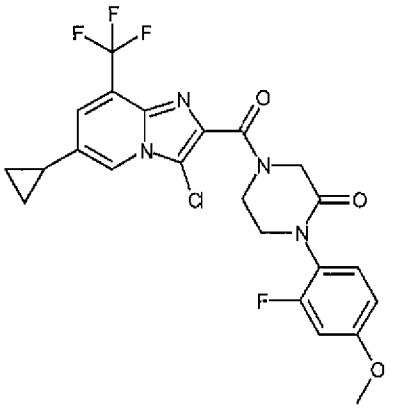
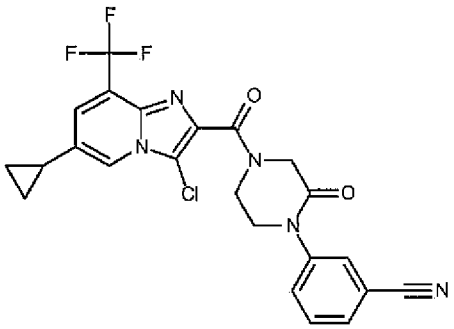
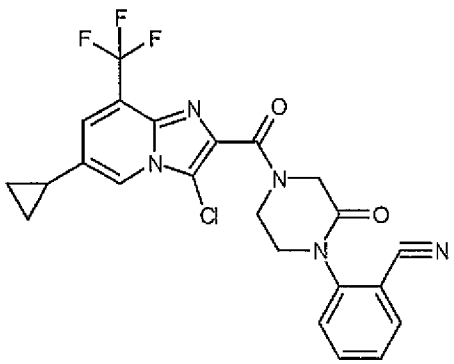
220		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone Enantiomer 2
221		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methylamino)cyclohexyl]-2-piperazinone
222		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone

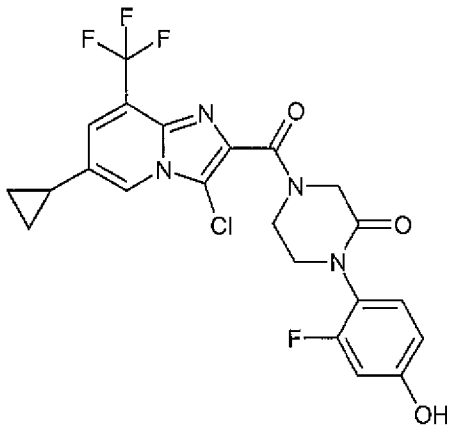
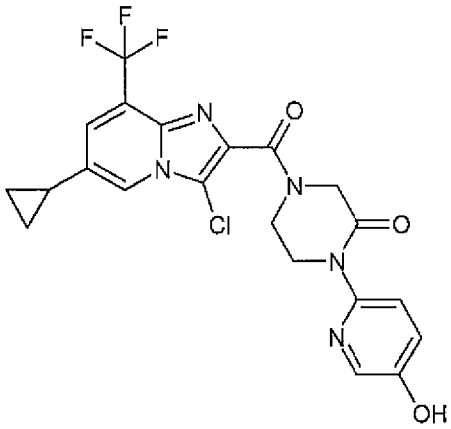
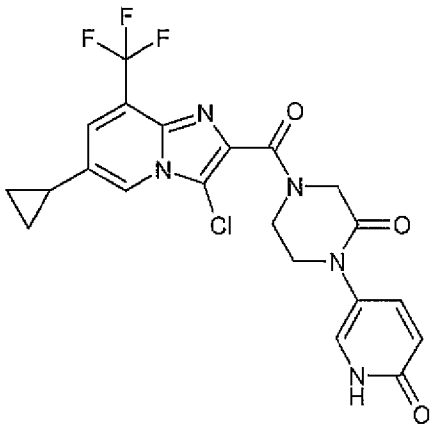
223		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone
224		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-methylcyclohexyl)-2-piperazinone
225		4-[(3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

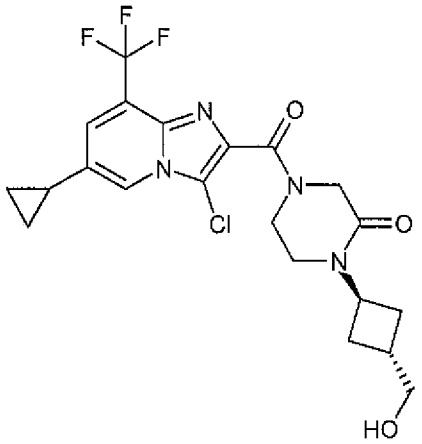
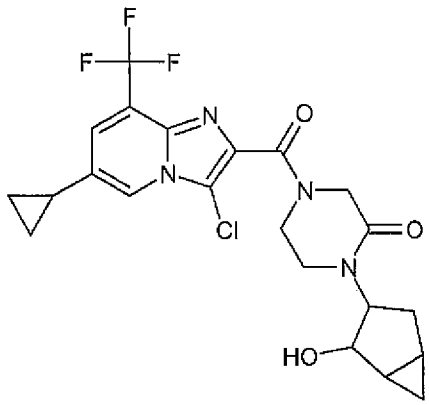
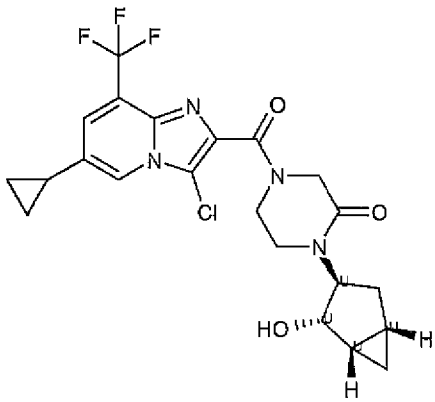
226		4-{[3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone
227		4-{[3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone
228		4-[(8-acetyl-3-chloro-6-cyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

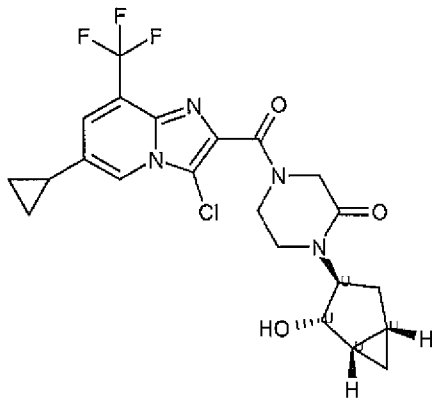
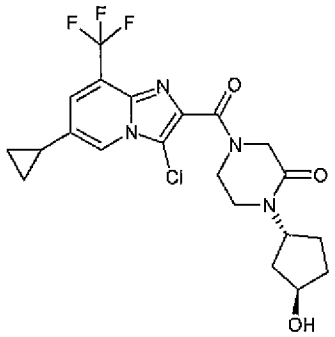
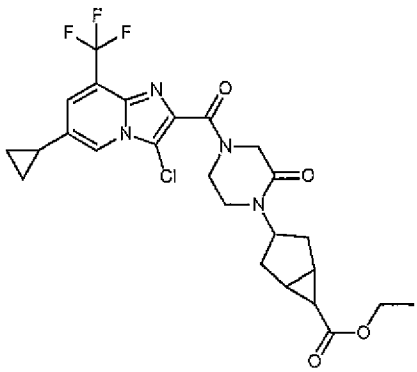
229		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-2-thienyl)-2-piperazinone
230		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-3-thienyl)-2-piperazinone
231		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

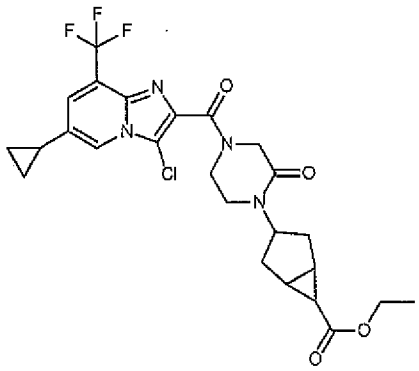
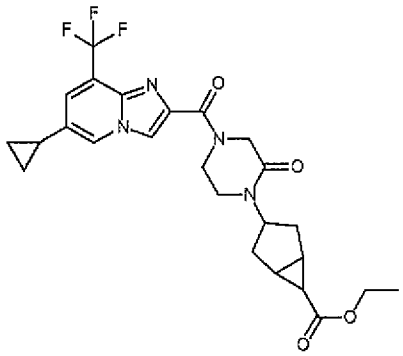
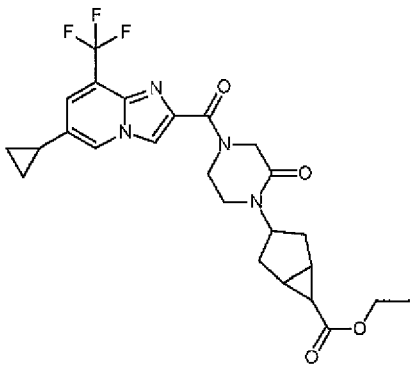
232		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone
233		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone
234		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone

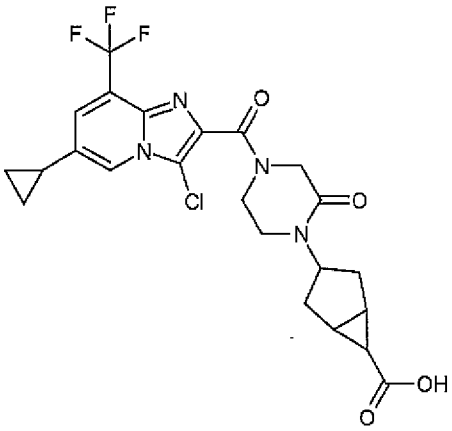
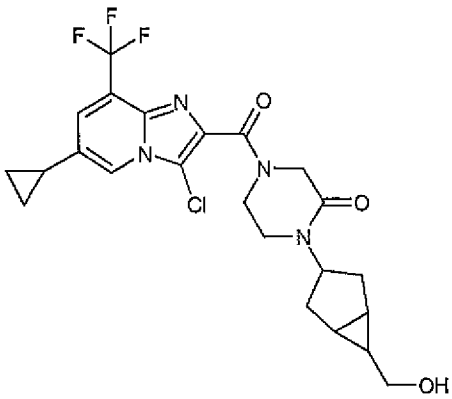
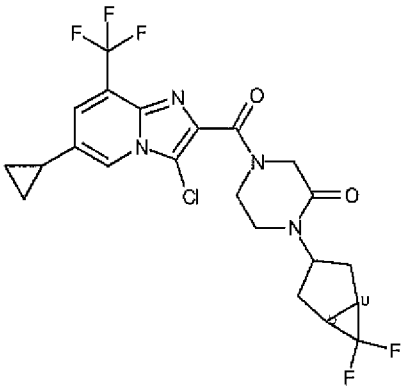
235		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone
236		3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile
237		2-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile

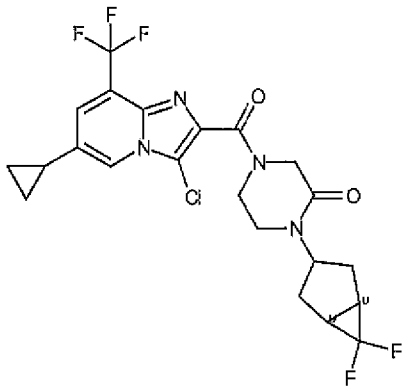
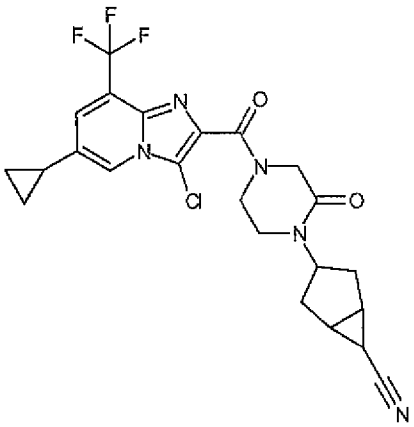
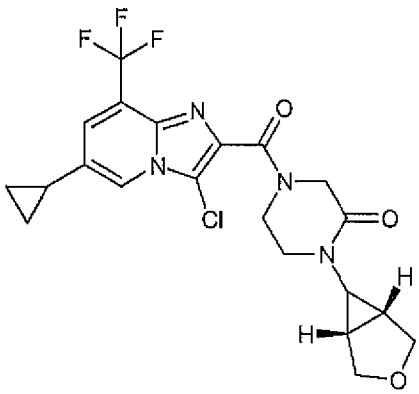
238		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluoro-4-hydroxyphenyl)-2-piperazinone
239		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-hydroxy-2-pyridinyl)-2-piperazinone
240		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxo-1,6-dihydro-3-pyridinyl)-2-piperazinone

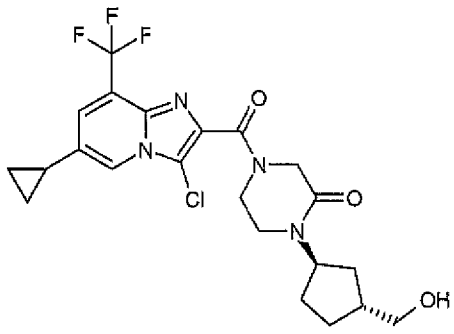
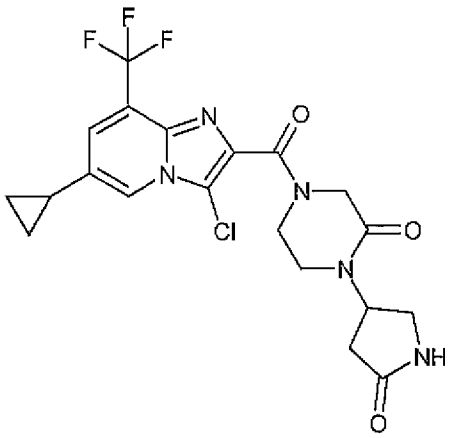
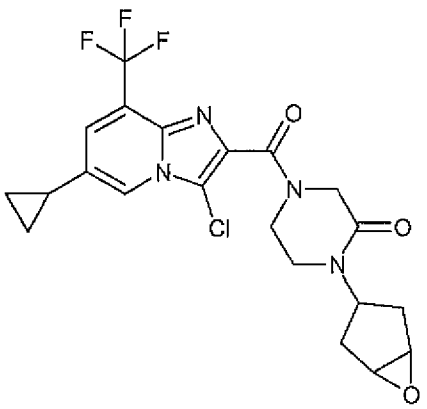
241		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-3-(hydroxymethyl)cyclobutyl]-2-piperazinone
242		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxybicyclo[3.1.0]hex-3-yl)-2-piperazinone
243		Enantiomer 1: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone

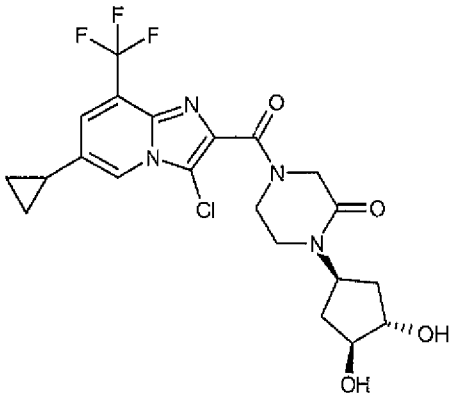
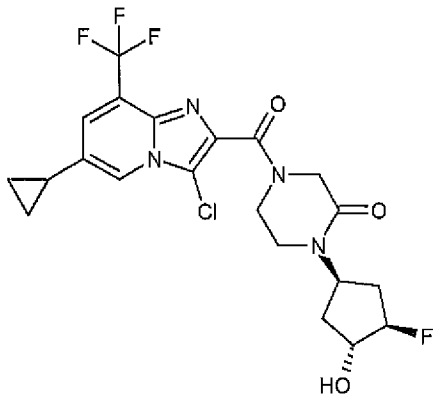
244		Enantiomer 2: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone
245		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone
247		Isomer1. ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate

248		Isomer2. ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate
249		Isomer1. ethyl 3-(4-{[6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate
250		Isomer2. ethyl 3-(4-{[6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate

251		Isomer2, 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylic acid
252		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(hydroxymethyl)bicyclo[3.1.0]hex-3-yl]-2-piperazinone
253		isomer1: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6,6-difluorobicyclo[3.1.0]hex-3-yl)-2-piperazinone

254		isomer2: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6,6-difluorobicyclo[3.1.0]hex-3-yl)-2-piperazinone
255		3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carbonitrile
256		(Trans)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone

257		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone
258		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-oxo-3-pyrrolidinyl)-2-piperazinone
259		4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxabicyclo[3.1.0]hex-3-yl)-2-piperazinone

260		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3,4-dihydroxycyclopentyl]-2-piperazinone
261		(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-fluoro-4-hydroxycyclopentyl]-2-piperazinone

[00112] The compounds of Table 1 were synthesized according to the Synthetic Methods, General Schemes, and the Examples described after Table 2.

[00113] In certain embodiments, the compound of the present invention is selected from the group consisting of:

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone,

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-2-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopropyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cycloheptyl-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylethyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-3-methylcyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-methylcyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2,6-piperazinedione,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone,

trans-4-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)cyclohexyl acetate,

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

(+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

(+/-)-4-{[3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

1-cyclopentyl-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone ,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,

4-{[3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone,
1-butyl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-butyl-2-piperazinone,
(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(+/-)-1-cyclobutyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylpropyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclopropylmethyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,

4-{[3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(2H-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
1-cyclohexyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-ethylpropyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-methylpropyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-3-furanyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dimethylethyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone ,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone,
4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methyloxy)phenyl]-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxyphenyl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclohexen-1-yl)-2-piperazinone,

methyl (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetate,

(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetic acid,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-(methyloxy)phenyl]-2-piperazinone,

4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone,
4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone,
4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
6-cyclopropyl-2-{[4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone,
6-cyclopropyl-2-{[4-(3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone,
(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone,

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone,
(cis/trans mixture)-1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
(cis/trans mixture)-1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone ,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3,4-dihydroxycyclopentyl)-2-piperazinone ,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone ,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
6-cyclopropyl-2-{[4-(cis-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
6-cyclopropyl-2-{[4-(trans-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(5S)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(5R)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-(hydroxymethyl)-2-piperazinone,
1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-5-methyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxocyclopentyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclobutylmethyl)-2-piperazinone,
4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-anti-hydroxy-5-methyloctahydro-2-pentalenyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-anti-hydroxyoctahydro-2-pentalenyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone,
1-[(1R,5S,6r)-bicyclo[3.1.0]hex-6-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone,
1-[(endo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
2-({4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinyl}carbonyl)-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
1-[(exo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(methyloxy)cyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-ethyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(hydroxymethyl)cyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone,
(+/-)-trans-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methylamino)cyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-methylcyclohexyl)-2-piperazinone,
4-[(3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-[(8-acetyl-3-chloro-6-cyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-2-thienyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-3-thienyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone,
3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile,
2-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluoro-4-hydroxyphenyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-hydroxy-2-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxo-1,6-dihydro-3-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-3-(hydroxymethyl)cyclobutyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxybicyclo[3.1.0]hex-3-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S)-3-hydroxycyclopentyl]-2-piperazinone,
ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate,
ethyl 3-(4-{[6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate,

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylic acid,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(hydroxymethyl)bicyclo[3.1.0]hex-3-yl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6,6-difluorobicyclo[3.1.0]hex-3-yl)-2-piperazinone,
3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carbonitrile,
(trans)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-oxo-3-pyrrolidinyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxabicyclo[3.1.0]hex-3-yl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3,4-dihydroxycyclopentyl]-2-piperazinone, and
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-fluoro-4-hydroxycyclopentyl]-2-piperazinone,
or a pharmaceutically acceptable salt thereof.

[00114] In further embodiments, the compound of the present invention is selected from the group consisting of:
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone,
1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
6-cyclopropyl-2-{[4-(4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile, and
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone;
or a pharmaceutically acceptable salt thereof.

[00115] In certain embodiments, the compound of the present invention is selected from the group consisting of:

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,
6-cyclopropyl-2-{[4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
6-cyclopropyl-2-{[4-(cis-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone, and
1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone,
or a pharmaceutically acceptable salt thereof.

[00116] In certain embodiments, the compound of the present invention is 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone, or a pharmaceutically acceptable salt thereof.

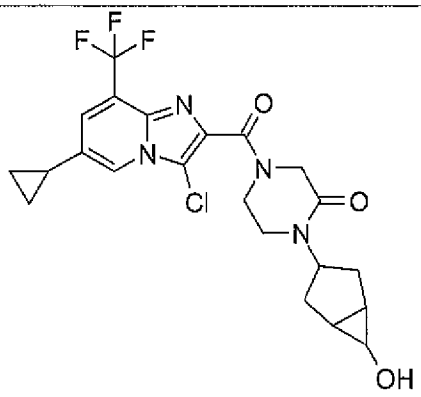
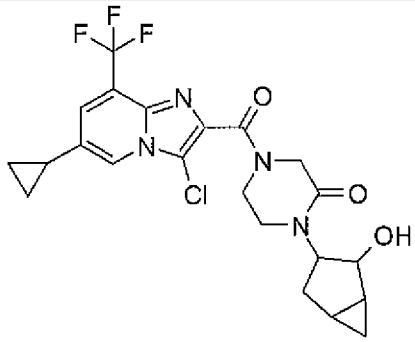
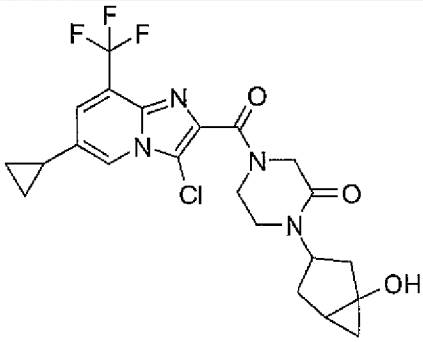
[00117] In certain embodiments, the compound of the present invention is 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone, or a pharmaceutically acceptable salt thereof.

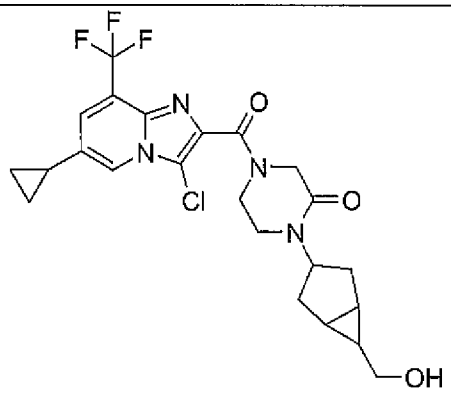
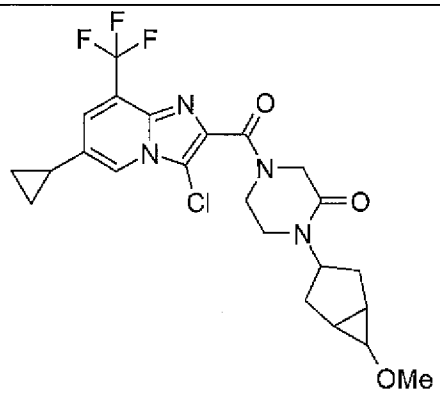
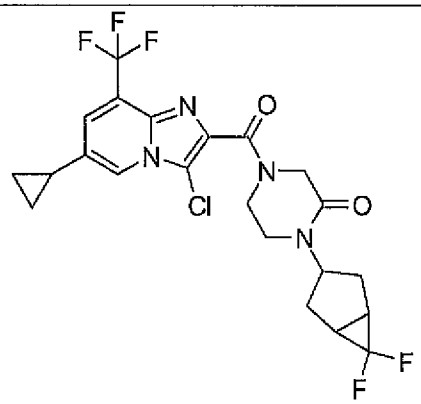
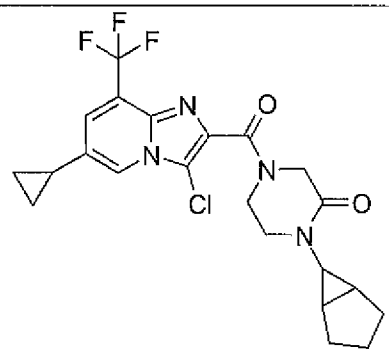
[00118] In certain embodiments, the compound of the present invention is 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone, or a pharmaceutically acceptable salt thereof.

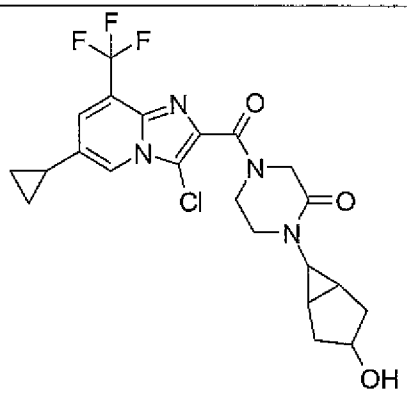
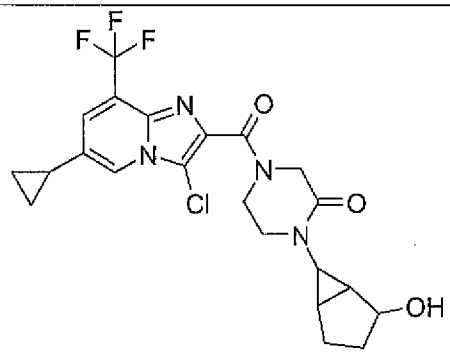
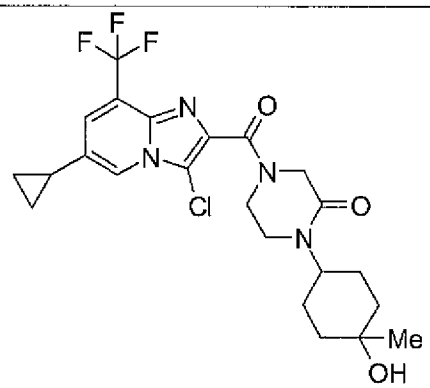
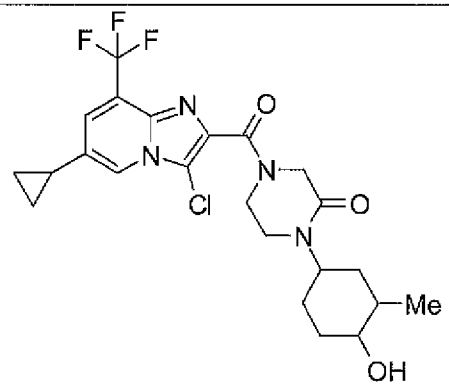
[00119] In certain embodiments, the compound of the present invention is 1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone, or a pharmaceutically acceptable salt thereof.

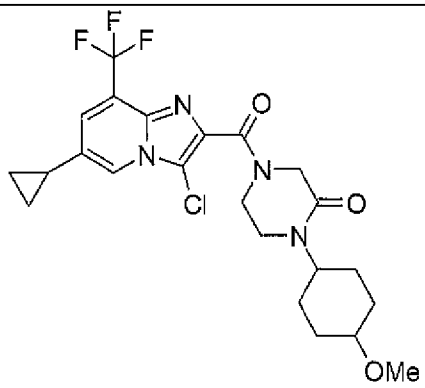
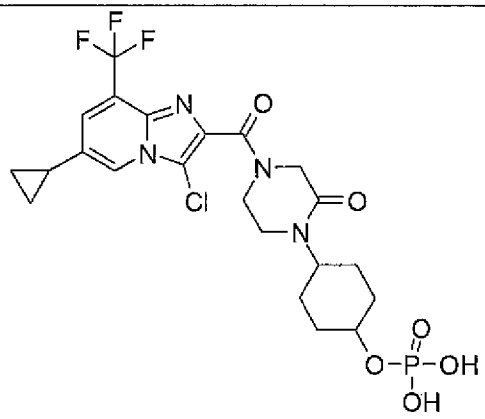
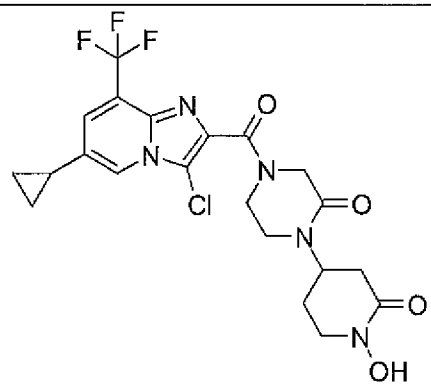
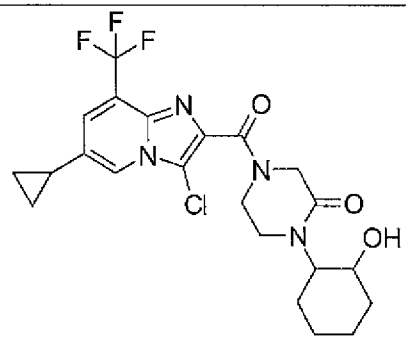
[00120] In other embodiments, the compound of the present invention, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of those compounds set forth in Table 2.

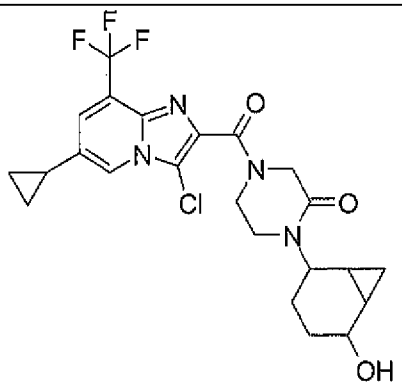
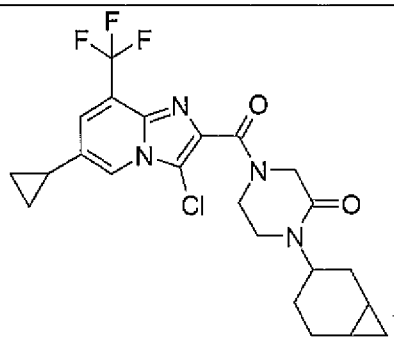
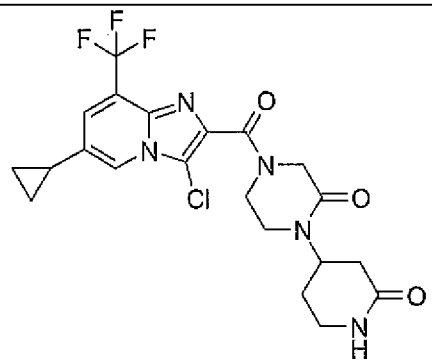
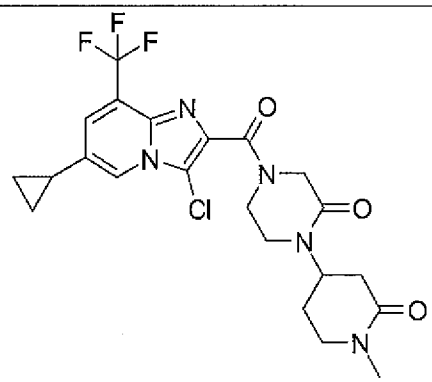
Table 2

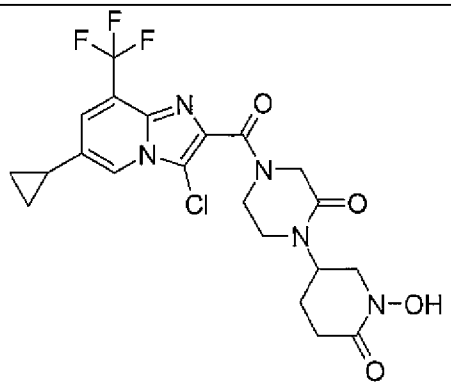
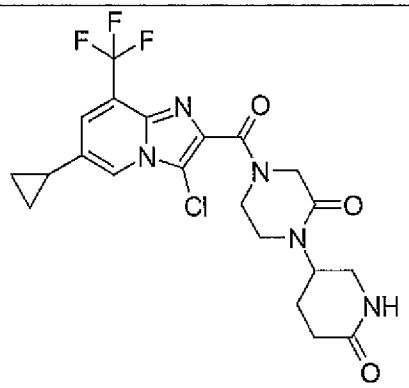
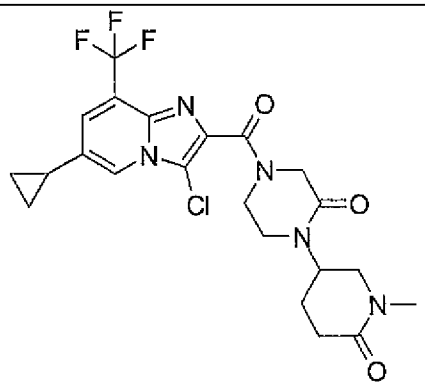
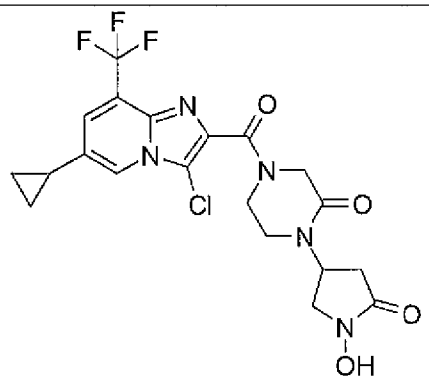
Compound Number	Structure
262	
263	
264	

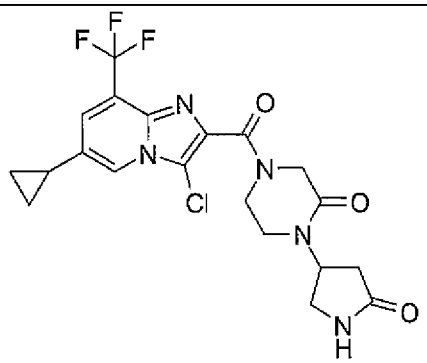
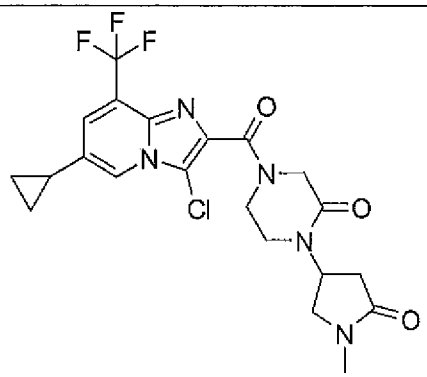
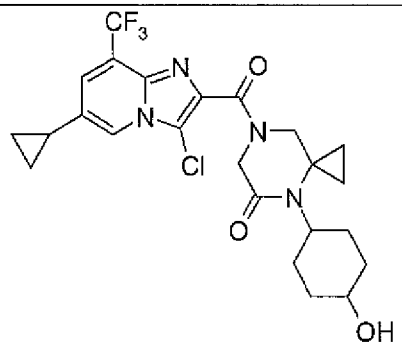
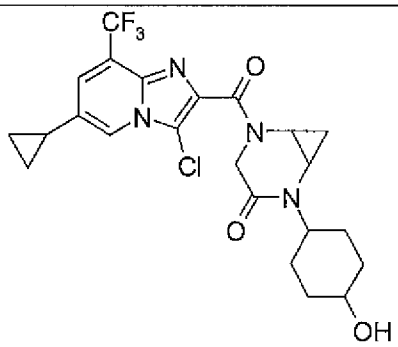
265	
266	
267	
268	

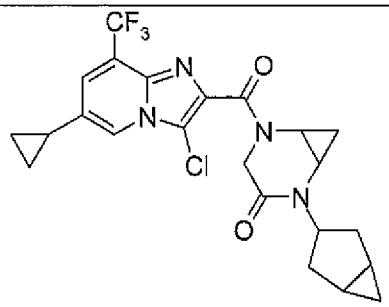
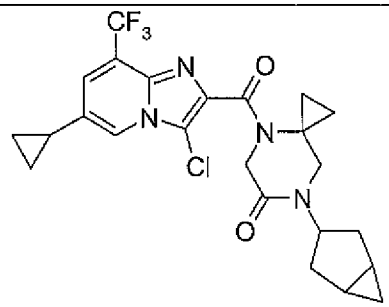
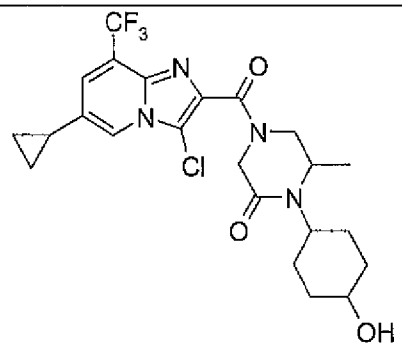
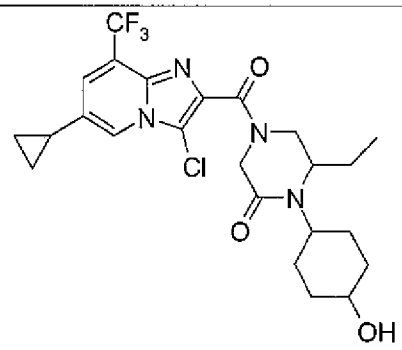
269	
270	
271	
272	

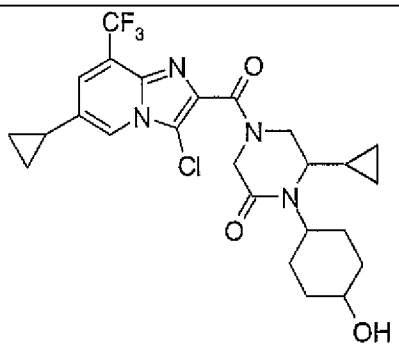
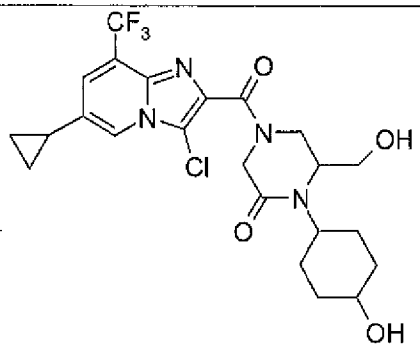
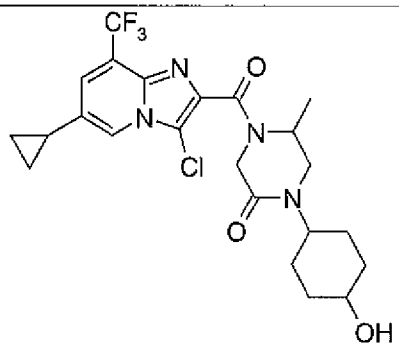
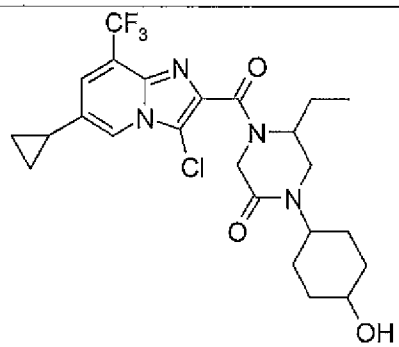
273	
274	
275	
276	

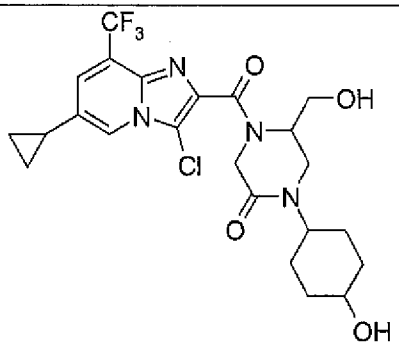
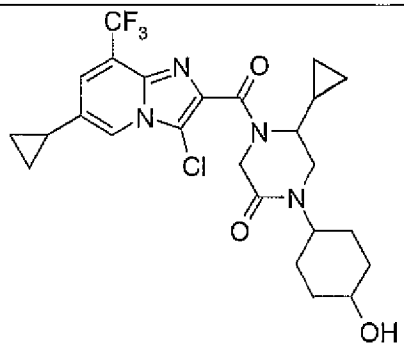
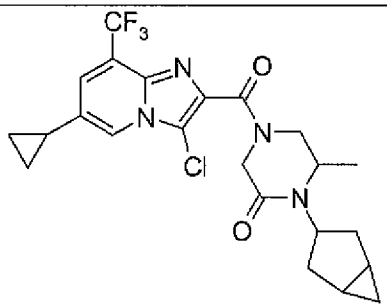
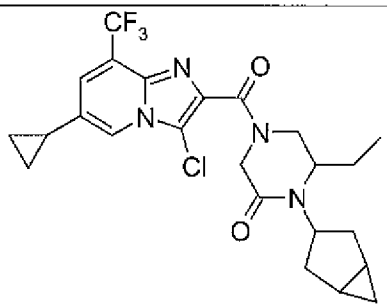
277	
278	
279	
280	

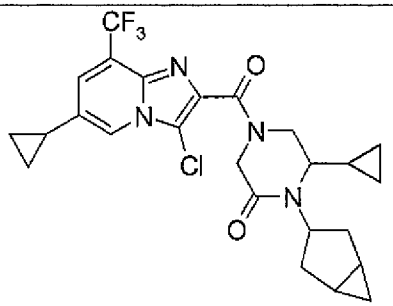
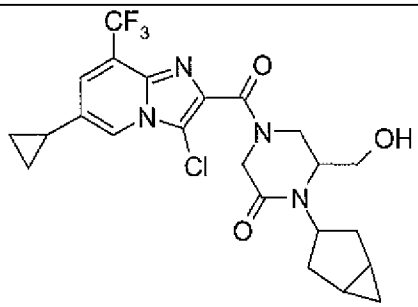
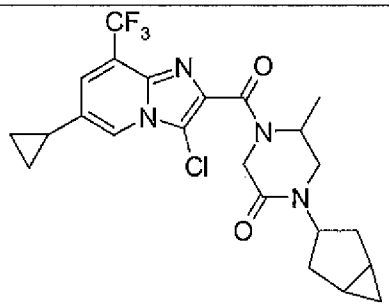
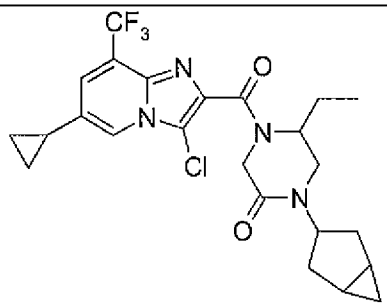
281	
282	
283	
284	

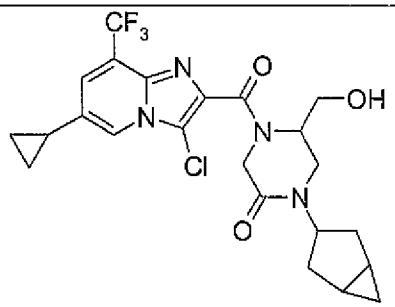
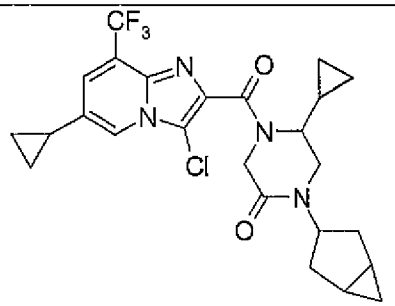
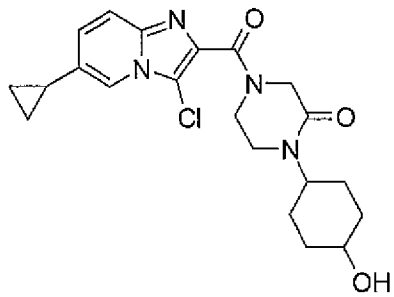
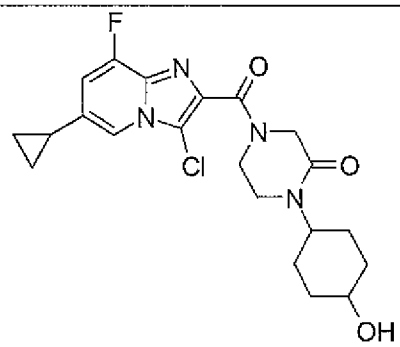
285	
286	
287	
288	

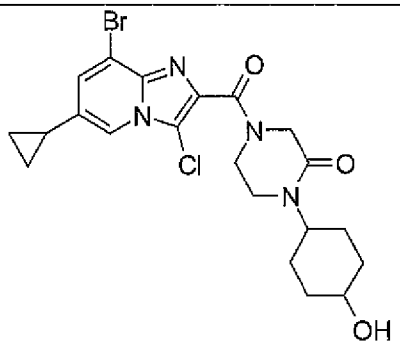
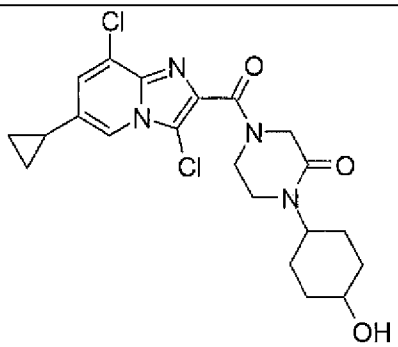
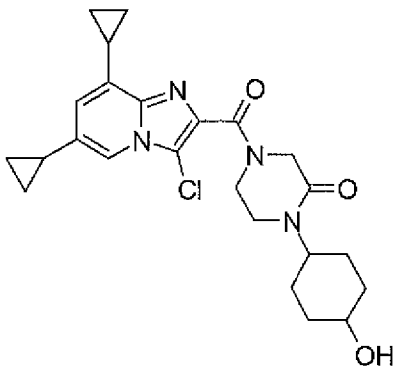
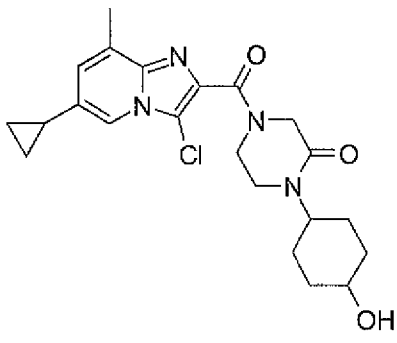
289	
290	
291	
292	

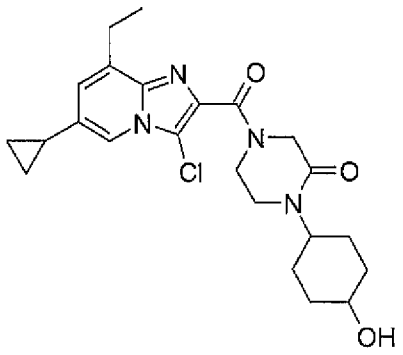
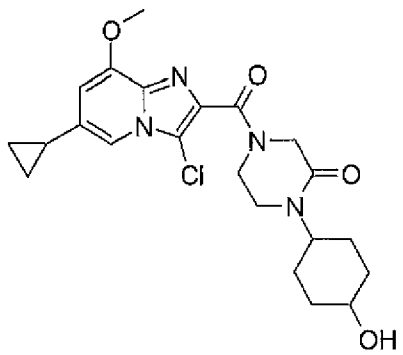
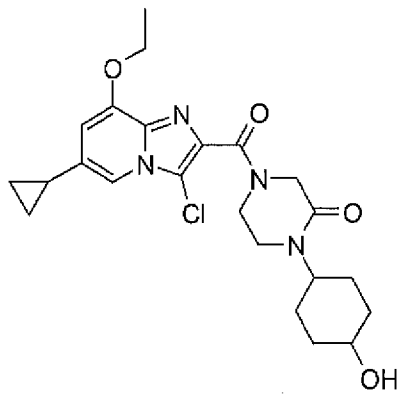
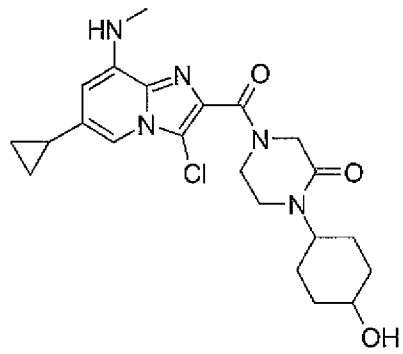
293	
294	
295	
296	

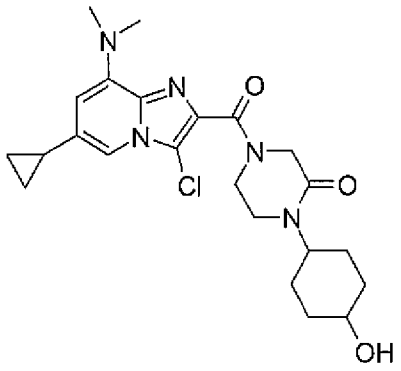
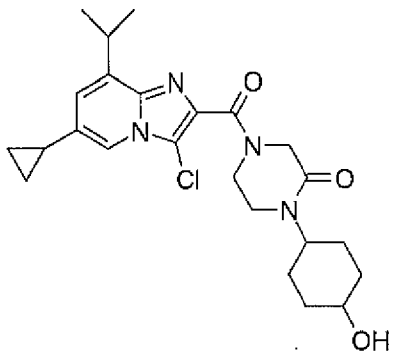
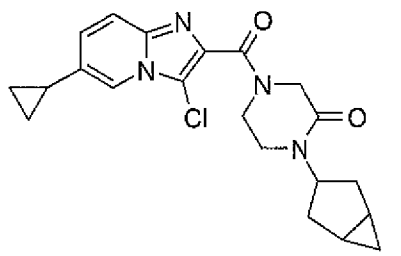
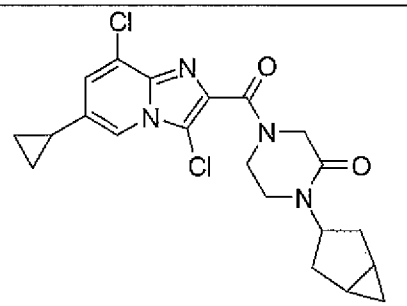
297	
298	
299	
300	

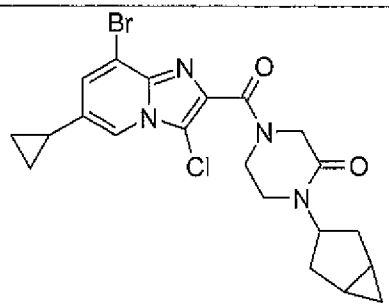
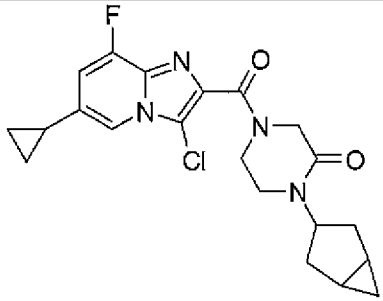
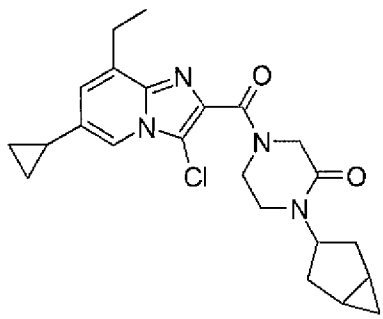
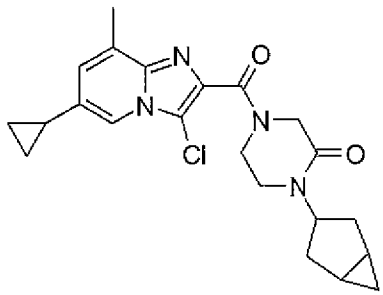
301	
302	
303	
304	

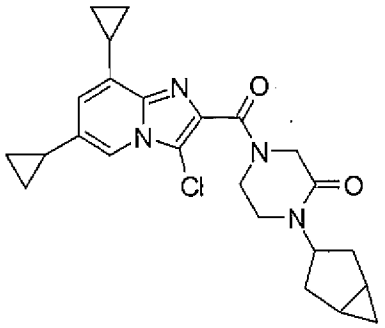
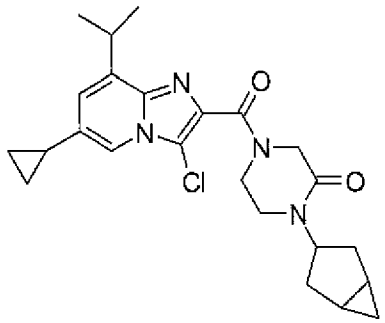
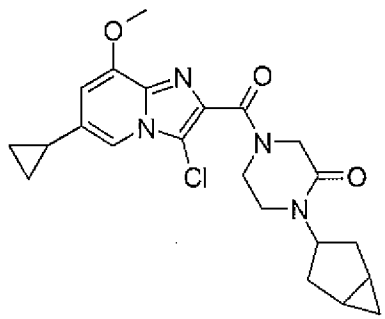
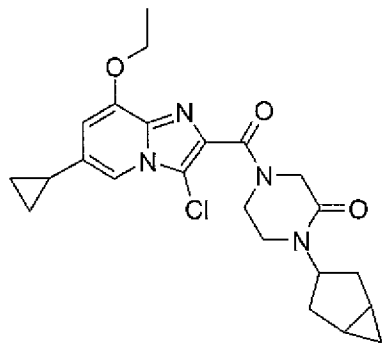
305	
306	
307	
308	

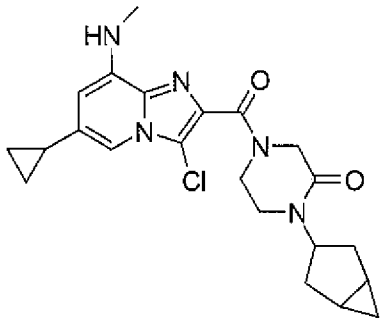
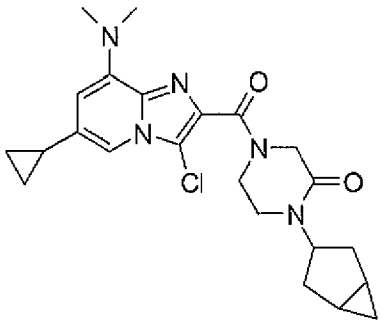
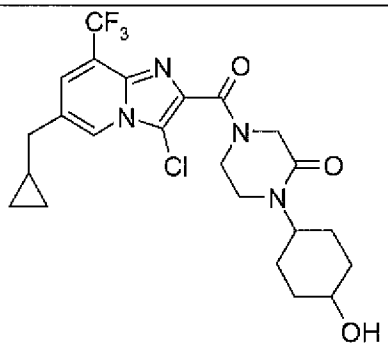
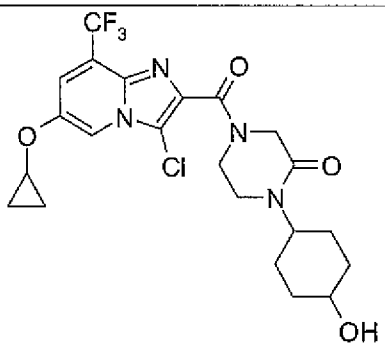
309	
310	
311	
312	

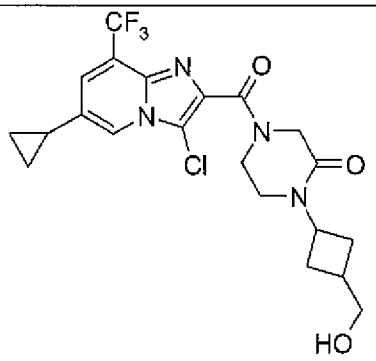
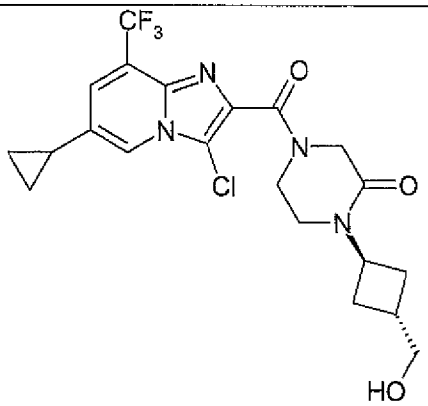
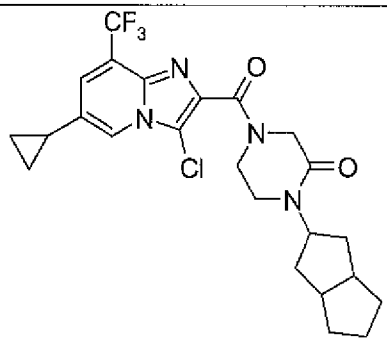
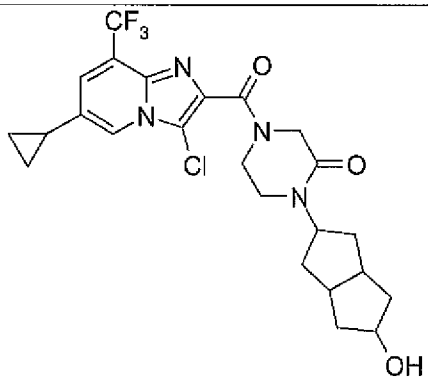
313	
314	
315	
316	

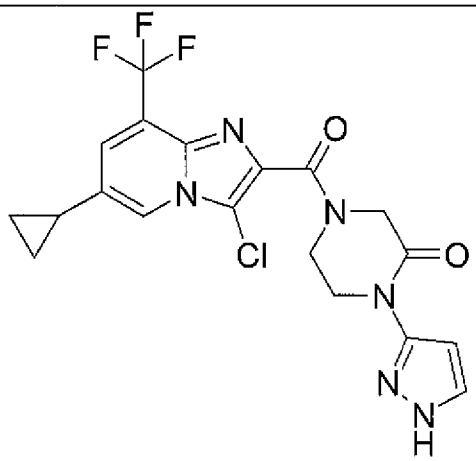
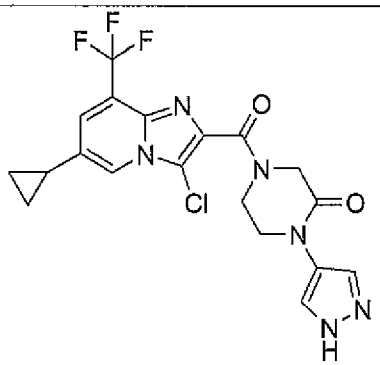
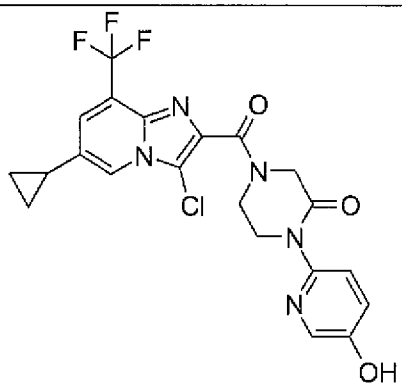
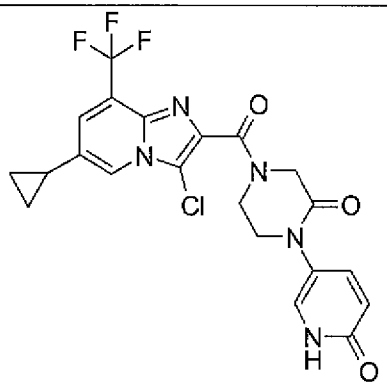
317	
318	
319	
320	

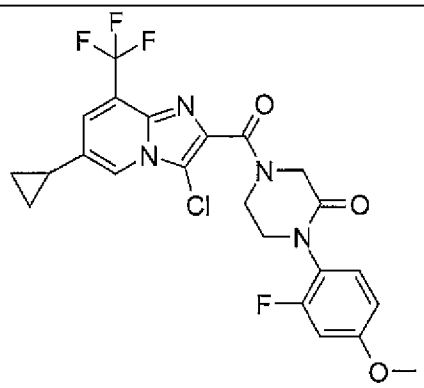
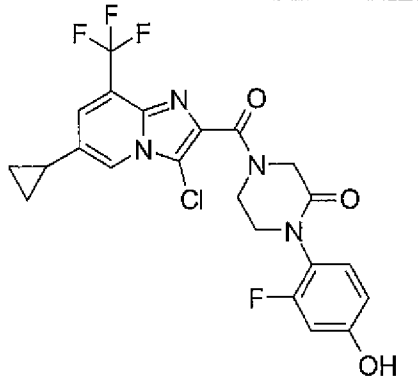
321	
322	
323	
324	

325	
326	
327	
328	

329	
330	
331	
332	

333	
334	
335	
336	

337	
338	
339	
340	

341	
342	

[00121] The compounds of Table 2 may be synthesized according to the following synthetic methods, schemes, and the Examples.

Synthetic Methods

[00122] The methods of synthesis for the provided chemical entities employ readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given; other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

[00123] Additionally, the methods of this invention may employ protecting groups which prevent certain functional groups from undergoing undesired reactions. Suitable protecting groups for various functional groups as well as suitable conditions for protecting and deprotecting particular functional groups are well known in the art. For example, numerous protecting groups are described in T. W. Greene and G. M. Wuts, Protecting Groups in Organic Synthesis, Third Edition, Wiley, New York, 1999, and references cited therein.

[00124] Furthermore, the provided chemical entities may contain one or more chiral centers and such compounds can be prepared or isolated as pure stereoisomers, i.e., as individual enantiomers or diastereomers, or as stereoisomer-enriched mixtures. All such stereoisomers (and enriched mixtures) are included within the scope of this specification, unless otherwise indicated. Pure stereoisomers (or enriched mixtures) may be prepared using, for example, optically active starting materials or stereoselective reagents well-known in the art. Alternatively, racemic mixtures of such compounds can be separated using, for example, chiral column chromatography, chiral resolving agents and the like.

[00125] The starting materials for the following reactions are generally known compounds or can be prepared by known procedures or obvious modifications thereof. For example, many of the starting materials are available from commercial suppliers such as Aldrich Chemical Co. (Milwaukee, Wisconsin, USA), Bachem (Torrance, California, USA), Emka-Chemce or Sigma (St. Louis, Missouri, USA). Others may be prepared by procedures, or obvious modifications thereof, described in standard reference texts such as Fieser and Fieser's Reagents for Organic Synthesis, Volumes 1-15 (John Wiley and Sons, 1991), Rodd's Chemistry of Carbon Compounds, Volumes 1-5 and Supplementals (Elsevier Science Publishers, 1989), Organic Reactions, Volumes 1-40 (John Wiley and Sons, 1991), March's Advanced Organic Chemistry, (John Wiley and Sons, 4th Edition), and Larock's Comprehensive Organic Transformations (VCH Publishers Inc., 1989).

[00126] Unless specified to the contrary, the reactions described herein take place at atmospheric pressure, generally within a temperature range from -78 °C to 200 °C. Further, except as employed in the Examples or as otherwise specified, reaction times and conditions are intended to be approximate, *e.g.*, taking place at about atmospheric pressure within a temperature range of about -78 °C to about 110 °C over a period of about 1 to about 24 hours; reactions left to run overnight average a period of about 16 hours.

[00127] The terms "solvent," "organic solvent," and "inert solvent" each mean a solvent inert under the conditions of the reaction being described in conjunction therewith, including, for example, benzene, toluene, acetonitrile, tetrahydrofuranyl ("THF"), dimethylformamide ("DMF"), chloroform, methylene chloride (or dichloromethane), diethyl ether, methanol, N-methylpyrrolidone ("NMP"), pyridine and the like.

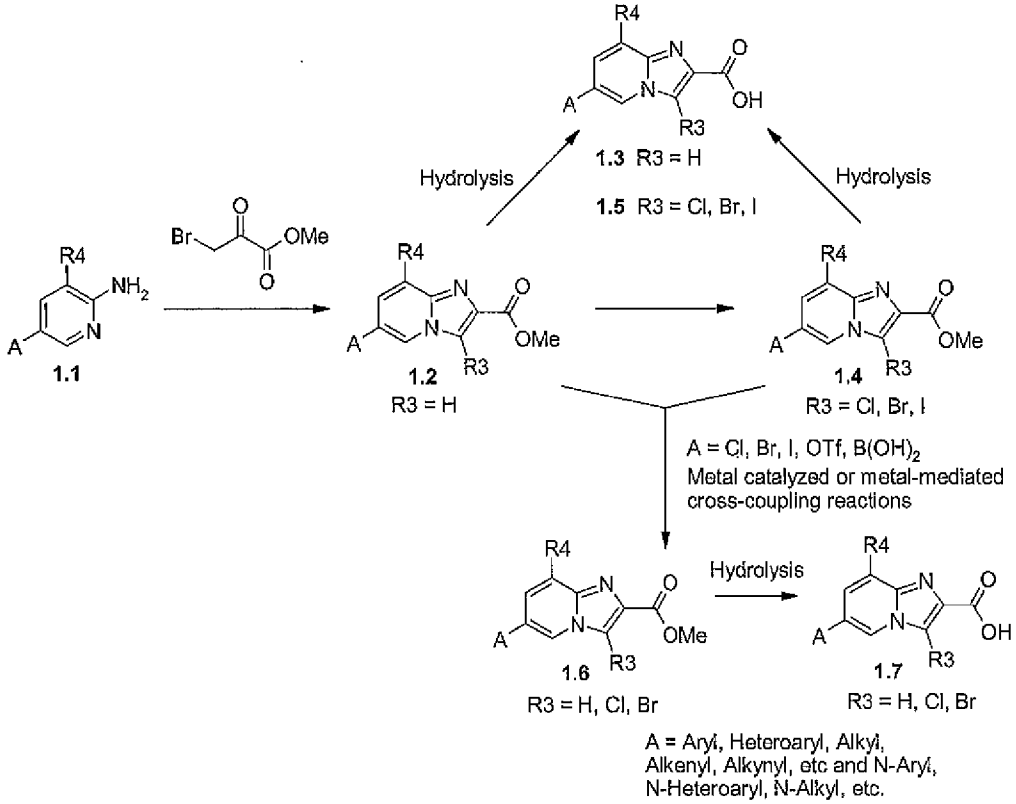
[00128] Isolation and purification of the chemical entities and intermediates described herein can be effected, if desired, by any suitable separation or purification procedure such as, for example, filtration, extraction, crystallization, column chromatography, thin-layer chromatography or thick-layer chromatography, or a combination of these procedures. Specific illustrations of suitable separation and isolation

procedures can be had by reference to the examples herein below. However, other equivalent separation or isolation procedures can also be used.

[00129] When desired, the (R)- and (S)-isomers may be resolved by methods known to those skilled in the art, for example by formation of diastereoisomeric salts or complexes which may be separated, for example, by crystallization; *via* formation of diastereoisomeric derivatives which may be separated, for example, by crystallization, gas-liquid or liquid chromatography; selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. Alternatively, a specific enantiomer may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer to the other by asymmetric transformation.

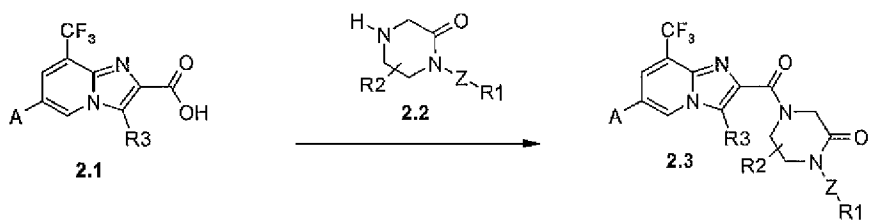
[00130] Scheme 1 shows a representative general synthesis of certain imidazo[1,2-*a*]pyridine-2-carboxylic acids (see, for example, WO09023179A2). Substituted 2-aminopyridine **1.1** can be cyclized with methyl bromopyruvate to afford the substituted imidazo[1,2-*a*]pyridine-2-carboxylic methyl ester **1.2**, which upon saponification can give the desired carboxylic acid **1.3**. Halogens (such as Cl, Br, I) can be introduced at R^3 by treating intermediate **1.2** with halogenating agents (such as NCS, NBS, or NIS) to yield compounds such as **1.4**, which upon saponification of the ester can give the corresponding carboxylic acids **1.5**. Esters **1.2** or **1.4** where A = Cl, Br, I, OTf, $B(OH)_2$ for example can undergo metal-catalyzed or metal-mediated cross-coupling reactions (including but not limited to Suzuki, Stille, Sonogashira, Negishi, and Buchwald-Hartwig reactions) to introduce new groups at position A (intermediate **1.6**) and subsequent saponification can yield the substituted acids **1.7**.

Scheme 1



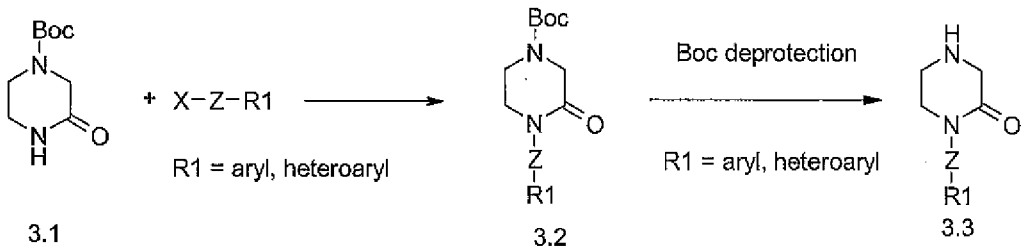
[00131] Scheme 2 shows that certain substituted imidazo[1,2-*a*]pyridine-2-carboxylic acids **2.1** can undergo amide formation with substituted 2-piperazinones **2.2** utilising standard coupling reagents such as, but not limited to, HATU ("2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate") HBTU ("O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate"), PyBrOP ("Bromotripyrrolidinophosphonium hexafluorophosphate, EDC/HOBt (EDC – "*N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide"; HOBt – "1-Hydroxybenzotriazole") to give the amides **2.3**. In addition, the carboxylic acid can first be converted to acid chloride via treatment with oxalyl chloride or thionyl chloride. Subsequent addition of a substituted 2-piperazinone can yield the corresponding amide.

Scheme 2



[00132] The general routes to prepare the amine fragments are depicted in Schemes 3-7. Substituted N-aryl or N-heteroaryl piperazinones can be prepared by metal-catalyzed or metal-mediated C-N cross-coupling of aryl halides or heteroaryl halides as depicted in Scheme 3 (see: *Ber. Dtsch. Chem. Ges.* **1906**, *39*, 1691; *J. Am. Chem. Soc.* **2002**, *124*, 7421). 1-Boc-3-oxopiperazine **3.1** can react with aryl iodide or aryl bromide in the presence of copper salt such as copper(I) iodide, copper (I) oxide and in the presence of a suitable base such as potassium carbonate, potassium phosphate, cesium carbonate or the like. This reaction can be carried out in solvents such as DMF, 1,4-dioxane, toluene, NMP, and the like and preferably in the presence of a diamine such as ethylenediamine, N,N'dimethylethylenediamine, or the like. This reaction is usually carried out at high temperatures, preferably 100-160°C and can also be performed with microwave irradiation. The resulting Boc-protected N-aryl or N-heteroaryl piperazinones **3.2** can be deprotected with acids such hydrogen chloride or trifluoroacetic acid or the like and in suitable solvents such as DCM, 1,4-dioxane, ether or the like to give the 1-substituted-2-piperazinone **3.3.** This chemistry can also be carried out with other protecting groups such as N-benzyl, N-tosyl, and the like.

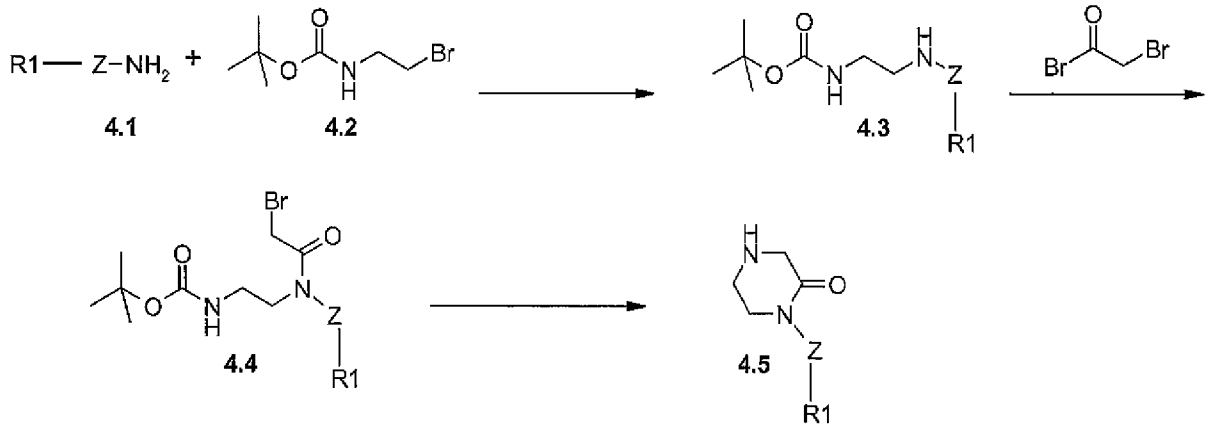
Scheme 3



3.1 3.2 3.3

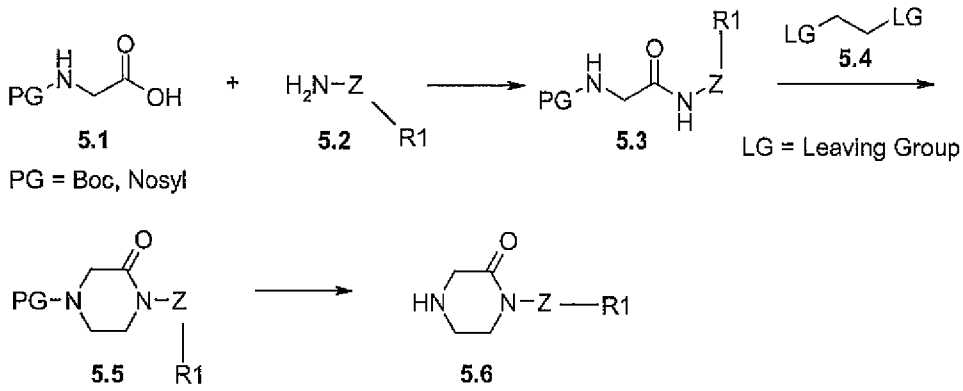
[00133] Scheme 4 shows that a number of synthetic routes can be employed to prepare certain 1-alkyl-2-piperazinones. In one approach (Scheme 4), a primary amine **4.1** can be treated with 1,1-dimethylethyl (2-bromoethyl)carbamate **4.2** to give intermediate **4.3.** The Boc-protected ethylenediamine **4.3** can be acylated with bromo acetylbromide to afford intermediate **4.4.** The Boc-group can be removed with acids such hydrogen chloride or trifluoroacetic acid or the like and in suitable solvents such as DCM, 1,4-dioxane, ether or the like and subsequent ring-closure (typically in the presence of a base) can yield the 1-substituted-2-piperazinone **4.5.**

Scheme 4



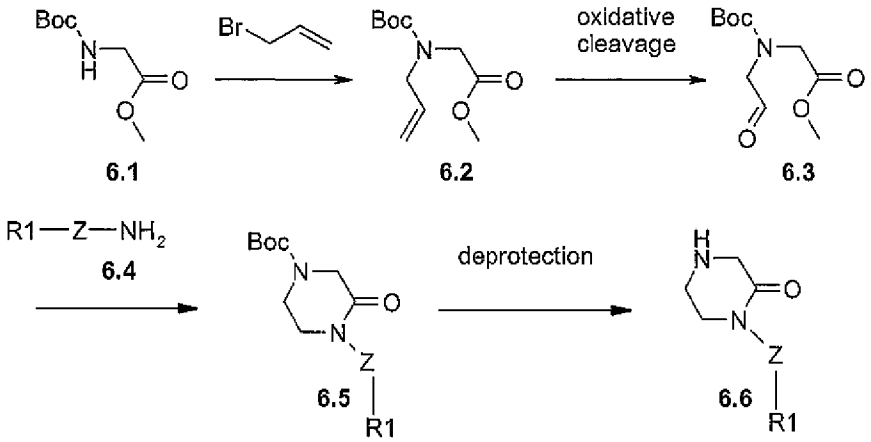
[00134] Scheme 5 shows that 1-substituted-2-piperazinone derivatives can alternatively be prepared from protected glycine (see: *J. Org. Chem.* **1997**, *62*, 1016; *Tetrahedron: Asymmetry*, **2008**, *19,* 1689). A group such as Boc (tert-butyloxycarbonyl), Nosyl (4-nitrobenzenesulfonyl) or the like can be used as a protecting group for glycine. Coupling of protected glycine **5.1** with an amine **5.2** can be performed under standard amide bond coupling conditions such as HATU, EDC/HOBt, DMTMM, or the like with a suitable base such as N,N-diisopropylethylamine, N-methylmorpholine, triethylamine or the like and in solvents such as DMF, THF or the like to afford intermediate **5.3.** Cyclization can be carried out with 1,2-dielectrophiles of ethylene **5.4** (where LG = leaving group) such as ethylene bistriflate, ethylene dibromide or the like in the presence of a base such as potassium carbonate, sodium hydride or the like and in solvents such as DMF, THF, acetonitrile or the like to give the protected piperazinone **5.5.** The reaction can be carried out at ambient temperature or with heating at 50 °C. Substituted piperazinones with Boc protecting group can be deprotected with hydrogen chloride or trifluoroacetic acid in solvents such as DCM, 1,4-dioxane the like to afford the 1-sustitutute-2-piperazinone **5.6**. Substituted piperazinones with Nosyl protecting group can be removed with thiophenol in the presence of a base such as potassium carbonate in solvents such as acetonitrile or DMF or the like and at temperatures around 50 °C to afford the 1-sustitutute-2-piperazinone **5.6**. The piperazinones can be stored as the free base or converted to a salt when treated with an acid (*e.g.*, HCl).

Scheme 5



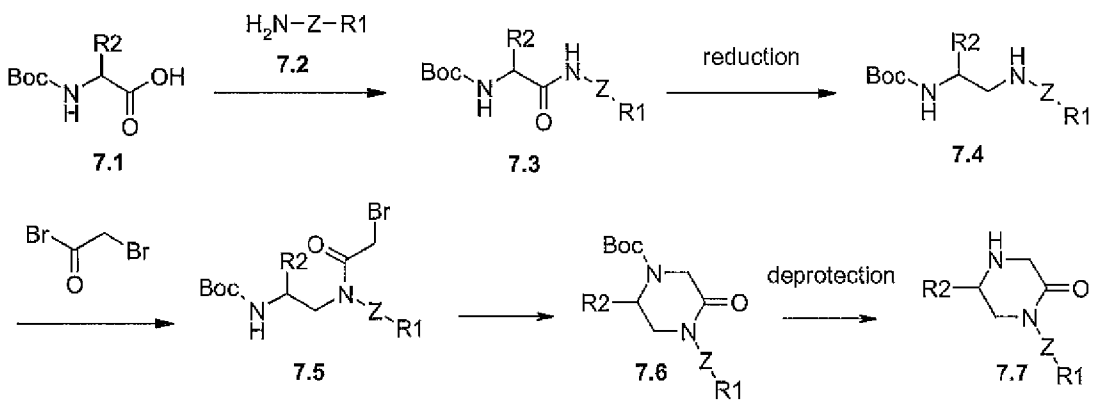
[00135] Scheme 6 shows that certain substituted piperazinone derivatives can also be prepared from methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}glycinate (see *Bioorg. Med. Chem. Lett.* **2007**, 2092). Alkylation of **6.1** with allyl bromide can be accomplished with a suitable base, such as sodium hydride, cesium carbonate, or the like in a solvent such as dimethylformamide, tetrahydrofuranyl, or the like. The olefin of **6.2** can be oxidatively cleaved with ozone in a suitable solvent such as methanol, chloroform, and preferably at reduced temperatures (-78 °C) to afford the aldehyde **6.3**. Oxidative cleavage of the olefin can also be performed using catalytic OsO_4 with $NaIO_4$ in a suitable solvent. Aldehyde **6.3** can undergo reductive amination with an amine **6.4** in a suitable solvent such as methanol, 1,2-dichloromethane, or the like with or without a water scavenging reagent such as sodium sulfate, molecular sieves, or the like and with a reducing agent such as sodium borohydride, sodium cyanoborohydride, sodium triacetoxyborohydride. The resulting amino ester can subsequently cyclize in the presence of a suitable base such as sodium methoxide, sodium hydride, 1,8-diazabicyclo(5.4.0)undec-7-ene, or the like in a suitable solvent such as methanol, tetrahydrofuranyl, or the like to give the protected 2-piperazinone **6.5**. Boc-deprotection can be achieved with hydrogen chloride or trifluoroacetic acid in solvents such as dichloromethane, 1,4-dioxane or the like to give the 1-substituted-2-piperazinone **6.6**.

Scheme 6



[00136] Scheme 7 shows that certain piperazinone derivatives can be prepared from a Boc-protected amino acid (see *J. Med. Chem.* **1999**, *42*, 3779). A Boc-protected amino acid **7.1** can undergo coupling with an amine **7.2** utilising standard coupling reagents such as HATU, HBTU, EDC/HOBt, or the like to give the amide **7.3.** The amide carbonyl of intermediate **7.3** can be reduced to the corresponding amine **7.4** with reducing agents such as sodium bis(2-methoxyethoxy)aluminumhydride, lithium aluminum hydride, or the like. The amine **7.4** can be acylated with bromoacetyl bromide and the resulting intermediate **7.5** can cyclize in the presence of an appropriate base such as cesium carbonate, sodium hydride, or the like in a suitable solvent such as dimethylformamide, tetrahydrofuranyl, or the like, with or without an iodide source (NaI, KI) to afford the protected piperazinones **7.6.** Deprotection of the Boc-group can be accomplished under acidic conditions such as hydrogen chloride, trifluoroacetic acid, or the like in solvents such as dichloromethane, 1,4-dioxane or the like to yield the substituted-2-piperazinones **7.7**.

Scheme 7



[00137] Additional synthetic protocols useful in making the synthetic intermediates for compounds according to Formula (I) may be found in PCT Published Application No. WO2009/023179 filed on August 8, 2008 and entitled "Certain Nitrogen Containing Bicyclic Chemical Entities for Treating Viral Infections."

EXAMPLES

[00138] The following examples serve to more fully describe the manner of making and using the above-described invention. It is understood that these examples in no way serve to limit the true scope of the invention, but rather are presented for illustrative purposes. In the examples below and the synthetic schemes above, the following abbreviations have the following meanings. If an abbreviation is not defined, it has its generally accepted meaning.

aq.	=	aqueous
µL	=	microliters
µM	=	micromolar
NMR	=	nuclear magnetic resonance
boc	=	tert-butoxycarbonyl
br	=	broad
Cbz	=	benzyloxycarbonyl
d	=	doublet
δ	=	chemical shift
°C	=	degrees celcius
DCM	=	dichloromethane
dd	=	doublet of doublets
DMEM	=	Dulbeco's Modified Eagle's Medium
DMF	=	N,N-dimethylformamide
DMSO	=	dimethylsulfoxide
EtOAc	=	ethyl acetate
g	=	gram
h or hr	=	hours
HCV	=	hepatitus C virus
HPLC	=	high performance liquid chromatography
Hz	=	hertz
IU	=	International Units
IC_{50}	=	inhibitory concentration at 50% inhibition

J	=	coupling constant (given in Hz unless otherwise indicated)
m	=	multiplet
M	=	molar
$M+H^+$	=	parent mass spectrum peak plus H^+
mg	=	milligram
mL	=	milliliter
mM	=	millimolar
mmol	=	millimole
MS	=	mass spectrum
nm	=	nanomolar
ppm	=	parts per million
q.s.	=	sufficient amount
s	=	singlet
sat.	=	saturated
t	=	triplet
TFA	=	trifluoroacetic acid

EXAMPLE 1

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone

(Compound 1)

Step A

5-bromo-3-(trifluoromethyl)-2-pyridinamine

[00139] To a solution of 2-amino-3-trifluoromethylpyridine (100 g, 0.62 mol) in DMF (500 mL) was added a solution of NBS (110 g, 0.62 mol) in DMF (500 mL) dropwise at room temperature. The solution was stirred at room temperature for 2 hours and then concentrated to 300 mL. The residue was added slowly to the beaker containing a mixture of 5% aqueous $NaHSO_3$ and H_2O (3 L, 1:10 v/v). The precipitate was filtered, washed with H_2O (2 x 500 mL) and dried under vacuum to give the title compound (120 g, 85%) as a light brown solid.

Step B

Methyl 6-bromo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00140] A solution of 5-bromo-3-(trifluoromethyl)-2-pyridinamine (100 g, 0.42 mol) and methyl 3-bromopyruvate (180 g, 1 mol) was heated at 50°C for 3 hours. The solvent was evaporated and the residue was poured slowly into ice water (3 L) to give a

precipitate. The suspension was stirred vigorously for 1 hour. The precipitate was filtered off, washed with H_2O (2 x 500 mL) and dried under vacuum to give the title compound (119 g, 82%) as a yellow powder.

Step C

Methyl 6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00141] DMF (155 mL) was added under argon to a mixture of methyl 6-bromo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (5 g, 15.47 mmol), 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyrazole-1-carboxylic acid tert-butyl ester (22.75 g, 77.40 mmol), tetrakis(triphenylphosphine)palladium(0) (1.79 g, 1.55 mmol), and cesium carbonate (50.4 g, 155 mmol). The reaction was heated to 80 °C for 20 minutes. After cooling in a water bath, the solvent was removed *in-vacuo*. To the resulting residue was added H_2O and diethyl ether and the mixture was sonicated for 30 minutes. The precipitate was filtered and washed successively with H_2O and diethyl ether, and then air dried to obtain the title compound (5.61 g, 90%) as a beige solid. ES-LCMS m/z: 410.9 (M+1).

Step D

Methyl 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00142] N-chlorosuccinimide (1.78 g, 13.4 mmol) was added to a suspension of methyl 6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1*H*-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (5 g, 12.2 mmol) in DMF (61 mL) at room temperature. The reaction was heated to 50 °C for 4 hours and then cooled to room temperature. After 18 hours, the reaction was quenched with 5 % aqueous $NaHSO_3$. The precipitate was filtered and washed successively with H_2O and diethyl ether, and then air dried to obtain the title compound (4.73 g, 87%) as a beige solid. ES-LCMS m/z: 445.0 (M+1).

Step E

3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00143] An aqueous solution of NaOH (1 M, 43 mL) was added slowly to a solution of methyl 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1*H*-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (4.732 g, 10.65 mmol) in THF and DMF (5:1 v/v, 146 mL) at room temperature. After 4 hours the pH was adjusted to 4 with aqueous citric acid (1 M). The residual THF was removed and the resulting precipitate was filtered and washed successively with H_2O and diethyl ether, and then air dried to obtain the title compound (3.04 g, 87%) as a beige solid. ES-LCMS m/z: 331.0 (M+1).

Step F

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone

[00144] HATU (207 mg, 0.544 mmol) was added to a solution of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.150 g, 0.454 mmol), 1-phenyl-2-piperazinone trifluoroacetate (Chembridge Corporation) (0.138 g, 0.454 mmol) and DIPEA (0.174 mL, 0.998 mmol) in DMF (1.5 mL). The mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with saturated sodium bicarbonate and water. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford 0.029 g (13%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.77 - 8.98 (m, 1 H) 8.59 (br. s., 1 H) 8.24 (br. s., 2 H) 7.32 - 7.53 (m, 4 H) 7.19 - 7.36 (m, 1 H) 4.69 (s, 1 H) 4.42 (s, 1 H) 4.23 (t, 1 H) 4.05 (t, 1 H) 3.85 (m, 2 H). ES-LCMS m/z: 489 (M+1).

EXAMPLE 2

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone

(Compound 2)

[00145] HATU (0.207 g, 0.544 mmol) was added to a solution of 3-chloro-6-(1*H*-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.150 g, 0.454 mmol), 1-methyl-2-piperazinone hydrochloride (0.068 g, 0.454 mmol) and DIPEA (0.174 mL, 0.998 mmol) in DMF (1.5 mL). The mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford 0.020 g (9%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.74 (s, 1 H) 8.18 - 8.49 (m, 2 H) 7.94 - 8.18 (m, 1 H) 4.10 - 4.63 (m, 2 H) 3.81 - 4.10 (m, 2 H) 3.39 (t, *J*=5.40 Hz, 2 H) 2.86 (s, 3 H). ES-LCMS m/z: 427 (M+1).

EXAMPLE 3

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone

(Compound 3)

Step A

Methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00146] A solution of methyl 6-bromo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (119 g, 0.37 mol) and NCS (51.5 g, 0.39 mol) in DMF (1 L) was heated at 50 °C for 1 hour. The mixture was diluted with EtOAc (1.5 L) and washed with H_2O (900 mL). The aqueous layer was extracted with EtOAc (2 x 300 mL). The combined organic extracts were washed successively with 5% aqueous $NaHSO_3$ (500 mL), saturated aqueous $NaHCO_3$ (500 mL), brine (500 mL) and dried over with anhydrous $MgSO_4$. After the removal of the organic solvent, the crude product was washed with Et_2O (2 x 300 mL) to give the title compound (120 g, 91.5%) as a yellow powder.

Step B

3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00147] To a solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (120 g, 0.34 mol) and furan-3-boronic acid (37.8 g, 0.34 mol) in acetonitrile (1 L), $Pd(dppf)Cl_2$ (8 g, 10.9 mmol) and 3M aqueous K_3PO_4 (300 mL) were added. After degassing and refilling with nitrogen (three times), the reaction mixture was heated under reflux for 2 hours. Then, after the addition of another batch of 3M aqueous K_3PO_4 (600 mL), the mixture was heated at reflux overnight. After the removal of solvents, H_2O (800 mL) was added and extracted with EtOAc (2 x 600 mL). The aqueous layer was acidified with concentrated HCl to pH 2~3 and then extracted with EtOAc (3 x 800 mL). The combined organic solution was dried over anhydrous $MgSO_4$. After concentration, the residue was washed with Et_2O (2 x 300 mL) to give the title compound (68 g, 61 %) as a brown solid. ^1H NMR (DMSO-d_6) δ 7.31 (s, 1H), 7.84 (s, 1H), 8.21 (s, 1H), 8.56 (s, 1H), 8.80 (s, 1H), 13.40 (s, 1H); ES-LCMS m/z: 331.0 (M+1).

Step C

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone

[00148] HATU (0.138 g, 0.363 mmol) was added to a solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-phenyl-2-piperazinone trifluoroacetate (Chembridge Corporation) (0.092 g, 0.302 mmol) and DIPEA (0.106 mL, 0.605 mmol) in DMF (1.5 mL). The mixture was stirred at room temperature for one hour. The reaction mixture was diluted with ethyl acetate and washed with saturated sodium bicarbonate and water. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford 0.061 g (41%) of the title compound as a white solid. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 8.84 (br. s., 1 H) 8.57 (br. s., 1 H) 8.23 (br. s., 1 H) 7.85 (br. s., 1 H) 7.04 - 7.53 (m, 6 H) 4.66 (br. s., 1 H) 4.41 (br. s., 1 H) 3.89 - 4.31 (m, 2 H) 3.82 (br. s., 2 H). ES-LCMS m/z: 489 (M+1).

EXAMPLE 4

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 4)

[00149] HATU (0.138 g, 0.363 mmol) was added to a solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 2-piperazinone hydrochloride (0.041 g, 0.302 mmol) and DIPEA (0.11 mL, 0.605 mmol) in DMF (1.5 mL). The mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to give 0.009 g (7%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.84 (br. s., 1 H) 8.58 (br. s., 1 H) 8.03 - 8.36 (m, 2 H) 7.85 (br. s., 1 H) 7.34 (br. s., 1 H) 4.38 (br. s., 1 H) 4.18 (br. s., 1 H) 3.65 - 4.02 (m, 2 H) 3.28 (m, 2H). ES-LCMS m/z: 412 (M+).

EXAMPLE 5

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone

(Compound 5)

[00150] HATU (0.138 g, 0.363 mmol) was added to a mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-methyl-2-piperazinone hydrochloride (0.045 g, 0.302 mmol) and DIPEA (0.11 mL, 0.605 mmol) in DMF (1.5 mL). The mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to afford 0.055 g of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.83 (d, *J*=6.96 Hz, 1 H) 8.58 (s, 1 H) 8.23 (s, 1 H) 7.85 (s, 1 H) 7.34 (s, 1 H) 4.46 (s, 1 H) 4.23 (s, 1 H) 4.05 (br. s., 1 H) 3.93 (br. s., 1 H) 3.43 (m, 2 H) 2.91 (s, 3 H). ES-LCMS m/z: 426 (M+).

EXAMPLE 6

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 6)

[00151] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.077 g, 0.302 mmol), DIPEA (0.16 mL, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford 0.043 g (28%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (d, J=5.13 Hz, 1 H) 8.59 (s, 1 H) 8.25 (s, 1 H) 7.86 (s, 1 H) 7.60 (d, J=3.48 Hz, 1 H) 7.23 - 7.44 (m, 2 H) 4.91 (s, 1 H) 4.61 (s, 1 H) 4.27 (s, 3 H) 4.12 (d, 1 H). ES-LCMS m/z: 495 (M+).

EXAMPLE 7

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 7)

[00152] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-cyclohexyl-2-piperazinone trifluoroacetate (Chembridge Corporation) (0.089 g, 0.302 mmol), DIPEA (0.16 mL, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford 0.080 g of the title compound as a beige solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.83 (d, 1 H) 8.58 (s, 1 H) 8.23 (s, 1 H) 7.85 (s, 1 H) 7.34 (s, 1 H) 4.46 (s, 1 H) 4.14 - 4.37 (m, 3 H) 4.02 (t, 1 H) 3.85 (t, 1 H) 1.77 (m, 2 H) 1.50 - 1.68 (m, 3 H) 1.39 - 1.52 (m, 2 H) 1.16 - 1.39 (m, 2 H) 0.97 - 1.16 (m, 2 H). ES-LCMS m/z: 494 (M+).

EXAMPLE 8

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone

(Compound 8)

Step A

1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate

[00153] Di-tert-butyl dicarbonate (3.92 g, 17.98 mmol) was added to a suspension of 2-piperazinone (1.50 g, 14.98 mmol) in dichloromethane (15 mL). The mixture was

stirred at room temperature for 5 hours. The solvent was evaporated to afford 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (2.99 g, quantitative) as an off-white solid.

Step B

1,1-dimethylethyl 4-(3-fluorophenyl)-3-oxo-1-piperazinecarboxylate

[00154] A mixture of 1,1-dimethylethyl-3-oxo-1-piperazinecarboxylate (0.549 g, 2.74 mmol), 1-bromo-3-fluorobenzene (0.25 mL, 2.286 mmol), copper(I) iodide (0.022 g, 0.114 mmol), potassium carbonate (0.632 g, 4.57 mmol) and N,N'-dimethyl-1,2-ethanediamine (0.025 mL, 0.229 mmol) in toluene (5 mL) was heated at reflux under nitrogen overnight. After cooling to room temperature the reaction mixture was filtered through silica gel eluting with DCM:EtOAc/1:1. The filtrate was concentrated and the residue was purified by silica gel chromatography (hexanes/EtOAc) to afford the title compound (0.473 g, 70%) as a white solid. ES-LCMS m/z: 295 (M+1).

Step C

1-(3-fluorophenyl)-2-piperazinone hydrochloride

[00155] A mixture of 1,1-dimethylethyl 4-(3-fluorophenyl)-3-oxo-1-piperazinecarboxylate (0.445 g, 1.512 mmol) and hydrogen chloride (4 N in 1,4-dioxane) (2 mL, 65.8 mmol) was stirred at room temperature for one hour. The solvent was evaporated to afford the title compound (0.358 g, quantitative) as a white solid.

Step D

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone

[00156] A mixture of 3-chloro-6-(1*H*-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(3-fluorophenyl)-2-piperazinone hydrochloride (0.070 g, 0.302 mmol), DIPEA (0.16 mL, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford the title compound (0.073 g, 47%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 13.21 (br. s., 1 H) 8.64 - 9.09 (m, 1 H) 8.37 - 8.72 (m, 1 H) 8.02 - 8.39 (m, 2 H) 6.68 - 7.71 (m, 4 H) 4.62 - 4.77 (m, 1 H) 4.31 - 4.50 (m, 1 H) 4.15 - 4.31 (m, 1 H) 3.94 - 4.10 (m, 1 H) 3.85 (br. s., 2 H). ES-LCMS m/z: 507 (M+1).

EXAMPLE 9

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone

(Compound 9)

[00157] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(3-fluorophenyl)-2-piperazinone hydrochloride (0.070 g, 0.302 mmol), DIPEA (0.16 mL, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford the title compound (0.067 g, 43%) as a beige solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.69 - 8.98 (m, 1 H) 8.57 (s, 1 H) 8.23 (s, 1 H) 7.85 (s, 1 H) 7.46 (d, 1 H) 7.19 - 7.40 (m, 3 H) 7.13 (d, 1 H) 4.69 (s, 1 H) 4.42 (s, 1 H) 4.22 (m, 1H) 4.04 (m, 1 H) 3.82 (m, 2 H). ES-LCMS m/z: 506 (M+).

EXAMPLE 10

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone

(Compound 10)

[00158] A mixture of 3-chloro-6-(1*H*-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(phenylmethyl)-2-piperazinone (0.057 g, 0.302 mmol), DIPEA (0.16 mL, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford the title compound (0.055 g, 36%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 13.01 - 13.42 (m, 1 H) 8.84 (s, 1 H) 8.40 - 8.70 (m, 1 H) 8.23 (d, 2 H) 7.17 - 7.49 (m, 5 H) 4.52 - 4.65 (m, 3 H) 4.35 (s, 1 H) 4.05 (m, 1 H) 3.92 (m., 1 H) 3.37 (m, 2 H). ES-LCMS m/z: 503 (M+1).

EXAMPLE 11

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone

(Compound 11)

[00159] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(phenylmethyl)-2-piperazinone (0.057 g, 0.302

mmol), DIPEA (0.16 mL, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) afforded the title compound (0.068 g, 44%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.71 - 9.05 (m, 1 H) 8.44 - 8.68 (m, 1 H) 8.23 (d, 1 H) 7.73 - 7.93 (m, 1 H) 7.09 - 7.52 (m, 6 H) 4.59 (d, 3 H) 4.21 - 4.46 (m, 1 H) 3.95 - 4.17 (m, 1 H) 3.77 - 3.98 (m, 1 H), 3.37 (m, 2H). ES-LCMS m/z: 503 (M+1).

EXAMPLE 12

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone

(Compound 12)

[00160] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.068 g, 0.205 mmol), 1-[2-(trifluoromethyl)phenyl]-2-piperazinone (0.050 g, 0.205 mmol), DIPEA (0.107 mL, 0.614 mmol) and HATU (0.093 g, 0.246 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford the title compound (0.058 g, 50%) a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.76 (s, 1 H) 8.45 (s, 1 H) 8.13 (s, 1 H) 7.67 - 7.88 (m, 3 H) 7.46 - 7.68 (m, 2 H) 7.21 (s, 1 H) 3.85 - 4.82 (m, 4 H) 3.67 - 3.87 (m, 1 H) 3.51 (m, 1 H). ES-LCMS m/z: 557 (M+1).

EXAMPLE 13

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone

(Compound 13)

[00161] A mixture of 3-chloro-6-(1*H*-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.067.7 g, 0.205 mmol), 1-[2-(trifluoromethyl)phenyl]-2-piperazinone (0.050 g, 0.205 mmol), DIPEA (0.11 mL, 0.614 mmol) and HATU (0.093 g, 0.246 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to afford the title compound (0.042 g, 35%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 13.12 (br. s., 1 H)

8.81 (s, 1 H) 8.39 - 8.65 (m, 1 H) 8.00 - 8.29 (m, 2 H) 7.67 - 7.91 (m, 2 H) 7.42 - 7.65 (m, 2 H) 4.48 - 4.81 (m, 1 H) 3.95 - 4.48 (m, 3 H) 3.63 - 3.93 (m, 1 H) 3.56 (br. s., 1 H). ES-LCMS m/z: 557 (M+1).

EXAMPLE 14

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone

(Compound 14)

Step A

1-(2-fluorophenyl)-2-piperazinone hydrochloride

[00162] A mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.200 g, 0.999 mmol), 1-bromo-2-fluorobenzene (0.146 g, 0.832 mmol), copper(I) iodide (0.0079 g, 0.042 mmol), potassium carbonate (0.230 g, 1.665 mmol) and N,N'-dimethyl-1,2-ethanediamine (0.009 mL, 0.083 mmol) in toluene (5 mL) was heated at reflux under nitrogen overnight. The reaction mixture was filtered through silica gel eluting with 1:1/DCM:EtOAc. The filtrate was evaporated and the residue was purified by silica gel chromatography (EtOAc:hexane) to afford 1,1-dimethylethyl 4-(2-fluorophenyl)-3-oxo-1-piperazinecarboxylate (0.189 g, 77%) as a white solid. Hydrogen chloride (4 N in 1,4-dioxane) (2 mL, 65.8 mmol) was added and the mixture was stirred at room temperature for one hour. The solvent was evaporated to give the title compound (0.125 g, 100%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.08 (br. s., 1 H) 7.40 - 7.49 (m, 2 H) 7.27 - 7.39 (m, 2 H) 3.92 (s, 2 H) 3.86 (t, *J*=5.40 Hz, 2 H) 3.50 - 3.57 (m, 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone

[00163] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.098 g, 0.264 mmol), 1-(2-fluorophenyl)-2-piperazinone hydrochloride (0.061 g, 0.264 mmol), DIPEA (0.139 mL, 0.793 mmol) and HATU (0.121 g, 0.317 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.068 g, 50%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.84 (br. s., 1 H) 8.57 (br. s., 1 H) 8.23 (br. s., 1 H) 7.84 (br. s., 1 H) 7.09 - 7.63 (m, 5 H) 4.71 (br. s., 1 H) 4.45 (br. s., 1 H) 4.23 (br. s., 1 H) 4.07 (br. s., 1 H) 3.39 (br. s., 2 H).

EXAMPLE 15

4-{[3-chloro-6-(1*H*-pyrazol-4-yl)-8-(trifluoromethyl)-1,8a-dihydroimidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone

(Compound 15)

[00164] A mixture of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.110 g, 0.334 mmol), 1-(2-fluorophenyl)-2-piperazinone hydrochloride (0.077 g, 0.334 mmol), DIPEA (0.175 mL, 1.001 mmol) and HATU (0.152 g, 0.401 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to afford the title compound (0.027 g, 16%) as a beige solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 13.15 (br. s., 1 H) 8.81 (br. s., 1 H) 7.97 - 8.59 (m, 3 H) 7.05 - 7.66 (m, 4 H) 4.67 (br. s., 1 H) 4.40 (br. s., 1 H) 4.19 (br. s., 1 H) 4.02 (br. s., 1 H) 3.72 (br. s., 2 H). ES-LCMS m/z: 507 (M+1).

EXAMPLE 16

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone

(Compound 16)

Step A

1-(4-fluorophenyl)-2-piperazinone hydrochloride

[00165] A mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.200 g, 0.999 mmol), 1-bromo-4-fluorobenzene (0.091 mL, 0.832 mmol), copper(I) iodide (0.008 g, 0.042 mmol), potassium carbonate (0.230 g, 1.665 mmol) and N,N'-dimethyl-1,2-ethanediamine (0.009 mL, 0.083 mmol) in toluene (5 mL) was heated at reflux under nitrogen overnight. The reaction mixture was filtered through silica gel. The filtrate was evaporated and the residue was purified by silica gel chromatography (EtOAc:hexane) to give1,1-dimethylethyl 4-(4-fluorophenyl)-3-oxo-1-piperazinecarboxylate (0.180 g, 73%) as a white solid. Hydrogen chloride (4 N in 1,4-dioxane) (4 mL, 132 mmol) was added and the mixture was stirred at room temperature for several hours. The solvent was evaporated to give the title compound (0.135 g, quantitative) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.79 (br. s., 1 H) 7.34 - 7.41 (m, 2 H) 7.25 - 7.34 (m, 2 H) 3.82 - 3.92 (m, 4 H) 3.53 (d, 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone

[00166] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.107 g, 0.290 mmol), 1-(4-fluorophenyl)-2-piperazinone hydrochloride (0.067 g, 0.290 mmol), DIPEA (0.152 mL, 0.871 mmol) and HATU (0.133 g, 0.349 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.059 g, 36%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.71 - 9.06 (m, 1 H) 8.58 (s, 1 H) 8.08 - 8.33 (m, 1 H) 7.86 (s, 1 H) 7.40 - 7.48 (m, 2 H) 7.35 (s, 1 H) 7.26 (t, 2 H) 4.68 (s, 1 H) 4.42 (s, 1 H) 4.22 (br. s., 1 H) 4.05 (br. s., 1 H) 3.76 - 3.89 (m, 2 H). ES-LCMS m/z: 507 (M+1).

EXAMPLE 17

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone

(Compound 17)

[00167] A mixture of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.097 g, 0.295 mmol), 1-(4-fluorophenyl)-2-piperazinone hydrochloride (0.068 g, 0.295 mmol), DIPEA (0.154 mL, 0.884 mmol) and HATU (0.135 g, 0.354 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.045 g, 29%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 13.19 (br. s., 1 H) 8.87 (s, 1 H) 8.59 (m, 1 H) 8.24 (m, 2 H) 7.33 - 7.61 (m, 2 H) 7.26 (t, 2 H) 4.69 (s, 1 H) 4.42 (m, 1 H) 4.13 - 4.29 (m, 1 H) 3.99 - 4.13 (m, 1 H) 3.81 (m, 2 H). ES-LCMS m/z: 507 (M+1).

EXAMPLE 18

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-2-pyridinyl)-2-piperazinone

(Compound 18)

Step A

1-(3-fluoro-2-pyridinyl)-2-piperazinone dihydrochloride

[00168] A mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.200 g, 0.999 mmol), 2-chloro-3-fluoropyridine (0.083 mL, 0.832 mmol), copper(I) iodide (0.008 mg, 0.042 mmol), potassium carbonate (0.230 g, 1.665 mmol) and N,N'-dimethyl-1,2-

ethanediamine (0.009 mL, 0.083 mmol) in toluene (5 mL) was heated at reflux under nitrogen overnight. The reaction mixture was filtered through silica gel eluting with 1:1/DCM:EtOAc. The filtrate was evaporated and the residue was purified by silica gel chromatography (EtOAc:hexane) to give 1,1-dimethylethyl 4-(3-fluoro-2-pyridinyl)-3-oxo-1-piperazinecarboxylate (0.040 g, 16%) as a white solid. Hydrogen chloride (4 N in 1,4-dioxane) (2 mL) was added and the mixture was stirred at room temperature for 2 hours. The solvent was evaporated to afford the title compound (0.037 g, 100%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.97 (br. s., 2 H) 8.38 (d, 1 H) 7.88 (ddd, 1 H) 7.52 (dt, 4.10 Hz, 1 H) 5.18 - 6.00 (m, 4 H) 3.88 - 4.09 (m, 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-2-pyridinyl)-2-piperazinone

[00169] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.068 g, 0.184 mmol), 1-(3-fluoro-2-pyridinyl)-2-piperazinone dihydrochloride (0.036 g, 0.184 mmol), DIPEA (0.129 mL, 0.738 mmol) and HATU (0.084 g, 0.221 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.041 g, 41%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.85 (br. s., 1 H) 8.58 (br. s., 1 H) 8.38 (br. s., 1 H) 8.24 (br. s., 1 H) 7.85 (br. s., 2 H) 7.51 (br. s., 1 H) 7.34 (br. s., 1 H) 4.76 (br. s., 1 H) 4.50 (br. s., 1 H) 4.22 (br. s., 1 H) 4.09 (br. s., 1 H) 3.95 (br. s., 2 H). ES-LCMS m/z: 508 (M+1).

EXAMPLE 19

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-pyridinyl)-2-piperazinone

(Compound 19)

Step A

1-(2-pyridinyl)-2-piperazinone dihydrochloride

[00170] A mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.234 g, 1.171 mmol), 2-iodopyridine (0.200 g, 0.976 mmol), copper(I) iodide (0.009 mg, 0.049 mmol), potassium phosphate tribasic (0.412 g, 1.951 mmol) and (1R, 2R)-1,2-cyclohexanediamine (0.011 mL, 0.098 mmol) in toluene (2 mL) was heated at reflux under nitrogen overnight. The reaction mixture was filtered through silica gel eluting with 1:1/DCM:EtOAc. The filtrate was evaporated and the residue was purified by silica gel

chromatography (EtOAc:hexane) to give 1,1-dimethylethyl 3-oxo-4-(2-pyridinyl)-1-piperazinecarboxylate (0.086 g, 31%) as a yellow oil. Hydrogen chloride (4 N in 1,4-dioxane) (1.5 mL, 49 mmol) was added and the mixture was stirred at room temperature for one hour. The solvent was evaporated to afford the title compound (0.083 g, 100%) as a white solid.

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-pyridinyl)-2-piperazinone

[00171] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (100 mg, 0.270 mmol), 1-(2-pyridinyl)-2-piperazinone dihydrochloride (67.6 mg, 0.270 mmol), DIPEA (0.189 mL, 1.082 mmol) and HATU (123 mg, 0.325 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.048 g, 36%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.75 - 9.03 (m, 1 H) 8.53 - 8.73 (m, 1 H) 8.36 - 8.55 (m, 1 H) 8.10 - 8.38 (m, 1 H) 7.71 - 8.09 (m, 3 H) 7.12 - 7.49 (m, 2 H) 4.66 - 4.99 (m, 1 H) 4.40 - 4.60 (m, 1 H) 3.89 - 4.31 (m, 4 H). ES-LCMS m/z: 490 (M+1).

EXAMPLE 20

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-pyridinyl)-2-piperazinone

(Compound 20)

Step A

1-(3-pyridinyl)-2-piperazinone dihydrochloride

[00172] To a mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.234 g, 1.171 mmol), 3-iodopyridine (0.200 g, 0.976 mmol), copper(I) iodide (0.009 g, 0.049 mmol) and potassium phosphate tribasic (0.412 g, 1.951 mmol) in toluene (2 mL) under nitrogen, was added N,N'-dimethyl-1,2-ethanediamine (0.010 mL, 0.098 mmol). The reaction mixture was heated at 110°C overnight, cooled to room temperature and filtered through silica gel. The filter was washed with 1:1/EtOAc:DCM. The combined filtrates were concentrated. Purification by silica gel chromatography (MeOH:DCM) gave 1,1-dimethylethyl 3-oxo-4-(3-pyridinyl)-1-piperazinecarboxylate (0.119 g, 44%) as a white solid. HCl (4 N in 1,4-dioxane) (1.5 mL, 6.00 mmol) was added. The mixture was stirred

at room temperature for one hour. The solvent was evaporated to give the title compound (0.110 g, quantitative) as a yellow solid. ES-LCMS m/z : 178 (M+1).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-pyridinyl)-2-piperazinone

[00173] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.149 g, 0.404 mmol), 1-(3-pyridinyl)-2-piperazinone dihydrochloride (0.101 g, 0.404 mmol), DIPEA (0.282 mL, 1.615 mmol) and HATU (0.184 g, 0.485 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.049 g, 23%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (s, 1 H) 8.65 (s, 1 H) 8.59 (s, 1 H) 8.42 - 8.53 (m, 1 H) 8.25 (s, 1 H) 7.77 - 7.91 (m, 2 H) 7.42 - 7.54 (m, 1 H) 7.29 - 7.38 (m, 1 H) 4.67 - 4.79 (m, 1 H) 4.40 - 4.53 (m, 1 H) 4.19 - 4.32 (m, 1 H) 4.03 - 4.13 (m, 1 H) 3.91 (d, 2 H). ES-LCMS m/z: 489 (M+).

EXAMPLE 21

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 21)

Step A

1,1-dimethylethyl [2-(cyclopentylamino)ethyl]carbamate

[00174] A mixture of 1,1-dimethylethyl (2-bromoethyl)carbamate (1.32 g, 5.87 mmol), cyclopentylamine (0.58 mL, 5.87 mmol) and potassium carbonate (1.62 g, 11.74 mmol) in DMF (10 mL) was heated at 60 °C for 30 minutes. The reaction mixture was diluted with EtOAc and water was added. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to give a yellow oil. The crude product was carried on to the next step without further purification.

Step B

1,1-dimethylethyl {2-[(bromoacetyl)(cyclopentyl)amino]ethyl}carbamate

[00175] To a cooled solution of bromoacetyl bromide (0.38 mL, 4.39 mmol) in dichloromethane (8 mL) was added a solution of 1,1-dimethylethyl [2-(cyclopentylamino)ethyl]carbamate (0.911 g, 3.99 mmol) and triethylamine (0.61 mL, 4.39 mmol) in dichloromethane (6 mL). The mixture was stirred while cooling in an ice bath for 30 minutes. The solvent was evaporated and EtOAc and water were added to the

residue. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (EtOAc:hexane) gave the title compound (0.706 g, 51%). ES-LCMS m/z: 349 (M+1).

Step C

1-cyclopentyl-2-piperazinone

[00176] TFA (2 mL, 26.0 mmol) was added to a solution of 1,1-dimethylethyl {2-[(bromoacetyl)(cyclopentyl)amino]ethyl}carbamate (0.680 g, 1.947 mmol) in dichloromethane (10 mL). The mixture was stirred at room temperature for 30 minutes. The solvent was evaporated to give a colorless oil which was dissolved in ethanol (10 mL). Potassium carbonate (807 mg, 5.84 mmol) was added and the mixture was heated at reflux for 30 minutes. The solvent was evaporated and the residue was taken up in DCM and water. The aqueous layer was back-extracted with DCM. The combined organic layers were dried over sodium sulfate and concentrated. Purification by silica gel chromatography (MeOH:DCM) afforded the title compound (0.112 g, 34%) as a colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 4.76 - 4.96 (m, 1 H) 3.43 (s, 2 H) 3.08 - 3.17 (m, 2 H) 2.90 - 3.03 (m, 2 H) 1.90 (br. s., 1 H) 1.65 - 1.77 (m, 2 H) 1.54 - 1.65 (m, 2 H) 1.46 - 1.54 (m, 2 H) 1.34 - 1.45 (m, 2 H).

Step D

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00177] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.165 g, 0.446 mmol), 1-cyclopentyl-2-piperazinone (0.075 g, 0.446 mmol), DIPEA (0.23 mL, 1.337 mmol) and HATU (0.203 g, 0.535 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.048 g, 29%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (br. s., 1 H) 8.60 (br. s., 1 H) 8.25 (br. s., 1 H) 7.87 (br. s., 1 H) 7.36 (br. s., 1 H) 4.80 (br. s., 1 H) 4.49 (br. s., 1 H) 4.25 (br. s., 1 H) 4.05 (br. s., 1 H) 3.88 (br. s., 1 H), 3.5 (m, 2H), 1.39 - 1.96 (m, 8 H). ES-LCMS m/z: 480 (M+1).

EXAMPLE 22

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-pyridinyl)-2-piperazinone

(Compound 22)

Step A

1-(4-pyridinyl)-2-piperazinone dihydrochloride

[00178] To a mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.234 g, 1.171 mmol), 4-iodopyridine (0.200 g, 0.976 mmol), copper(I) iodide (0.0093 mg, 0.049 mmol) and potassium phosphate tribasic (0.412 g, 1.951 mmol) in toluene (2 mL) in a microwave vial, was added N,N'-dimethyl-1,2-ethanediamine (0.010 mL, 0.098 mmol). The mixture was heated at 150 °C in a microwave reactor for 20 minutes. The reaction mixture was filtered through silica gel eluting with 1:1/ EtOAc:DCM. The filtrate was concentrated, dissolved in EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. Purification by silica gel chromatography (MeOH:DCM) gave 1,1-dimethylethyl 3-oxo-4-(4-pyridinyl)-1-piperazinecarboxylate (0.075 g, 28%). HCl (4 N in 1,4-dioxane) (2 mL, 8.00 mmol) was added and the mixture was stirred at room temperature for one hour. The solvent was evaporated to give the title compound (0.058 g, 88%) as a solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 - 10.49 (m, 1 H) 9.75 (br. s., 2 H) 8.85 (d, *J*=7.04 Hz, 1 H) 8.30 (br. s., 1 H) 8.06 (d, *J*=7.04 Hz, 1 H) 4.09 - 4.22 (m, 1 H) 3.54 - 3.64 (m, 3 H) 3.34 - 3.44 (m, 1 H) 3.27 (br. s., 1 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-pyridinyl)-2-piperazinone

[00179] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.072 g, 0.196 mmol), 1-(4-pyridinyl)-2-piperazinone dihydrochloride (0.049 g, 0.196 mmol), DIPEA (0.14 mL, 0.784 mmol) and HATU (0.089 g, 0.235 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.021 g, 22%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (br. s., 1 H) 8.59 (br. s., 2 H) 8.25 (s, 1 H) 8.10 - 8.20 (m, 1 H) 7.86 (br. s., 1 H) 7.54 (d, *J*=4.88 Hz, 2 H) 7.35 (s, 1 H) 4.62 - 4.83 (m, 1 H) 4.47 (br. s., 1 H) 4.15 - 4.33 (m, 1 H) 3.81 - 4.12 (m, 3 H). ES-LCMS m/z: 490 (M+1).

EXAMPLE 23

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopropyl-2-piperazinone

(Compound 23)

Step A

1-cyclopropyl-2-piperazinone

[00180] 1-Cyclopropyl-2-piperazinone (0.038 g, 10% over 3 steps) was prepared from cyclopropylamine (0.303 mL, 4.38 mmol) by the procedure described for Example 21. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 3.52 (s, 2 H) 3.27 (t, *J*=5.47 Hz, 2 H) 3.02 - 3.10 (m, 2 H) 2.75 (tt, *J*=7.33, 3.91 Hz, 1 H) 0.77 - 0.88 (m, 2 H) 0.62 - 0.71 (m, 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopropyl-2-piperazinone

[00181] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.095 g, 0.257 mmol), 1-cyclopropyl-2-piperazinone (0.036 g, 0.257 mmol), DIPEA (0.090 mL, 0.514 mmol) and HATU (0.117 g, 0.308 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.047 g, 36%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.69 - 8.94 (m, 1 H) 8.56 (s, 1 H) 8.19 - 8.28 (m, 1 H) 7.84 (s, 1 H) 7.23 - 7.43 (m, 1 H) 4.35 - 4.54 (m, 1 H) 4.12 - 4.27 (m, 1 H) 3.93 - 4.08 (m, 1 H) 3.77 - 3.93 (m, 1 H), 3.5 (m, 2H), 2.64 - 2.82 (m, 1 H) 0.65 (m, 4 H). ES-LCMS m/z: 453 (M+1).

EXAMPLE 24

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cycloheptyl-2-piperazinone

(Compound 24)

Step A

1-cycloheptyl-2-piperazinone

[00182] 1-cycloheptyl-2-piperazinone (0.245 g, 35% over 3 steps) was prepared from cycloheptylamine by the procedure described for Example 21. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.39 - 4.82 (m, 1 H) 3.50 (s, 2 H) 3.45 (s, 1 H) 3.22 (t, 2 H) 3.02 (t, *J*=5.37 Hz, 2 H) 1.38 - 1.81 (m, 12 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cycloheptyl-2-piperazinone

[00183] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.107 g, 0.290 mmol), 1-cycloheptyl-2-piperazinone

(0.057.0 g, 0.290 mmol), DIPEA (0.10 mL, 0.581 mmol) and HATU (0.132 g, 0.348 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.067 g, 43%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.82 (d, 1 H) 8.56 (s, 1 H) 8.22 (s, 1 H) 7.84 (s, 1 H) 7.32 (s, 1 H) 4.43 (br. s., 2 H) 4.19 (s, 1 H) 4.00 (br. s., 1 H) 3.83 (br. s., 1 H) 3.26 - 3.49 (m, 2 H) 1.31 - 1.75 (m, 12 H). ES-LCMS m/z: 509 (M+1).

EXAMPLE 25

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 25)

Step A

1-cyclobutyl-2-piperazinone

[00184] 1-Cyclobutyl-2-piperazinone (0.108 g, 14% over 3 steps) was prepared from cyclobutylamine (0.350 g, 4.92 mmol) by the procedure described for Example 21. ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 4.77 - 5.20 (m, 1 H) 3.49 (s, 2 H) 3.31 (t, *J*=5.46 Hz, 2 H) 3.07 (t, *J*=5.46 Hz, 2 H) 2.03 - 2.19 (m, 3 H) 1.59 - 1.74 (m, 3 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00185] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.122 g, 0.331 mmol), 1-cyclobutyl-2-piperazinone (0.051.0 g, 0.331 mmol), DIPEA (0.12 mL, 0.661 mmol) and HATU (0.151 g, 0.397 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.055 g, 35%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.83 (d, 1 H) 8.57 (s, 1 H) 8.23 (br. s., 1 H) 7.84 (s, 1 H) 7.33 (s, 1 H) 4.70 - 5.05 (m, 1 H) 4.45 (s, 1 H) 4.21 (s, 1 H) 4.05 (t, 1 H) 3.89 (t, 1 H) 3.41 - 3.59 (m, 2 H) 2.08 - 2.30 (m, 2 H) 1.99 (br. s., 2 H) 1.41 - 1.75 (m, 2 H). ES-LCMS m/z: 467 (M+1).

EXAMPLE 26

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylethyl)-2-piperazinone

(Compound 26)

Step A

1-(1-methylethyl)-2-piperazinone

[00186] 1-(1-Methylethyl)-2-piperazinone (0.099g, 13% over 3 steps) was prepared from isopropylamine (0.300 g, 5.08 mmol) by the procedure described for Example 21. ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 4.88 (spt, *J*=6.83 Hz, 1 H) 3.50 (s, 2 H) 3.10 - 3.26 (m, 2 H) 2.88 - 3.10 (m, 2 H) 1.10 (d, 6 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylethyl)-2-piperazinone

[00187] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.112 g, 0.302 mmol), 1-(1-methylethyl)-2-piperazinone (0.043 g, 0.302 mmol), DIPEA (0.11 mL, 0.605 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.050 g, 34%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.64 - 8.93 (m, 1 H) 8.52 (s, 1 H) 8.18 (s, 1 H) 7.80 (s, 1 H) 7.11 - 7.42 (m, 1 H) 4.49 - 4.73 (m, 1 H) 4.40 (s, 1 H) 4.16 (s, 1 H) 3.88 - 4.05 (m, 1 H) 3.64 - 3.89 (m, 1 H) 3.22 - 3.38 (m, 2 H), 1.02-1.04 (m, 6 H). ES-LCMS m/z: 454 (M+1).

EXAMPLE 27

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

(Compound 27)

Step A

1-(3-thienyl)-2-piperazinone hydrochloride

[00188] A mixture of 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.489 g, 2.44 mmol), 3-bromothiophene (0.332 g, 2.036 mmol), copper(I) iodide (0.019 g, 0.102 mmol), potassium carbonate (0.563 g, 4.07 mmol) and trans-N,N-dimethyl-cyclohexane-1,2-diamine (0.029, 0.204 mmol) in 1,4-dioxane (5 mL) was heated at reflux under nitrogen for 24 hours. After cooling to room temperature, the reaction mixture was filtered through

silica gel eluting with DCM:EtOAc/1:1. The filtrate was concentrated and the residue was purified by silica gel chromatography to afford 1,1-dimethylethyl 3-oxo-4-(3-thienyl)-1-piperazinecarboxylate (0.305 g, 53%) as a white solid. Hydrogen chloride (4 N in 1,4-dioxane) (1.5 mL, 6.00 mmol) was added and the mixture was stirred at room temperature for one hour. The solvent was evaporated to give 1-(3-thienyl)-2-piperazinone hydrochloride (0.240 g, 44% overall) as a light gray solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.91 (br. s., 2 H) 7.57 (d, 2 H) 7.27 - 7.48 (m, 1 H) 3.97 (t, 2 H) 3.53 (t, 2 H) 3.38 - 3.49 (m, 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

[00189] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid potassium salt (0.100 g, 0.270 mmol), 1-(3-thienyl)-2-piperazinone hydrochloride (0.059 g, 0.270 mmol), DIPEA (0.094 mL, 0.541 mmol) and HATU (0.123 g, 0.325 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.055 g, 41%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.84 (d, J=6.84 Hz, 1 H) 8.57 (s, 1 H) 8.23 (s, 1 H) 7.85 (t, J=1.56 Hz, 1 H) 7.49 - 7.59 (m, 2 H) 7.39 (d, J=5.08 Hz, 1 H) 7.34 (s, 1 H) 4.69 (s, 1 H) 4.43 (s, 1 H) 4.22 (t, J=4.98 Hz, 1 H) 3.95 - 4.07 (m, 1 H) 3.78 - 3.96 (m, 2 H). ES-LCMS m/z: 495 (M+1).

EXAMPLE 28

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

(Compound 28)

Step A

methyl 3-chloro-6-(1-methylethenyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00190] A solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (6 g, 16.78 mmol-- see PCT Int. Appl. WO 2009023179), potassium isopropenyl trifluoroborate (3.75 g, 25.2 mmol), triethylamine (11.70 mL, 84 mmol), and $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.685 g, 0.839 mmol) in propanol (75 mL) was maintained with stirring at 100 °C for 2 hours. The mixture was cooled to room

temperature, poured into ethyl acetate, and washed with saturated sodium chloride (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford methyl 3-chloro-6-(1-methylethenyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (3.78 g, 11.86 mmol, 71 % yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.45 (s, 1H), 8.16 (s, 1H), 5.81 (s, 1H), 5.38 (s, 1H), 3.92 (s, 3H), 2.23 (s, 3H).

Step B

methyl 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00191] A nitrogen purged solution of methyl 3-chloro-6-(1-methylethenyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (3.80 g, 11.92 mmol) and phenyl disulfide (0.397 mL, 2.385 mmol) in ethyl acetate (150 mL) was added to 10% Pd/C (1.903 g, 1.789 mmol) and maintained under 50 psi of hydrogen for 5 hours (no additional hydrogen absorption was observed after 2 hours). The mixture was filtered through Celite, concentrated, and the resulting residue was purified by column chromatography to afford methyl 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (3 g, 9.35 mmol, 78% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.46 (s, 1H), 7.97 (s, 1H), 3.91 (s, 3H), 3.18 (spt, J = 6.9 Hz, 1H), 1.30 (d, 6H).

Step C

3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00192] A solution of methyl 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (3 g, 9.35 mmol) in tetrahydrofuran (60 mL)/water (60 mL) was treated with sodium hydroxide (1 M, 23.39 mL, 23.39 mmol), stirred rapidly for 45 minutes, and quenched via slow addition of HCl (1 M, 37.4 mL, 37.4 mmol). Ethyl acetate was added and the organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (2.31 g, 7.53 mmol, 81% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ ppm 13.37 (br. s., 1H), 8.43 (s, 1H), 7.94 (s, 1H), 3.17 (spt, J = 6.8 Hz, 1H), 1.30 (d, J = 7.0 Hz, 6H).

Step D

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

[00193] A mixture of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.326 mmol), 1-(3-thienyl)-2-piperazinone hydrochloride (0.071 g, 0.326 mmol), DIPEA (0.11 mL, 0.652 mmol) and HATU (0.149 g, 0.391 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was

dried over sodium sulfate and concentrated. The residue was purified by silica gel chromatography (MeOH:DCM) to give the title compound (0.055 g, 61%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.47 (d, 1 H) 7.95 (s, 1 H) 7.50 - 7.59 (m, 2 H) 7.40 (d, 1 H) 4.68 (s, 1 H) 4.43 (s, 1 H) 4.15 - 4.28 (m, 1 H) 4.03 (d, 1 H) 3.83 - 3.96 (m, 2 H) 3.19 (m, 6.76 Hz, 1 H) 1.31 (d, 6 H). ES-LCMS m/z: 471 (M+1).

EXAMPLE 29

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone

(Compound 29)

Step A

1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone hydrochloride

[00194] 1-(4-Methyl-1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.322 g, 49% over 2 steps) was prepared from 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.675 g, 3.37 mmol) and 2-bromo-4-methyl-1,3-thiazole (0.500 g, 2.81 mmol) as described in Example 27. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.09 (br. s., 1 H) 6.96 (d, 1 H) 4.29 (t, 2 H) 3.92 - 4.15 (m, 2 H) 3.57 (d, 2 H) 2.31 (s, 3 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone

[00195] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (100 mg, 0.302 mmol), 1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone hydrochloride (70.7 mg, 0.302 mmol), DIPEA (0.106 mL, 0.605 mmol) and HATU (138 mg, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for 1 hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by prep LCMS (acetonitrile:water with 0.1% formic acid) to give 76 mg (49%) of desired product as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (d, J=4.68 Hz, 1 H) 8.59 (s, 1 H) 8.13 - 8.32 (m, 1 H) 7.64 - 7.97 (m, 1 H) 7.13 - 7.43 (m, 1 H) 6.75 - 7.04 (m, 1 H) 4.84 - 4.95 (m, 1 H) 4.48 - 4.65 (m, 1 H) 4.15 - 4.36 (m, 3 H) 4.01 - 4.15 (m, 1 H) 2.32 (br. s., 3 H). ES-LCMS m/z: 510 (M+1).

EXAMPLE 30

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone

(Compound 30)

[00196] A mixture of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.075 g, 0.245 mmol), 1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.057 g, 0.245 mmol), DIPEA (0.063 g, 0.489 mmol) and HATU (0.112 g, 0.293 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.067 g, 56%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.47 (d, J=6.05 Hz, 1 H) 7.96 (s, 1 H) 6.91 (d, J=5.66 Hz, 1 H) 4.87 (s, 1 H) 4.57 (s, 1 H) 4.16 - 4.32 (m, 3 H) 4.00 - 4.13 (m, 1 H) 3.10 - 3.22 (m, 1 H) 2.31 (s, 3 H) 1.31 (d, 6 H). ES-LCMS m/z: 486 (M+1).

EXAMPLE 31

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone

(Compound 31)

Step A

1-(1,3-thiazol-4-yl)-2-piperazinone hydrochloride

[00197] 1-(1,3-thiazol-4-yl)-2-piperazinone hydrochloride (0.829 g, 58% over 2 steps) was prepared from 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (1.553 g, 7.75 mmol) and 4-bromo-1,3-thiazole (1.06 g, 6.46 mmol) as described in Example 27. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.22 (br. s., 2 H) 9.06 (d, 1 H) 7.92 (d, 1 H) 4.25 (t, 2 H) 3.92 (br. s., 2 H) 3.53 (br. s., 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone

[00198] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(1,3-thiazol-4-yl)-2-piperazinone hydrochloride (0.066 g, 0.302 mmol), DIPEA (0.078 g, 0.605 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.056 g, 37%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.06 (s, 1 H) 8.86 (d, J=4.88 Hz, 1 H) 8.59 (s, 1 H) 8.25 (s, 1 H) 7.87 - 8.00 (m, 1 H) 7.86 (s, 1 H) 7.35 (s, 1 H) 4.77 (s, 1 H) 4.50 (s, 1 H) 4.11 - 4.28 (m, 3 H) 4.05 (d, 1 H). ES-LCMS m/z: 496 (M+1).

EXAMPLE 32

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone

(Compound 32)

[00199] A mixture of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.075 g, 0.245 mmol), 1-(1,3-thiazol-4-yl)-2-piperazinone hydrochloride (0.053 g, 0.245 mmol), DIPEA (0.063 g, 0.489 mmol) and HATU (0.112 g, 0.293 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.052 g, 45%) as a white solid . ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.04 (d, 1 H) 8.46 (d, 1 H) 7.94 (s, 1 H) 7.88 (d, 1 H) 4.74 (s, 1 H) 4.48 (s, 1 H) 4.10 - 4.27 (m, 3 H) 4.02 (t, 1 H) 3.18 (m,1 H) 1.30 (d, 6 H). ES-LCMS m/z: 472 (M+1).

EXAMPLE 33

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone

(Compound 33)

Step A

1-(2-thienyl)-2-piperazinone hydrochloride

[00200] 1-(2-thienyl)-2-piperazinone hydrochloride (0.525 g, 78% over 2 steps) was prepared from 1,1-dimethylethyl 3-oxo-1-piperazinecarboxylate (0.737 g, 3.68 mmol) and 2-bromothiophene (0.500 g, 3.07 mmol) as described in Example 27. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.05 (br. s., 2 H) 7.14 - 7.20 (m, 1 H) 6.97 (dd, 4.00 Hz, 1 H) 6.89 (d, 1 H) 4.08 (t, 2 H) 3.99 (s, 2 H) 3.60 (t, 2 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone

[00201] Method A: A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(2-thienyl)-2-piperazinone hydrochloride (0.066 g, 0.302 mmol), DIPEA (0.078 g, 0.605 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated.

[00202] Method B: A suspension of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol) in thionyl chloride (2 mL, 27.4 mmol) was heated at reflux for one hour. The solvent was evaporated, and the residue was suspended in toluene and evaporated again, and then dissolved in dichloromethane. A solution of 1-(2-thienyl)-2-piperazinone hydrochloride (0.066 g, 0.302 mmol) and DIPEA (0.156 g, 1.21 mmol) in dichloromethane (2 mL) was added. After stirring at room temperature for 15 minutes, the reaction mixture was diluted with dichloromethane. The organic layer was washed with saturated sodium bicarbonate, water and brine, dried over sodium sulfate and concentrated.

[00203] The crude products from Methods A and B above (in DMSO solution) were combined and diluted with EtOAc. Water was added and the organic layer was washed once more with water, dried over sodium sulfate and the solvent was evaporated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.033 g, 11%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (d, *J*=9.37 Hz, 1 H) 8.59 (s, 1 H) 8.25 (s, 1 H) 7.86 (s, 1 H) 7.35 (s, 1 H) 7.07 - 7.19 (m, 1 H) 6.91 - 7.00 (m, 1 H) 6.76 - 6.91 (m, 1 H) 4.83 (s, 1 H) 4.54 (s, 1 H) 4.28 - 4.39 (m, 1 H) 4.07 - 4.19 (m, 1 H) 3.94 - 4.06 (m, 2 H). ES-LCMS m/z: 495 (M+1).

EXAMPLE 34

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 34)

Step A

3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride

[00204] 3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.163 g, 31% over 2 steps) was prepared from 1,1-dimethylethyl 2,2-dimethyl-3-oxo-1-piperazinecarboxylate (0.575 g, 2.52 mmol) and 2-bromo-1,3-thiazole (0.344 g, 2.1 mmol) as described in Example 27. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.68 (br. s, 2 H) 7.58 (d, 1 H) 7.39 (d, 1 H) 4.35 (t, 2 H) 3.62 (d, 2 H) 1.64 (s, 6 H).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone

[00205] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.074 g, 0.302 mmol), DIPEA (0.117 g, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature overnight. The reaction

mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.082 g, 51%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.86 (s, 1 H) 8.58 (s, 1 H) 8.24 (s, 1 H) 7.81 - 7.90 (m, 1 H) 7.61 (d,1 H) 7.40 (d, 1 H) 7.35 (d, 1 H) 4.21 - 4.40 (m, 2 H) 3.85 - 4.04 (m, 2 H) 1.88 (s, 6 H). ES-LCMS m/z: 524 (M+1).

EXAMPLE 35

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone

(Compound 35)

Step A

1-(4,4-difluorocyclohexyl)-2-piperazinone hydrochloride

[00206] 1-(4,4-difluorocyclohexyl)-2-piperazinone hydrochloride (0.118 g, 17% over 4 steps) was prepared from (4,4-difluorocyclohexyl)amine hydrochloride (357 mg, 2.64 mmol) by the procedure described in Example 21. ES-LCMS m/z: 218 (M+).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone

[00207] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(4,4-difluorocyclohexyl)-2-piperazinone hydrochloride (0.077 g, 0.302 mmol), DIPEA (0.117 g, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.053 g, 33%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.78 (d, 1 H) 8.52 (s, 1 H) 8.18 (s, 1 H) 7.80 (s, 1 H) 7.28 (d, 1 H) 4.44 (s, 1 H) 4.27 - 4.41 (m, 1 H) 4.19 (s, 1 H) 3.92 - 4.02 (m, 1 H) 3.76 - 3.85 (m, 1 H) 3.30 - 3.38 (m, 2 H) 1.82 - 2.11 (m, 4 H) 1.53 - 1.77 (m, 4 H). ES-LCMS m/z: 531 (M+1).

EXAMPLE 36

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 36)

Step A

(+/-)-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride

[00208] (+/-)-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.334 g, 47% over 2 steps) was prepared from (+/-)-1,1-dimethylethyl 2-methyl-3-oxo-1-piperazinecarboxylate (630 mg, 2.94 mmol) and 2-bromo-1,3-thiazole (0.262 mL, 2.94 mmol) using the procedure described in Example 27. ES-LCMS m/z: 198 (M+1).

Step B

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone

[00209] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), (+/-)-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (0.070 g, 0.302 mmol), DIPEA (0.117 g, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.046 g, 29%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.85 (d, 1 H) 8.58 (s, 1 H) 8.24 (s, 1 H) 7.85 (s, 1 H) 7.59 (d,1 H) 7.26 - 7.42 (m, 2 H) 5.34 and 5.19 (m, 1 H) 4.67 (m, 1 H) 4.42 (m, 1 H) 4.07 and 3.94 (m, 1 H) 3.83 and 3.56 (m, 1 H) 1.75 and 1.60 (d, 3 H). ES-LCMS m/z: 510 (M+1).

EXAMPLE 37

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 37)

Step A

6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00210] Methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (20 g, 55.9 mmol) was dissolved in THF (360 mL) then water (360 mL) and aqueous solution 1 N NaOH (140 mL, 140 mmol) were added. After 10 minutes, TLC and LCMS showed no remaining starting material. The orange solution was poured slowly into a flask containing a vigorously stirred solution of 1 N HCl (145 mL) and water (350 mL). After stirring for 1 hour, the mixture was filtered and the solid was dried under vacuum to give the title compound (11.8 g, 34.4 mmol, 61.4 % yield) as an off-white powder. The filtrate was extracted with ethyl acetate (2 x 500 mL) and the organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The material was recrystallized

from hot EtOH (~200 mL) to give the title compound (2.34 g, 6.81 mmol, total combined 73% yield). 1H NMR (400 MHz, DMSO-d_6) δ ppm 13.45 (br. s., 1 H) 8.94 (d, 1 H) 8.04 (s, 1 H).

Step B

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00211] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.291 mmol), 1-cyclopentyl-2-piperazinone hydrochloride (0.059 g, 0.291 mmol), DIPEA (0.113 g, 0.873 mmol) and HATU (0.133 g, 0.349 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.049 g, 31%) as a beige solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.82 - 9.14 (m, 1 H) 7.91 - 8.21 (m, 1 H) 4.62 - 4.95 (m, 1 H) 4.29 - 4.50 (m, 1 H) 4.09 - 4.30 (m, 1 H) 3.88 - 4.06 (m, 1 H) 3.75 - 3.89 (m, 1 H) 3.40 (m, 2H) 1.25 - 1.85 (m, 8 H). ES-LCMS m/z: 493, 495.

EXAMPLE 38

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

(Compound 38)

Step A

1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone hydrochloride

[00212] 1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone hydrochloride (0.260 g, 10 % over 4 steps) was prepared from 1,1-dimethylethyl (2-bromoethyl)carbamate (2.69 g, 11.99 mmol) and tetrahydro-2H-pyran-4-amine hydrochloride (1.650 g, 11.99 mmol) using the procedure described in Example 21. ES-LCMS m/z: 185 (M+1).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

[00213] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone hydrochlroride (0.055 g, 0.302 mmol), DIPEA (0.117 g, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was triturated with

methanol and air-dried to give the title compound (0.026 g, 18%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.76 - 8.87 (m, 1 H) 8.57 (s, 1 H) 8.23 (s, 1 H) 7.85 (s, 1 H) 7.33 (s, 1 H) 4.41 - 4.56 (m, 2 H) 4.24 (s, 1 H) 4.02 (t, *J*=5.08 Hz, 1 H) 3.78 - 3.96 (m, 3 H) 3.35 - 3.45 (m, 4 H) 1.74 (t, *J*=11.73 Hz, 2 H) 1.49 (d, 2 H). ES-LCMS m/z: 497 (M+1).

EXAMPLE 39

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

(Compound 39)

Step A

1-(4-oxocyclohexyl)-2-piperazinone hydrochloride

[00214] 1-(4-oxocyclohexyl)-2-piperazinone hydrochloride (0.066 g, 5% over 4 steps) was prepared from 1,1-dimethylethyl (2-bromoethyl)carbamate (1.376 g, 6.14 mmol) and 4-aminocyclohexanone (0.695 g, 6.14 mmol) as described in Example 21. ES-LCMS m/z: 257 (M+1).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

[00215] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.093 g, 0.280 mmol), 1-(4-oxocyclohexyl)-2-piperazinone hydrochloride (0.065 g, 0.280 mmol), DIPEA (0.145 g, 1.121 mmol) and HATU (0.128 g, 0.336 mmol) in DMF (10 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.012 g, 8%) as a beige solid. ^{1}H NMR (400 MHz, methanol-d_4) δ ppm 8.68 (s, 1 H) 8.19 (s, 1 H) 8.08 (s, 1 H) 7.66 (t, 1 H) 7.02 (d, 1 H) 4.85 (m, 1H) 4.65 (s, 1 H) 4.40 (s, 1 H) 4.18 (t, 1 H) 3.96 - 4.03 (m, 1 H) 3.49 - 3.55 (m, 2 H) 2.52 - 2.69 (m, 2 H) 2.37 (d, 2 H) 1.94 - 2.12 (m, 4 H). ES-LCMS m/z: 509 (M+1).

EXAMPLE 40

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone

(Compound 40)

Step A

1-(3,3-difluorocyclobutyl)-2-piperazinone hydrochloride

[00216] 1-(3,3-difluorocyclobutyl)-2-piperazinone hydrochloride (0.084 g, 11% over 4 steps) was prepared from 1,1-dimethylethyl (2-bromoethyl)carbamate (780 mg, 3.48 mmol) and (3,3-difluorocyclobutyl)amine hydrochloride (Chinglu Pharmaceutical Research) as described in Example 21 (0.500g, 3.48 mmol).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone

[00217] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.302 mmol), 1-(3,3-difluorocyclobutyl)-2-piperazinone hydrochloride (0.057 g, 0.302 mmol), DIPEA (0.117 g, 0.907 mmol) and HATU (0.138 g, 0.363 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.045 g, 29%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.78 (d, J=8.20 Hz, 1 H) 8.52 (s, 1 H) 8.18 (s, 1 H) 7.80 (s, 1 H) 7.28 (s, 1 H) 4.51 - 4.67 (m, 1 H) 4.47 (s, 1 H) 4.21 (s, 1 H) 4.06 (t, 1 H) 3.87 (t,1 H) 3.37 - 3.53 (m, 2 H) 2.81 - 3.01 (m, 2 H) 2.66 - 2.80 (m, 2 H). ES-LCMS m/z: 503 (M+1).

EXAMPLE 41

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 41)

[00218] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.100 g, 0.291 mmol), 1-cyclobutyl-2-piperazinone hydrochloride (0.045 g, 0.291 mmol), DIPEA (0.113 g, 0.873 mmol) and HATU (0.133 g, 0.349 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.076 g, 54%) as a light beige solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.02 (d, 1 H) 8.11 (d, 1 H) 4.71 - 5.01 (m, 1 H) 4.40 (s, 1 H) 4.21 (s, 1 H) 4.00 (t, 1 H) 3.89 (t, 1 H) 3.48 (m, 5.17 Hz, 2 H) 2.07 - 2.30 (m, 2 H) 2.00 (d, 2 H) 1.41 - 1.74 (m, 2 H). ES-LCMS m/z: 479, 491.

EXAMPLE 42

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone

(Compound 42)

[00219] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.081 g, 0.236 mmol), 1-(4,4-difluorocyclohexyl)-2-piperazinone hydrochloride (0.060 g, 0.236 mmol), DIPEA (0.091 g, 0.707 mmol) and HATU (0.107 g, 0.283 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.024 g, 24%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.96 (d, 1 H) 8.06 (s, 1 H) 4.21 - 4.50 (m, 2 H) 4.18 (s, 1 H) 3.91 (t, 1 H) 3.79 (t, 1 H) 3.28 - 3.38 (m, 2 H) 2.01 (br. s., 4 H) 1.53 (m, 4 H). ES-LCMS m/z: 543, 545.

EXAMPLE 43

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

(Compound 43)

Step A

methyl 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00220] $Pd(OAc)_2$ (8 g, 0.036 mol) and $(cyclohexyl)_3P$ (10 g, 0.036 mol) were added to a solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (110 g, 0.31 mol), cyclopropylboronic acid (29 g, 0.34 mol) and K_3PO_4-$3H_2O$ (313 g, 0.93 mol) in toluene (1.1 L). After degassing and refilling with Nitrogen (three times), the reaction mixture was heated at 110 °C for 3 hours. The reaction solution was filtered through Celite. After the addition of H_2O (800 mL) and EtOAc (800 mL), the organic layer was separated and then dried over anhydrous $MgSO_4$. After concentration, the residue was purified with silica gel chromatography [petroleum ether: EtOAc (10:1 v/v)] to give the title compound (65 g, 66.3%) as light yellow solid.

Step B

3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00221] Lithium hydroxide monohydrate (42 g, 1 mol) was added to a solution of methyl 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (65 g, 0.2 mol) in a mixture of MeOH/THF/H_2O (600 mL/600 mL/300 mL) and the reaction mixture was stirred at room temperature for 1 hour. After the removal of organic solvents,

the aqueous solution was acidified with concentrated HCl to pH 2 and then extracted with EtOAc (3 x 300 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated to give the title compound (56 g, 90%) as light yellow solid. ^{1}H NMR(300MHz, DMSO-d_6) δ 0.88 (m, 2 H), 1.05 (m, 2 H), 2.18 (m, 1 H), 7.57 (s, 1 H), 8.43 (s, 1 H), 13.32 (s, 1H); ES-LCMS m/z: 305 (M+1).

Step C:

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

[00222] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.082 g, 0.270 mmol), 1-(4-oxocyclohexyl)-2-piperazinone hydrochloride (0.053 g, 0.270 mmol), DIPEA (0.105 g, 0.810 mmol) and HATU (0.123 g, 0.324 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) and silica gel chromatography gave the title compound (0.011 g, 8%)as a white solid. ^{1}H NMR (400 MHz, methanol-d_4) δ ppm 8.31 (s, 1 H) 7.58 (s, 1 H), 4.85 (m, 1H), 4.62 (s, 1 H) 4.39 (s, 1 H) 4.15 (m, 1 H) 3.98 (m, 1 H) 3.37 - 3.56 (m, 2 H) 2.47 - 2.70 (m, 2 H) 2.37 (d, 2 H) 2.06 - 2.17 (m, 1 H) 1.83 - 2.07 (m, 4 H) 0.97 - 1.17 (m, 2 H) 0.85 (d, 2 H). ES-LCMS m/z: 483 (M+1).

EXAMPLE 44

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

(Compound 44)

[00223] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.105 g, 0.306 mmol), 1-(4-oxocyclohexyl)-2-piperazinone hydrochloride (0.060 g, 0.306 mmol), DIPEA (0.119 g, 0.917 mmol) and HATU (0.140 g, 0.367 mmol) in DMF (2 mL) was stirred at room temperature. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.009 g, 5.1%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.78 - 9.19 (m, 1 H) 8.05 (s, 1 H) 4.55 - 4.96 (m, 1 H) 4.39 (s, 1 H) 4.20 (s, 1 H) 3.92 (s, 1 H) 3.71 - 3.86 (m, 1 H), 3.30 (m, 2H), 2.60 (m, 2H), 2.09 - 2.27 (m, 2 H) 1.70 - 2.03 (m, 4 H). ES-LCMS m/z: 521, 523.

EXAMPLE 45

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone

(Compound 45)

[00224] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.094 g, 0.274 mmol), 1-(3,3-difluorocyclobutyl)-2-piperazinone hydrochloride (0.062 g, 0.274 mmol), DIPEA (0.106 g, 0.821 mmol) and HATU (0.125 g, 0.328 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.045 g, 32%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.02 (d, 1 H) 7.90 - 8.21 (m, 1 H) 4.56 - 4.80 (m, 1 H) 4.45 (m, 1 H) 4.25 (m, 1 H) 4.04 (m, 1 H) 3.91 (m, 1 H) 3.50 (m, 2 H) 2.92 (m, 2 H) 2.80 (m, 2 H). ES-LCMS m/z: 515, 517.

EXAMPLE 46

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone

(Compound 46)

[00225] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.083 g, 0.274 mmol), 1-(3,3-difluorocyclobutyl)-2-piperazinone hydrochloride (0.062 g, 0.274 mmol), DIPEA (0.106 g, 0.821 mmol) and HATU (0.125 g, 0.328 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to afford the title compound (0.022 g, 17%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.36 - 8.73 (m, 1 H) 7.42 - 7.85 (m, 1 H) 4.42 - 4.93 (m, 2 H) 4.19 - 4.38 (m, 1 H) 4.02 - 4.20 (m, 1 H) 3.81 - 4.02 (m, 1 H) 3.46 - 3.62 (m, 2 H) 2.69 - 3.11 (m, 4 H) 2.15 - 2.38 (m, 1 H) 0.76 - 1.23 (m, 4 H). ES-LCMS m/z: 477 (M+1).

EXAMPLE 47

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone

(Compound 47)

Step A

1,1-dimethylethyl (trans-3-hydroxycyclobutyl)carbamate

[00226] A mixture of trans-3-({[(1,1-dimethylethyl)oxy]carbonyl}amino)cyclobutyl 1H-imidazole-1-carboxylate (5.00 g, 17.77 mmol) (prepared as described on page 20 WO2007062332A2) and 1 N aqueous sodium hydroxide (40 mL, 40.0 mmol) was stirred at room temperature overnight. After evaporating most of the organic solvent, EtOAc was added and the organic layer was washed twice with 1 N aqueous HCl, dried over sodium sulfate and concentrated to afford 1,1-dimethylethyl (trans-3-hydroxycyclobutyl)carbamate (2.45 g, 76%) as a white solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 4.71 (br. s., 1 H) 4.36 - 4.52 (m, 1 H) 4.19 (br. s., 1 H) 2.26 (dd, 4.39 Hz, 2 H) 2.13 - 2.23 (m, 2 H) 1.30 - 1.54 (m, 9 H).

Step B

trans-3-{[tris(1-methylethyl)silyl]oxy}cyclobutanamine trifluoroacetate

[00227] A solution of 1,1-dimethylethyl (trans-3-hydroxycyclobutyl)carbamate (2.76 g, 14.74 mmol), TIPSCl (4.26 g, 22.11 mmol) and imidazole (2.51 g, 36.9 mmol) in DMF (60 mL) was stirred at room temperature for on hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to afford 1,1-dimethylethyl (trans-3-{[tris(1-methylethyl)silyl]oxy}cyclobutyl)carbamate (5.06 g, quantitative) as a colorless oil. The oil was dissolved in dichloromethane (40 mL) and TFA (5 mL, 64.9 mmol) was added. The solution was stirred at room temperature for overnight. The solvent was evaporated to afford trans-3-{[tris(1-methylethyl)silyl]oxy}cyclobutanamine trifluoroacetate (5.25 g, quantitative). ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 10.52 (br. s., 2 H) 7.36 - 7.63 (m, 2 H) 4.64 (quin, *J*=6.00 Hz, 1 H) 3.72 - 4.05 (m, 1 H) 2.30 - 2.50 (m, 4 H) 0.71 - 1.15 (m, 21 H).

Step C

1-(trans-3-{[tris(1-methylethyl)silyl]oxy}cyclobutyl)-2-piperazinone hydrochloride

[00228] 1-(trans-3-{[tris(1-methylethyl)silyl]oxy}cyclobutyl)-2-piperazinone hydrochloride (0.140 g, 15% over 4 steps) was prepared from 1,1-dimethylethyl (2-bromoethyl)carbamate (1.19 g, 5.33 mmol) and trans-3-{[tris(1-methylethyl)silyl]oxy}cyclobutanamine trifluoroacetate (1.90 g, 5.33 mmol) by the procedure described in Example 21. ES-LCMS m/z: 327 (M+1).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone

[00229] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.219 g, 0.661 mmol), 1-(trans-3-hydroxycyclobutyl)-2-piperazinone hydrochloride (0.137 g, 0.661 mmol), DIPEA (0.256 g, 1.98 mmol) and HATU (0.276 g, 0.727 mmol) in DMF (2 mL) was stirred at room temperature for 2 hours. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was treated with hydrogen chloride (4 N in 1,4-dioxane) (1 mL, 4 mmol) for 1 hour. The solvent was evaporated and the residue was purified by silica gel chromatography, followed by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.017 g, 5%) as an off-white solid. ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 8.63 (m, 1 H) 8.16 (d, 1 H) 8.03 (d, 1 H) 7.64 (s, 1 H) 6.99 (br. s., 1 H) 5.01 - 5.31 (m, 1 H) 4.52 - 4.65 (m, 1 H) 4.24 - 4.43 (m, 2 H) 4.09 - 4.27 (m, 1 H) 4.01 (m, 1 H) 3.48 - 3.68 (m, 2 H) 2.39 - 2.69 (m, 2 H) 2.10 - 2.37 (m, 2 H). ES-LCMS m/z: 483 (M+1).

EXAMPLE 48

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

(Compound 48)

Step A

trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate

[00230] A solution of 1,1-dimethylethyl (trans-4-hydroxycyclohexyl)carbamate (CombiBlocks) (1.000 g, 4.64 mmol), triisopropylsilyl chloride (1.34 g, 6.97 mmol) and imidazole (0.791 g, 11.61 mmol) in DMF (40 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc and washed with water and brine, dried over sodium sulfate and concentrated to an off-white solid. The crude product was dissolved in DCM (40 mL) and trifluoroacetic acid (3 mL, 38.9 mmol) was added. The solution was stirred at room temperature for one hour. The solvent was evaporated to afford trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate (1.59 g, 89%). ES-LCMS m/z: 272 (M+1).

Step B

1,1-dimethylethyl {2-[(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate

[00231] A mixture of trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate (1.59 g, 4.13 mmol), 1,1-dimethylethyl (2-bromoethyl)carbamate (0.927 g, 4.13 mmol) and potassium carbonate (1.714 g, 12.40 mmol) in DMF (40 mL) was heated at 60°C overnight. The reaction mixture was diluted with EtOAc and water was added.

The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to the title compound as a colorless oil (1.18 g). ES-LCMS m/z: 415 (M+1). The crude product was used for the next step without further purification.

Step C

1,1-dimethylethyl {2-[(bromoacetyl)(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate

[00232] A solution of bromoacetyl bromide (0.621 g, 3.08 mmol) in DCM (5 mL) was added to a solution of 1,1-dimethylethyl {2-[(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate (1.160 g, 2.80 mmol) and triethylamine (0.429 mL, 3.08 mmol) in DCM (30 mL) at 0 °C. The mixture was stirred for 30 minutes. The solvent was evaporated and EtOAc and water were added. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Silica gel chromatography gave 1,1-dimethylethyl {2-[(bromoacetyl)(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate (0.300 g, 20%). ES-LCMS m/z: 536 (M+1).

Step D

1,1-dimethylethyl 3-oxo-4-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-1-piperazinecarboxylate

[00233] To a solution of 1,1-dimethylethyl {2-[(bromoacetyl)(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate (0.291 g, 0.543 mmol) in DMF (4 mL) at 0 °C was added sodium hydride (60% oil dispersion) (0.024 g, 0.598 mmol). The reaction mixture was stirred for 30 minutes, poured into ice-water and extracted with EtOAc. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to give 1,1-dimethylethyl 3-oxo-4-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-1-piperazinecarboxylate (0.199 g, 81%) as a yellow oil. ES-LCMS m/z: 455 (M+1).

Step E

1-(trans-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate

[00234] Trifluoroacetic acid (1 mL, 13 mmol) was added to a solution of 1,1-dimethylethyl 3-oxo-4-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-1-piperazinecarboxylate (0.187 g, 0.411 mmol) in DCM (3 mL). The mixture was stirred at room temperature for one hour. The solvent was evaporated to give 1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate (0.192 g). The crude product was used for the next step without further purification. ES-LCMS m/z: 199 (M+1).

Step F

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00235] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.063 g, 0.193 mmol), 1-(trans-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate (0.060 g, 0.193 mmol), DIPEA (0.075 g, 0.578 mmol) and HATU (0.081 g, 0.212 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (EtOAc:hexanes) gave the title compound (0.033 g, 33%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.78 (d,1 H) 8.52 (s, 1 H) 8.18 (s, 1 H) 7.80 (t, 1 H) 7.28 (s, 1 H) 4.40 - 4.68 (m, 1 H) 4.30 - 4.45 (m, 1 H) 3.99 - 4.26 (m, 2 H) 3.87 - 4.03 (m, 1 H) 3.61 - 3.87 (m, 1 H) 3.29 - 3.34 (m, 2 H) 1.66 - 1.99 (m, 2 H) 1.37 - 1.63 (m, 4 H) 1.01 - 1.30 (m, 2 H). ES-LCMS m/z: 511 (M+1).

EXAMPLE 49

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

(Compound 49)

[00236] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.061 g, 0.177 mmol), 1-(trans-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate (0.055 g, 0.177 mmol), DIPEA (0.068 g, 0.530 mmol) and HATU (0.074 g, 0.194 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to an oil. Purification by silica gel chromatography (methanol:DCM) gave the title compound (0.027 g, 29%) as a pink solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.00 (d, 1 H) 8.10 (s, 1 H) 4.58 (br. s., 1 H) 4.38 (s, 1 H) 3.99 - 4.27 (m, 3 H) 3.94 (t, 1 H) 3.81 (t, 1 H) 3.16 (m, 2H) 1.86 (m, 2 H) 1.38 - 1.61 (m, 4 H) 1.15 (m, 2 H). ES-LCMS m/z: 523, 525.

EXAMPLE 50

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

(Compound 50(a))

ROUTE A

Step A

trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate

[00237] A solution of 1,1-dimethylethyl (trans-4-hydroxycyclohexyl)carbamate (CombiBlocks) (1.000 g, 4.64 mmol), triisopropylsilyl chloride (1.34 g, 6.97 mmol) and imidazole (0.791 g, 11.61 mmol) in DMF (40 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to an off-white solid. The crude product was dissolved in DCM (40 mL) and trifluoroacetic acid (3 mL, 38.9 mmol) was added. The solution was stirred at room temperature for one hour. The solvent was evaporated to afford trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate (1.59 g, 89%). ES-LCMS m/z: 272 (M+1).

Step B

1,1-dimethylethyl {2-[(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate

[00238] A mixture of trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate (1.59 g, 4.13 mmol), 1,1-dimethylethyl (2-bromoethyl)carbamate (0.927 g, 4.13 mmol) and potassium carbonate (1.714 g, 12.40 mmol) in DMF (40 mL) was heated at 60 °C overnight. The reaction mixture was diluted with EtOAc and water was added. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to give the title compound as a colorless oil (1.18 g). ES-LCMS m/z: 415 (M+1). The crude product was used without further purification.

Step C

1,1-dimethylethyl {2-[(bromoacetyl)(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate

[00239] A solution of bromoacetyl bromide (0.621 g, 3.08 mmol) in DCM (5 mL) was added to a solution of 1,1-dimethylethyl {2-[(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate (1.160 g, 2.80 mmol) and triethylamine (0.429 mL, 3.08 mmol) in DCM (30 mL) at 0 °C. The mixture was stirred for 30 minutes. The solvent was evaporated and EtOAc and water were added. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Silica gel chromatography (hexanes/EtOAc) gave the title compound (0.300 g, 20%). ES-LCMS m/z: 536 (M+1).

Step D

1,1-dimethylethyl 3-oxo-4-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-1-piperazinecarboxylate

[00240] To a solution of 1,1-dimethylethyl {2-[(bromoacetyl)(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)amino]ethyl}carbamate (0.291 g, 0.543 mmol) in DMF (4 mL) at 0 °C was added sodium hydride (60% oil dispersion) (0.024 g, 0.598 mmol). The reaction mixture was stirred for 30 minutes, poured into ice-water and extracted with EtOAc. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to give 1,1-dimethylethyl 3-oxo-4-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-1-piperazinecarboxylate (0.199 g, 81%) as a yellow oil. ES-LCMS m/z: 455 (M+1).

Step E

1-(trans-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate

[00241] Trifluoroacetic acid (1 mL, 13 mmol) was added to a solution of 1,1-dimethylethyl 3-oxo-4-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-1-piperazinecarboxylate (0.187 g, 0.411 mmol) in DCM (3 mL). The mixture was stirred at room temperature for one hour. The solvent was evaporated to give 1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate (0.192 g). The crude product was used without further purification. ES-LCMS m/z: 199 (M+1).

Step F

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00242] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.054 g, 0.177 mmol), 1-(trans-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate (0.055 g, 0.177 mmol), DIPEA (0.068 g, 0.530 mmol) and HATU (0.074 g, 0.194 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was separated and washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (DCM:MeOH) followed by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.011 g, 12%) as a white solid. ^{1}H NMR (400 MHz, methanol-d_4) δ ppm 8.31 (s, 1 H) 7.58 (s, 1 H) 4.56 (s, 1 H) 4.24 - 4.41 (m, 2 H) 4.11 (t, 1 H) 3.95 (m, 1 H) 3.39 - 3.57 (m, 3 H) 2.04 - 2.21 (m, 1 H) 1.88 - 2.07 (m, 2 H) 1.54 - 1.76 (m, 4 H) 1.29 - 1.48 (m, 2 H) 0.97 - 1.16 (m, 2 H) 0.73 - 0.90 (m, 2 H). ES-LCMS m/z: 485 (M+1).

ROUTE B

Step A

N-[(4-nitrophenyl)sulfonyl]glycine

[00243] To a solution of glycine (10 g, 133 mmol) in 1 N sodium hydroxide (140 mL, 140 mmol) at 0 °C was added 4-nitrobenzenesulfonyl chloride (29.5 g, 133 mmol) to give a suspension. After 30 minutes, the cooling bath was removed and 1 N sodium hydroxide solution was added to maintain the pH>9. After 2 hours, the mixture was diluted with 1 N sodium hydroxide and water and extracted with EtOAc (250 mL). The insoluble material was filtered off, and the aqueous phase was separated and further extracted with EtOAc (250 mL, 100 mL). The aqueous phase was then acidified with 6 N HCl to pH 1 to precipitate the product. The precipitate was filtered and dried under high vacuum to afford the title compound (20.88 g, 60.2 %) as a white solid. ES-LCMS m/z: 259 (M-1)

Step B

N1-(trans-4-hydroxycyclohexyl)-N2-[(4-nitrophenyl)sulfonyl]glycinamide

[00244] A mixture of 1,1-dimethylethyl (trans-4-hydroxycyclohexyl)carbamate (Combi Blocks) (1.000 g, 4.64 mmol) and HCl (4 N in 1,4-dioxane) (10 mL, 40 mmol) was stirred at room temperature for one hour. The solvent was evaporated to give trans-4-aminocyclohexanol hydrochloride (0.704 g, quant.) as a white solid. HATU (2.104 g, 5.53 mmol) was added to a mixture of N-[(4-nitrophenyl)sulfonyl]glycine (1.200 g, 4.61 mmol), trans-4-aminocyclohexanol hydrochloride (0.699 g, 4.61 mmol) and DIPEA (1.79 g, 13.83 mmol) in DMF (20 mL). The mixture was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc and water was added. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography gave the title compound (0.740 g, 45%). ES-LCMS m/z: 357 (M+).

Step C

N2-[(4-nitrophenyl)sulfonyl]-N1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)glycinamide

[00245] A mixture of N1-(trans-4-hydroxycyclohexyl)-N2-[(4-nitrophenyl)sulfonyl]glycinamide (0.200 g, 0.560 mmol), triisopropylsilyl chloride (0.162 g, 0.839 mmol) and imidazole (0.095 g, 1.399 mmol) in DMF (5 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc and water was added. The organic layer was washed with water and brine, dried over sodium sulfate and the solvent was evaporated to give the title compound (0.287 g). The crude product was used for the next step without further purification. ES-LCMS m/z: 514 (M+1).

Step D

4-[(4-nitrophenyl)sulfonyl]-1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone

[00246] A mixture of N^2-[(4-nitrophenyl)sulfonyl]-N1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)glycinamide (0.380 g, 0.740 mmol) and potassium carbonate (1.02 g, 7.40 mmol) in DMF (8 mL) was heated at 60 °C for 30 minutes. 1,2-dibromoethane (0.64 mL, 7.40 mmol) was added and heating was continued overnight. EtOAc and water were added to the reaction mixture. The aqueous layer was back extracted with EtOAc and the combined organic layers were washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (EtOAc:hexane) gave the title compound (0.262 g, 66%) as a white solid. ES-LCMS m/z: 540 (M+1).

Step E

1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone

[00247] Thiophenol (0.134 g, 1.214 mmol) was added to a suspension of potassium carbonate (0.235 g, 1.699 mmol) in acetonitrile (5 mL) at 50 °C. After 30 minutes, 4-[(4-nitrophenyl)sulfonyl]-1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone (0.262 g, 0.485 mmol) in acetonitrile (10 mL) was added dropwise. After 1 hour, the reaction mixture was cooled to room temperature and the solvent was evaporated. Purification by silica gel chromatography (MeOH:DCM) gave the title compound (0.110 g, 64%) as a white solid. ES-LCMS m/z: 355 (M+1).

Step F

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00248] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.084 g, 0.276 mmol), 1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone (0.098 g, 0.276 mmol), DIPEA (0.107 g, 0.829 mmol) and HATU (0.126 g, 0.332 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (EtOAc:hexane) gave 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone (0.128 g, 71%). Hydrogen chloride (4 N in 1,4-dioxane) (2 mL, 65.8 mmol) was added and the mixture was stirred at room temperature for 15 minutes. The solvent was evaporated. The residue was triturated with ether and dried under vacuum to give the title compound (0.084 g, 63%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.16 - 8.62 (m, 1 H) 7.58 (s, 1 H) 4.41 (s, 1 H) 4.17 (s, 1 H) 3.97 (t, 1 H) 3.79 (t, 1 H) 3.24 - 3.40 (m, 4 H) 2.05 - 2.32 (m, 1 H) 1.71 - 1.93 (m, 2

H) 1.37 - 1.62 (m, 4 H) 1.15 - 1.29 (m, 2 H) 0.94 - 1.04 (m, 2 H) 0.84 - 0.90 (m, 2 H). ES-LCMS m/z: 485 (M+1).

ROUTE C

Step A

methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-2-propen-1-ylglycinate

[00249] To a solution of N-(tert-butoxycarbonyl)-glycine methyl ester (39.3 mL, 266 mmol) in DMF (600 mL) at 0 °C was added allyl bromide (28.8 mL, 332 mmol) followed by sodium hydride (60%, 12.76 g, 319 mmol). After 75 minutes, saturated aqueous NH_4Cl (100 mL) was added and the suspension was stirred for 30 minutes. The white precipitate was filtered off through a pad of Celite and the filtrate was concentrated under reduced pressure. The residue was diluted with EtOAc (400 mL) and washed with brine (100 mL). The aqueous phase was separated and further extracted with EtOAc (200 mL). The combined organic phase was dried over $MgSO_4$, filtered and concentrated to give 55 g of crude product as an oil which was purified on silica gel (0-15% EtOAc/ hexanes) to give the title compound (24.89 g, 109 mmol, 40.8 % yield) as a colorless oil. ES-LCMS m/z: 174 (M+1).

Step B

methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate

[00250] A solution of methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-2-propen-1-ylglycinate (12 g, 52.3 mmol) in methanol (374 mL) was cooled to -78 °C before ozone was bubbled into the mixture. Ozone was applied until the reaction mixture turned blue and TLC indicated consumption of the starting material. Nitrogen was bubbled into the reaction mixture until the blue solution became colorless, and then bubbled with nitrogen for 25 more minutes. Dimethyl sulfide (19.36 mL, 262 mmol) was added slowly and the mixture was allowed to slowly come to room temperature as the cold-bath warmed overnight. The mixture was concentrated and the residue was taken up in ethyl acetate (750 mL). The organic phase was washed with water (250 mL), washed with brine (250 mL), dried over sodium sulfate, and concentrated to give the title compound (12.7 g, 99%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 9.59 - 9.77 (m, 1 H), 4.13 (s, 1 H), 4.05 (s, 1 H), 4.00 (s, 1 H), 3.90 (s, 1 H), 3.72 - 3.80 (m, 3 H), 1.39 - 1.54 (m, 9 H). Spectral data matches that reported previously in the literature: Bioorg. Med. Chem., 2007 (15), 2092-2105.

Step C

1,1-dimethylethyl 4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinecarboxylate

[00251] To a solution of methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (12.7 g, 52.2 mmol) in methanol (200 mL) was added sodium sulfate (46.3 g, 326 mmol) followed by trans-4-aminocyclohexanol hydrochloride (9.49 g, 62.6

mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (10.93 mL, 62.6 mmol). The mixture was stirred for 60 minutes before sodium borohydride (2.369 g, 62.6 mmol) was added portionwise in order to control effervescence. A mild exotherm was observed. After 2 hours, LC-MS showed the uncyclized amine/ester. Sodium hydride (60% in mineral oil) (3.99 g, 100 mmol) was added portionwise in order to control effervescence. The reaction appeared to be complete after 1 hour. The reaction was stirred for an additional hour and was concentrated. The mixture was quenched with 30% citric acid trisodium salt. 1 N Hydrochloric acid was added until pH~7, and then solid citric acid was added until pH~5. The mixture was extracted three times with ethyl acetate and the combined organic layers were washed with brine. The organic phase was dried over sodium sulfate and concentrated. Solids precipitated while concentrating. Once the volume reached ~100-150 mL, hexanes were added (400 mL). Solids were collected by filtration, washed with hexanes, and dried under vacuum to give the title compound (10.65 g, 68%). ES-LCMS m/z: 299 (M+1).

Step D

1-(trans-4-hydroxycyclohexyl)-2-piperazinone hydrochloride

[00252] To a solution of 1,1-dimethylethyl 4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinecarboxylate (10.65 g, 35.7 mmol) in dichloromethane (DCM) (100 mL) was added a solution of 4 N HCl in 1,4-dioxane (89 mL, 357 mmol). After 6 hours, the solvent was removed under reduced pressure to give 1-(trans-4-hydroxycyclohexyl)-2-piperazinone hydrochloride (9.78 g, 36.4 mmol, quantitative) as a white solid. The compound contained ~0.23 eq DCM and ~0.16 eq of 1,4-dioxane. ES-LCMS m/z: 199.3 (M+1).

Step E

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00253] To a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (218 mg, 0.716 mmol), 1-(trans-4-hydroxycyclohexyl)-2-piperazinone hydrochloride (230 mg, 0.859 mmol), N,N-diisopropylethylamine (625 µl, 3.58 mmol) in DMF (1.8 mL) at room temperature was added HATU (278 mg, 0.730 mmol) in one portion. After 25 minutes, the mixture was diluted with EtOAc (20 mL), and washed with 1 N HCl (5 mL), saturated aqueous NH_4Cl (8 mL), then brine (8 mL), dried over Na_2SO_4, filtered and concentrated to give a foam (~400 mg). The foam was dissolved in absolute EtOH (1.5 mL) and added dropwise to water (15 mL). The precipitate was filtered and dried under high vacuum to give the title compound (272.2 mg, 0.550 mmol, 77 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.84 - 0.95 (m, 2 H),

0.97 - 1.07 (m, 2 H), 1.10 - 1.33 (m, 2 H), 1.44 - 1.63 (m, 4 H), 1.84 (m, 2 H), 2.15 - 2.28 (m, 1 H), 3.24 - 3.40 (m, 3 H), 3.81 (t, J=5.0 Hz, 1 H), 3.98 (t, J=4.9 Hz, 1 H), 4.07 - 4.28 (m, 2 H), 4.43 (s, 1 H), 4.58 (t, J=3.9 Hz, 1 H), 7.59 (s, 1 H), 8.40 - 8.49 (m, 1 H); ES-LCMS m/z: 485.2 (M+1).

ROUTE D

Step A

methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-2-propen-1-ylglycinate

[00254] Et_3N (106 mL, 762 mmol) was added dropwise to a solution of methyl bromoacetate (70.2 mL, 762 mmol) in THF (600 mL). The cloudy solution was cooled to 0 °C and allylamine (43.5 g, 762 mmol) was added in one portion and the resulting mixture was stirred at 0 °C for 15 mins. The cooling bath was removed and stirring was continued at room temperature for 1.5 hours. A small aliquot was analyzed by NMR and showed a 89:11 ratio of methyl *N*-2-propen-1-ylglycinate to the dialkylated amine. The reaction mixture was filtered to remove the $Et_3N.HBr$ salt and washed with Et_2O. The filtrate was concentrated to give the crude methyl *N*-2-propen-1-ylglycinate as a clear oil. A solution of this oil in CH_2Cl_2 (600 mL) was cooled to 0 °C. Boc_2O (150 g, 686 mmol) and DMAP (9.3 g, 76 mmol) were added in portions. Evolution of CO_2 was observed. The reaction mixture was allowed to stir at room temperature for 1.5 hours, washed with 0.5 M HCl (2 x 600 mL), aq. $NaHCO_3$, brine, dried (Na_2SO_4), filtered and evaporated to give a brown oil. Purification by high vacuum distillation provided the title compound (125.8 g, 72%) as a clear liquid. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.71 - 5.86 (m, *J*=16.4, 10.9, 5.4, 5.4, 5.4 Hz, 1 H), 5.06 - 5.24 (m, 2 H), 3.81 - 4.03 (m, 4 H), 3.74 (s, 3 H), 1.38 - 1.52 (m, 9 H).

EXAMPLE 51

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone

(Compound 51)

Step A

cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate

[00255] Cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate (1.73 g) was prepared from 1,1-dimethylethyl (cis-4-hydroxycyclohexyl)carbamate (Biofine International) and triisopropylsilyl chloride by the procedure described in Example 50.

Step B

1-(cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone trifluoroacetate

[00256] 1-(cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone trifluoroacetate (0.294 g, 13% over 4 steps) was prepared by the procedure described in Example 50 starting with cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexanamine trifluoroacetate and 1,1-dimethylethyl (2-bromoethyl)carbamate. ES-LCMS m/z: 355 (M+1).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone

[00257] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.060 g, 0.197 mmol), 1-(cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone trifluoroacetate (0.070 g, 0.197 mmol), DIPEA (0.077 g, 0.592 mmol) and HATU (0.090 g, 0.237 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to an oil. Purification by silica gel chromatography (EtOAc:hexane) gave 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)-1,8a-dihydroimidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(*cis*-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone. 4 N HCl in 1,4-dioxane (2.5 mL, 10.00 mmol) was added and the mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% ammonia) to give the title compound (0.013 g, 13%) as a white solid. ^{1}H NMR (400 MHz, methanol-d_4) δ ppm 8.09 - 8.53 (m, 1 H) 7.46 - 7.69 (m, 1 H) 4.48 - 4.66 (m, 1 H) 4.27 - 4.46 (m, 2 H) 4.01 - 4.18 (m, 1 H) 3.86 - 4.01 (m, 2 H) 3.42 - 3.65 (m, 2 H) 2.13 (br. s., 1 H) 1.88 (d, 4 H) 1.53 - 1.72 (m, 2 H) 1.34 - 1.53 (m, 2 H) 1.09 (d, 2 H) 0.66 - 0.91 (m, 2 H). ES-LCMS m/z: 485 (M+1).

EXAMPLE 52

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone

(Compound 52)

[00258] A mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.077 g, 0.225 mmol), 1-(cis-4-hydroxycyclohexyl)-2-piperazinone trifluoroacetate (0.070 g, 0.225 mmol), DIPEA (0.087 g, 0.675 mmol) and HATU (0.103 g, 0.270 mmol) in DMF (2 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to an oil. 4 N HCl in 1,4-dioxane (2.5 mL, 10.00 mmol) was added and the mixture was stirred at room temperature overnight.

The solvent was evaporated and the residue was purified by prep LCMS (acetonitrile:water with 0.1% ammonia) to give the title compound (0.028 g, 23%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.02 (d, J=11.32 Hz, 1 H) 7.82 - 8.33 (m, 1 H) 4.40 (s, 2 H) 4.28 (d, J=12.49 Hz, 1 H) 4.22 (s, 2 H) 3.95 (t, J=4.78 Hz, 1 H) 3.74 - 3.88 (m, 2 H) 1.78 - 1.92 (m, 2 H) 1.73 (d, J=13.46 Hz, 2 H) 1.39 - 1.57 (m, 2 H) 1.26 (m, 2 H). ES-LCMS m/z: 525 (M+1).

EXAMPLE 53

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone

(Compound 53)

[00259] A mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.065 g, 0.197 mmol), 1-(cis-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone trifluoroacetate (0.070 g, 0.197 mmol), DIPEA (0.103 mL, 0.592 mmol) and HATU (90 mg, 0.237 mmol) in DMF (2 mL) was stirred at room temperature. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to an oil. Purification by silica gel chromatography (EtOAc:hexane) gave the title compound (0.033 g, 24%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.84 (d, J=7.61 Hz, 1 H) 8.58 (s, 1 H) 8.23 (s, 1 H) 7.86 (s, 1 H) 7.34 (s, 1 H) 4.40 (s, 2 H) 4.25 - 4.36 (m, 3 H) 3.95 (m, 1 H) 3.76 - 3.91 (m, 2 H) 1.84 (d, 2 H) 1.74 (d, 2 H) 1.38 - 1.58 (m, 2 H) 1.17 - 1.43 (m, 2 H). ES-LCMS m/z: 511 (M+1).

EXAMPLE 54

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone

(Compound 54)

Step A

(3-methylcyclobutyl)amine hydrochloride

[00260] A solution of 3-methylcyclobutanecarboxylic acid (Parkway Scientific) (6.60 g, 57.8 mmol), diphenylphosphoryl azide (23.85 g, 87 mmol) and triethylamine (11.70 g, 116 mmol) in tert-butanol (100 mL) was heated at reflux overnight. Saturated aqueous sodium bicarbonate was added followed by evaporation of most of the tert-butanol under reduced pressure. The resulting suspension was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulfate and concentrated to give 1,1-dimethylethyl (3-methylcyclobutyl)carbamate (10.6 g). Hydrogen chloride (4 N in 1,4-

dioxane) (100 mL, 400 mmol) was added and the mixture was stirred at room temperature for one hour. The solvent was evaporated to give the title compound (4.00 g, 58%) as a white solid (4.00 g, 58%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.26 (br.s., 2 H) 3.64 - 3.81 and 3.40 - 3.52 (m, 1 H) 2.4 and 2.2 (m, 1 H) 2.16 - 2.35 (m, 2 H) 1.85 and 1.70 (m, 2 H) 1.06 and 1.04 (d, 3 H).

Step B

2-bromo-N-(3-methylcyclobutyl)acetamide

[00261] Bromoacetyl bromide (5.22 g, 25.8 mmol) was added to a solution of (3-methylcyclobutyl)amine hydrochloride (2.00 g, 23.49 mmol) and DIPEA (9.11 g, 70.5 mmol) in DCM (20 mL) at 0 °C. The mixture was stirred for one hour. The reaction mixture was poured into saturated sodium bicarbonate and the organic layer was separated, dried over sodium sulfate and concentrated to a brown oil. Purification by silica gel chromatography (EtOAc:hexane) gave the title compound (2.27 g, 47%) as a light yellow solid. ES-LCMS m/z: 206, 208.

Step C

N2-(2-hydroxyethyl)-N1-(3-methylcyclobutyl)glycinamide

[00262] A mixture of 2-bromo-N-(3-methylcyclobutyl)acetamide (2.240 g, 10.87 mmol) and ethanolamine (0.697 g, 11.41 mmol) in ethanol (40 mL) was heated at 60 °C for 1.5 hours. The reaction mixture was cooled to room temperature and the solvent was evaporated. Purification by silica gel chromatography (DCM/MeOH) gave the title compound (0.944 g, 47%) as a white solid. ES-LCMS m/z: 187 (M+1).

Step D

3-chloro-6-cyclopropyl-N-(2-hydroxyethyl)-N-{2-[(3-methylcyclobutyl)amino]-2-oxoethyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide

[00263] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (1.323 g, 4.34 mmol), N2-(2-hydroxyethyl)-N1-(3-methylcyclobutyl)glycinamide (0.809 g, 4.34 mmol), DIPEA (1.684 g, 13.03 mmol) and HATU (1.982 g, 5.21 mmol) in DMF (20 mL) was stirred at room temperature for one hour. EtOAc and water were added. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (DCM/MeOH) gave the title compound (0.784 g, 38%). ES-LCMS m/z: 473 (M+1).

Step E

3-chloro-N-(2-chloroethyl)-6-cyclopropyl-N-{2-[(3-methylcyclobutyl)amino]-2-oxoethyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide

[00264] Methanesulfonyl chloride (0.159 mL, 2.038 mmol) was added to a solution of 3-chloro-6-cyclopropyl-N-(2-hydroxyethyl)-N-{2-[(3-methylcyclobutyl)amino]-2-oxoethyl}-

8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (0.771 g, 1.630 mmol) and DIPEA (0.632 g, 4.89 mmol) in DCM (15 mL) at 0 °C. The mixture was stirred for 30 minutes. Stirring was continued at room temperature overnight. Saturated sodium bicarbonate was added, the organic layer was separated, dried over sodium sulfate and the solvent was evaporated to give the title compound (0.649 g, 81%). ES-LCMS m/z: 513 (M+Na).

Step F

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone

[00265] A 60% dispersion of sodium hydride in mineral oil (0.018 g, 0.448 mmol) was added to a mixture of 3-chloro-N-(2-chloroethyl)-6-cyclopropyl-N-{2-[(3-methylcyclobutyl)amino]-2-oxoethyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (0.200 g, 0.407 mmol) and sodium iodide (0.122 g, 0.814 mmol) in DMF (2 mL) at room temperature. The mixture was stirred for one hour. The reaction mixture was poured into ice water and extracted with EtOAc. The organic layer was washed with water and brine and dried over sodium sulfate. Evaporation of the solvent gave the title compound (0.176 g, 86%) as an off-white foam. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, 1 H) 7.60 (d, 1 H) 4.86 - 5.30 (m, 0.5 H) 4.53 - 4.74 (m, 0.5 H) 4.43 (s, 1 H) 4.19 (d, 1 H) 3.96 - 4.12 (m, 1 H) 3.76 - 3.95 (m, 1 H) 3.38 - 3.60 (m, 2 H) 2.29 - 2.44 (m, 1 H) 2.07 - 2.27 (m, 2.5 H) 1.87 - 2.07 (m, 0.5 H) 1.59 - 1.85 (m, 2 H) 1.11 - 1.17 (m, 1.5 H) 0.96 - 1.08 (m, 3.5 H) 0.84 - 0.94 (m, 2 H). ES-LCMS m/z: 455 (M+1).

EXAMPLE 55

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-3-methylcyclobutyl)-2-piperazinone

(Compound 55)

[00266] The title compound (0.052 g) was obtained from the mixture of cis and trans isomers (Example 54) after chromatographic separation on a Chiralcel ADH column (250x10 mm i.d., 5um; Daicel Chemical Ind.; Osaka, Japan) under supercritical conditions maintained at 40 °C, 140 bar with methanol modified CO_2 (20%MeOH, 80% CO_2) delivered at a combined flow rate of 10mL/min on a Berger MiniGram SFC system (Berger Instruments, Inc.; Newark, De). The isomers were detected using a Knauer selectable wavelength UV-Vis detector at 280nm.

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 8.44 (d, 1 H) 7.60 (d, 1 H) 4.56 - 4.82 (m, 1 H) 4.43 (s, 1 H) 4.19 (s, 1 H) 4.04 (br. s., 1 H) 3.80 - 3.93 (m, 1 H) 3.44 (m, 2 H) 2.06 - 2.29 (m, 3 H) 1.86 - 2.06 (m, 1 H) 1.73 (t, 2 H) 0.95 - 1.11 (m, 5 H) 0.78 - 0.95 (m, 2 H). ES-LCMS m/z: 455 (M+1).

EXAMPLE 56

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-methylcyclobutyl)-2-piperazinone

(Compound 56)

[00267] The title compound (0.050 g) was obtained from the mixture of cis and trans isomers (Example 54) as described in Example 55. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 8.26 - 8.60 (m, 1 H) 7.41 - 7.74 (m, 1 H) 4.96 - 5.21 (m, 1 H) 4.34 - 4.57 (m, 1 H) 4.19 (s, 1 H) 3.91 - 4.11 (m, 1 H) 3.71 - 3.90 (m, 1 H) 3.35 - 3.54 (m, 2 H) 2.27 - 2.44 (m, 2 H) 2.15 - 2.25 (m, 2 H) 1.58 - 1.79 (m, 2 H) 1.15 (d, 3 H) 0.96 - 1.07 (m, 2 H) 0.84 (m, 2 H). ES-LCMS m/z: 455 (M+1).

EXAMPLE 57

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2,6-piperazinedione

(Compound 57)

Step A

1,1-dimethylethyl 3,5-dioxo-1-piperazinecarboxylate

[00268] Di-tert-butyl dicarbonate (2.87 g, 13.15 mmol) was added to a suspension of 2,6-piperazinedione (1.00 g, 8.76 mmol) in DCM (40 mL). The mixture was stirred at room temperature overnight. The solvent was evaporated to give 1,1-dimethylethyl 3,5-dioxo-1-piperazinecarboxylate as a white solid. The crude product was carried further without additional purification. ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 8.26 (br. s., 1 H), 4.29 (s, 4 H) 1.3 (s, 9H).

Step B

1-cyclopentyl-2,6-piperazinedione hydrochloride

[00269] To a mixture of 1,1-dimethylethyl 3,5-dioxo-1-piperazinecarboxylate (0.233 g, 1.086 mmol), cyclopentanol (0.085 g, 0.987 mmol) and triphenylphosphine (0.285 g, 1.086 mmol) in THF (4 mL) was added DIAD (0.220 g, 1.086 mmol). The mixture was stirred at room temperature overnight. The solvent was evaporated. Purification by silica gel chromatography gave 1,1-dimethylethyl 4-cyclopentyl-3,5-dioxo-1-piperazinecarboxylate (0.083 g). Hydrogen chloride (4 N in 1,4-dioxane) (2 mL, 8.00 mmol) was added and the mixture was stirred at room temperature overnight. The solvent was evaporated to give 1-cyclopentyl-2,6-piperazinedione hydrochloride (0.054 g, 27% over 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.06 (br. s., 1 H) 4.81 - 5.05 (m, 1 H) 4.04 (s, 4 H) 1.62 - 1.98 (m, 4 H) 1.31 - 1.60 (m, 2 H) 0.98 - 1.28 (m, 2 H).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2,6-piperazinedione

[00270] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.084 g, 0.274 mmol), 1-cyclopentyl-2,6-piperazinedione hydrochloride (0.050 g, 0.274 mmol), DIPEA (0.106 g, 0.823 mmol) and HATU (0.125 g, 0.329 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to a brown solid. Trituration with methanol gave the title compound (0.045 g, 33%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.47 (s, 1 H) 7.63 (s, 1 H) 4.95 (br. s., 2 H) 4.83 - 4.91 (m, 1 H) 4.60 (br. s., 2 H) 2.11 - 2.34 (m, 1 H) 1.67 - 1.95 (m, 6 H) 1.43 - 1.59 (m, 2 H) 0.99 - 1.09 (m, 2 H) 0.84 - 0.94 (m, 2 H).

EXAMPLE 58

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone

(Compound 58)

[00271] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.114 g, 0.375 mmol), 1-(trans-1-methyl-3-{[tris(1-methylethyl)silyl]oxy}cyclobutyl)-2-piperazinone trifluoroacetate (0.170 g, 0.375 mmol), DIPEA (0.145 g, 1.124 mmol) and HATU (0.171 g, 0.450 mmol) in DMF (2 mL) was stirred at room temperature for 2 hours. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was treated with hydrogen chloride (4 N in 1,4-dioxane) (1 mL, 4 mmol) for 1 hour. The solvent was evaporated and residue was subjected to silica gel chromatography (DCM/MeOH) and reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.020 g, 11.5%) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.44 (d, J=6.64 Hz, 1 H) 7.38 - 7.69 (m, 1 H) 5.06 - 5.20 (m, 1 H) 5.04 (d, 1 H) 4.43 (s, 1 H) 4.19 (s, 2 H) 3.98 - 4.08 (m, 1 H) 3.81 - 3.91 (m, 1 H) 3.39 - 3.50 (m, 2 H) 2.30 - 2.44 (m, 2 H) 2.21 (dd, 1 H) 1.93 - 2.06 (m, 2 H) 1.01 (d, 2 H) 0.89 (d, 2 H). ES-LCMS m/z: 457 (M+1).

EXAMPLE 59

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone

(Compound 59)

Step A

(3-fluorocyclobutyl)amine hydrochloride

[00272] (3-Fluorocyclobutyl)amine hydrochloride (0.756 g, 64% over 2 steps) was prepared from 3-fluorocyclobutanecarboxylic acid (1.00 g, 8.47 mmol) by the procedure described in Example 54. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.41 (br. s., 1 H) 5.01 - 5.54 (m, 1 H) 4.05 - 4.36 and 3.71 - 3.97 (m, 1 H) 2.41 - 2.61 (m, 2 H) 2.31 - 2.45 (m, 1 H) 2.09 - 2.29 (m, 1 H).

Step B

1-(3-fluorocyclobutyl)-2-piperazinone hydrochloride

[00273] 1-(3-fluorocyclobutyl)-2-piperazinone hydrochloride (0.099 g, 24% over 2 steps) was prepared from (3-fluorocyclobutyl)amine hydrochloride (0.376 g, 3.0 mmol) and methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (462 mg, 2.0 mmol) and sodium cyanoborohydride (0.188 g, 3.0 mmol), followed by deprotection with hydrogen chloride in 1,4-dioxane as described herein. ES-LCMS m/z: 273 (M+1).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone

[00274] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.137 g, 0.450 mmol), 1-(3-fluorocyclobutyl)-2-piperazinone hydrochloride (0.094 g, 0.450 mmol), DIPEA (0.175 g, 1.351 mmol) and HATU 0.(206 g, 0.541 mmol) in DMF (2 mL) was stirred at room temperature for 2 hours. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was treated with hydrogen chloride (4 N in 1,4-dioxane) (1 mL, 4 mmol) for one hour. The solvent was evaporated and the residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid)to afford the title compound (0.014 g, 7%). ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 8.31 (br. s., 1 H) 7.57 (s, 1 H) 5.00 - 5.28 (m, 2 H) 4.55 (s, 1 H) 4.33 (s, 1 H) 4.16 (t, 1 H) 4.00 (t, 1 H) 3.50 - 3.61 (m, 2 H) 2.52 - 2.72 (m, 2 H) 2.35 - 2.53 (m, 2 H) 2.03 - 2.19 (m, 1 H) 0.98 - 1.13 (m, 2 H) 0.75 - 0.88 (m, 2 H). ES-LCMS m/z: 459 (M+1).

EXAMPLE 60

trans-4-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)cyclohexyl acetate

(Compound 60)

[00275] To a mixture of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone (0.040 g, 0.082 mmol) and TEA (0.017 g, 0.165 mmol) in DCM (1.5 mL) was added acetyl chloride (0.007 mL, 0.099 mmol). After stirring at room temperature for one hour, the reaction mixture was diluted with DCM. The organic layer was separated, washed with water and brine and concentrated. The residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to give the title compound (0.015 g, 34%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, 1 H) 7.60 (m, 1 H) 4.58 (m, 1 H) 4.44 (s, 1 H) 4.02 - 4.36 (m, 2 H) 4.00 (m, 1 H) 3.82 (br. s., 1 H) 3.33 (m, 2 H) 2.2 - 2.31 (m, 1 H) 1.98 (s, 3 H) 1.88 - 1.97 (m, 2 H) 1.51 - 1.70 (m, 4 H) 1.44 (br. s., 2 H) 0.96 - 1.06 (m, 2 H) 0.83 - 0.94 (m, 2 H). ES-LCMS m/z: 527 (M+1).

EXAMPLE 61

(+/-)-cis-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxycyclohexyl)-2-piperazinone

(Compound 61)

Step A

(+/-)-cis-1-(3-hydroxycyclohexyl)-2-piperazinone

[00276] (+/-)-cis-1-(3-hydroxycyclohexyl)-2-piperazinone (0.557 g, 8.4%) was prepared from 3-amino-cyclohexanol (cis, trans mixture) (4.03 g, 35 mmol) and N-[(4-nitrophenyl)sulfonyl]glycine (9.85 g, 33.3 mmol) by the procedure described herein.

Step B

cis-(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxycyclohexyl)-2-piperazinone

[00277] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid 0.(814 g, 2.67 mmol), (+/-)-cis-1-(3-hydroxycyclohexyl)-2-piperazinone (0.530 g, 2.67 mmol), DIPEA (1.04 g, 8.02 mmol) and HATU (1.22 g, 3.21 mmol) in DMF (2 mL) was stirred at room temperature for one hour. The reaction mixture was diluted with EtOAc and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. Purification by silica gel chromatography (MeOH:DCM) gave the title compound (0.805 g) in 86% purity as an off-white foam. A portion (0.080 g) of this material was purified by reverse phase HPLC (acetonitrile:water

with 0.1% formic acid) to afford the title compound (0.062 g) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.31 - 8.51 (m, 1 H) 7.49 - 7.71 (m, 1 H) 4.76 (m, 1 H) 4.44 (m, 1 H) 4.23 - 4.33 (m, 2 H) 3.98 (d, 1 H) 3.79 - 3.87 (m, 1 H) 3.41 - 3.57 (m, 2 H) 2.22 (m, 1 H) 1.62 - 1.85 (m, 3 H) 1.41 - 1.56 (m, 1 H) 1.33 (d, 4 H) 1.02 (d, 2 H) 0.90 (d, 2 H). ES-LCMS m/z: 485 (M+1).

EXAMPLE 62

4-{[3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 62)

Step A:

methyl 3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00278] [1,1'-Bis(diphenylphosphino)ferrocene] dichloropalladium (II) dichloromethane adduct (57.1 mg, 0.070 mmol) was added to methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (250 mg, 0.699 mmol) in tetrahydrofuran (5 mL). Propylzinc bromide (0.5M in tetrahydrofuran) (2.098 mL, 1.049 mmol) was then added slowly dropwise (1 drop every 2-3 seconds) at room temperature (25 °C). The reaction appeared to be complete within 2 hours and only trace starting material remained. The mixture was diluted with dichloromethane. The organic phase was washed once with water, washed two times with brine, dried over sodium sulfate, and concentrated. The residue was purified by reverse phase HPLC to give the title compound (96 mg, 43%). ES-LCMS m/z: 321, 323 (M+1).

Step B

3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00279] Methyl 3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (94 mg, 0.293 mmol) was dissolved in tetrahydrofuran (1954 µl) and then water (1954 µl) added. Sodium hydroxide (1 M) (733 µl, 0.733 mmol) was added and the mixture stirred at room temperature for 3 hours. The mixture was quenched with hydrochloric acid (1 M) (1172 µl, 1.172 mmol) and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated to give the title compound (87mg, 97%). ES-LCMS m/z: 307, 309 (M+1).

Step C

4-{[3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

[00280] To a mixture of 3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (45 mg, 0.147 mmol) and 1-cyclohexyl-2-piperazinone trifluoroacetate (47.8 mg, 0.161 mmol) in DMF was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.103 mL, 0.587 mmol). N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (67.0 mg, 0.176 mmol) was added and the mixture stirred at room temperature for 1 hour. The mixture was diluted with ethyl acetate. The organic phase was washed with water, washed with brine, washed with 5% lithium chloride (aqueous), dried over sodium sulfate, and concentrated. The residue was subject to silica chromatography eluting with a gradient of 0% to 4% 2 M ammonia/methanol in dichloromethane. Appropriate fractions were concentrated and the residue dissolved in minimal dichloromethane. Hexanes were added to give a cloudy mixture that was concentrated by rotovap. The residue was dried under high vacuum to give the title compound (52mg; 74%) as a solid. ^{1}H NMR (DMSO-d_6) δ: 8.46 (d, 1H), 7.84 (s, 1H), 4.39 (s, 1H), 4.15 (m, 2H), 3.94 (t, 1H), 3.77 (m, 1H), 3.30 (m, 2H), 2.69 (t, 2H), 1.66 - 1.78 (m, 2H), 1.58 - 1.66 (m, 2H), 1.49 (br. s., 2H), 1.33 - 1.46 (m, 2H), 1.21 (m, 3H), 1.03 (m, 1H), 0.88 (t, J = 7.3 Hz, 3H). ES-LCMS m/z: 471, 473 (M+1).

EXAMPLE 63

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 63)

Step A

methyl 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00281] [1,1'-Bis(diphenylphosphino)ferrocene] dichloropalladium (II) dichloromethane adduct (1.713 g, 2.098 mmol) was added to a mixture of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (7.5 g, 20.98 mmol) in tetrahydrofuran (70 mL). Isobutylzinc bromide (0.5M in tetrahydrofuran) (52.4 mL, 26.2 mmol) was then added slowly dropwise at room temperature. The reaction was stirred for 4 hours. The reaction appeared to be about 94% complete by LC-MS. An additional 0.17g of PdCl2(dppf)-dichloromethane adduct catalyst was added followed by slow dropwise addition of an additional 5.2mL of isobutylzinc bromide (0.5 M in tetrahydrofuran). Conversion appeared to be complete within an hour. The mixture was concentrated. The residue was adsorbed onto 20 g of Celite by slurry in dichloromethane and evaporation to dryness. Purification by silica chromatography, eluting with a gradient

of 15% to 25% ethyl acetate in hexanes gave the title compound (3.9g; 55%). ES-LCMS m/z: 335, 337 (M+1).

Step B

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

[00282] Methyl 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (95 mg, 0.284 mmol) was dissolved in tetrahydrofuran (2 mL) and water (2 mL) added. Sodium hydroxide (1 M) (0.710 mL, 0.710 mmol) was added and the mixture stirred at room temperature for 1 hour. The mixture was quenched with 1 M hydrochloric acid (1.135 mL, 1.135 mmol) and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was dissolved in 2 mL of thionyl chloride and refluxed for 1 hour. The mixture was concentrated and the residue co-evaporated 2 times with toluene via rotovap, dried under vacuum, and the acid chloride dissolved in dichloromethane (4mL). 2mL of the acid chloride solution was added dropwise to a mixture of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.099 mL, 0.568 mmol) and 1-cyclohexyl-2-piperazinone trifluoroacetate (42.0 mg, 0.142 mmol) in dichloromethane. The reaction was complete within 1 hour. The mixture was quenched with saturated sodium bicarbonate and extracted with dichloromethane. The organic phase was washed with brine, concentrated, and the residue purified by silica chromatography eluting with a gradient of 0% to 4% 2 M ammonia/methanol in dichloromethane to give the title compound (28mg, 40%) as a solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.50 (s, 1 H), 7.85 (s, 1 H), 4.44 (s, 1 H), 4.13 - 4.32 (m, 2 H), 3.95 - 4.04 (m, 1 H), 3.76 - 3.86 (m, 1 H), 3.35 - 3.44 (m, 1 H), 2.64 (d, 2 H), 1.86 - 2.07 (m, 1 H), 1.68 - 1.83 (m, 2 H), 1.51 - 1.67 (m, 3 H), 1.38 - 1.50 (m, 2 H), 1.20 - 1.38 (m, 3 H), 0.98 - 1.19 (m, 1 H), 0.90 (d, 6 H). ES-LCMS m/z: 485, 487 (M+1).

EXAMPLE 64

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 64)

Step A

methyl 6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00283] [1,1'-Bis(diphenylphosphino)ferrocene] dichloropalladium (II)dichloromethane adduct (113 mg, 0.139 mmol) was added to methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (496 mg, 1.39 mmol) in tetrahydrofuran (10 mL). Butylzinc bromide (0.5M in tetrahydrofuran) (4.16 mL, 2.08 mmol)

was then added slowly dropwise (1 drop every 2-3 sec) at room temperature. The reaction appeared to be complete within 1 hour. The mixture was diluted with dichloromethane, washed one time with water and two times with brine, dried over anhydrous sodium sulfate, and concentrated. Purification by silica chromatography eluting with a gradient of 0% to 2% acetonitrile in dichloromethane gave the title compound (143mg; 30.8%). ES-LCMS m/z: 335, 337 (M+1).

Step B

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

[00284] Methyl 6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (143 mg, 0.427 mmol) was dissolved in tetrahydrofuran (2 mL) and then water (2 mL) added. Sodium hydroxide (1 M) (1.068 mL, 1.068 mmol) was added and the mixture stirred at room temperature for 1 hour. The mixture was quenched with hydrochloric acid (1 M) (1.709 mL, 1.709 mmol) and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was dissolved in thionyl chloride (5.00 mL, 68.5 mmol), refluxed for one hour, and concentrated. The residue was co-evaporated two times with toluene and then dissolved in of dichloromethane (3 mL). A 1 mL aliquot of the dichloromethane solution was added dropwise to a stirring mixture of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.097 mL, 0.56 mmol) and 1-cyclohexyl-2-piperazinone trifluoroacetate (50.6 mg, 0.171 mmol) in dichloromethane (2 mL). The reaction was stirred for 1 hour, quenched with saturated sodium bicarbonate, extracted with dichloromethane, and concentrated. The residue was triturated in dichloromethane and hexanes. Solids were collected by filtration, washed with hexanes, and dried under vacuum to give the title compound (64 mg; 93%). ^{1}H NMR (DMSO-d_6) δ ppm 8.37 - 8.55 (m, 1 H), 7.84 (s, 1 H), 4.39 (s, 1 H), 4.07 - 4.30 (m, 2 H), 3.88 - 4.02 (m, 1 H), 3.72 - 3.84 (m, 1 H), 3.29 - 3.36 (m, 2 H), 2.71 (t, 2 H), 1.71 (d, 2 H), 1.46 - 1.67 (m, 5 H), 1.34 - 1.45 (m, 2 H), 1.13 - 1.35 (m, 4 H), 0.94 - 1.14 (m, 1 H), 0.87 (t, 3 H). ES-LCMS m/z: 485, 487 (M+1).

EXAMPLE 65

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 65)

[00285] Methyl 6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (143 mg, 0.427 mmol) was dissolved in tetrahydrofuran (2 mL) and then water

(2 mL) was added. Sodium hydroxide (1 M) (1.068 mL, 1.068 mmol) was added and the mixture stirred at room temperature for 1 hour. The mixture was quenched with hydrochloric acid (1 M) (1.709 mL, 1.709 mmol) and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was dissolved in thionyl chloride (5.00 mL, 68.5 mmol), refluxed for one hour, and concentrated. The residue was co-evaporated two times with toluene and then dissolved in 3 mL of dichloromethane. A 1 mL aliquot of the dichloromethane solution was added dropwise to a stirring mixture of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.097 mL, 0.56 mmol) and 1-(1,3-thiazol-2-yl)-2-piperazinone dihydrochloride (43.8 mg, 0.171 mmol) in dichloromethane (2 mL). The reaction was stirred for 1 hour, quenched with saturated sodium bicarbonate, extracted with dichloromethane, and concentrated. The residue was triturated in ethyl ether and hexanes. Solids were collected by filtration, washed with hexanes, and dried under vacuum to give the title compound (39 mg; 38%). ^{1}H NMR (DMSO-d_6) δ ppm 8.49 (d, 1 H), 7.86 (s, 1 H), 7.54 (d, 1 H), 7.32 (dd, 1 H), 4.84 (s, 1 H), 4.54 (s, 1 H), 4.20 (s, 3 H), 4.05 (br. s., 1 H), 2.72 (t, 2 H), 1.58 (t, 2 H), 1.24 - 1.40 (m, 2 H), 0.88 (t, 3 H). ES-LCMS m/z: 486, 488 (M+1).

EXAMPLE 66

(+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 66)

Step A

(+/-)-Methyl 3-chloro-6-(2,5-dihydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00286] Methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (2.0 , 5.6 mmol), palladium(II) acetate (0.13 g, 0.56 mmol), potassium acetate (1.4 g, 14 mmol), 2,3-dihydrofuran (1.96 g, 28.0 mmol), and tetrabutylammonium bromide (1.8 g, 5.6 mmol) in N,N-dimethylformamide (30 mL) were stirred at 80 °C for 1 hour. The mixture was allowed to cool, diluted with water, and extracted with ethyl acetate. The organic phase was washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 10% ethyl acetate in dichloromethane to give the title compound (970 mg, 50%). ES-LCMS m/z: 347, 349 (M+1).

Step B

(+/-)-Methyl 3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00287] (+/-)-Methyl 3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (342 mg, 0.986 mmol) and diphenyl sulfide (0.033 mL, 0.20 mmol) were degassed with nitrogen before 10% palladium on carbon (157 mg, 0.148 mmol) was added. The mixture was stirred under 40 psi of hydrogen for 3 hours. The catalyst was filtered off over Celite and the filtrate concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 5% acetonitrile in dichloromethane to give the title compound (293 mg, 85%). ES-LCMS m/z: 349, 351 (M+1).

Step C

(+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00288] (+/-)-Methyl 3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (293 mg, 0.840 mmol) was dissolved in tetrahydrofuran (11 mL). water (11 mL) and sodium hydroxide (1 M) (2.101 mL, 2.101 mmol) were added and the mixture stirred for 1 hour at room temperature. 4 mL of 1 N hydrochloric acid were added and the mixture extracted two times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was slurried in thionyl chloride (1000 mg, 8.40 mmol) and the mixture heated to reflux. The mixture became homogeneous after 15 minutes. LC-MS showed a complete reaction. The thionyl chloride was removed by rotovap and the residue co-evaporated two times with toluene. The residue was dissolved in 3mL of dichloromethane. An 1 mL aliquot of the acid chloride solution was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.176 mL, 1.1 mmol) and 1-cyclopentyl-2-piperazinone hydrochloride (69 mg, 0.34 mmol) in dichloromethane (2 mL). The reaction was complete within 10 minutes. The reaction mixture was diluted with dichloromethane, washed with water, and the organic layer concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 2% 2 M ammonia/methanol in dichloromethane. The product was further purified by reverse phase HPLC to give the title compound (59 mg; 43%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.19 - 8.34 (m, 1 H), 7.54 (s, 1 H), 4.79 - 5.09 (m, 2 H), 4.57 (s, 1 H), 4.39 (s, 1 H), 4.22 - 4.34 (m, 1 H), 4.05 - 4.21 (m, 1 H), 3.86 - 4.05 (m, 2 H), 3.39 (dt, 2 H), 2.42 (dq, 1 H), 2.05 (quin, 2 H), 1.75 - 1.94 (m, 3 H), 1.37 - 1.74 (m, 6 H). ES-LCMS m/z: 485, 487 (M+1).

EXAMPLE 67

4-{[3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 67)

Step A

Methyl 3-chloro-6-hydroxy-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00289] Methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (5 g, 13.99 mmol), potassium acetate (4.12 g, 42.0 mmol), bis(pinacolato)diboron (7.99 g, 31.5 mmol), and [1,1'-bis(diphenylphosphino)ferrocene] dichloropalladium (II)dichloromethane adduct (1.142 g, 1.399 mmol) in 1,4-dioxane (200 mL) were heated to 100 °C for 2 hours. The mixture was cooled to room temperature before acetic acid (1.60 mL, 28.0 mmol) and water (4 mL) were added. The mixture was stirred for 1 hour and 30% hydrogen peroxide (2.86 mL, 28.0 mmol) was added. After 3 hours, the mixture was quenched with a sodium thiosulfate solution, extracted with ethyl acetate, washed with brine, and concentrated. The residue was slurried in dichloromethane/ether and solids were collected by filtration. The product was dried under vacuum to give the title compound (3.48g, 76%) as a solid. ES-LCMS m/z: 295, 297 (M+1).

Step B

methyl 3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00290] Methyl 3-chloro-6-hydroxy-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (360 mg, 1.22 mmol), potassium carbonate (338 mg, 2.44 mmol), and ethyl iodide (0.099 mL, 1.22 mmol) in DMF (5 mL) were stirred at room temperature for 2 hours. The mixture was diluted with water and extracted with ethyl acetate. The organic phase was washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, concentrated, and the residue purified by silica chromatography eluting with a gradient of 0% to 5% ethyl acetate in dichloromethane to give the title compound (250mg; 63%). ES-LCMS m/z: 323, 325 (M+1).

Step C

4-{[3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00291] Methyl 3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (250 mg, 0.775 mmol) was dissolved in tetrahydrofuran (10 mL). Water (10 mL) and sodium hydroxide (1.937 mL, 1.937 mmol) were added and the mixture stirred for 1 hour at room temperature. 1 N Hydrochloric acid (4 mL) was added and the mixture extracted two times with ethyl acetate. The combined organic layers were washed with

brine, dried over sodium sulfate, and concentrated. The residue was slurried in thionyl chloride (1000 mg, 8.40 mmol) and the mixture heated to reflux. The mixture became homogeneous after 15 minutes. The thionyl chloride was removed by rotovap and the residue co-evaporated two times with toluene. The residue was dissolved in 3 mL of dichloromethane. A 1 mL aliquot of the acid chloride solution was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.162 mL, 0.930 mmol) and 1-cyclopentyl-2-piperazinone hydrochloride (55 mg, 0.27 mmol) in dichloromethane (5 mL). The reaction was stirred for 10 minutes and then diluted with dichloromethane, washed with saturated sodium bicarbonate, and the organic layer concentrated. The residue was purified by reverse phase HPLC to give the title compound (63 mg, 53%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 7.60 - 7.76 (m, 1 H), 7.41 (s, 1 H), 4.79 - 5.06 (m, 1 H), 4.59 (s, 1 H), 4.37 (s, 1 H), 4.25 - 4.34 (m, 1 H), 4.07 (q, 2 H), 3.91 (t, 1 H), 3.38 (dt, 2 H), 1.82 (br. s., 2 H), 1.62 - 1.74 (m, 2 H), 1.53 - 1.62 (m, 2 H), 1.38 - 1.53 (m, 5 H). ES-LCMS m/z: 459, 461 (M+1).

EXAMPLE 68

4-{[3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 68)

Step A

methyl 3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00292] To a mixture of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (600 mg, 1.68 mmol), 3-pyridinylboronic acid (309 mg, 2.52 mmol), and 3M potassium phosphate tribasic (1.68 mL, 5.03 mmol) in acetonitrile (10 mL) was added [1,1'-bis(diphenylphosphino)ferrocene] dichloropalladium (II)dichloromethane adduct (137 mg, 0.168 mmol), and the mixture heated to 80 °C for 2 hours. The mixture was allowed to cool to room temperature, diluted with water, and extracted with ethyl acetate. The organic phase was washed with 5% lithium chloride (aqueous), washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 50% ethyl acetate in dichloromethane to give the title compound (260 mg, 44%). ES-LCMS m/z: 356, 358 (M+1).

Step B

4-{[3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00293] Methyl 3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (250 mg, 0.703 mmol) was dissolved in tetrahydrofuran (10 mL). Water (10

mL) and sodium hydroxide (1 M) (1.757 mL, 1.757 mmol) were added and the mixture stirred for 1 hour at room temperature. Hydrochloric acid (1 M) (10 mL) was added and the mixture concentrated. The residue was co-evaporated 2 times with toluene and dried under high vacuum, and the split into 3 equal portions of the acid. To one portion of the acid was added N,N-dimethylformamide (3 mL), 1-cyclopentyl-2-piperazinone hydrochloride (50 mg, 0.25 mmol), *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.246 mL, 1.41 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (94 mg, 0.25 mmol). After stirring for 1 hour, the mixture was quenched with saturated sodium bicarbonate and extracted with ethyl acetate. The organic phase was washed with brine, concentrated, and the residue purified by reverse phase HPLC. The sample was recrystallized with dichloromethane and hexanes to give the title compound (55 mg, 48%) as a solid. ^{1}H NMR (DMSO-d_6) δ ppm 9.07 - 9.16 (m, 1 H), 8.94 - 9.07 (m, 1 H), 8.67 - 8.78 (m, 1 H), 8.33 - 8.39 (m, 1 H), 8.28 - 8.33 (m, 1 H), 7.54 - 7.70 (m, 1 H), 4.64 - 4.97 (m, 1 H), 4.39 - 4.55 (m, 1 H), 4.25 (s, 1 H), 4.00 - 4.12 (m, 1 H), 3.81 - 3.95 (m, 1 H), 3.33 - 3.46 (m, 2 H), 1.62 - 1.83 (m, 4 H), 1.47 - 1.62 (m, 4 H). ES-LCMS m/z: 492, 494 (M+1).

EXAMPLE 69

(+/-)-4-{[3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 69)

Step A

(+/-)-Methyl 3-chloro-6-(2,3-dihydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00294] Methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (2.0 , 5.6 mmol), palladium(II) acetate (0.13 g, 0.56 mmol), potassium acetate (1.4g, 14 mmol), 2,5-dihydrofuran (1.96g, 28 mmol), and tetrabutylammonium bromide (1.8 g, 5.6 mmol) in *N,N*-dimethylformamide (30 mL) were stirred at 80 °C for 1 hour. The mixture was allowed to cool, diluted with water, extracted with ethyl acetate, washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 10% ethyl acetate in dichloromethane to give the title compound (310 mg, 16%). ES-LCMS m/z: 347, 349 (M+1).

Step B

(+/-)-Methyl 3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00295] (+/-)-Methyl 3-chloro-6-(2,3-dihydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (310 mg, 0.894 mmol) and diphenyl sulfide (0.030 mL, 0.179 mmol) were degassed with nitrogen before 10% palladium on carbon (143 mg, 0.134 mmol) was added. The mixture was stirred under 40 psi hydrogen for 3 hours. The catalyst was filtered off over Celite and the filtrate concentrated. The residue was subject to silica chromatography eluting with a gradient of 0% to 20% ethyl acetate in dichloromethane to give the title compound (255 mg; 82%). ES-LCMS m/z: 349, 351 (M+1).

Step C

(+/-)-4-{[3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00296] (+/-)-Methyl 3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (255 mg, 0.731 mmol) was dissolved in tetrahydrofuran (5 mL). Water (5 mL) and sodium hydroxide (1 M) (1.828 mL, 1.828 mmol) were added and the mixture stirred for 1 hour at room temperature. 10 mL of 1 N hydrochloric acid were added and the mixture extracted two times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was slurried in thionyl chloride (870 mg, 7.31 mmol) and the mixture heated to reflux. The mixture became homogeneous after 15 minutes. The thionyl chloride was removed by rotovap and the residue co-evaporated two times with toluene. The residue was dissolved in 3mL of dichloromethane. A 1mL aliquot of the acid chloride solution was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.153 mL, 0.878 mmol) and 1-cyclopentyl-2-piperazinone hydrochloride (59 mg, 0.29 mmol) in dichloromethane (2 mL). After 15 minutes, the mixture was diluted with dichloromethane and washed with saturated sodium bicarbonate. The organic layer was concentrated and the residue purified by reverse phase HPLC to give the title compound (24 mg; 20%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.13 (d, 1 H), 7.59 (s, 1 H), 4.81 - 5.09 (m, 1 H), 4.59 (s, 1 H), 4.41 (s, 1 H), 4.29 (t, 1 H), 4.05 - 4.23 (m, 2 H), 3.89 - 4.02 (m, 2 H), 3.84 (ddd, 1 H), 3.53 (quin, 1 H), 3.42 (dt, 2 H), 2.36 - 2.62 (m, 1 H), 1.94 - 2.15 (m, 1 H), 1.78 - 1.94 (m, 2 H), 1.56 - 1.78 (m, 4 H), 1.39 - 1.56 (m, 2 H). ES-LCMS m/z: 485, 487(M+1).

EXAMPLE 70

4-{[3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 70)

Step A

Methyl 3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00297] Methyl 3-chloro-6-hydroxy-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (495 mg, 1.680 mmol), potassium carbonate (464 mg, 3.36 mmol), and 2-iodopropane (0.185 mL, 1.85 mmol) in DMF (5 mL) were stirred at room temperature for 2 hours. The mixture was diluted with water and extracted with ethyl acetate. The organic phase was washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, concentrated, and the residue was purified by silica chromatography eluting with a gradient of 0% to 5% ethyl acetate in dichloromethane to give the title compound (325 mg, 57%). ES-LCMS m/z: 337, 339 (M+1).

Step B

4-{[3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00298] Methyl 3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (325 mg, 0.965 mmol) was dissolved in tetrahydrofuran (5 mL). Water (5 mL) and sodium hydroxide (1 M) (2.413 mL, 2.413 mmol) were added and the mixture stirred for 1 hour at room temperature. 10 mL of 1 N hydrochloric acid were added and the mixture extracted two times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was slurried in thionyl chloride (1150 mg, 9.65 mmol) and the mixture heated to reflux. After 15 minutes, the mixture became homogeneous. The thionyl chloride was removed by rotovap and the residue co-evaporated two times with toluene. The residue was dissolved in dichloromethane (8 mL). A 2 mL aliquot of the acid chloride solution was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.202 mL, 1.16 mmol) and 1-cyclopentyl-2-piperazinone hydrochloride (49 mg, 0.24 mmol) in dichloromethane (2 mL). After 10 minutes, the mixture was diluted with dichloromethane and washed with saturated sodium bicarbonate. The organic layer was concentrated and the residue purified by silica chromatography eluting with a gradient of 25% to 50% ethyl acetate in hexanes to give the title compound (55 mg, 48%). ^{1}H NMR (DMSO-d_6) δ ppm 8.12 - 8.33 (m, 1 H), 7.72 (s, 1 H), 4.66 - 4.97 (m, 2 H), 4.46 (s, 1 H), 4.22 (s, 1 H), 3.99 - 4.12 (m, 1 H), 3.80 - 3.95 (m, 1 H), 3.34 - 3.48 (m, 2 H), 1.61 - 1.81 (m, 4 H), 1.53 (br. s., 4 H), 1.34 (d, 6 H). ES-LCMS m/z: 473, 475 (M+1).

EXAMPLE 71

1-cyclopentyl-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 71)

Step A

5-chloro-3-(trifluoromethyl)-2-pyridinamine

[00299] To a solution of 3-(trifluoromethyl)-2-pyridinamine (12.2 g, 75.2 mmol) in *N,N*-dimethylformamide (100 mL) was added N-chlorosuccinimide (10.55 g, 79.01 mmol). The mixture was heated to 60 °C and stirred for 1 hour. The mixture was allowed to cool to room temperature and was concentrated. The residue purified by passing through a silica plug, eluting with dichloromethane to give the title compound (13 g, 88%). ES-LCMS m/z: 197, 199 (M+1).

Step B

ethyl 6-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00300] 5-chloro-3-(trifluoromethyl)-2-pyridinamine (3.00 g, 15.3 mmol) and ethyl bromopyruvate (4.27 mL, 30.5 mmol) in *N,N*-dimethylformamide (50 mL) were stirred at 60 °C for 3 hours. The mixture was allowed to cool to room temperature and then poured into stirring iced water. The precipitate was stirred for 5 minutes, collected by filtration, washed with water, and dried under vacuum to give the title compound (3.5g, 78%) as a solid. ES-LCMS m/z: 293, 295 (M+1).

Step C

ethyl 3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00301] To a solution of ethyl 6-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (3.5 g, 12.0 mmol) in *N,N*-dimethylformamide (50 mL) was added N-chlorosuccinimide (1.677 g, 12.56 mmol). The mixture was heated to 60 °C and after 2 hours was allowed to cool to room temperature and concentrated to ~10 mL. The mixture was partitioned between ethyl acetate and water, and extracted 2 times with ethyl acetate. The combined organic layers were washed with saturated sodium thiosulfite, washed with saturated sodium bicarbonate, brine, dried over sodium sulfate, and concentrated. The residue was dried under vacuum to give the title compound (3.9 g, 99%) as a solid. ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.35 (d, 1 H), 7.64 (d, 1 H), 4.48 (q, 2 H), 1.44 (t, 3 H).

Step D

3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00302] Ethyl 3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (1.93 g, 5.90 mmol) was dissolved in tetrahydrofuran (50 mL). Water (50 mL) and sodium hydroxide (1 M) (11.80 mL, 11.80 mmol) were added and the mixture stirred for 2 hours at

room temperature. The mixture was quenched with 1 N hydrochloric acid and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated to give the title compound (1.67 g, 85%); ES-LCMS m/z: 299, 301 (M+1).

Step E

1-cyclopentyl-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

[00303] 3,6-Dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (417 mg, 1.39 mmol) was slurried in thionyl chloride (1659 mg, 13.94 mmol) and the mixture heated to 75 °C. After 15 minutes, the mixture became homogeneous. The thionyl chloride was removed by rotovap and the residue co-evaporated 2 times with toluene. The residue was dissolved in dichloromethane (8 mL). A 2 mL aliquot of the acid chloride solution was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.292 mL, 1.67 mmol) and 1-cyclopentyl-2-piperazinone hydrochloride (114 mg, 0.558 mmol) in dichloromethane (2 mL). After 15 minutes, the mixture was diluted with dichloromethane and the organic phase washed with saturated sodium bicarbonate. The organic layer was concentrated and the residue purified by reverse phase HPLC. The product was triturated in ether before collecting by filtration to give the title compound (37 mg; 24%) as a solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.87 - 9.13 (m, 1 H), 8.08 (s, 1 H), 4.65 - 4.92 (m, 1 H), 4.41 (s, 1 H), 4.22 (s, 1 H), 3.93 - 4.06 (m, 1 H), 3.81 - 3.93 (m, 1 H), 3.37 - 3.43 (m, 1 H), 3.35 (br. s., 1 H), 1.68 (br. s., 4 H), 1.53 (br. s., 4 H). ES-LCMS m/z: 449, 451 (M+1).

EXAMPLE 72

4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 72)

[00304] A 2 mL aliquot of the acid chloride solution from the above example was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.292 mL, 1.67 mmol) and 1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (123 mg, 0.558 mmol) in dichloromethane (2 mL). After 15 minutes, the mixture was diluted with dichloromethane and the organic phase washed with saturated sodium bicarbonate. The organic layer was concentrated and the residue was triturated in ethyl ether before collecting by filtration to give the title compound (89 mg; 55%) as a solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.94 - 9.13 (m, 1 H), 8.11 (s, 1 H), 7.60 (d, 1 H), 7.32 - 7.44 (m, 1 H), 4.85 (s, 1 H), 4.60 (s, 1 H), 4.17 - 4.37 (m, 3 H), 4.11 (br. s., 1 H). ES-LCMS m/z: 464, 466 (M+1).

EXAMPLE 73

4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (Enantiomer 1)

(Compound 73)

[00305] Enantiomeric separation of (+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (42 mg; Example 66) was performed on a Chiralcel OJH column (250x10 mm i.d., 5 um; Daicel Chemical Ind., Osaka Japan) maintained at 40 °C and under supercritical conditions (140 bar) with methanol modified carbon dioxide (8% MeOH, 92% carbon dioxide) delivered at a combined flow rate of 10 mL/min on a Thar Discovery Supercritical Fluid Chromatography system (Thar Instruments, Inc., Pittsburgh, PA). The enantiomers were monitored using a Gilson 151 UV/Vis detector (Gilson, INC., Middleton, WI) at 254nm. Concentration of the early eluting peak gave the title compound (11 mg). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.18 - 8.37 (m, 1 H), 7.56 (br. s., 1 H), 4.82 - 5.10 (m, 2 H), 4.59 (s, 1 H), 4.41 (s, 1 H), 4.30 (t, 1 H), 4.15 (q, 1 H), 3.86 - 4.08 (m, 2 H), 3.42 (dt, 2 H), 2.44 (dq, 1 H), 2.08 (quin, 2 H), 1.77 - 1.96 (m, 3 H), 1.55 - 1.77 (m, 4 H), 1.41 - 1.55 (m, 2 H). ES-LCMS m/z: 485, 487(M+1).

EXAMPLE 74

4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (Enantiomer 2)

(Compound 74)

[00306] Enantiomeric separation of (+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (42 mg; Example 66) as described in the previous example. Concentration of the late eluting peak gave the title compound (17 mg). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.17 - 8.42 (m, 1 H), 7.56 (s, 1 H), 4.92 - 5.11 (m, 2 H), 4.59 (s, 1 H), 4.41 (s, 1 H), 4.29 (t, 1 H), 4.08 - 4.23 (m, 1 H), 3.90 - 4.09 (m, 2 H), 3.30 - 3.57 (m, 2 H), 2.44 (dq, 1 H), 2.08 (quin, 2 H), 1.77 - 1.92 (m, 3 H), 1.56 - 1.77 (m, 4 H), 1.43 - 1.56 (m, 2 H). ES-LCMS m/z: 485, 487(M+1).

EXAMPLE 75

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 75)

Step A

3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00307] Methyl 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (1.7 g, 5.1 mmol) was dissolved in tetrahydrofuran (35 mL). Water (35 mL) and sodium hydroxide (1 M) (10.16 mL, 10.16 mmol) were added sequentially and the mixture was stirred for 2 hours at room temperature. The mixture was quenched with 1 N hydrochloric acid and extracted two times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated to give the title compound (1.6 g; 99%) as a solid. ES-LCMS m/z: 321, 323 (M+1).

Step B

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

[00308] To a mixture of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (50 mg, 0.16 mmol) and 1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (39 mg, 0.18 mmol) in dimethylformamide (520 µl) was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (136 µl, 0.780 mmol). N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (71.1 mg, 0.187 mmol) was added and the mixture stirred at room temperature for 30 minutes. The mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The ethyl acetate layers were combined, washed with water, washed with 5% lithium chloride (aqueous), washed with brine, concentrated, and the residue subjected to silica chromatography eluting with a gradient of 0% to 3% 2 M NH_3/methanol in dichloromethane. Appropriate fractions were concentrated and the residue dissolved in minimal dichloromethane. Hexanes were added to give a cloudy mixture that was concentrated by rotovap. The residue was dried under high vacuum to give the title compound (59 mg, 79%) as a solid. ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.02 (br. s., 1 H), 7.46 - 7.59 (m, 2 H), 7.00 - 7.11 (m, 1 H), 5.08 (s, 1 H), 4.70 (s, 1 H), 4.51 - 4.63 (m, 1 H), 4.32 - 4.51 (m, 2 H), 4.17 (br. s., 1 H), 2.57 (d, 2 H), 1.80 - 2.06 (m, 1 H), 0.96 (d, 6 H). ES-LCMS m/z: 486, 488 (M+1).

EXAMPLE 76

4-{[3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 76)

Step A

methyl 3-chloro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00309] A mixture of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (5.0 g, 14 mmol), bis(pinacolato)diboron (8.88 g, 35.0 mmol), potassium acetate (4.12 g, 42.0 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane adduct (0.512 g, 0.699 mmol) was heated at 100 °C in 1,4-dioxane (186 mL). After 3.5 hours, the reaction was cooled to room temperature. The solid was filtered and the black solution was absorbed on silica gel and chromatographed [ISCO 220 g column, 0-15% ethyl acetate in n-hexanes (15 minutes), 15% ethyl acetate in n-hexanes (10 minutes), (15-40% ethyl acetate in n-hexanes, 10 minutes). The compound eluted with 30% ethyl acetate in n-hexanes. Appropriate fractions were concentrated to give the title compound (4.544 g, 11.23 mmol, 80 % yield) as a white solid. ES-LCMS m/z: 404, 407 (M+1).

Step B

methyl 3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00310] Methyl 3-chloro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (1.5 g, 3.7 mmol), copper (I) oxide (0.265 g, 1.85 mmol), and (0.303 g, 4.45 mmol) in methanol (10 mL) were stirred at room temperature for 1 day. LC-MS showed no conversion. Air was bubbled through the reaction and then heated to 35-40 °C. No conversion was observed after 2 hours. The mixture was allowed to cool to room temperature. One drop of water was added and the mixture allowed to stir over the weekend. The reaction had gone dry over the weekend. Methanol (5 mL) was added and the mixture continued to stir for 2 hours. LC-MS showed a small amount of desired product had formed. An additional 0.4 equivalents of copper (I) oxide (0.21g, 1.5 mmol) were added and the mixture continued to stir at room temperature overnight. LC-MS showed ~50% conversion. An additional 0.5 equivalents of copper (I) oxide (265mg, 1.85mmol) was added and the mixture continued to stir at room temperature. After 24 hours, the reaction was filtered through a pad of Celite, washed with methanol and dichloromethane, and the filtrate concentrated to give the title compound (1.6 g, >99%, 79% purity) as a solid. ES-LCMS m/z: 345, 347 (M+1).

Step C

4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00311] Methyl 3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (117 mg, 0.268 mmol) was slurried in tetrahydrofuran (1 mL) before water (1 mL) and sodium hydroxide (1 M) (0.536 mL, 0.536 mmol) were added. The mixture was stirred at room temperature for 1 hour. The mixture was concentrated and the residue slurried in *N,N*-dimethylformamide (2 mL). *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.187 mL, 1.07 mmol) and 1-cyclobutyl-2-piperazinone hydrochloride (56.2 mg, 0.295 mmol) were added followed by N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (122 mg, 0.322 mmol). The mixture was stirred at room temperature for 1 hour. The mixture was diluted with brine and extracted 2 times with ethyl acetate. The combined ethyl acetate layers were washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with gradient of 0% to 4% 2 M ammonia/methanol in dichloromethane. Appropriate fractions were concentrated to give the title compound (25 mg, 20%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.42 (d, 1 H), 7.88 (s, 1 H), 7.75 (s, 1 H), 7.32 (s, 2 H), 4.87 - 5.15 (m, 1 H), 4.60 (s, 1 H), 4.41 (s, 1 H), 4.31 (d, 1 H), 4.00 (d, 1 H), 3.47 - 3.64 (m, 2 H), 2.07 - 2.22 (m, 4 H), 1.63 - 1.81 (m, 2 H). ES-LCMS m/z: 467, 469 (M+1).

EXAMPLE 77

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 77)

[00312] To a mixture of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (45 mg, 0.14 mmol) and 1-cyclopentyl-2-piperazinone hydrochloride (32mg, 0.15 mmol) in dimethylformamide (1 mL) was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.123 mL, 0.702 mmol). N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (64.0 mg, 0.168 mmol) was added and the mixture stirred at room temperature for 30 minutes. The mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The ethyl acetate layers were combined, washed with water, washed with 5% lithium chloride (aqueous), washed with brine, concentrated, and the residue subject to silica chromatography eluting with a gradient of 0% to 3% 2 M ammonia/methanol in dichloromethane. Appropriate fractions were concentrated and the residue dissolved in minimal dichloromethane. Hexanes were added to give a cloudy mixture that was concentrated by rotovap. The residue was dried under high vacuum to give the title compound (24 mg, 36%) as a solid. ^{1}H NMR

(CHLOROFORM-*d*) δ ppm 7.92 - 8.12 (m, 1 H), 7.50 (s, 1 H), 4.83 - 5.10 (m, 1 H), 4.59 (s, 1 H), 4.42 (s, 1 H), 4.28 - 4.35 (m, 1 H), 3.89 - 4.01 (m, 1 H), 3.33 - 3.51 (m, 2 H), 2.58 (d, 2 H), 1.78 - 2.05 (m, 2 H), 1.55 (s, 7 H), 0.97 (d, 6 H). ES-LCMS m/z: 471, 473 (M+1).

EXAMPLE 78

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 78)

[00313] To a mixture of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (45 mg, 0.14 mmol) and 1-cyclobutyl-2-piperazinone hydrochloride (29 mg, 0.15 mmol) in dimethylformamide (1 mL) was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.123 mL, 0.702 mmol). N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (64.0 mg, 0.168 mmol) was added and the mixture stirred at room temperature for 30 minutes. The mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The ethyl acetate layers were combined, washed with water, washed with 5% LiCl (aqueous), washed with brine, concentrated, and the residue subject to silica chromatography eluting with a gradient of 0% to 3% 2 M NH_3/methanol in dichloromethane. Appropriate fractions were concentrated and the residue dissolved in minimal dichloromethane. Hexanes were added to give a cloudy mixture that was concentrated by rotovap. The residue was dried under high vacuum to give the title compound (35 mg, 55%) as a solid. ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.02 (d, 1 H), 7.50 (s, 1 H), 4.86 - 5.16 (m, 1 H), 4.58 (s, 1 H), 4.40 (s, 1 H), 4.33 (t, 1 H), 3.99 (t, 1 H), 3.53 (dt, 2 H), 2.58 (d, 2 H), 2.05 - 2.24 (m, 4 H), 1.85 - 2.03 (m, 1 H), 1.62 - 1.81 (m, 2 H), 0.97 (d, 6 H). ES-LCMS m/z: 457, 459 (M+1).

EXAMPLE 79

4-{[3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 79)

Step A

Methyl 3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00314] Methyl 3-chloro-6-hydroxy-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (350 mg, 1.19 mmol), potassium carbonate (328 mg, 2.38 mmol), and methyl iodide (0.089 mL, 1.4 mmol) in dimethylformamide (5 mL) were stirred at room temperature for 2 hours. The mixture was diluted with water and extracted with ethyl

acetate. The organic phase was washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, and concentrated. The residue purified by silica chromatography eluting with a gradient of 0% to 5% ethyl acetate in dichloromethane to give the title compound (325 mg, 89%). ES-LCMS m/z: 309, 311 (M+1).

Step B

4-{[3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00315] Water (2mL) was added to methyl 3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (100 mg, 0.324 mmol) in tetrahydrofuran (2 mL) followed by sodium hydroxide (1 M) (0.648 mL, 0.648 mmol). The mixture was stirred for 1 hour, quenched with 1 N hydrochloric acid, and extracted two times with ethyl acetate. The combined organic layers were washed with brine and concentrated. The residue was dissolved in 2 mL of dimethylformamide. To a 1 mL aliquot of the carboxylic acid solution was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.131 mL, 0.583 mmol), 1-cyclobutyl-2-piperazinone hydrochloride (37 mg, 0.19 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (67.8 mg, 0.178 mmol). The mixture was stirred for 1 hour, diluted with ethyl acetate, washed with brine, washed with 5% lithium chloride, dried over sodium sulfate, and concentrated. The residue purified by reverse phase HPLC to give the title compound (39 mg, 56%). ^{1}H NMR (DMSO-d_6) δ ppm 8.17 (s, 1 H), 7.76 (br. s., 1 H), 4.71 - 5.02 (m, 1 H), 4.47 (s, 1 H), 4.20 (s, 1 H), 4.08 (br. s., 1 H), 3.96 (s, 3 H), 3.83 - 3.93 (m, 1 H), 3.40 - 3.56 (m, 2 H), 2.18 (br. s., 2 H), 2.00 (br. s., 2 H), 1.64 (d, 2 H). ES-LCMS m/z: 431, 433 (M+1).

EXAMPLE 80

(+/-)-4-{[3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 80)

Step A

tributyl[1-methyl-1-propen-1-yl]stannane

[00316] Tributyl(chloro)stannane (2.89 mL, 10.7 mmol) was added to bromo[(1E)-1-methyl-1-propen-1-yl]magnesium (0.5M in tetrahydrofuran) (53.8 mL, 26.9 mmol) and the mixture stirred at reflux for 5 hours. The mixture was cooled to room temperature and quenched with saturated ammonium chloride. The organic phase separated, washed with saturated sodium bicarbonate, washed with brine, dried over sodium sulfate, concentrated, and the residue passed through a silica plug eluting with ethyl ether. The

filtrate was concentrated to give the title compound as a mixture of E and Z isomers. ^{1}H NMR (CHLOROFORM-*d*) δ ppm 6.01 - 6.17 (m, 0.7 H (major isomer)), 5.55 - 5.67 (m, 0.3 H (minor isomer)), 1.78 - 1.93 (m, 3 H), 1.60 - 1.72 (m, 3 H), 1.37 - 1.56 (m, 6 H), 1.20 - 1.38 (m, 7 H), 0.77 - 0.96 (m, 14 H).

Step B

methyl 3-chloro-6-[1-methyl-1-propen-1-yl]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (mixture of E and Z isomers)

[00317] Methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (0.50g, 1.4 mmol), tributyl[1-methyl-1-propen-1-yl]stannane (0.58g, 1.7 mmol), and $Pd(PPh_3)_4$ (0.16 g, 0.14 mmol) in *N,N*-dimethylformamide (10 mL) were purged with nitrogen for 5 minutes and then heated to 85 °C for 2 hours. LC-MS showed no reaction. The mixture was heated to 110 °C. No reaction after 1 hour. 80 mg of trans-benzyl(chloro)bis(triphenylphosphine)palladium (II) was added and the mixture continued to stir at 110 °C. After 1hr, LC-MS showed ~5:1 starting material/desired product. The mixture was heated for 2 hours. Starting material was consumed and the product was observed by LC-MS, along with several other components. The mixture was allowed to cool to room temperature and stirred overnight. The mixture was diluted with ethyl acetate, washed with brine, washed with 5% lithium chloride, dried over sodium sulfate, concentrated, and the residue purified by silica chromatography eluting with 25% ethyl acetate in hexanes to give the title compound (214mg, 46%) as a mixture (~7:3) of isomers. ES-LCMS m/z: 333, 335 (M+1).

Step C

(+/-)-methyl 3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00318] Methyl 3-chloro-6-[1-methyl-1-propen-1-yl]-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (184 mg, 0.553 mmol) was dissolved in ethanol (10 mL) and tetrahydrofuran (5 mL). 3% platinum on carbon (90 mg, 0.014 mmol) was added under nitrogen. The mixture was purged with nitrogen and then stirred under hydrogen (balloon pressure) for 3 hours. The mixture was then stirred under 30psi of hydrogen overnight. The catalyst was filtered off over Celite® and the wash concentrated. The residue was purified by silica chromatography eluting with 25% ethyl acetate in hexanes to give the title compound (128 mg, 69%). ES-LCMS m/z: 335, 337 (M+1).

Step D

(+/-)-4-{[3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00319] (+/-)-Methyl 3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (63 mg, 0.19 mmol) was dissolved in tetrahydrofuran (2.5 mL) before sodium hydroxide (1 M) (0.376 mL, 0.376 mmol) and water (2.5 mL) were added. The mixture was stirred for 1 hour, quenched with 1 N hydrochloric acid, and extracted two times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was dissolved in dichloromethane (3 mL) before oxalyl chloride (2 M in dichloromethane) (0.188 mL, 0.376 mmol) was added dropwise. The mixture was stirred for 1 hour, concentrated, and co-evaporated with hexanes. The acid chloride was dissolved in 2 mL of dichloromethane. A 1 mL aliquot of the acid chloride solution was added dropwise to a solution of *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.053 mL, 0.30 mmol) and 1-cyclobutyl-2-piperazinone hydrochloride (20 mg, 0.10 mmol) in dichloromethane (2 mL). The mixture was stirred for 1 hour, concentrated, and the residue purified by silica chromatography eluting with a gradient of 0% to 3% 2 M ammonium/methanol in dichloromethane to give the title compound (22 mg, 51%) as a foam. ^{1}H NMR (DMSO-d_6) δ ppm 8.31 - 8.51 (m, 1 H), 7.83 (br. s., 1 H), 4.68 - 4.95 (m, 1 H), 4.39 (s, 1 H), 4.15 (s, 1 H), 3.99 (br. s., 1 H), 3.75 - 3.90 (m, 1 H), 3.40 (br. s., 2 H), 2.77 - 2.97 (m, 1 H), 2.12 (br. s., 2 H), 1.84 - 2.04 (m, 2 H), 1.45 - 1.74 (m, 4 H), 1.14 - 1.32 (m, 3 H), 0.77 (t, 3 H). ES-LCMS m/z: 457, 459 (M+1).

EXAMPLE 81

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 81)

Step A

methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-2-propen-1-ylglycinate

[00320] N-Boc-glycine methyl ester (1.758 mL, 11.89 mmol) in *N,N*-dimethylformamide (30 mL) was cooled to 5 °C before allyl bromide (1.544 mL, 17.84 mmol) was added, followed by sodium hydride (0.713 g, 17.8 mmol) . The mixture was stirred for 2 hours, quenched with saturated ammonium chloride and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The product was purified by silica chromatography eluting with a gradient of 0% to 50% ethyl acetate in hexanes to give the title compound (1.57 g, 57%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 5.63 - 5.90 (m, 1 H), 4.99 - 5.25 (m, 2 H), 3.94 (br. s., 2 H), 3.87 (d, 1 H), 3.83 (s, 1 H), 1.43 (d, 9 H).

Step B

methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate

[00321] A solution of methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-2-propen-1-ylglycinate (1.57 g, 6.85 mmol) in methanol (50 mL) was cooled to -78 °C before ozone was bubbled into the mixture. Ozone was applied until the reaction mixture turned blue and thin layer chromatography indicated consumption of the starting material. Nitrogen was bubbled into the reaction mixture until the blue solution became colorless, and then bubbled with nitrogen for 15 more minutes. Dimethyl sulfide (2.79 mL, 37.7 mmol) was added and the mixture allowed to slowly come to room temperature as the cold-bath warmed overnight. The mixture was concentrated and the residue taken up in ethyl acetate. The organic phase was washed 2 times with water, dried over sodium sulfate and concentrated to give the title compound (1.6 g, >99%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 9.51 - 9.73 (m, 1 H), 4.10 (s, 1 H), 4.02 (s, 1 H), 3.97 (s, 1 H), 3.87 (d, 1 H), 3.68 - 3.75 (m, 3 H), 1.38 - 1.44 (m, 9 H).

Step C

1,1-dimethylethyl 4-cyclobutyl-3-oxo-1-piperazinecarboxylate

[00322] Cyclopropylamine (4.23 mL, 49.6 mmol) was added to a solution of methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (7.8 g, 33mmol) in methanol (100 mL) and the mixture stirred for 5 minutes. Sodium cyanoborohydride (3.12 g, 49.6 mmol) was added. An exotherm was observed such that the internal temperature reached 35 °C. The mixture was stirred for 2.5 hours. Another portion of sodium cyanoborohydride (3.12 g, 49.6 mmol) was added and the mixture stirred overnight at room temperature. The mixture was concentrated, the residue diluted with 1 M sodium hydroxide, and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 30% ethyl acetate in dichloromethane to give the title compound (2.9 g, 33%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 4.90 - 5.12 (m, 1 H), 4.04 (s, 2 H), 3.55 - 3.67 (m, 2 H), 3.31 - 3.41 (m, 2 H), 2.11 (d, 4 H), 1.69 (s, 2 H), 1.45 (s, 9 H).

Step D

1-cyclobutyl-2-piperazinone trifluoroacetate

[00323] 1,1-dimethylethyl 4-cyclobutyl-3-oxo-1-piperazinecarboxylate (2.9 g, 11 mmol) was stirred in dichloromethane (25 mL) and trifluoroacetic acid (25 mL) for 2 hours. The mixture was concentrated and dried under vacuum to give a pinkish oil. The oil was stirred vigorously in diethyl ether. Solids formed and were triturated by stirring. Solids were collected by filtration and dried under vacuum to give the title compound (2.57 g, 84%). ^{1}H NMR (DMSO-d_6) δ ppm 9.28 (br. s., 2 H), 4.70 - 4.95 (m, 1 H), 3.71 (s, 2 H), 3.48 - 3.59 (m, 2 H), 3.31 - 3.47 (m, 2 H), 2.09 - 2.30 (m, 2 H), 1.91 - 2.09 (m, 2 H), 1.65 (td, 2 H).

Step E

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00324] 3-Chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (2.92 g, 9.58 mmol) was slurried in dichloromethane (96 mL) with stirring. *N,N*-dimethylformamide (0.037 mL, 0.479 mmol) was added and then oxalyl chloride (2 M in dichloromethane) (9.58 mL, 19.2 mmol) was added slowly dropwise. Complete dissolution occurred within 90 minutes after the last portion of oxalyl chloride was added. The mixture was concentrated and the residue co-evaporated 1 time with hexanes. The residue was dissolved in dichloromethane (60 mL) and added slowly dropwise to a mixture of 1-cyclobutyl-2-piperazinone trifluoroacetate (2.57 g, 9.58 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (6.68 mL, 38.3 mmol) in dichloromethane (100 mL). After stirring for 1 hour the mixture was diluted with dichloromethane. The organic phase was washed 1 time with saturated sodium bicarbonate, washed 1 time with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 35% ethyl acetate in dichloromethane. Appropriate fractions were concentrated to leave a white foam. The product was recrystallized from ethyl ether and hexanes to give the title compound (2.8 g, 66%). ^{1}H NMR (DMSO-d_6) δ ppm 8.31 - 8.49 (m, 1 H), 7.44 - 7.66 (m, 1 H), 4.64 - 4.95 (m, 1 H), 4.38 (s, 1 H), 4.15 (s, 1 H), 3.94 - 4.07 (m, 1 H), 3.78 - 3.91 (m, 1 H), 3.40 (br. s., 2 H), 2.15 (br. s., 3 H), 1.86 - 1.99 (m, 2 H), 1.57 (br. s., 2 H), 0.97 (d, 2 H), 0.85 (d, 2 H). ES-LCMS m/z: 441, 443 (M+1).

EXAMPLE 82

4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 82)

[00325] Methyl 3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (434 mg, 0.995 mmol) was slurried in tetrahydrofuran (7 mL) before water (7 mL) and sodium hydroxide (1 M) (1.989 mL, 1.989 mmol) were added. The mixture was stirred at room temperature for 2 hours and concentrated. The residue slurried in *N,N*-dimethylformamide (10 mL) and split into 2 equal 5 mL aliquots of sodium 3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate. To one 5 mL aliquot of the sodium 3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate slurry was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.695 mL, 3.98 mmol), 1-cyclopentyl-2-piperazinone

hydrochloride (112 mg, 0.547 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (227 mg, 0.597 mmol). The mixture was stirred at room temperature for 1 hour. The reaction was diluted with brine and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with gradient of 0% to 4% 2 M ammonium/methanol in dichloromethane. The product was additionally purified by reverse phase HPLC to give the title compound (15 mg, 6%). ^{1}H NMR (DMSO-d_6) δ ppm 9.03 (d, 1 H), 8.39 (s, 1 H), 8.27 (s, 1 H), 7.94 (s, 1 H), 7.14 (s, 1 H), 4.62 - 4.86 (m, 1 H), 4.39 (s, 1 H), 4.18 (s, 1 H), 3.95 (d, 1 H), 3.81 (br. s., 1 H), 3.29 - 3.43 (m, 2 H), 1.63 (br. s., 4 H), 1.48 (br. s., 4 H). ES-LCMS m/z: 481, 483 (M+1).

EXAMPLE 83

4-{[3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 83)

[00326] To the remaining 5 mL dimethyl formamide aliquot of sodium 3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate from the above example was added *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.695 mL, 3.98 mmol), 1-cyclohexyl-2-piperazinone hydrochloride (162 mg, 0.547 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (227 mg, 0.597 mmol). The mixture was stirred at room temperature for 1 hour. The reaction was diluted with brine and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with gradient of 0% to 4% 2 M ammonium/methanol in dichloromethane. The product was additionally purified by reverse phase HPLC to give the title compound (35 mg, 13%). ^{1}H NMR (DMSO-d_6) δ ppm 8.99 - 9.12 (m, 1 H), 8.39 (s, 1 H), 8.25 - 8.32 (m, 1 H), 7.93 (s, 1 H), 7.04 - 7.19 (m, 1 H), 4.32 - 4.45 (m, 1 H), 4.17 (s, 2 H), 3.91 - 3.98 (m, 1 H), 3.77 - 3.83 (m, 1 H), 3.29 - 3.43 (m, 2 H), 1.63 - 1.83 (m, 2 H), 1.46 - 1.61 (m, 3 H), 1.32 - 1.46 (m, 2 H), 1.15 - 1.33 (m, 2 H), 0.94 - 1.14 (m, 1 H). ES-LCMS m/z: 495, 497 (M+1).

EXAMPLE 84

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone

(Compound 84)

Step A

1,1-dimethylethyl 3-oxo-4-propyl-1-piperazinecarboxylate

[00327] Sodium cyanoborohydride (0.061 g, 0.97 mmol) was added to a solution of methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (0.15 g, 0.65 mmol) and n-propylamine (0.081 mL, 0.97 mmol) in methanol (2 mL). The mixture was stirred at room temperature for 2 hours and then sodium cyanoborohydride (0.061 g, 0.97 mmol) was added again. The mixture was stirred at room temperature overnight. The mixture was concentrated and the residue diluted with 1 M sodium hydroxide. The mixture was extracted 2 times with ethyl acetate and the combined organic layers washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 25% ethyl acetate in dichloromethane to give the title compound (56 mg, 36%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 4.01 (s, 2 H), 3.57 (d, 2 H), 3.22 - 3.38 (m, 4 H), 1.53 (d, 2 H), 1.41 (s, 9 H), 0.86 (t, 3 H).

Step B

1-propyl-2-piperazinone trifluoroacetate

[00328] 1,1-Dimethylethyl 3-oxo-4-propyl-1-piperazinecarboxylate (55 mg, 0.227 mmol) was stirred in dichloromethane (1 mL) and trifluoroacetic acid (1 mL) for 1 hour. The mixture was concentrated, co-evaporated with hexanes, and dried under vacuum to give the title compound (55 mg, 95%). ^{1}H NMR (METHANOL-d_4) δ ppm 3.81 (s, 2 H), 3.56 - 3.65 (m, 2 H), 3.48 - 3.54 (m, 2 H), 3.36 - 3.45 (m, 2 H), 1.53 - 1.71 (m, 2 H), 0.92 (t, 3 H).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone

[00329] To a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (26.8 mg, 0.088 mmol), 1-propyl-2-piperazinone trifluoroacetate (25 mg, 0.098 mmol), and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.068 mL, 0.390 mmol) in *N,N*-dimethylformamide (1 mL) was added N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (40.8 mg, 0.107 mmol). The mixture was stirred for 30 minutes and diluted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride and concentrated. The residue was purified by reverse

phase HPLC to give the title compound (24 mg, 57%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.02 (d, 1 H), 7.38 (s, 1 H), 4.57 (s, 1 H), 4.39 (s, 1 H), 4.29 (t, 1 H), 3.97 (t, 1 H), 3.42 - 3.54 (m, 2 H), 3.37 (dt, 2 H), 1.93 - 2.13 (m, 1 H), 1.47 - 1.66 (m, 2 H), 1.00 - 1.18 (m, 2 H), 0.83 - 0.98 (m, 3 H), 0.72 - 0.82 (m, 2 H). ES-LCMS m/z: 429, 431 (M+1).

EXAMPLE 85

1-butyl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 85)

Step A

1,1-dimethylethyl 4-butyl-3-oxo-1-piperazinecarboxylate

[00330] n-Butylamine (0.078 mL, 0.787 mmol) was added to a solution of methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (140 mg, 0.605 mmol) in methanol (2 mL) and the mixture stirred for 5 minutes. Sodium cyanoborohydride (57.1 mg, 0.908 mmol) was added and the mixture stirred at room temperature for 6 hours. The mixture was concentrated and the residue diluted with 1 M sodium hydroxide before being extracted 2 times with ethyl acetate. The combined organic layers were washed with brine and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 30% ethyl acetate in dichloromethane to give the title compound (48 mg, 31%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 4.01 (s, 2 H), 3.53 - 3.64 (m, 2 H), 3.32 - 3.40 (m, 2 H), 3.23 - 3.32 (m, 2 H), 1.44 - 1.56 (m, 2 H), 1.42 (s, 9 H), 1.21 - 1.36 (m, 2 H), 0.89 (t, 3 H).

Step B

1-butyl-2-piperazinone trifluoroacetate

[00331] 1,1-Dimethylethyl 4-butyl-3-oxo-1-piperazinecarboxylate (48 mg, 0.19 mmol) was stirred in dichloromethane (1 mL) and trifluoroacetic acid (1 mL) for 1 hour. The mixture was concentrated and co-evaporated with hexanes. The residue was dried under vacuum to give the title compound (50 mg, 99%). ^{1}H NMR (METHANOL-d_4) δ ppm 3.82 (s, 2 H), 3.56 - 3.66 (m, 2 H), 3.47 - 3.55 (m, 2 H), 3.44 (t, 2 H), 1.48 - 1.68 (m, 2 H), 1.26 - 1.43 (m, 2 H), 0.94 (t, 3 H).

Step C

1-butyl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

[00332] To a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (26.8 mg, 0.088 mmol), 1-butyl-2-piperazinone trifluoroacetate (26 mg, 0.098 mmol), and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.068 mL, 0.390

mmol) in *N,N*-dimethylformamide (1 mL) was added N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (40.8 mg, 0.107 mmol). The mixture was stirred for 30 minutes and diluted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride and concentrated. The residue was purified by reverse phase HPLC to give the title compound (18 mg; 42%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.02 (d, 1 H), 7.38 (s, 1 H), 4.57 (s, 1 H), 4.38 (s, 1 H), 4.23 - 4.34 (m, 1 H), 3.90 - 4.05 (m, 1 H), 3.50 (t, 1 H), 3.41 - 3.47 (m, 2 H), 3.34 - 3.41 (m, 1 H), 1.93 - 2.08 (m, 1 H), 1.41 - 1.60 (m, 2 H), 1.18 - 1.40 (m, 2 H), 1.04 - 1.14 (m, 2 H), 0.87 - 0.96 (m, 3 H), 0.72 - 0.80 (m, 2 H). ES-LCMS m/z: 443, 445 (M+1).

EXAMPLE 86

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone

(Compound 86)

[00333] To a mixture of 3-chloro-6-bromo-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (33.5 mg, 0.098 mmol), 1-propyl-2-piperazinone trifluoroacetate (25 mg, 0.098 mmol), and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.068 mL, 0.390 mmol) in *N,N*-dimethylformamide (1 mL) was added N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (40.8 mg, 0.107 mmol). The mixture was stirred for 30 minutes and diluted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by reverse phase HPLC to give the title compound (12 mg, 26%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.44 (d, 1 H), 7.72 (s, 1 H), 4.58 (s, 1 H), 4.41 (s, 1 H), 4.23 - 4.36 (m, 1 H), 3.93 - 4.09 (m, 1 H), 3.53 (t, 1 H), 3.48 (t, 1 H), 3.33 - 3.44 (m, 2 H), 1.46 - 1.72 (m, 2 H), 0.84 - 1.02 (m, 3 H). ES-LCMS m/z: 467, 469, 471 (M+1).

EXAMPLE 87

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-butyl-2-piperazinone

(Compound 87)

[00334] To a mixture of 3-chloro-6-bromo-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (33.5 mg, 0.098 mmol), 1-butyl-2-piperazinone trifluoroacetate (26 mg, 0.098 mmol), and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.068 mL, 0.39 mmol) in *N,N*-dimethylformamide (1 mL) was added N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-

3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (40.8 mg, 0.107 mmol). The mixture was stirred for 30 minutes and diluted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by reverse phase HPLC to give the title compound (16 mg, 34%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.44 (d, 1 H), 7.72 (s, 1 H), 4.58 (s, 1 H), 4.40 (s, 1 H), 4.23 - 4.35 (m, 1 H), 3.91 - 4.06 (m, 1 H), 3.53 (t, 1 H), 3.37 - 3.49 (m, 3 H), 1.43 - 1.65 (m, 2 H), 1.26 - 1.43 (m, 2 H), 0.89 - 0.99 (m, 3 H). ES-LCMS m/z: 481, 483, 485 (M+1).

EXAMPLE 88

(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

(Compound 88)

Step A

(+/-)-1,1-dimethylethyl [2-(cyclobutylamino)-1-methyl-2-oxoethyl]carbamate

[00335] To a solution of (+/-)-*N*-{[(1,1-dimethylethyl)oxy]carbonyl}alanine (2.24 g, 11.84 mmol) in *N,N*-dimethylformamide (50 mL) was added cyclobutylamine (1.112 mL, 13.02 mmol), *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (6.20 mL, 35.5 mmol), and *N*-[(dimethylamino)(3*H*-[1,2,3]triazolo[4,5-*b*]pyridin-3-yloxy)methylidene]-*N*-methylmethanaminium hexafluorophosphate (HATU) (5.40 g, 14.2 mmol). The mixture was stirred for 2 hours, quenched with water, and extracted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride, dried over sodium sulfate and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 50% ethyl acetate in dichloromethane to give the title compound (2.4 g, 84%). ES-LCMS m/z: 243 (M+1).

Step B

(+/-)-1,1-dimethylethyl [2-(cyclobutylamino)-1-methylethyl]carbamate

[00336] To a 5 °C slurry of (+/-)-1,1-dimethylethyl [2-(cyclobutylamino)-1-methyl-2-oxoethyl]carbamate (1.2 g, 4.9 mmol) in tetrahydrofuran (12 mL) and toluene (12 mL) was added sodium bis(2-methoxyethoxy)aluminumhydride (4.53 mL, 14.9 mmol) slowly dropwise. The mixture was allowed to warm to room temperature and then heated to 35 °C for 16 hours. The mixture was cooled in an ice-bath and was carefully quenched with dropwise addition of sodium hydroxide (5M, 10 mL) to keep internal temperature below 20 °C. The mixture was stirred for 20 minutes at room temperature before toluene (30 mL) was added. The layers were separated and the organic phase washed 2 times with sodium hydroxide (5M, 10 mL), dried over sodium sulfate, and concentrated to give the title compound (1.1 g, 97%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 4.55 - 4.81 (m, 1 H), 3.58

- 3.80 (m, 1 H), 3.14 - 3.32 (m, 1 H), 2.51 (d, 2 H), 2.17 (br. s., 2 H), 1.55 - 1.73 (m, 4 H), 1.43 (s, 9 H), 1.11 (d, 3 H).

Step C

(+/-)-1,1-dimethylethyl {2-[(bromoacetyl)(cyclobutyl)amino]-1-methylethyl}carbamate

[00337] To a solution of (+/-)-1,1-dimethylethyl [2-(cyclobutylamino)-1-methylethyl]carbamate (1.1 g, 4.8 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (2.52 mL, 14.4 mmol) in dichloromethane (50 mL) at 5 °C was added bromoacetyl bromide (0.461 mL, 5.30 mmol). The mixture was stirred at 5 °C for 2 hours and quenched with saturated sodium bicarbonate. The mixture was extracted with dichloromethane and the organic phase washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography (ethyl acetate/dichloromethane) to give the title compound (340 mg, 20%). ES-LCMS m/z: 349, 351 (M+1).

Step D

(+/-)-1,1-dimethylethyl 4-cyclobutyl-2-methyl-5-oxo-1-piperazinecarboxylate

[00338] (+/-)-1,1-Dimethylethyl {2-[(bromoacetyl)(cyclobutyl)amino]-1-methylethyl}carbamate (340 mg, 0.973 mmol) and cesium carbonate (747 mg, 2.29 mmol) in *N,N*-dimethylformamide (20 mL) were stirred at room temperature for 2 hours and then at 45 °C for 1 hour. Catalytic sodium iodide was added and the mixture heated to 65 °C for 2 hours. The mixture was allowed to cool to room temperature and was diluted with water. The mixture was extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5%, dried over sodium sulfate, and concentrated to give the title compound (294 mg, 99%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 4.98 - 5.15 (m, 1 H), 4.36 - 4.51 (m, 1 H), 4.17 (d, 1 H), 3.78 (d, 1 H), 3.39 - 3.51 (m, 1 H), 3.19 - 3.29 (m, 1 H), 1.95 - 2.29 (m, 4 H), 1.63 - 1.78 (m, 2 H), 1.44 (s, 9 H), 1.16 (d, 3 H).

Step E

(+/-)-1-cyclobutyl-5-methyl-2-piperazinone trifluoroacetate

[00339] (+/-)-1,1-Dimethylethyl 4-cyclobutyl-2-methyl-5-oxo-1-piperazinecarboxylate (294 mg, 0.975 mmol) was stirred in dichloromethane (5 mL) and trifluoroacetic acid (5 mL) for 1 hour. The mixture was concentrated to give the title compound (275 mg, 99%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 7.56 - 7.75 (m, 1 H), 4.75 - 4.92 (m, 1 H), 3.80 - 4.05 (m, 2 H), 3.68 (d, 1 H), 3.48 - 3.60 (m, 2 H), 1.99 - 2.25 (m, 4 H), 1.63 - 1.87 (m, 2 H), 1.51 (d, 3 H).

Step F

(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

[00340] N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (112 mg, 0.293 mmol) was added to a mixture of 6-Bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (84 mg, 0.24 mmol), (+/-)-1-cyclobutyl-5-methyl-2-piperazinone trifluoroacetate (69 mg, 0.24 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.341 mL, 1.95 mmol) in *N,N*-dimethylformamide (2 mL). The reaction was stirred for 2 hours and diluted with water. The mixture was extracted with ethyl acetate and the organic phase washed with water, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 30% ethyl acetate in dichloromethane to give the title compound (50 mg, 41%) as a white solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.90 - 9.11 (m, 1 H), 8.10 (br. s., 1 H), 4.78 - 5.03 (m, 1 H), 4.64 - 4.78 (m, 1 H), 4.35 - 4.59 (m, 1 H), 3.76 - 4.19 (m, 1 H), 3.36 - 3.66 (m, 2 H), 2.04 - 2.23 (m, 2 H), 1.91 - 2.04 (m, 2 H), 1.53 - 1.72 (m, 2 H), 1.23 (d, 3 H). ES-LCMS m/z: 493, 495, 497 (M+1).

EXAMPLE 89

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

(Compound 89)

[00341] N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (112 mg, 0.293 mmol) was added to a mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (81 mg, 0.24 mmol), (+/-)-1-cyclobutyl-5-methyl-2-piperazinone trifluoroacetate (69 mg, 0.24 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.341 mL, 1.95 mmol) in N,N-dimethylformamide (2 mL). The reaction was stirred for 2 hours and diluted with water. The mixture was extracted with ethyl acetate and the organic phase washed with water, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 3% 2 M ammonia/methanol in dichloromethane to give the title compound (26 mg, 22%) as a white solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.75 - 8.92 (m, 1 H), 8.56 (s, 1 H), 8.22 (s, 1 H), 7.84 (s, 1 H), 7.33 (s, 1 H), 4.66 - 5.02 (m, 2 H), 4.35 - 4.64 (m, 1 H), 3.75 - 4.24 (m, 1 H), 3.37 - 3.72 (m, 2 H), 2.05 - 2.24 (m, 2 H), 1.90 - 2.06 (m, 2 H), 1.52 - 1.72 (m, 2 H), 1.24 (d, 3 H). ES-LCMS m/z: 481, 483 (M+1).

EXAMPLE 90

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

(Compound 90)

[00342] N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (112 mg, 0.293 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (74.5 mg, 0.24 mmol), (+/-)-1-cyclobutyl-5-methyl-2-piperazinone trifluoroacetate (69 mg, 0.24 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.341 mL, 1.95 mmol) in *N,N*-dimethylformamide (2 mL). The reaction was stirred for 2 hours and diluted with water. The mixture was extracted with ethyl acetate and the organic phase washed with water, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 50% ethyl acetate in dichloromethane to give the title compound (34 mg, 31%) as a white solid. ^{1}H NMR (DMSO-d_6) δ ppm 8.40 - 8.53 (m, 1 H), 7.56 - 7.69 (m, 1 H), 4.64 - 4.99 (m, 2 H), 4.37 - 4.63 (m, 1 H), 3.73 - 4.19 (m, 1 H), 3.37 - 3.67 (m, 2 H), 2.04 - 2.30 (m, 3 H), 1.91 - 2.04 (m, 2 H), 1.55 - 1.69 (m, 2 H), 1.22 (d, 3 H), 0.96 - 1.06 (m, 2 H), 0.84 - 0.92 (m, 2 H). ES-LCMS m/z: 455, 457 (M+1).

EXAMPLE 91

(+/-)-1-cyclobutyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-5-methyl-2-piperazinone

(Compound 91)

Step A

methyl 6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00343] A mixture of 6-bromo-8-trifluoromethyl-imidazo[1,2-a]pyridine-2-carboxylic acid methyl ester (600 mg, 1.85 mmol), furan-3-boronic acid (291 mg, 2.60 mmol), tetrakis(triphenylphosphine)palladium(0) (107 mg, 0.0928 mmol) in 1 M K_3PO_4 (2.5 mL) and 1,4-dioxane (12.5 mL) was heated at 90 °C for 135 minutes. The mixture was diluted with ethyl acetate (120 mL) and washed with saturated aqueous sodium bicarbonate (20 mL), and brine (20 mL). The solution was diluted with hexanes (50 mL) and loaded on a short pad of silica gel which was eluted with ethyl acetate/hexanes (2:1 v/v) to give 6-furan-3-yl-8-trifluoromethyl-imidazo[1,2-a]pyridine-2-carboxylic acid methyl ester (653.7 mg) as a light brown solid. The partially purified methyl ester was dissolved in tetrahydrofuran (90 mL) treated with lithium hydroxide monohydrate (220 mg, 5.24 mmol) in water (30 mL). After 4.5 hours, the solvent was removed under reduced pressure,

diluted with 10% sodium hydroxide (20 mL) and washed with ethyl ether (100 mL). The aqueous phase was acidified with 6 N hydrochloric acid, extracted with ethyl acetate (2 x 100 mL). The filtrate was dried (sodium sulfate), filtered and concentrated to give 6-furan-3-yl-8-trifluoromethyl-imidazo[1,2-a]pyridine-2-carboxylic acid (520 mg, 84%) a light yellow solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.01 (dd, 1H, J = 0.8, 1.7 Hz), 7.83 (t, 1H, J = 1.7 Hz), 8.11 (brs, 1H), 8.44 (brs, 1H), 8.51 (s, 1H), 9.11 (s, 1H), 13.00 (brs, 1H); ES-LCMS m/z: 297 (M+1).

Step B

(+/-)-1-cyclobutyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-5-methyl-2-piperazinone

[00344] N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (112 mg, 0.293 mmol) was added to a mixture of 6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (72 mg, 0.24 mmol), (+/-)-1-cyclobutyl-5-methyl-2-piperazinone trifluoroacetate (69 mg, 0.24 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.341 mL, 1.95 mmol) in N,N-dimethylformamide (2 mL). The reaction was stirred for 2 hours and diluted with water. The mixture was extracted with ethyl acetate and the organic phase washed with water, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 100% ethyl acetate in dichloromethane. The compound was further purified by reverse phase HPLC to give the title compound (15 mg, 14%). ^{1}H NMR (METHANOL-d_4) δ ppm 8.89 (s, 1 H), 8.34 (s, 1 H), 8.08 (s, 1 H), 7.94 (s, 1 H), 7.62 (s, 1 H), 6.88 (d, 1 H), 5.15 - 5.91 (m, 1 H), 4.89 - 5.07 (m, 1 H), 4.19 - 4.71 (m, 1 H), 3.83 - 4.07 (m, 1 H), 3.43 - 3.72 (m, 2 H), 2.00 - 2.39 (m, 4 H), 1.72 (s, 2 H), 1.33 (d, 3 H). ES-LCMS m/z: 447 (M+1).

EXAMPLE 92

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(1-methylpropyl)-2-piperazinone

(Compound 92)

Step A

(+/-)-1,1-dimethylethyl 4-(1-methylpropyl)-3-oxo-1-piperazinecarboxylate

[00345] Methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (0.5 g, 2.119 mmol) was added to (+/-)-(1-methylpropyl)amine (0.258 mL, 2.54 mmol) and stirred neat for 1 hour. Methanol (20 mL) was added and then sodium cyanoborohydride (0.200 g, 3.18 mmol). The mixture was stirred overnight at room temperature, concentrated, and diluted with 1 M sodium hydroxide (aqueous). The mixture was

extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, concentrated, and the residue purified by silica chromatography eluting with a gradient of 0% to 25% ethyl acetate in dichloromethane to give the title compound (34 mg, 6%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 4.51 - 4.74 (m, 1 H), 4.03 (s, 2 H), 3.56 (d, 2 H), 3.05 - 3.33 (m, 2 H), 1.31 - 1.65 (m, 11 H), 1.02 - 1.17 (m, 3 H), 0.82 (t, 3 H).

Step B

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylpropyl)-2-piperazinone

[00346] (+/-)-1,1-dimethylethyl 4-(1-methylpropyl)-3-oxo-1-piperazinecarboxylate (34.1 mg, 0.133 mmol) was dissolved in dichloromethane (5 mL) and trifluoroacetic acid (5 mL, 64.9 mmol) was added. The mixture was stirred for 1 hour, concentrated, and the residue dried under vacuum. The residue was dissolved in *N,N*-dimethylformamide (3 mL) before 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (40.5 mg, 0.133 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.116 mL, 0.665 mmol) were added. N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (55.6 mg, 0.146 mmol) was added and the mixture was stirred for 2 hours. The mixture was diluted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with ethyl acetate/dichloromethane to give the title compound (39 mg, 66%). ^{1}H NMR (METHANOL-d_4) δ ppm 8.29 (s, 1 H), 7.56 (s, 1 H), 4.56 (s, 2 H), 4.35 (s, 1 H), 4.06 - 4.19 (m, 1 H), 3.86 - 4.05 (m, 1 H), 3.32 - 3.52 (m, 2 H), 2.00 - 2.23 (m, 1 H), 1.40 - 1.67 (m, 2 H), 1.13 (d, 3 H), 1.01 - 1.10 (m, 2 H), 0.76 - 0.91 (m, 5 H). ES-LCMS m/z: 443, 445 (M+1).

EXAMPLE 93

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclopropylmethyl)-2-piperazinone

(Compound 93)

Step A

1,1-dimethylethyl {2-[(cyclopropylmethyl)amino]ethyl}carbamate

[00347] A suspension of (cyclopropylmethyl)amine (1.98 g, 27.9 mmol), 1,1-dimethylethyl (2-bromoethyl)carbamate (2.5 g, 11 mmol), and potassium carbonate (4.63 g, 33.5 mmol) in *N,N*-dimethylformamide (30 mL) was maintained with stirring at 60 °C in a sealed pressure flask for 24 hours. The mixture was cooled, poured into ethyl acetate, and washed sequentially with water, 5% lithium chloride (aqueous), and saturated sodium

chloride (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford the title compound (2.35 g, 10.97 mmol, 98 % yield) as a yellow oil. ^{1}H NMR (DMSO-d_6) δ ppm 6.67 - 6.81 (m, 1 H), 2.99 (d, 2 H), 2.46 - 2.61 (m, 3 H), 2.35 (d, 2 H), 1.38 (s, 9 H), 0.74 - 0.99 (m, 1 H), 0.38 (dd, 2 H), 0.08 (dd, 2 H).

Step B

1,1-dimethylethyl {2-[(bromoacetyl)(cyclopropylmethyl)amino]ethyl}carbamate

[00348] To a solution of 1,1-dimethylethyl {2-[(cyclopropylmethyl)amino]ethyl}carbamate (2.07 g, 9.66 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (5.06 mL, 29.0 mmol) in dichloromethane (50 mL) at 5 °C was added bromoacetyl bromide (0.924 mL, 10.6 mmol). The mixture was stirred at 5 °C for 2 hours, quenched with saturated sodium bicarbonate, and extracted with dichloromethane. The organic phase was washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 30% ethyl acetate in dichloromethane to give the title compound (1.55 g, 48%). ES-LCMS m/z: 335, 337 (M+1).

Step C

1,1-dimethylethyl 4-(cyclopropylmethyl)-3-oxo-1-piperazinecarboxylate

[00349] 1,1-Dimethylethyl {2-[(bromoacetyl)(cyclopropylmethyl)amino]ethyl}carbamate (1.55 g, 4.62 mmol) and cesium carbonate (3.77 g, 11.6 mmol) were stirred overnight in *N,N*-dimethylformamide at room temperature. The mixture was quenched with water and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5% lithium chloride (aqueous), dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a 0% to 35% gradient of ethyl acetate in dichloromethane to give the title compound (564 mg, 48%). ES-LCMS m/z: 255 (M+1).

Step D

1-(cyclopropylmethyl)-2-piperazinone hydrochloride

[00350] 1,1-dimethylethyl 4-(cyclopropylmethyl)-3-oxo-1-piperazinecarboxylate (564 mg, 2.22 mmol) was dissolved in dichloromethane (10 mL) before hydrogen chloride (4 N in 1,4-dioxane) (5 mL, 20mmol) was added. The mixture was stirred for 2 hours, concentrated, and dried under vacuum to give the title compound (410 mg, 97%). ^{1}H NMR (DMSO-d_6) δ ppm 9.87 (br. s., 2 H), 3.67 (s, 2 H), 3.58 - 3.65 (m, 2 H), 3.35 - 3.40 (m, 2 H), 3.23 (d, 2 H), 0.94 (ddd, 1 H), 0.41 - 0.50 (m, 2 H), 0.16 - 0.28 (m, 2 H).

Step E

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclopropylmethyl)-2-piperazinone

[00351] 3-Chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (75 mg, 0.25 mmol) and 1-(cyclopropylmethyl)-2-piperazinone hydrochloride (46.9 mg, 0.246 mmol) were dissolved in *N,N*-dimethylformamide (3 mL) before *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.215 mL, 1.23 mmol) was added followed by N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (103 mg, 0.271 mmol). The mixture was stirred for 2 hours and diluted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 5% 2 M ammonium/methanol in dichloromethane to give the title compound (80 mg, 70%). ^{1}H NMR (CHLOROFORM-*d*) δ ppm 8.04 (d, 1 H), 7.40 (s, 1 H), 4.61 (s, 1 H), 4.42 (s, 1 H), 4.32 (t, 1 H), 3.98 - 4.08 (m, 1 H), 3.63 (t, 1 H), 3.57 (t, 1 H), 3.35 (d, 1 H), 3.30 (d, 1 H), 1.94 - 2.09 (m, 1 H), 1.06 - 1.15 (m, 2 H), 0.91 - 1.06 (m, 1 H), 0.75 - 0.82 (m, 2 H), 0.48 - 0.57 (m, 2 H), 0.20 - 0.31 (m, 2 H). ES-LCMS m/z: 441, 443 (M+1).

EXAMPLE 94

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone

(Compound 94)

Step A

(+/-)-1,1-Dimethylethyl (2-aminopropyl)carbamate (major) and (+/-)-1,1-dimethylethyl (2-amino-1-methylethyl)carbamate (minor)

[00352] (+/-)-1,2-diaminopropane (2.30 mL, 27.0 mmol) was dissolved in ethanol (100 mL) and 1,1-dimethylethyl phenyl carbonate (9.98 mL, 54.0 mmol) added. The mixture was heated to reflux for 16 hours, cooled to room temperature, and concentrated by rotovap. The residue was diluted with water before hydrochloric acid (1 M) was added carefully until the pH was ~3. The aqueous phase was washed 3 times with dichloromethane and then made strongly basic with sodium hydroxide (1 M). The aqueous phase and extracted 3 times with dichloromethane and the combined organic layers dried over sodium sulfate before being concentrated to give the title compound (2.98 g, 63%) as a mixture (~85:15) of regioisomers. ES-LCMS m/z: 175 (M+1).

Step B

(+/-)-1,1-dimethylethyl [2-(cyclopentylamino)-1-methylethyl]carbamate and (+/-)-1,1-dimethylethyl [2-(cyclopentylamino)propyl]carbamate

[00353] To a mixture of (+/-)-1,1-dimethylethyl (2-aminopropyl)carbamate and (+/-)-1,1-dimethylethyl (2-amino-1-methylethyl)carbamate (1.2 g, 5.9 mmol), cyclopentanone (0.524 mL, 5.85 mmol), and acetic acid (0.101 mL, 1.76 mmol) in 1,2-dichloroethane (10 mL) was added sodium triacetoxyborohydride (3.72 g, 17.6 mmol). The mixture was stirred at room temperature overnight and then quenched with saturated sodium bicarbonate. The mixture was extracted with dichloromethane and the organic phase washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 5% 2 M ammonium/methanol in dichloromethane to give the title compound (1.1 g, 78%). ES-LCMS m/z: 243 (M+1).

Step C

(+/-)-1,1-dimethylethyl {2-[(bromoacetyl)(cyclopentyl)amino]-1-methylethyl}carbamate and (+/-)-1,1-dimethylethyl {2-[(bromoacetyl)(cyclopentyl)amino]propyl}carbamate

[00354] To a solution of (+/-)-1,1-Dimethylethyl [2-(cyclopentylamino)-1-methylethyl]carbamate and (+/-)-1,1-dimethylethyl [2-(cyclopentylamino)propyl]carbamate (1.1 g, 4.5 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (2.378 mL, 13.62 mmol) in dichloromethane (50 mL) at 5 °C was added bromoacetyl bromide (0.434 mL, 4.99 mmol). The mixture was stirred at 5 °C for 2 hours and quenched with saturated sodium bicarbonate. The mixture was extracted with dichloromethane and the organic phase washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 30% ethyl acetate in dichloromethane to give the title compound (560 mg; 34%). ES-LCMS m/z: 363, 365 (M+1).

Step D

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone andy (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone

[00355] (+/-)-1,1-Dimethylethyl {2-[(bromoacetyl)(cyclopentyl)amino]-1-methylethyl}carbamate and (+/-)-1,1-dimethylethyl {2-[(bromoacetyl)(cyclopentyl)amino]propyl}carbamate (560 mg, 1.541 mmol) and cesium carbonate (1260 mg, 3.85 mmol) were stirred in *N,N*-dimethylformamide overnight at room temperature. The mixture was quenched with water and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5% lithium chloride (aqueous), dried over sodium sulfate, and concentrated to give a mixture of (+/-)-

1,1-dimethylethyl 4-cyclopentyl-3-methyl-5-oxo-1-piperazinecarboxylate and (+/-)-1,1-dimethylethyl 4-cyclopentyl-2-methyl-5-oxo-1-piperazinecarboxylate (350 mg, 80%). The residue was dissolved in dichloromethane (10 mL) before hydrogen chloride (4 N in 1,4-dioxane) (2.5 mL, 10mmol) was added. The mixture was stirred for 2 hours, concentrated, and dried under vacuum to give a mixture of (+/-)-1-cyclopentyl-6-methyl-2-piperazinone and (+/-)-1-cyclopentyl-5-methyl-2-piperazinone (228 mg, 84%). To the mixture of (+/-)-1-cyclopentyl-6-methyl-2-piperazinone and (+/-)-1-cyclopentyl-5-methyl-2-piperazinone (179 mg, 0.985 mmol) and *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.686 mL, 3.94 mmol) in dichloromethane (150 mL) was added dropwise a dichloromethane (60 mL) solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carbonyl chloride (0.985 mmol) (formed by adding oxalyl chloride (2 M in dichloromethane) (0.985 mL, 1.969 mmol) slowly dropwise to a stirring slurry of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (300 mg, 0.985 mmol) in dichloromethane (10 mL) with dimethylformamide (3.80 µl, 0.049 mmol) and working up as described elsewhere in this document). After stirring for 1 hour, the mixture was diluted with dichloromethane and the organic phase washed with saturated sodium bicarbonate, washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 25% ethyl acetate in dichloromethane to give the title compounds (165 mg, 36%) as a mixture of regioisomers. ES-LCMS m/z: 469, 471 (M+1).

Step E

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone

[00356] The regioisomers (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone and (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone (165 mg) were separated by reverse phase HPLC. The early eluting peak was isolated to give the title compound (54 mg; 33%). ^{1}H NMR (DMSO-d_6) δ ppm (rotomeric) 8.44 (br. s., 1 H), 7.59 (s, 1 H), 4.66 - 4.95 (m, 2 H), 4.56 (d, 0.45 H), 4.45 (d, 0.55 H), 4.16 (br. s., 0.45 H), 3.82 (d, 0.55 H), 3.50 (d, 1 H), 3.19 - 3.28 (m, 0.45 H), 3.14 (d, 0.55 H), 2.14 - 2.30 (m, 1 H), 1.58 - 1.79 (m, 4 H), 1.34 - 1.58 (m, 4 H), 1.23 (d, 3 H), 0.97 - 1.06 (m, 2 H), 0.83 - 0.95 (m, 2 H). ES-LCMS m/z: 469, 471 (M+1).

EXAMPLE 95

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone

(Compound 95)

[00357] The regioisomers (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone and (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone (165 mg; Example 94) were separated by reverse phase HPLC. The late eluting peak was isolated to give the title compound (61 mg; 37%). ^{1}H NMR (DMSO-d_6) δ ppm (rotomeric) 8.39 - 8.50 (m, 1 H), 7.59 (s, 1 H), 4.59 (d, 0.4 H), 4.42 - 4.50 (m, 1.2 H), 4.38 (d, 0.4 H), 4.06 - 4.23 (m, 1.4 H), 3.85 (d, 0.6 H), 3.73 - 3.79 (m, 0.4 H), 3.61 - 3.68 (m, 0.6 H), 3.52 (dd, 0.6 H), 3.25 (dd, 0.4 H), 2.11 - 2.30 (m, 1 H), 1.58 - 1.87 (m, 6 H), 1.40 - 1.57 (m, 2 H), 1.14 - 1.25 (m, 3 H), 0.97 - 1.07 (m, 2 H), 0.83 - 0.95 (m, 2 H). ES-LCMS m/z: 469, 471 (M+1).

EXAMPLE 96

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone (Enantiomer 1)

(Compound 96)

[00358] (+/-)-4-{[3-Chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone (89 mg; Example 90) was resolved by chiral HPLC under the following conditions: The compound was separated on an ChiralPak AD-H column (30X250mm) using 30% ethanol (0.1% diethylamine) in hexane(0.1% diethylamine). Flow rate was 42.5ml/min and collection was triggered on 254nm. The early eluting peak was isolated to give the title compound as a single unknown enantiomer (25 mg). ^{1}H NMR (CHLOROFORM-*d*) δ ppm (rotomeric) 7.94 - 8.15 (m, 1 H), 7.40 (s, 1 H), 5.45 (br. s., 0.6 H), 4.95 - 5.25 (m, 1.4 H), 4.87 (d, 0.4 H), 4.75 (d, 0.6 H), 4.19 (d, 0.4 H), 3.96 (d, 0.6 H), 3.55 - 3.75 (m, 1 H), 3.31 (d, 1 H), 1.96 - 2.24 (m, 5 H), 1.64 - 1.79 (m, 2 H), 1.31 - 1.42 (m, 3 H), 1.05 - 1.17 (m, 2 H), 0.74 - 0.85 (m, 2 H). ES-LCMS m/z: 455, 457 (M+1).

EXAMPLE 97

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone (Enantiomer 2)

(Compound 97)

[00359] Racemic (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone (89 mg) was resolved chiral HPLC under the following conditions: The compound was separated on an ChiralPak AD-H column (30X250mm) using 30% ethanol (0.1% diethylamine) in hexane(0.1% diethylamine). Flow rate was 42.5ml/min and collection was triggered on 254nm. The late eluting peak was isolated to give the title compound as a single unknown enantiomer (24 mg). ^{1}H NMR (CHLOROFORM-*d*) δ ppm (rotomeric) 8.04 (d, 1 H), 7.41 (s, 1 H), 5.45 (br. s., 0.6 H), 4.95 - 5.23 (m, 1.4 H), 4.87 (d, 0.4 H), 4.75 (d, 0.6 H), 4.20 (d, 0.4 H), 3.97 (d, 0.6 H), 3.65 (t, 1 H), 3.31 (d, 1 H), 1.96 - 2.25 (m, 5 H), 1.65 - 1.78 (m, 2 H), 1.28 - 1.44 (m, 3 H), 1.02 - 1.17 (m, 2 H), 0.70 - 0.85 (m, 2 H). ES-LCMS m/z: 455, 457 (M+1).

EXAMPLE 98

4-{[3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 98)

Step A

methyl 3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00360] A solution of methyl 3-chloro-6-hydroxy-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (0.25 g, 0.84 mmol), chlorodifluoroacetic acid sodium salt (0.27 g, 1.94 mmol), and Cs_2CO_3 (0.38 g, 1.18 mmol) in DMF (23.4 mL) was stirred at 90 °C for 4 hours. The reaction was then diluted with EtOAc, the combined organic phase was washed with 5% LiCl (2x), brine, dried ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (0-3% MeOH/DCM) to give the title compound (0.12 g, 42%). ES-LCMS m/z: 345.3 (M+1).

Step B

3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00361] A solution of methyl 3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (0.12 g, 0.35 mmol) in THF (2.35 mL) and water (2.35 mL) was treated with 1 M NaOH (0.70 mL, 0.70 mmol). The reaction was stirred at room temperature for 30 minutes. The reaction was then quenched by the addition of 1 M HCl (0.70 mL, 0.70 mmol). The reaction was diluted with EtOAc and the layers were separated. The combined organics phase was washed with brine, dried ($MgSO_4$), filtered, and evaporated to give the title compound as a residue that was used without further purification (0.117 g, 100%). ES-LCMS m/z: 331.0 (M+1).

Step C

4-{[3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00362] A solution of 1-cyclobutyl-2-piperazinone HCl (0.03 g, 0.13 mmol) and 3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (.05 g, 0.16 mmol) in DMF (0.73 mL) was treated with DIPEA (0.06 mL, 0.36 mmol) and HATU (0.06 g, 0.16 mmol). The reaction was stirred at room temperature for 2.5 hours. The reaction was then diluted with EtOAc, the combined organic phase was washed with 5% LiCl (x2), brine, dried ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (0-3% MeOH/DCM) to give the title compound (0.55 g, 81%). ^{1}H NMR (DMSO-d_6) δ: 8.61 - 8.87 (m, 1H), 7.92 - 8.04 (m, 1H), 7.12 - 7.61 (m, 1H), 4.72 - 4.95 (m, 1H), 4.40 (s, 1H), 4.20 (s, 1H), 3.97 - 4.10 (m, 1H), 3.82 - 3.95 (m, 1H), 3.40 - 3.57 (m, 2H), 2.10 - 2.27 (m, 2H), 1.91 - 2.07 (m, 2H), 1.54 - 1.75 (m, 2H). ES-LCMS m/z: 467.2 (M+1).

EXAMPLE 99

4-{[3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 99)

Step A

methyl 3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00363] A solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.60 g, 1.68 mmol), 3-thienylboronic acid (0.32 g, 2.52 mmol), and 3M tripotassium phosphate (1.68 mL, 5.03 mmol) in acetonitrile (13.99 mL) was treated with $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.14 g, 0.17 mmol). The reaction was heated to 85 °C for 1 hour. The reaction was cooled to room temperature and diluted with water. The mixture was extracted with DCM, the combined organic phase was washed with brine, dried ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (0-100% EtOAc/Hexanes) to give the title compound (0.47 g, 78%). ES-LCMS m/z: 360.8, 363.1 (M+1).

Step B

3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00364] A solution of methyl 3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.47 g, 1.31 mmol) in THF (8.70 mL) and H_2O (8.70 mL) was treated by the addition of 1.0 M NaOH (2.61 mL, 2.61 mmol). The reaction was stirred at room temperature for 1 hour and quenched by the addition of 1 M HCl (3.92 mL, 3.92

mmol). The reaction was diluted with EtOAc, the combined organic phase was washed with brine, dried ($MgSO_4$), filtered, and evaporated to yield the title compound that was used without purification and assumed to be quantitative. ES-LCMS m/z: 347.1 (M+1).

Step C

4-{[3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00365] A solution of 3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.070 g, 0.20 mmol) and 1-cyclobutyl-2-piperazinone HCl (0.035 g, 0.18 mmol) in DMF (0.92 mL) was treated by the addition of DIPEA (0.096 mL, 0.55 mmol) and HATU (0.077 g, 0.20 mmol). The reaction was stirred at room temperature for 2 hours and diluted with EtOAc. The combined organic phase was washed with 5% LiCl, saturated $NaHCO_3$, brine, ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (1-4% MeOH/DCM) to give the title compound (0.81 g, 91%). ^{1}H NMR (DMSO-d_6) δ: 8.84 - 8.95 (m, 1H), 8.31 (br. s., 2H), 7.83 - 7.89 (m, 1H), 7.72 - 7.79 (m, 1H), 4.78 - 4.93 (m, 1H), 4.45 (s, 1H), 4.21 (s, 1H), 4.00 - 4.10 (m, 1H), 3.86 - 3.93 (m, 1H), 3.43 - 3.54 (m, 2H), 2.11 - 2.26 (m, 2H), 1.95 - 2.05 (m, 2H), 1.56 - 1.69 (m, 2H). ES-LCMS m/z: 483.2 (M+1).

EXAMPLE 100

4-{[3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 100)

Step A

methyl 3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00366] A solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.60 g, 1.68 mmol), 2-furanylboronic acid (0.28 g, 2.52 mmol), and 3M tripotassium phosphate (1.68 mL, 5.03 mmol) in ACN (13.99 mL) was treated with PdCl2(dppf)-CH2Cl2 adduct (0.14 g, 0.17 mmol). The reaction was heated to 85 °C for 1 hour. The reaction was cooled to room temperature, diluted with water, and was extracted with DCM. The combined organic phase was washed with brine, dried ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (0-1% MeOH/DCM) to give the title compound (0.46 g, 79%). ES-LCMS m/z: 345.4, 347.1 (M+1).

Step B

3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00367] A solution of methyl 3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.46 g, 1.32 mmol) in THF (8.80 mL) and water (8.80 mL) was

treated by the addition of 1 N NaOH (2.64 mL, 2.64 mmol). The reaction was stirred at room temperature for 7 hours and then acidified with 1 N HCl (3.96 mL, 3.96 mmol). The reaction was extracted with EtOAc. The combined organic phase was washed with brine, dried ($MgSO_4$), filtered, and the solvent was evaporated to give the title compound that was used without purification (0.42 g, 97%). ES-LCMS m/z: 330.8, 333.1 (M+1).

Step C

4-{[3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00368] A solution of 3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.067 g, 0.20 mmol) and 1-cyclobutyl-2-piperazinone HCl (0.035 g, 0.18 mmol) in DMF (0.92 mL) was treated with DIPEA (0.096 mL, 0.55 mmol) and HATU (0.077 g, 0.20 mmol). The reaction was stirred at room temperature for 2 hours and diluted with EtOAc. The combined organic phase was washed with 5% LiCl, saturated $NaHCO_3$, brine, dried ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (1-4% MeOH/DCM) to yield the product as a yellow solid. The yellow solid was then triturated with Et_2O to give the title compound (0.054 g, 63%) as a pale yellow solid. ^{1}H NMR (DMSO-d_6) δ: 8.65 - 8.76 (m, 1H), 8.27 (br. s., 1H), 7.89 (s, 1H), 7.40 (br. s., 1H), 6.71 (br. s., 1H), 4.76 - 4.94 (m, 1H), 4.45 (s, 1H), 4.21 (s, 1H), 3.99 - 4.12 (m, 1H), 3.85 - 3.98 (m, 1H), 3.43 - 3.58 (m, 2H), 2.09 - 2.30 (m, 2H), 1.93 - 2.08 (m, 2H), 1.53 - 1.71 (m, 2H). ES-LCMS m/z: 467.2 (M+1).

EXAMPLE 101

4-{[3-chloro-6-(1*H*-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 101)

Step A

methyl 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00369] A solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.60 g, 1.68 mmol), 1,1-dimethylethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrole-1-carboxylate (0.54 g, 1.85 mmol), and 3M tripotassium phosphate (1.68 mL, 5.03 mmol) in ACN (13.99 mL) was treated with $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.14 g, 0.17 mmol). The reaction was heated to 85 °C for 1 hour. The reaction was cooled to room temperature and diluted with water. The mixture was extracted with DCM, the combined organic phase was washed with brine, dried

($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (0-5% MeOH/DCM) to give the title compound (0.78 g, 100%). ES-LCMS m/z: 444.2 (M+1).

Step B

3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00370] A solution of methyl 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.78 g, 1.76 mmol) in THF (11.70 mL) and water (11.70 mL) was treated by the addition of 1 N NaOH (2.63 mL, 2.63 mmol). The reaction was stirred at room temperature overnight. The reaction was extracted with EtOAc and set aside. The aqueous phase was then acidified with 1 N HCl (5.27 mL, 5.27 mmol) and then was extracted with EtOAc. The combined organic phase was washed with brine, dried ($MgSO_4$), filtered, concentrated and used without purification (0.470 g, 62.3%). ES-LCMS m/z: 430.1 (M+1).

Step C

1,1-dimethylethyl 3-[3-chloro-2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-1H-pyrrole-1-carboxylate

[00371] A solution of 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.087 g, 0.20 mmol)and 1-cyclobutyl-2-piperazinone HCl (0.035 g, 0.18 mmol) in DMF (0.92 mL) was treated with DIPEA (0.096 mL, 0.55 mmol) and HATU (0.077 g, 0.20 mmol). The reaction was stirred at room temperature for 2 hours and diluted with EtOAc. The combined organic phase was washed with 5% LiCl, saturated $NaHCO_3$, brine, dried ($MgSO_4$), filtered, evaporated and purified by silica gel chromatography (1-5% MeOH/DCM) to give the title compound (0.080 g, 77%). ES-LCMS m/z: 566.3 (M+1).

Step D

4-{[3-chloro-6-(1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00372] A solution of 1,1-dimethylethyl 3-[3-chloro-2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-1H-pyrrole-1-carboxylate (0.080 g, 0.14 mmol) in DCM (2.0 mL) was treated by the addition of 4 N in 1,4-dioxanes HCl (0.50 mL, 16.46 mmol). The reaction was stirred at room temperature for 8 hours. The reaction was concentrated, the residue was taken up in DCM (2.0 mL), and treated with TFA (0.11 mL, 1.41 mmol). The reaction was stirred at room temperature overnight. The reaction was then treated with 4 N HCl in 1,4-dioxanes and the reaction was stirred at room temperature overnight. The solvents were removed under reduced pressure. The residue was taken up in MeOH and treated with 2 M ammonia in MeOH

(0.20 mL, 0.40 mmol), evaporated and purified by silica gel chromatography (0-5% MeOH/DCM) to give the title compound (0.035 g, 53%). ^{1}H NMR (DMSO-d_6) δ: 11.21 (br. s., 1H), 8.48 - 8.69 (m, 1H), 8.15 (s, 1H), 7.61 (br. s., 1H), 6.85 - 6.97 (m, 1H), 6.60 - 6.78 (m, 1H), 4.74 - 5.00 (m, 1H), 4.47 (s, 1H), 4.20 (s, 1H), 4.03 - 4.11 (m, 1H), 3.85 - 3.92 (m, 1H), 3.44 - 3.54 (m, 2H), 2.11 - 2.26 (m, 2H), 1.94 - 2.05 (m, 2H), 1.56 - 1.69 (m, 2H). ES-LCMS m/z: 466.4 (M+1).

EXAMPLE 102

4-{[3-chloro-6-(2*H*-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 102)

Step A

methyl 3-chloro-8-(trifluoromethyl)-6-[(trimethylsilyl)ethynyl]imidazo[1,2-a]pyridine-2-carboxylate

[00373] A solution of methyl 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.80 g, 2.24 mmol), trimethylsilylethyne (0.35 mL, 2.46 mmol), copper(I) iodide (10.65 mg, 0.056 mmol), TEA (1.72 mL, 12.31 mmol), bis(triphenylphosphine)palladium(II) chloride (0.039 g, 0.056 mmol) in benzene (11.19 mL) was purged with nitrogen and was stirred at room temperature for 3 hours and then concentrated. The dark brown residue was purified by silica gel chromatography (100% DCM) to give the title product as a light brown solid (0.79 g, 94%). ES-LCMS m/z: 376.7 (M+1).

Step B

methyl 3-chloro-6-ethynyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00374] A solution of methyl 3-chloro-8-(trifluoromethyl)-6-[(trimethylsilyl)ethynyl]imidazo[1,2-a]pyridine-2-carboxylate (.79 g, 2.10 mmol) in THF (21.05 mL) was treated by the addition of 1.0M TBAF in THF (2.10 mL, 2.10 mmol). After stirring at room temperature for 20 minutes, the reaction was diluted with EtOAc and the combined organic phase was washed with water (3x), brine, dried ($MgSO_4$), filtered, and concentrated. The crude black residue was purified by silica gel chromatography (0-50% EtOAc/Hexanes) to give mostly pure product. The residue was then re-purified by silica gel chromatography (0-30% EtOAc/Hexanes) to give the title product as a white solid (0.183 g, 29%). ES-LCMS m/z: 303.1 (M+1).

Step C

methyl 3-chloro-6-[2-(hydroxymethyl)-2H-1,2,3-triazol-4-yl]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00375] A 0 °C mixture of 37% aqueous formaldehyde (0.34 mL, 4.56 mmol), glacial acetic acid (0.039 mL, 0.68 mmol), and 1,4-dioxane (0.34 mL) was stirred for 15 minutes and then was treated with sodium azide (0.044 g, 0.68 mmol), followed by methyl 3-chloro-6-ethynyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.138 g, 0.46 mmol). After an additional 10 minutes of stirring, sodium ascorbate (0.018 g, 0.091 mmol) was added, followed by copper(II) sulfate (3.64 mg, 0.023 mmol) in water (0.10 mL). The suspension was stirred with warming to room temperature overnight. The suspension was diluted with water and extracted with DCM. The combined organic phase was washed with brine, dried ($MgSO_4$), filtered, evaporated, and the crude residue was used without further purification (0.147 g, 86%). ES-LCMS m/z: 376.1 (M+1).

Step D

3-chloro-6-(2H-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00376] A suspension of methyl 3-chloro-6-[2-(hydroxymethyl)-2H-1,2,3-triazol-4-yl]-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.147 g, 0.39 mmol) in THF (2.61 mL) and water (2.61 mL) was treated by the addition of 1 M NaOH (1.17 mL, 1.17 mmol). The reaction became clear and was stirred at room temperature for 1.5 hours and then treated by the addition of 1 N HCl (1.17 mL, 1.17 mmol). The reaction was diluted with EtOAc, the combine organic phase was washed with brine, dried ($MgSO_4$), filtered, and concentrated to give the title product that was used without purification (0.098 g, 76%). ES-LCMS m/z: 332.1 (M+1).

Step E

4-{[3-chloro-6-(2H-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00377] A solution of 3-chloro-6-(2H-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.024 g, 0.072 mmol) and 1-cyclobutyl-2-piperazinone HCl (0.017 g, 0.087 mmol) in DMF (0.36 mL) was treated by the addition of DIPEA (0.032 mL, 0.18 mmol) and HATU (0.030 g, 0.080 mmol). The reaction was stirred at room temperature for 2 hours and diluted with EtOAc. The combined organic phase was washed with 5% LiCl, saturated $NaHCO_3$, brine, dried ($MgSO_4$), filtered, concentrated, and the residue was triturated with Et_2O to yield the title compound (0.019 g, 56%). ^1H NMR (DMSO-d_6) δ: 9.01 - 9.10 (m, 1H), 8.60 - 8.72 (m, 1H), 8.28 - 8.41 (m, 1H), 4.73 - 4.93 (m, 1H), 4.45 (s, 1H), 4.22 (s, 1H), 4.01 - 4.08 (m, 1H), 3.86 - 3.94 (m, 1H), 3.44 - 3.53 (m, 2H), 2.06 - 2.25 (m, 2H), 1.93 - 2.06 (m, 2H), 1.56 - 1.70 (m, 2H). ES-LCMS m/z: 468.3 (M+1).

EXAMPLE 103

4-{[3-chloro-6-(1*H*-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 103)

Step A

methyl 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00378] A solution of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.60 g, 1.68 mmol), (1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-2-yl)boronic acid (0.43 g, 2.01 mmol), and 3M tripotassium phosphate (1.68 mL, 5.03 mmol) in acetonitrile (13.99 mL) was treated with $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.14 g, 0.17 mmol). The reaction was heated to 85 °C for 1 hour. The reaction was cooled to room temperature, diluted with water, and extracted with DCM. The combined organic phase was washed with brine, dried ($MgSO_4$), filtered and concentrated to yield a reddish-brown residue that was purified by silica gel chromatography (0-1% MeOH/DCM) to yield mostly pure product. The crude product was re-purified by silica gel chromatography (10-30% EtOAc/Hexanes) to give the title compound (0.504 g, 68%). ES-LCMS m/z: 444.5, 446.2 (M+1).

Step B

3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00379] A suspension of methyl 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.504 g, 1.14 mmol) in water (7.57 mL) and THF (7.57 mL) was treated by the addition of 1 M NaOH (2.27 mL, 2.27 mmol). The reaction became clear and was stirred at room temperature for 1.5 hours and then treated by the addition of 1 N HCl (3.41 mL, 3.41 mmol). The reaction was diluted with EtOAc and the combined organic phase was washed with brine, dried ($MgSO_4$), filtered and concentrated to yield the title product which was used without purification (0.506 g, 100%). ES-LCMS m/z: 430.2 (M+1).

Step C

1,1-dimethylethyl 2-[3-chloro-2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-1H-pyrrole-1-carboxylate

[00380] A solution of 3-chloro-6-(1-{[(1,1-dimethylethyl)oxy]carbonyl}-1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.087 g, 0.20 mmol) and 1-cyclobutyl-2-piperazinone HCl (0.035 g, 0.18 mmol) in DMF (0.92 mL) was treated by the addition of DIPEA (0.096 mL, 0.55 mmol) and HATU (0.077 g, 0.20 mmol). The reaction

was stirred at room temperature for 2 hours and diluted with EtOAc. The combined organic phase was washed with 5% LiCl, saturated $NaHCO_3$, brine, dried ($MgSO_4$), filtered and concentrated and used without purification (0.100 g, 96%). ES-LCMS m/z: 566.3 (M+1).

Step D

4-{[3-chloro-6-(1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00381] A solution of 1,1-dimethylethyl 2-[3-chloro-2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-1H-pyrrole-1-carboxylate (0.10 g, 0.18 mmol) in DCM (2.00 mL) was treated by the addition of 4 N in 1,4-dioxanes HCl (0.50 mL, 2.00 mmol). The reaction was stirred at room temperature for 48 hours and concentrated. The residue was taken up in MeOH and basified with 2 M ammonia in MeOH (3.82 µL, 0.18 mmol). The solvents were then evaporated and the crude residue was purified by silica gel chromatography (1-4% MeOH/DCM) to yield the title product (0.029 g, 35%). ^{1}H NMR (DMSO-d_6) δ: 11.74 (s., 1H), 8.84 (s, 1H), 8.21 (s, 1H), 7.02 (s, 1H), 6.88 (s, 1H), 6.20 (s, 1H), 4.74 - 4.95 (m, 1H), 4.47 (s, 1H), 4.20 (s, 1H), 4.00 - 4.11 (m, 1H), 3.87 – 3.89 (m, 1H), 3.39 - 3.56 (m, 2H), 2.10 - 2.28 (m, 2H), 1.90 - 2.06 (m, 2H), 1.53 - 1.70 (m, 2H). ES-LCMS m/z: 466.2 (M+1).

EXAMPLE 104

1-cyclohexyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 104)

[00382] A solution of 6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (125 mg, 0.422 mmol – see PCT Int. Appl. WO 2009023179), 1-cyclohexyl-2-piperazinone (156 mg, 0.528 mmol, AniChem LLC), HATU (201 mg, 0.528 mmol), and DIPEA (0.295 mL, 1.688 mmol) in N,N-dimethylformamide (5 mL) was maintained with stirring for 2 hours. The mixture was poured into ethyl acetate and washed twice with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 1-cyclohexyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone (117 mg, 0.254 mmol, 60% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ: 9.17 (s, 1H), 8.46 (s, 1H), 8.45 (s, 1H), 8.14 (s, 1H), 7.85 (s, 1H), 7.04 (d, J = 1.0 Hz, 1H), 4.84 (br. s., 1H), 4.41 (br. s., 1H), 4.22 (br. s., 2H), 3.84 (br. s., 1H), 3.39 (br. s., 2H), 1.77 (m, 2H), 1.39 - 1.66 (m, 5H), 1.30 - 1.38 (m, 2H), 1.03 - 1.17 (m, 1H). ES-LCMS m/z: 461.24 m/z (M+1).

EXAMPLE 105

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 105)

[00383] A solution of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (185 mg, 0.603 mmol), 1-(1,3-thiazol-2-yl)-2-piperazinone (193 mg, 0.754 mmol, AniChem LLC), HATU (287 mg, 0.754 mmol), and DIPEA (0.316 mL, 1.810 mmol) in N,N-dimethylformamide(4 mL) was maintained with stirring at room temperature for 2 hours. The reaction was poured into ethyl acetate and extracted three times with 5% LiCl(aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone (200 mg, 0.424 mmol, 70% yield) as a yellow foam. ^{1}H NMR (80°C, DMSO-d_6) δ: 8.37 (s, 1H), 7.85 (s, 1H), 7.52 (d, J = 3.5 Hz, 1H), 7.29 (d, J = 3.5 Hz, 1H), 4.85 (br. s., 1H), 4.56 (br. s., 1H), 4.23 (br. s., 2H), 4.10 (br. s., 2H), 3.11 - 3.20 (m, 1H), 1.28 (d, J = 7.0 Hz, 6H). ES-LCMS m/z: 472.09 (M+1).

EXAMPLE 106

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 106)

[00384] A solution of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (125 mg, 0.408 mmol), 1-cyclohexyl-2-piperazinone (121 mg, 0.408 mmol, AniChem LLC), HATU (194 mg, 0.510 mmol), and DIPEA (0.214 mL, 1.223 mmol) in N,N-dimethylformamide (4 mL) was maintained with stirring at room temperature for 2 hours. The solution was poured into ethyl acetate and washed three times with 5% LiCl(aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone (111 mg, 0.236 mmol, 57% yield) as a white foam. ^{1}H NMR (DMSO-d_6) δ: 8.35 (s, 1H), 7.83 (s, 1H), 4.38 (br. s., 1H), 4.17 (br. s., 2H), 3.69 - 4.03 (m, 2H), 3.32 (br. s., 2H), 3.13 - 3.18 (m, 1H), 1.66 - 1.78 (m, 2H), 1.49 - 1.60 (m, 3H), 1.34 - 1.49 (m, 2H), 1.27 (d, J = 6.8 Hz, 6H), 1.18 - 1.24 (m, 1H), 1.00 - 1.13 (m, 2H). ES-LCMS m/z: 470.90, 471.57 (M+1).

EXAMPLE 107

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 107)

[00385] A solution of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (80 mg, 0.262 mmol), 1-cyclopentyl-2-piperazinone (40 mg, 0.238 mmol), HATU (113 mg, 0.297 mmol), and DIPEA (0.125 mL, 0.713 mmol) in N,N-dimethylformamide (4 mL) was maintained with stirring at room temperature for 4 hours. The mixture was poured into ethyl acetate and extracted three times with 5% LiCl(aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (26 mg, 0.057 mmol, 24% yield) as a yellow foam. ^{1}H NMR (two rotameric forms evident at room temperature, DMSO-d_6) δ: 8.43 - 8.48 (m, 1H), 7.94 (s, 1H), 4.70 - 4.86 (m, 1H), 4.45 (s, 1H), 4.22 (s, 1H), 3.96 - 4.07 (m, 1H), 3.78 - 3.92 (m, 1H), 3.36 - 3.43 (m, 2H), 3.11 - 3.25 (m, 1H), 1.45 - 1.79 (m, 8H), 1.31 (d, 6H). ES-LCMS m/z: 457.21 (M+1).

EXAMPLE 108

4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone

(Compound 108)

[00386] A solution of 3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (150 mg, 0.489 mmol), 1-(3-fluorophenyl)-2-piperazinone (128 mg, 0.556 mmol), HATU (220 mg, 0.578 mmol), and DIPEA (0.233 mL, 1.334 mmol) in N,N-dimethylformamide (4 mL) was maintained with stirring for 2 hours. The mixture was poured into ethyl acetate and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone (121 mg, 0.251 mmol, 56% yield) as a white foam. ^{1}H NMR (DMSO-d_6) δ: 8.47 (br. s., 1H), 7.95 (s, 1H), 7.42 - 7.51 (m, 1H), 7.30 - 7.38 (m, 1H), 7.24 - 7.29 (m, 1H), 7.09 - 7.19 (m, 1H), 4.68 (s, 1H), 4.42 (s, 1H), 4.16 - 4.26 (m, 1H), 3.99 - 4.07 (m, 1H), 3.80 - 3.92 (m, 2H), 3.19 (spt, J = 6.9 Hz, 1H), 1.31 (d, J = 6.8 Hz, 6H). ES-LCMS m/z: 483.15 (M+1).

EXAMPLE 109

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-ethylpropyl)-2-piperazinone

(Compound 109)

Step A

1,1-dimethylethyl {2-[(1-ethylpropyl)amino]ethyl}carbamate

[00387] A suspension of 1,1-dimethylethyl (2-bromoethyl)carbamate (2 g, 8.92 mmol), potassium carbonate (3.70 g, 26.8 mmol), and 1-ethyl-propylamine (1.040 mL, 8.92 mmol) in N,N-dimethylformamide (15 mL) was maintained at 60°C for 16 hours. The mixture was poured into ethyl acetate and washed twice with 5% LiCl (aqueous) and once with saturated sodium chloride (aqueous). The organic layer was dried over sodium sulfate, filtered, and all volatiles were removed under reduced pressure to afford 1,1-dimethylethyl {2-[(1-ethylpropyl)amino]ethyl}carbamate (1.64 g, 7.12 mmol, 80% yield) as a clear oil (85% purity). ^{1}H NMR (DMSO-d_6) δ: 6.73 (br. s., 1H), 2.91 - 3.04 (m, 2H), 2.44 - 2.49 (m, 2H), 2.27 (d, J = 11.5 Hz, 1H), 1.38 (s, 9H), 1.32 (br. s., 4H), 0.81 (t, J = 7.4 Hz, 6H).

Step B

1,1-dimethylethyl {2-[(bromoacetyl)(1-ethylpropyl)amino]ethyl}carbamate

[00388] A solution of 1,1-dimethylethyl {2-[(1-ethylpropyl)amino]ethyl}carbamate (1.64 g, 7.12 mmol), triethylamine (1.141 mL, 8.19 mmol), and bromoacetyl bromide (0.712 mL, 8.19 mmol) in dichloromethane (50 mL) was maintained with stirring at 0°C for 2 hours. The solution was poured into saturated aqueous sodium bicarbonate and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 1,1-dimethylethyl {2-[(bromoacetyl)(1-ethylpropyl)amino]ethyl}carbamate (1.48 g, 4.21 mmol, 59% yield) as a yellow oil. ES-LCMS m/z: 351.17, 353.20 (M+1).

Step C

N-(2-aminoethyl)-2-bromo-N-(1-ethylpropyl)acetamide

[00389] A solution of 1,1-dimethylethyl {2-[(bromoacetyl)(1-ethylpropyl)amino]ethyl}carbamate (1.48 g, 4.21 mmol) in dichloromethane (50 mL) was treated with TFA (6.49 mL, 84 mmol) and maintained with stirring at room temperature for 2 hours. All volatiles were removed under reduced pressure to afford N-(2-aminoethyl)-2-bromo-N-(1-ethylpropyl)acetamide (1.73 g, 4.03 mmol, 96% yield) as a yellow unstable oil which was used immediately in the subsequent transformation.

Step D

1-(1-ethylpropyl)-2-piperazinone

[00390] A solution of N-(2-aminoethyl)-2-bromo-N-(1-ethylpropyl)acetamide (1.73 g, 4.74 mmol) in ethanol (50 mL) was treated with potassium carbonate (2.62 g, 18.95 mmol) and maintained at reflux for 1 hour. The EtOH was removed under reduced pressure and the solids were suspended in dichloromethane and stirred vigorously for 30 minutes. The solids were removed via vacuum filtration and the filtrates were dried over sodium sulfate, filtered, and taken to a residue under reduced pressure to afford 1-(1-ethylpropyl)-2-piperazinone (410 mg, 2.408 mmol, 50% yield) as a viscous yellow oil. ^{1}H NMR (DMSO-d_6) δ: 4.24 - 4.36 (m, 1H), 3.21 (br. s., 2H), 2.91 - 3.00 (m, 2H), 2.80 - 2.88 (m, 2H), 1.26 - 1.48 (m, 4H), 0.76 (t, 6H).

Step E

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-ethylpropyl)-2-piperazinone

[00391] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (150 mg, 0.454 mmol), 1-(1-ethylpropyl)-2-piperazinone (103 mg, 0.603 mmol), DIPEA (0.238 mL, 1.361 mmol), and HATU (207 mg, 0.544 mmol) in N,N-dimethylformamide (4 mL) was maintained with stirring at room temperature for 2 hours. The mixture was poured into ethyl acetate and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-ethylpropyl)-2-piperazinone (90 mg, 0.186 mmol, 41% yield) as a white foam. ^{1}H NMR (DMSO-d_6 ,400MHz) δ: 8.76 - 8.92 (m, 1 H), 8.58 (s, 1 H), 8.23 (s, 1 H), 7.85 (s, 1 H), 7.34 (s, 1 H), 4.48 (s, 1 H), 4.19 - 4.37 (m, 2 H), 3.97 - 4.10 (m, 1 H), 3.80 - 3.94 (m, 1 H), 3.10 - 3.31 (m, 2 H), 1.33 - 1.60 (m, 4 H), 0.69 - 0.94 ppm (m, 6 H). ES-LCMS m/z: 483.16 (M+1).

EXAMPLE 110

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-methylpropyl)-2-piperazinone

(Compound 110)

Step A

1,1-dimethylethyl {2-[(2-methylpropyl)amino]ethyl}carbamate

[00392] A thick-walled glass pressure flask was charged with isobutylamine (3.21 mL, 33.5 mmol), 1,1-dimethylethyl (2-bromoethyl)carbamate (3 g, 13.39 mmol), potassium carbonate (5.55 g, 40.2 mmol), and N,N-dimethylformamide (15 mL). The resulting solution was sealed and maintained at 65°C for 16 hours. The mixture was cooled and poured into 5% LiCl (aqueous) and diluted with ethyl acetate. The organic layer was

washed with additional 5% LiCl (aqueous) and saturated sodium chloride (aqueous), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 1,1-dimethylethyl {2-[(2-methylpropyl)amino]ethyl}carbamate (2.9 g, 13.41 mmol, 100% yield) as a clear oil. ^{1}H NMR (DMSO-d_6) δ: 6.72 (br. s., 1H), 2.90 - 3.06 (m, 2H), 2.47 - 2.49 (m, 2H), 2.21 - 2.33 (m, 2H), 1.57 - 1.70 (m, 1H), 1.38 (s, 9H), 0.85 (d, 6H).

Step B

1,1-dimethylethyl {2-[(bromoacetyl)(2-methylpropyl)amino]ethyl}carbamate

[00393] A solution of 1,1-dimethylethyl {2-[(2-methylpropyl)amino]ethyl}carbamate (2.9 g, 13.41 mmol) and triethylamine (2.80 mL, 20.11 mmol) in dichloromethane (75 mL) was treated dropwise with bromoacetyl bromide (1.341 mL, 15.42 mmol) while maintaining an internal temperature below 5 °C. The mixture was stirred for 2 hours and then poured into saturated sodium bicarbonate. The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 1,1-dimethylethyl {2-[(bromoacetyl)(2-methylpropyl)amino]ethyl}carbamate (2.98 g, 8.84 mmol, 66% yield) as a yellow oil. ^{1}H NMR (DMSO-d_6) δ: 6.80 - 7.04 (m, 1H), 4.07 - 4.15 (m, 2H), 3.25 - 3.40 (m, 2H), 2.96 - 3.20 (m, 4H), 1.86 - 1.97 (m, 1H), 1.38 (s, 9H), 0.75 - 0.94 (m, 6H).

Step C

N-(2-aminoethyl)-2-bromo-N-(2-methylpropyl)acetamide

[00394] A solution of 1,1-dimethylethyl {2-[(bromoacetyl)(2-methylpropyl)amino]ethyl}carbamate (3 g, 8.90 mmol) in dichloromethane (75 mL) was treated with TFA (13.71 mL, 178 mmol) and maintained with stirring at room temperature for 2 hours. All volatiles were removed under reduced pressure to afford N-(2-aminoethyl)-2-bromo-N-(2-methylpropyl)acetamide (3.78 g, 8.07 mmol, 91% yield) as a viscous yellow unstable oil used immediately in the next transformation.

Step D

1-(2-methylpropyl)-2-piperazinone

[00395] A solution of N-(2-aminoethyl)-2-bromo-N-(2-methylpropyl)acetamide (3.78 g, 8.07 mmol) in ethanol (50 mL) was treated with potassium carbonate (4.46 g, 32.3 mmol) and maintained at reflux for 1 hour. The solution was cooled and all solids removed via vacuum filtration. The filtrates were concentrated, resuspended in dichloromethane, refiltered, and the filtrates concentrated under reduced pressure to afford 1-(2-methylpropyl)-2-piperazinone (760 mg, 4.86 mmol, 60% yield) as a yellow oil. ^{1}H NMR (DMSO-d_6) δ: 3.15 - 3.18 (m, 4H), 3.10 (d, J = 7.6 Hz, 2H), 2.81 - 2.93 (m, 2H), 1.85 - 2.00 (m, 1H), 0.83 (d, 6H).

Step E

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-methylpropyl)-2-piperazinone

[00396] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (150 mg, 0.454 mmol), 1-(2-methylpropyl)-2-piperazinone (94 mg, 0.603 mmol), DIPEA (0.238 mL, 1.361 mmol), and HATU (207 mg, 0.544 mmol) in N,N-dimethylformamide (4 mL) was maintained with stirring at room temperature for 2 hours. The mixture was poured into ethyl acetate and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-methylpropyl)-2-piperazinone (106 mg, 0.226 mmol, 50% yield) as a white foam. ^{1}H NMR (DMSO-d_6) δ: 8.78 - 8.90 (m, 1H), 8.58 (s, 1H), 8.23 (s, 1H), 7.86 (s, 1H), 7.34 (s, 1H), 4.48 (br. s., 1H), 4.25 (s, 1H), 3.99 - 4.11 (m, 1H), 3.83 - 3.98 (m, 1H), 3.40 - 3.49 (m, 2H), 3.09 - 3.24 (m, 2H), 1.86 - 2.04 (m, 1H), 0.78 - 0.93 (m, 6H). ES-LCMS m/z: 469.06 (M+1).

EXAMPLE 111

(±)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-3-furanyl)-2-piperazinone

(Compound 111)

Step A

(±)-1,1-dimethylethyl [2-(tetrahydro-3-furanylamino)ethyl]carbamate

[00397] A suspension of (±)-tetrahydro-3-furanamine (1.1 g, 8.90 mmol, Small Molecules Inc., NJ, USA), 1,1-dimethylethyl (2-bromoethyl)carbamate (1.995 g, 8.90 mmol), and potassium carbonate (3.69 g, 26.7 mmol) in N,N-dimethylformamide (15 mL) was maintained at 50 °C in a sealed pressure vessel for 16 hours. The mixture was cooled, diluted with ethyl acetate, and poured into water. The organic layer was washed twice with 5% LiCl (aqueous), dried over sodium sulfate, and taken to a residue under reduced pressure to afford 1,1-dimethylethyl [2-(tetrahydro-3-furanylamino)ethyl]carbamate (1.33 g, 5.77 mmol, 65% yield, roughly 50% purity) as a clear oil used immediately in the subsequent transformation.

Step B

(±)-1,1-dimethylethyl {2-[(bromoacetyl)(tetrahydro-3-furanyl)amino]ethyl}carbamate

[00398] A solution of (±)-1,1-dimethylethyl [2-(tetrahydro-3-furanylamino)ethyl]carbamate (1.35 g, 5.86 mmol), bromoacetyl bromide (0.561 mL, 6.45 mmol), and triethylamine (2.043 mL, 14.65 mmol) in dichloromethane (25 mL) was

maintained with stirring at room temperature for 45 minutes. The mixture was poured into saturated sodium bicarbonate and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 1,1-dimethylethyl {2-[(bromoacetyl)(tetrahydro-3-furanyl)amino]ethyl}carbamate (470 mg, 1.338 mmol, 23% yield) as a yellow oil. ES-LCMS m/z: 373.09, 375.09 (M+Na).

Step C

(±)-1,1-dimethylethyl 3-oxo-4-(tetrahydro-3-furanyl)-1-piperazinecarboxylate

[00399] A solution of (±)-1,1-dimethylethyl {2-[(bromoacetyl)(tetrahydro-3-furanyl)amino]ethyl}carbamate (430 mg, 1.224 mmol) in N,N-dimethylformamide (10 mL) was treated with NaH (196 mg, 2.448 mmol) and maintained with stirring at room temperature for 1 hour. The mixture was quenched via addition of ammonium chloride and diluted with ethyl acetate. The organic layer was washed successively with aqueous LiCl and NaCl, dried over sodium sulfate, and concentrated to a residue under reduced pressure to afford 1,1-dimethylethyl 3-oxo-4-(tetrahydro-3-furanyl)-1-piperazinecarboxylate (260 mg, 0.962 mmol, 79% yield) as a clear oil. ES-LCMS m/z: 270.21(M+Na).

Step D

(±)-1-(tetrahydro-3-furanyl)-2-piperazinone

[00400] A solution of (±)-1,1-dimethylethyl 3-oxo-4-(tetrahydro-3-furanyl)-1-piperazinecarboxylate (260 mg, 0.962 mmol) in dichloromethane (10 mL) was treated with TFA (0.741 mL, 9.62 mmol) and maintained with stirring at room temperature for 45 minutes. The mixture was concentrated under reduced pressure to afford 1-(tetrahydro-3-furanyl)-2-piperazinone (285 mg, 1.003 mmol, quant. yield) as a yellow oil. ^{1}H NMR (DMSO-d_6) δ: 9.24 (br. s., 1H), 4.98 - 5.22 (m, 1H), 3.87 - 4.01 (m, 1H), 3.70 - 3.81 (m, 3H), 3.53 - 3.68 (m, 2H), 3.23 - 3.52 (m, 4H), 2.11 - 2.26 (m, 1H), 1.80 - 1.97 (m, 1H).

Step E

(±)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-3-furanyl)-2-piperazinone

[00401] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (220 mg, 0.665 mmol), (±)-1-(tetrahydro-3-furanyl)-2-piperazinone (236 mg, 0.832 mmol), DIPEA (0.581 mL, 3.33 mmol), and HATU (316 mg, 0.832 mmol) in N,N-dimethylformamide (5 mL) was maintained at room temperature for 45 minutes. The mixture was poured into ethyl acetate and washed sequentially with aqueous LiCl and NaCl. The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford (±)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-3-furanyl)-2-

piperazinone (250 mg, 0.518 mmol, 78% yield) as a white foam. ^{1}H NMR (DMSO-d_6) δ: 8.71 - 8.84 (m, 1H), 8.52 (s, 1H), 8.17 (s, 1H), 7.80 (s, 1H), 7.28 (s, 1H), 4.90 - 5.18 (m, 1H), 4.44 (s, 1H), 4.19 (s, 1H), 3.93 - 4.09 (m, 1H), 3.78 - 3.93 (m, 2H), 3.65 - 3.75 (m, 1H), 3.47 - 3.65 (m, 2H), 3.32 - 3.47 (m, 2H), 2.03 - 2.17 (m, 1H), 1.75 - 1.90 (m, 1H). ES-LCMS m/z: 483.27 (M+1).

EXAMPLE 112

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dimethylethyl)-2-piperazinone

(Compound 112)

Step A

1,1-dimethylethyl {2-[(1,1-dimethylethyl)amino]ethyl}carbamate

[00402] A solution of 1,1-dimethylethyl (2-bromoethyl)carbamate (3 g, 13.39 mmol), potassium carbonate (5.55 g, 40.2 mmol), and t-butyl amine (2.94 g, 40.2 mmol) in N,N-dimethylformamide (15 mL) was maintained at 60 °C in a sealed pressure tube for 16 hours. The mixture was cooled, poured into ethyl acetate, and washed with water. The organic layer was washed with additional 5% LiCl (aqueous) and saturated NaCl (aqueous), separated, dried over sodium sulfate, filtered, and taken to a residue under reduced pressure to afford 1,1-dimethylethyl {2-[(1,1-dimethylethyl)amino]ethyl}carbamate (2.74 g, 12.67 mmol, 95% yield) as a clear oil. ^{1}H NMR (DMSO-d_6) δ: 6.70 (br. s., 1H), 2.88 - 3.02 (m, 2H), 2.43 - 2.47 (m, 2H), 1.38 (s, 9H), 1.00 (s, 9H).

Step B

1,1-dimethylethyl {2-[(bromoacetyl)(1,1-dimethylethyl)amino]ethyl}carbamate

[00403] A solution of 1,1-dimethylethyl {2-[(1,1-dimethylethyl)amino]ethyl}carbamate (2.74 g, 12.67 mmol), bromoacetyl bromide (1.267 mL, 14.57 mmol), and triethylamine (2.65 mL, 19.00 mmol) in dichloromethane (75 mL) was maintained at 0 °C with stirring for 45 minutes. The mixture was poured into saturated sodium bicarbonate (aqueous) and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 1,1-dimethylethyl {2-[(bromoacetyl)(1,1-dimethylethyl)amino]ethyl}carbamate (2.50 g, 7.41 mmol, 59% yield) as a clear oil. ES-LCMS m/z: 359.05, 361.06 (M+Na).

Step C

N-(2-aminoethyl)-2-bromo-N-(1,1-dimethylethyl)acetamide

[00404] A solution of 1,1-dimethylethyl {2-[(bromoacetyl)(1,1-dimethylethyl)amino]ethyl}carbamate (2.50 g, 7.41 mmol) in dichloromethane (75 mL) was

treated with TFA (11.42 mL, 148 mmol) and maintained with stirring at room temperature for 2 hours. The solution was concentrated under reduced pressure to afford N-(2-aminoethyl)-2-bromo-N-(1,1-dimethylethyl)acetamide (4.1 g, 7.59 mmol, quant. yield) as an unstable yellow oil used immediately in the subsequent transformation.

Step D

1-(1,1-dimethylethyl)-2-piperazinone

[00405] A solution of N-(2-aminoethyl)-2-bromo-N-(1,1-dimethylethyl)acetamide (4.1 g, 17.29 mmol) and potassium carbonate (9.56 g, 69.2 mmol) in ethanol (50 mL) was maintained at reflux for 1 hour. The reaction was cooled and filtered to remove solid potassium carbonate. The filtrates were concentrated onto Celite® and purified by silica gel chromatography to afford 1-(1,1-dimethylethyl)-2-piperazinone (105 mg, 0.672 mmol, 4% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ: 7.71 (br. s., 1H), 3.06 - 3.13 (m, 2H), 3.02 (s, 2H), 2.56 - 2.65 (m, 2H), 1.02 (s, 9H).

Step E

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dimethylethyl)-2-piperazinone

[00406] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (135 mg, 0.408 mmol), 1-(1,1-dimethylethyl)-2-piperazinone (67.0 mg, 0.429 mmol), DIPEA (0.214 mL, 1.225 mmol), and HATU (171 mg, 0.449 mmol) was dissolved in N,N-dimethylformamide (4 mL) and maintained with stirring for 1 hour. No conversion to desired product was observed by LCMS. Reaction mixture was warmed to 75°C and then 95°C over three hours, cooled to room temperature, and poured into ethyl acetate/5% LiCl (aqueous). The organic layer was washed with additional aq. LiCl and NaCl, concentrated under reduced pressure, and purified by reverse phase HPLC. HPLC fractions containing product were re-purified by column chromatography to afford 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dimethylethyl)-2-piperazinone (3 mg, 6.40 µmol, 2% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ: 8.82 (s, 1H), 8.56 (s, 1H), 8.21 (s, 1H), 7.85 (s, 1H), 7.32 (s, 1H), 3.73 (br. s., 2H), 3.38 (s, 2H), 2.88 (br. s., 2H), 1.09 (s, 9H). ES-LCMS m/z: 469.12 (M+1).

EXAMPLE 113

(±) 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone

(Compound 113)

Step A

(±)-1,1-dimethylethyl {2-[(3,3-difluorocyclopentyl)amino]ethyl}carbamate

[00407] A mixture of (±)-(3,3-difluorocyclopentyl)amine (760 mg, 4.82 mmol, see *BOMCL*, 2009, *v.* 18(2) p. 554-559), 1,1-dimethylethyl (2-bromoethyl)carbamate (1189 mg, 5.30 mmol), and potassium carbonate (2000 mg, 14.47 mmol) in N,N-dimethylformamide (25 mL) was maintained at 60°C in a sealed pressure tube for 18 hours. The mixture was cooled, poured into ethyl acetate, and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford (±)-1,1-dimethylethyl {2-[(3,3-difluorocyclopentyl)amino]ethyl}carbamate (1.00 g, 1.324 mmol, 28% yield) with roughly 35-50% purity. This was used directly in the next step without further purification.

Step B

(±)-dimethylethyl {2-[(bromoacetyl)(3,3-difluorocyclopentyl)amino]ethyl}carbamate

[00408] A solution of (±)-1,1-dimethylethyl {2-[(3,3-difluorocyclopentyl)amino]ethyl}carbamate (1 g, 1.892 mmol) and DIPEA (0.991 mL, 5.68 mmol) in dichloromethane (50 mL) at 0°C was treated with bromoacetyl bromide (0.249 mL, 2.84 mmol) and stirred for 3 hours. The solution was poured into saturated sodium bicarbonate and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford (±)-dimethylethyl {2-[(bromoacetyl)(3,3-difluorocyclopentyl)amino]ethyl}carbamate (400 mg, 0.519 mmol, 27% yield) with roughly 50% purity contaminated with a non-UV active component. Product used in subsequent transformations without further purification. ES-LCMS m/z: 285.02 (M+1- BOC).

Step C

(±)-(1,1-dimethylethyl 4-(3,3-difluorocyclopentyl)-3-oxo-1-piperazinecarboxylate

[00409] A solution of (±)-1,1-dimethylethyl {2-[(bromoacetyl)(3,3-difluorocyclopentyl)amino]ethyl}carbamate (400 mg, 1.038 mmol) in N,N-dimethylformamide (12 mL) was treated with NaH (41.5 mg, 1.038 mmol) and maintained with stirring until bubbling ceased (1 hour). The mixture was diluted with saturated ammonium chloride (aqueous) and ethyl acetate. The organic layer was dried over sodium sulfate, filtered, and taken to a residue under reduced pressure. A roughly 1:1 mixture of two products evident (150 mg total): (±)-(1,1-dimethylethyl 4-(3,3-difluorocyclopentyl)-3-oxo-1-piperazinecarboxylate and (±)-1,1-dimethylethyl {2-[(3,3-difluorocyclopentyl)amino]ethyl}carbamate. ES-LCMS m/z: 305.10 (M+1).
The mixture was taken on to next transformation.

Step D

(±)-1-(3,3-difluorocyclopentyl)-2-piperazinone

[00410] A solution of (±)-1,1-dimethylethyl 4-(3,3-difluorocyclopentyl)-3-oxo-1-piperazinecarboxylate and (±)-1,1-dimethylethyl {2-[(3,3-difluorocyclopentyl)amino]ethyl}carbamate (150 mg total mixture) in Dichloromethane (DCM) (15 mL) was treated with TFA (0.380 mL, 4.93 mmol) and maintained with stirring at room temperature for 1 hours. The mixture was concentrated under reduced pressure to afford an inseparable mixture (100 mg) of 1-(3,3-difluorocyclopentyl)-2-piperazinone and N-(3,3-difluorocyclopentyl)-1,2-ethanediamine which was used crude in the subsequent transformation used directly in the next transformation.

Step E

(±) 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone

[00411] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (135 mg, 0.408 mmol), (±)-1-(3,3-difluorocyclopentyl)-2-piperazinone (130 mg, 0.408 mmol, crude mixture from above), DIPEA (0.285 mL, 1.633 mmol), and HATU (186 mg, 0.490 mmol) in N,N-dimethylformamide (5 mL) was maintained with stirring at room temperature for 3 hours. The mixture was poured into ethyl acetate and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford eluting first (±)-3-chloro-N-{2-[(3,3-difluorocyclopentyl)amino]ethyl}-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (49 mg, 0.103 mmol, 25.2 % yield) and eluting second (±) 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone (71 mg, 0.137 mmol, 34% yield) as white solids. ^{1}H NMR (DMSO-d_6) δ: 8.70 - 8.88 (m, 1H), 8.52 (s, 1H), 8.18 (s, 1H), 7.80 (s, 1H), 7.28 (s, 1H), 4.76 - 5.06 (m, 1H), 4.46 (s, 1H), 4.20 (s, 1H), 4.02 (br. s., 1H), 3.84 (br. s., 1H), 3.32 - 3.44 (m, 2H), 2.12 - 2.30 (m, 3H), 1.94 - 2.10 (m, 1H), 1.84 (br. s., 2H). ES-LCMS m/z: 517.55 (M+1).

EXAMPLE 114

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone (Enantiomer 1)

(Compound 114)

[00412] (±) 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone (32 mg) was dissolved in MeOH. An analytical resolution method was employed using a Chiralpak ADH column (4.6 x

250mm) at 2 mL/min, 140 bar, 40°C with 20% MeOH as modifier. Preparative resolution of the constituent enantiomers was performed using a Chiralpak ADH 10 x 250mm, 10 mL/min, 140 bar, 40°C using with 20% MeOH as modifier. Retention times for the two enantiomers were ~13.5 minutes and 16 minutes for analytical and ~12 minutes and 15 minutes for the prep respectively. Approximately 10 mg of each enantiomer was isolated. Absolute configurational assignments of each enantiomer were not made. First Eluting Enantiomer: ^{1}H NMR (DMSO-d_6) δ: 8.77 - 8.91 (m, 1H), 8.58 (s, 1H), 8.24 (s, 1H), 7.86 (s, 1H), 7.34 (s, 1H), 4.97 (dt, J = 18.1, 9.0 Hz, 1H), 4.52 (s, 1H), 4.26 (s, 1H), 4.08 (br. s., 1H), 3.90 (br. s., 1H), 3.42 (br. s., 2H), 2.17 - 2.37 (m, 3H), 2.09 (d, J = 8.8 Hz, 1H), 1.82 - 2.01 (m, 2H). ES-LCMS m/z: 517.31 (M+1).

EXAMPLE 115

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone (Enantiomer 2)

(Compound 115)

[00413] Second Eluting Enantiomer: ^{1}H NMR (DMSO-d_6) δ: 8.78 - 8.92 (m, 1H), 8.58 (s, 1H), 8.24 (s, 1H), 7.86 (s, 1H), 7.34 (s, 1H), 4.78 - 5.10 (m, 1H), 4.52 (s, 1H), 4.26 (s, 1H), 4.08 (br. s., 1H), 3.91 (br. s., 1H), 3.43 - 3.52 (m, 2H), 2.17 - 2.38 (m, 3H), 2.01 - 2.19 (m, 1H), 1.84 - 2.00 (m, 2H). ES-LCMS m/z: 517.30 (M+1).

EXAMPLE 116

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone

(Compound 116)

Step A

1,1-dimethylethyl (3,3-dimethylcyclobutyl)carbamate

[00414] A solution of 3,3-dimethylcyclobutanecarboxylic acid (2.80 g, 21.85 mmol) and

triethylamine (6.09 mL, 43.7 mmol) in tert-butanol (85 mL) was treated with diphenylphosphorylazide (7.08 mL, 32.8 mmol) and maintained at reflux for 16 hours. The mixture was cooled, diluted with saturated sodium bicarbonate, and all tert-butanol was removed under reduced pressure. The suspension was diluted with diethyl ether and the aqueous layer was extracted with additional diethyl ether. The combined ether layers were washed twice with saturated sodium chloride (aqueous), separated, dried over sodium sulfate, filtered, and taken to a residue under reduced pressure to afford 1,1-dimethylethyl (3,3-dimethylcyclobutyl)carbamate (5 g, 12.54 mmol, 57% yield) of sufficient

purity for direct use in the subsequent transformation.

Step B

(3,3-dimethylcyclobutyl)amine

[00415] A solution of crude product containing 1,1-dimethylethyl (3,3-dimethylcyclobutyl)carbamate (5 g, 12.54 mmol, 50% purity) was dissolved in 1,4-dioxane (50 mL) and treated with HCl in 1,4-dioxanes (4 M, 12.54 mL, 125 mmol) and maintained with stirring at room temperature overnight. The mixture was concentrated under reduced pressure and triturated with diethyl ether to afford (3,3-dimethylcyclobutyl)amine (812 mg, 5.99 mmol, 48% yield) HCl salt as a hygroscopic white solid. ^{1}H NMR (DMSO-d_6) δ: 8.25 (br. s., 3H), 3.60 - 3.71 (m, 1H), 1.83 - 2.13 (m, 4H), 1.11 (s, 6H).

Step C

2-bromo-N-(3,3-dimethylcyclobutyl)acetamide

[00416] A solution of (3,3-dimethylcyclobutyl)amine•HCl (200 mg, 1.475 mmol), bromoacetyl bromide (0.142 mL, 1.622 mmol), and DIPEA (0.773 mL, 4.42 mmol) in dichloromethane (15 mL) was maintained at 0 °C for 2 hours. The mixture was poured into saturated sodium bicarbonate (aqueous) and the organic layer was separated, dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 2-bromo-N-(3,3-dimethylcyclobutyl)acetamide (320 mg, 1.454 mmol, 99% yield) as a yellow solid. ES-LCMS m/z: 221.11, 223.13 (M+1).

Step D

N1-(3,3-dimethylcyclobutyl)-N2-(2-hydroxyethyl)glycinamide

[00417] A mixture of 2-bromo-N-(3,3-dimethylcyclobutyl)acetamide (310 mg, 1.408 mmol) and ethanolamine (0.089 mL, 1.479 mmol) in ethanol (7 mL) was maintained at 60°C for 45 minutes. The solution was cooled, concentrated under reduced pressure, and purified by column chromatography to afford N1-(3,3-dimethylcyclobutyl)-N2-(2-hydroxyethyl)glycinamide (200 mg, 0.999 mmol, 71% yield) as a pale yellow oil. ES-LCMS m/z: 201.19 (M+1).

Step E

3-chloro-6-cyclopropyl-N-{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}-N-(2-hydroxyethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide

[00418] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (135 mg, 0.443 mmol), N1-(3,3-dimethylcyclobutyl)-N2-(2-hydroxyethyl)glycinamide (98 mg, 0.487 mmol), HATU (202 mg, 0.532 mmol), and DIPEA (0.310 mL, 1.773 mmol) in N,N-dimethylformamide (5 mL) was maintained with stirring at room temperature for 45 minutes. The solution was poured into ethyl acetate and washed with LiCl (aq, 5%) three times. The organic layer was dried over sodium sulfate, filtered,

taken to a residue under reduced pressure, and purified by column chromatography to afford 3-chloro-6-cyclopropyl-N-{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}-N-(2-hydroxyethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (128 mg, 0.263 mmol, 59% yield) as a white solid. ES-LCMS m/z: 487.19 (M+1).

Step F

2-({[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}amino)ethyl methanesulfonate

[00419] A solution of 3-chloro-6-cyclopropyl-N-{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}-N-(2-hydroxyethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (85 mg, 0.175 mmol) and DIPEA (91 µl, 0.524 mmol) in dichloromethane was cooled to 0°C and treated with MsCl (17.00 µl, 0.218 mmol) in one portion. The mixture was stirred for 30 minutes at which time all starting material has been consumed. The mixture was poured into saturated sodium bicarbonate and the organic layer was dried over sodium sulfate, filtered, and taken to a residue under reduced pressure to afford 2-({[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}amino)ethyl methanesulfonate (95 mg, 0.168 mmol, 96% yield) as a yellow solid. ES-LCMS m/z: 565.32, 566.38, 567.37, 568.34 (M+1).

Step G

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone

[00420] A solution of 2-({[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}amino)ethyl methanesulfonate (95 mg, 0.168 mmol, 96% yield) was dissolved in N,N-dimethylformamide (2 mL), cooled to 0°C, and treated with NaH (6.37 mg, 0.265 mmol) in one portion. The mixture was stirred for 45 minutes, diluted with ethyl acetate, and quenched via addition of saturated sodium bicarbonate (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone (35 mg, 0.075 mmol, 42% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ: 8.20 - 8.44 (m, 1H), 7.57 (s, 1H), 4.68 - 4.84 (m, 1H), 4.24 (br. s., 2H), 3.93 (br. s., 2H), 3.26 - 3.51 (m, 2H), 2.16 (d, J = 10.0 Hz, 1H), 1.73 - 2.06 (m, 4H), 1.13 (s, 3H), 1.07 (s, 3H), 0.94 - 1.04 (m, 2H), 0.84 (d, 2H). ES-LCMS m/z: 469.24 (M+1).

EXAMPLE 117

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone

(Compound 117)

Step A

3-chloro-N-{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}-6-(3-furanyl)-N-(2-hydroxyethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide

[00421] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (150 mg, 0.454 mmol), N1-(3,3-dimethylcyclobutyl)-N2-(2-hydroxyethyl)glycinamide (100 mg, 0.499 mmol), HATU (207 mg, 0.544 mmol), and DIPEA (0.317 mL, 1.815 mmol) in N,N-dimethylformamide (5 mL) was maintained with stirring at room temperature for 45 minutes. The mixture was diluted with ethyl acetate and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 3-chloro-N-{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}-6-(3-furanyl)-N-(2-hydroxyethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (95 mg, 0.185 mmol, 41% yield) as a white solid. ES-LCMS m/z: 513.24 (M+1).

Step B

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone

[00422] A solution of 3-chloro-N-{2-[(3,3-dimethylcyclobutyl)amino]-2-oxoethyl}-6-(3-furanyl)-N-(2-hydroxyethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (95 mg, 0.185 mmol), DIPEA (0.097 mL, 0.556 mmol), and MsCl (0.018 mL, 0.232 mmol) in dichloromethane (5 mL) was maintained with stirring at 0°C for 30 minutes. The mixture was poured into saturated sodium bicarbonate and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and redissolved in N,N-dimethylformamide (5.00 mL). NaH (4.44 mg, 0.185 mmol) was added and the mixture was monitored by TLC/LCMS. No conversion was observed by LCMS at room temperature after 45 minutes. The mixture was poured into ethyl acetate and washed three times with saturated sodium bicarbonate. The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and azeotroped three times with toluene. The residue was dissolved in N,N-dimethylformamide (5.00 mL) and treated with NaH (4.44 mg, 0.185 mmol). The mixture was poured into ethyl acetate, washed three times with 5% LiCl (aqueous), and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-

a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone (6 mg, 0.012 mmol, 7% yield) as a white solid. ^{1}H NMR (DMSO-d_6) δ: 8.76 - 8.89 (m, 1H), 8.57 (s, 1H), 8.23 (br. s., 1H), 7.85 (br. s., 1H), 7.33 (br. s., 1H), 4.74 - 4.99 (m, 1H), 4.45 (s, 1H), 4.21 (br. s., 1H), 4.06 (br. s., 1H), 3.89 (br. s., 1H), 3.41 - 3.54 (m, 2H), 1.79 - 2.08 (m, 4H), 1.16 (br. s., 3H), 1.06 - 1.14 (m, 3H). ES-LCMS m/z: 495.38 (M+1).

EXAMPLE 118

(±)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone

(Compound 118)

Step A

(±)-1,1-dimethylethyl {2-[(2,2-difluorocyclopentyl)amino]ethyl}carbamate

[00423] A solution of (±)-(2,2-difluorocyclopentyl)amine (650 mg, 4.12 mmol, PCT Int. App. (2007) WO2007011810), 1,1-dimethylethyl (2-bromoethyl)carbamate (1017 mg, 4.54 mmol), and potassium carbonate (1995 mg, 14.44 mmol) in N,N-dimethylformamide (15 mL) was maintained at 60°C for 16 hours. The mixture was cooled to room temperature and poured into ethyl acetate. The suspension was washed three times with 5% LiCl (aqueous) and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and taken crude for the subsequent transformation (< 65% purity achieved).

Step B

(±)-1,1-dimethylethyl {2-[(bromoacetyl)(2,2-difluorocyclopentyl)amino]ethyl}carbamate

[00424] A solution of (±)-1,1-dimethylethyl {2-[(2,2-difluorocyclopentyl)amino]ethyl}carbamate (720 mg, 2.72 mmol), bromoacetyl bromide (0.478 mL, 5.45 mmol), and DIPEA (1.903 mL, 10.90 mmol) in dichloromethane (50 mL) was maintained at room temperature with stirring for 3 hours. The mixture was poured into saturated sodium bicarbonate (aqueous) and the organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford (±)-1,1-dimethylethyl {2-[(bromoacetyl)(2,2-difluorocyclopentyl)amino]ethyl}carbamate (290 mg, 0.753 mmol, 28% yield) as a yellow oil. ES-LCMS m/z: 285.02, 287.02 (M+1 - BOC).

Step C

(±)-1,1-dimethylethyl 4-(2,2-difluorocyclopentyl)-3-oxo-1-piperazinecarboxylate

[00425] A solution of (±)-1,1-dimethylethyl {2-[(bromoacetyl)(2,2-difluorocyclopentyl)amino]ethyl}carbamate (290 mg, 0.753 mmol) in N,N-dimethylformamide (5 mL) was treated with NaH (60.2 mg, 1.506 mmol) and maintained

with stirring for 45 minutes. The mixture was quenched via dropwise addition of saturated ammonium chloride (aqueous) and diluted with ethyl acetate. The organic layer was washed twice with 5% aq. LiCl and separated, dried over sodium sulfate, filtered, and taken to a residue under reduced pressure to afford a roughly 1:1 mixture of (±)-1,1-dimethylethyl 4-(2,2-difluorocyclopentyl)-3-oxo-1-piperazinecarboxylate (185 mg combined mass, 0.608 mmol, 81 % yield) and (±)-1,1-dimethylethyl {2-[(2,2-difluorocyclopentyl)amino]ethyl}carbamate as a yellow oil. ES-LCMS m/z: 305.21 (M+1).

Step D

(±)-1-(2,2-difluorocyclopentyl)-2-piperazinone

[00426] A solution of the crude mixture from above containing (±)-1,1-dimethylethyl 4-(2,2-difluorocyclopentyl)-3-oxo-1-piperazinecarboxylate (175 mg, 0.575 mmol in dichloromethane (8 mL) was treated with TFA (0.443 mL, 5.75 mmol) and maintained with stirring at room temperature for 45 minutes. The mixture was concentrated under reduced pressure to afford a crude mixture of (±)-1-(2,2-difluorocyclopentyl)-2-piperazinone and N-(2,2-difluorocyclopentyl)-1,2-ethanediamine (170 mg combined, quant. yield) suitable for use directly in the next transformation.

Step E

(±)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone

[00427] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (115 mg, 0.348 mmol), (±)-1-(2,2-difluorocyclopentyl)-2-piperazinone (166 mg, crude mixture described above, 0.522 mmol), HATU (198 mg, 0.522 mmol), and DIPEA (0.304 mL, 1.739 mmol) in N,N-dimethylformamide (5 mL) was maintained with stirring at room temperature for 45 minutes. The solution was poured into ethyl acetate and washed three times with 5% LiCl (aqueous). The organic layer was dried over sodium sulfate, filtered, taken to a residue under reduced pressure, and purified by column chromatography to afford eluting first (±)-3-chloro-N-{2-[(2,2-difluorocyclopentyl)amino]ethyl}-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide (12 mg, 0.025 mmol, 7% yield) and eluting second (±)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (33 mg, 0.064 mmol, 18% yield), both as white solids. ^{1}H NMR (DMSO-d_6) δ: 8.77 - 8.90 (m, 1H), 8.58 (s, 1H), 8.24 (s, 1H), 7.86 (s, 1H), 7.34 (s, 1H), 4.94 - 5.15 (m, 1H), 4.48 - 4.71 (m, 1H), 4.25 - 4.43 (m, 1H), 4.06 - 4.20 (m, 0.5H), 3.92 - 4.04 (m, 1H), 3.67 - 3.81 (m, 0.5H), 3.42 - 3.62 (m, 2H), 1.60 - 2.34 (m, 6H). ES-LCMS m/z: 517.15 (M+1).

EXAMPLE 119

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (Enantiomer 1)

(Compound 119)

[00428] (±) 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (15 mg) was resolved into individual enantiomers via dissolution in methanol and separation using supercritical fluid chromatography (20% MeOH/CO_2, 140 bar, 10 mL/min, ChiralPak AD-H 25 x 1 cm, 200 nM) affording 4.2 mg and 4.3 mg of early and later eluting enantiomers respectively. Absolute configurational assignments of the two enantiomers were not made. First Eluting Enantiomer: ^{1}H NMR (DMSO-d_6) δ: 8.70 - 8.95 (m, 1H), 8.58 (s, 1H), 8.24 (s, 1H), 7.86 (s, 1H), 7.34 (s, 1H), 4.91 - 5.19 (m, 1H), 4.49 - 4.72 (m, 1H), 4.26 - 4.43 (m, 1H), 4.07 - 4.17 (m, 0.5H), 3.92 - 4.05 (m, 1H), 3.68 - 3.79 (m, 0.5H), 3.42 - 3.61 (m, 2H), 1.61 - 2.28 (m, 6H). ES-LCMS m/z: 517.16 (M+1).

EXAMPLE 120

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (Enantiomer 2)

(Compound 120)

[00429] (±) 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone (15 mg) was resolved into individual enantiomers via dissolution in methanol and separation using supercritical fluid chromatography (20% MeOH/CO_2, 140 bar, 10 mL/min, ChiralPak AD-H 25 x 1 cm, 200 nM) affording 4.2 mg and 4.3 mg of early and later eluting enantiomers respectively. Absolute configurational assignments of the two enantiomers were not made. Second Eluting Enantiomer: ^{1}H NMR (DMSO-d_6) δ: 8.70 - 8.95 (m, 1H), 8.58 (s, 1H), 8.24 (s, 1H), 7.86 (s, 1H), 7.34 (s, 1H), 4.91 - 5.19 (m, 1H), 4.49 - 4.72 (m, 1H), 4.26 - 4.43 (m, 1H), 4.07 - 4.17 (m, 0.5H), 3.92 - 4.05 (m, 1H), 3.68 - 3.79 (m, 0.5H), 3.42 - 3.61 (m, 2H), 1.61 - 2.28 (m, 6H). ES-LCMS m/z: 517.16 (M+1).

EXAMPLE 121

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 121)

[00430] To a suspension of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (150 mg, 0.454 mmol), 1-

cyclopentyl-2-piperazinone (111 mg, 0.544 mmol), N,N-diisopropylethylamine (0.396 mL, 2.268 mmol) in DMF (2 mL) was added bromo-tris-pyrrolidino phosphoniumhexafluorophosphate (PyBrOP) (233 mg, 0.499 mmol). The mixture was stirred overnight and diluted with EtOAc (50 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL), brine (25 mL), dried ($MgSO_4$), filtered and concentrated. The crude was purified by silica gel chromatography (0-10% MeOH in DCM) to give the title compound (38.2 mg, 18%) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.42 - 1.82 (m, 8 H), 3.33 - 3.45 (m, 2 H), 3.85 (t, *J*=5.2 Hz, 1 H), 3.97 - 4.09 (m, 1 H), 4.22 (s, 1 H), 4.47 (s, 1 H), 4.67 - 4.89 (m, 1 H), 8.17 - 8.33 (m, 2 H), 8.57 (br. s., 1 H), 8.84 (d, *J*=6.8 Hz, 1 H), 13.17 (br. s., 1 H); ES-LCMS m/z: 481.1 (M+1).

EXAMPLE 122

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 122)

[00431] The title compound (150 mg, 67%) was prepared by PyBrOP coupling of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(1,3-thiazol-2-yl)-2-piperazinone in a manner analogous to that described in Example 121. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.10 (br. s., 1 H), 4.27 (br. s., 3 H), 4.59 (s, 1 H), 4.91 (s, 1 H), 7.36 (br. s., 1 H), 7.58 (d, *J*=3.2 Hz, 1 H), 8.15 - 8.37 (m, 2 H), 8.57 (br. s., 1 H), 8.85 (br. s., 1 H), 13.17 (br. s., 1 H); ES-LCMS m/z: 496.0 (M+1).

EXAMPLE 123

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 123)

[00432] The title compound (32 mg, 21%) was prepared by PyBrOP coupling of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-cyclobutyl-2-piperazinone in a manner analogous to that described in Example 121. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.55 - 1.69 (m, 2 H), 1.91 - 2.07 (m, 2 H), 2.18 (br. s., 2 H), 3.41 - 3.56 (m, 2 H), 3.89 (t, *J*=5 Hz, 1 H), 4.06 (t, *J*=5 Hz, 1 H), 4.21 (s, 1 H), 4.46 (s, 1 H), 4.86 (br. s., 1 H), 8.22 (br. s., 2 H), 8.56 (br. s., 1 H), 8.83 (d, *J*=8.7 Hz, 1 H), 13.17 (br. s., 1 H); ES-LCMS m/z: 467.2 (M+1).

EXAMPLE 124

4-{[3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 124)

Step A

5-iodo-3-(trifluoromethyl)-2-pyridinamine

[00433] A solution of N-iodosuccinimide (61 g, 0.272 mol) in DMF (200 mL) was rapidly added dropwise via an additional funnel to a stirred solution of 3-(trifluoromethyl)-2-pyridinamine (40 g, 0.247 mol) in N,N-dimethylformamide (200 mL) at room temperature. The mixture was allowed to stir at room temperature overnight. Part of the DMF (300 mL) was removed under reduced pressure and the residue was poured into 10% aqueous $Na_2S_2O_3$ and extracted with EtOAc. The organic phase was separated and washed with brine, dried and concentrated to give 5-iodo-3-(trifluoromethyl)-2-pyridinamine (50 g, 70%) as yellow solid.

Step B

methyl 6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00434] A solution of 5-iodo-3-(trifluoromethyl)-2-pyridinamine (45 g, 0.156 mol) and methyl bromopyruvate (70.6 g, 0.39 mol) in N,N-dimethylformamide (600 mL) was heated at 70 °C overnight. The reaction mixture was cooled to room temperature and poured into ice water. The mixture was stirred for 1 hour and filtered to give the title compound (37 g) as brown solid. This material was used for next step without further purification.

Step C

methyl 3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00435] To a solution of methyl 6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (37 g, 0.1 mol) in N,N-dimethylformamide (350 mL) was added N-bromosuccinimide (18.7 g, 0.105 mol). The mixture was heated at 50 °C for 3 hours. Upon cooling, the mixture was diluted with water and extracted with EtOAc. The organic layer was washed with brine, dried and concentrated. The crude was purified by silica gel chromatography [petroleum ether: EtOAc (10:1 v/v)] to give the title compound (32 g, 71%) as white solid.

Step D

3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00436] To a solution of methyl 3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (1 g, 2.227 mmol) in THF (11.93 mL) and water (3.98 mL) at room temperature was added a chilled solution of 1 N sodium hydroxide (3.90 mL, 3.90 mmol). After 35 minutes, the mixture was poured into chilled 1 N hydrochloric acid (5.57

mL, 5.57 mmol), and the mixture was stirred for 1 hour and the precipitate was filtered and dried under high vacuum to give 3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (834.7 mg, 1.823 mmol, 82 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.08 (s, 1 H), 8.85 (s, 1 H), 13.42 (br. s., 1 H); ES-LCMS m/z: 437.1 (M+1).

Step E

4-{[3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00437] The title compound (291 mg, 98%) was prepared by HATU coupling of 3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-cyclopentyl-2-piperazinone in a manner analogous to that described herein. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.41 - 1.83 (m, 8 H), 3.28-3.41 (m, 2 H), 3.86 (dt, *J*=15.5, 5.3 Hz, 2 H), 4.21 (s, 1 H), 4.32 (s, 1 H), 4.65 - 4.87 (m, 1 H), 8.09 (s, 1 H), 8.86 (m, 1 H); ES-LCMS m/z: 585.2, 587.1 (M+1).

EXAMPLE 125

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone

(Compound 125)

Step A

1-(3,5-difluorophenyl)-2-piperazinone hydrochloride

[00438] In a dried and nitrogen flushed three-necked round bottom flask, N-Boc piperazinone (1.1 g, 5.5 mmol), CuI (43.6 mg, 0.23 mmol), 1-bromo-3,5-difluorobenzene (0.882 g, 4.57 mmol), potassium carbonate (1.26 g, 9.14 mmol) and N,N'dimethylethylenediamine (4.0 mg, 0.455 mmol) was dispersed in anhydrous toluene (5 mL). The mixture was heated at 110 °C under nitrogen overnight. Upon consumption of bromide, the mixture was cooled to room temperature. The solid was filtered and the solvent was removed under reduced pressure. The crude product was purified by silica gel chromatography [petroleum ether: ethyl acetate (5:1 v/v) to petroleum ether: ethyl acetate (1:1 v/v)] to give 1,1-dimethylethyl 4-(3,5-difluorophenyl)-3-oxo-1-piperazinecarboxylate (500 mg, 36%) as yellow solid. 1,1-Dimethylethyl 4-(3,5-difluorophenyl)-3-oxo-1-piperazinecarboxylate was stirred in saturated HCl in 1,4-dioxane at room temperature until reaction was complete (2 hours). The solvent was then concentrated under reduced pressure to give a solid which was filtered, washed with Et_2O to give 1-(3,5-difluorophenyl)-2-piperazinone hydrochloride (400 mg, 59%) as white solid.

Step B

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone

[00439] A solution of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (67 mg, 0.21 mmol) and O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (TBTU) (80 mg, 0.25 mmol) was stirred in anhydrous DMF (10 mL) for 10 minutes at room temperature. 1-(3,5-Difluorophenyl)-2-piperazinone hydrochloride (62 mg, 0.25 mmol), and N,N-diisopropylethylamine (68 mg, 0.53 mmol) in DMF was added and the mixture was stirred for 2 hours. The mixture was diluted with ethyl acetate and washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by silica gel chromatography to give 4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone (80 mg, 73%) as solid. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 0.91 (d, J=6.5 Hz, 6 H), 1.83 - 2.06 (m, 1 H), 2.65 (d, J=7.1 Hz, 2 H), 3.78 - 3.95 (m, 2 H), 3.96 - 4.09 (m, 1 H), 4.16 - 4.28 (m, 1 H), 4.42 (s, 1 H), 4.70 (s, 1 H), 7.09 - 7.35 (m, 3 H), 7.86 (s, 1 H), 8.51 (br. s., 1 H); ES-LCMS m/z: 514.9 (M+1).

EXAMPLE 126

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 126)

[00440] A degassed suspension of 4-{[3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (Example 124) (50 mg, 0.085 mmol), cyclopropylboronic acid (11.01 mg, 0.128 mmol), 1 M tripotassium phosphate (256 µl, 0.256 mmol), $PdCl_2$(dppf)-CH_2Cl_2 adduct (3.49 mg, 4.27 µmol) in 1,4-dioxane (750 µl) was heated at 85 °C. After 16 hours, the brown mixture was diluted with EtOAc (20 mL) and washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated. The crude was purified by preparative HPLC (15-60% ACN gradient) to give 4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (17.2 mg, 0.034 mmol, 20 % yield) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.81 - 0.95 (m, 2 H), 0.95 - 1.09 (m, 2 H), 1.40 - 1.80 (m, 8 H), 2.17 - 2.30 (m, 1 H), 3.35 - 3.46 (m, 2 H), 3.84 (t, *J*=5.2 Hz, 1 H), 3.92 (t, *J*=5.1 Hz, 1 H), 4.21 (s, 1 H), 4.37 (s, 1 H), 4.60 - 4.93 (m, 1 H), 7.57 (s, 1 H), 8.43 (d, *J*=4.1 Hz, 1 H); ES-LCMS m/z: 499.3, 501.1 (M+1).

EXAMPLE 127

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 127)

[00441] To a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (114 mg, 0.374 mmol), 1-cyclopentyl-2-piperazinone (84 mg, 0.412 mmol), N,N-diisopropylethylamine (0.327 mL, 1.871 mmol) in DMF (1.5 mL) was added HATU (149 mg, 0.393 mmol) at room temperature. After 30 minutes, the mixture was diluted with EtOAc (25 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated. The crude was purified by silica gel chromatography (0-75% EtOAc in n-hexanes) to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (126.2 mg, 0.272 mmol, 72.7 % yield) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.83 - 0.94 (m, 2 H), 0.97 - 1.08 (m, 2 H), 1.43 - 1.79 (m, 8 H), 2.16 - 2.28 (m, 1 H), 3.34 - 3.44 (m, 2 H), 3.84 (t, *J*=5.3 Hz, 1 H), 3.96 - 4.09 (m, 1 H), 4.20 (s, 1 H), 4.44 (s, 1 H), 4.64 - 4.88 (m, 1 H), 7.60 (br. s., 1 H), 8.45 (d, *J*=4.9 Hz, 1 H); ES-LCMS m/z: 455.4 (M+1).

EXAMPLE 128

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methyloxy)phenyl]-2-piperazinone

(Compound 128)

[00442] The title compound (60 mg, 34%) was prepared similar to Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-[4-(methyloxy)phenyl]-2-piperazinone hydrochloride (prepared as in Step A of Example 125). ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.76 (br. s., 5 H), 4.03 (br. s., 1 H), 4.18 (br. s., 1 H), 4.38 (s, 1 H), 4.63 (s, 1 H), 6.97 (d, J=7.7 Hz, 2 H), 7.25 (d, J=8.1 Hz, 2 H), 7.34 (s, 1 H), 7.85 (s, 1 H), 8.23 (br. s., 1 H), 8.58 (s, 1 H), 8.85 (br. s., 1 H); ES-LCMS m/z: 518.8 (M+1).

EXAMPLE 129

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxyphenyl)-2-piperazinone

(Compound 129)

[00443] To a solution of 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-(methyloxy)phenyl]-2-piperazinone (Example 149) (200 mg, 0.4 mmol) in anhydrous DCM (10 mL) at -78 °C under nitrogen was added boron

tribromide (1 g, 4 mmol) dropwise. The mixture was allowed to stir at -78 °C for 30 minutes then warmed to room temperature for 1 hour. The reaction was quenched with saturated aqueous Na_2CO_3 and extracted with DCM. The combined organic solvent was dried (Na_2SO_4), filtered and concentrated. The crude product was purified by preparative TLC [petroleum ether: ethyl acetate (1:1 v/v)] to give the title compound (100 mg, 51%) as a light yellow solid. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.69 - 3.87 (m, 2 H), 3.96 - 4.09 (m, 1 H), 4.12 - 4.24 (m, 1 H), 4.39 (s, 1 H), 4.63 (s, 1 H), 6.67 (d, J=8.2 Hz, 1 H), 6.74 - 6.86 (m, 2 H), 7.19 (t, J=8.0 Hz, 1 H), 7.33 (d, J=1.1 Hz, 1 H), 7.84 (t, J=1.6 Hz, 1 H), 8.22 (s, 1 H), 8.57 (s, 1 H), 8.84 (s, 1 H), 9.60 (s, 1 H); ES-LCMS m/z: 504.8 (M+1).

EXAMPLE 130

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

(Compound 130)

Step A

N2-[(4-nitrophenyl)sulfonyl]-N1-(tetrahydro-2H-pyran-4-yl)glycinamide

[00444] To a solution of N-[(4-nitrophenyl)sulfonyl]glycine (5.91 g, 22.71 mmol),4-aminotetrahydropyran (2.76 g, 27.3 mmol), N,N-diisopropylethylamine (11.90 mL, 68.1 mmol) in DMF (125 mL) was added HATU (9.50 g, 24.98 mmol) in one portion. After 30 minutes, the mixture was diluted with EtOAc (500 mL), washed with 1 N HCl (2 x 100 mL), saturated aqueous $NaHCO_3$ (100 mL), brine (100 mL), dried (Na_2SO_4), filtered and concentrated to give crude N2-[(4-nitrophenyl)sulfonyl]-N1-(tetrahydro-2H-pyran-4-yl)glycinamide (7.00 g, 20.39 mmol, 90 % yield) as white solid. This was used for the next step without further purification. ES-LCMS m/z: 344.4 (M+1).

Step B

4-[(4-nitrophenyl)sulfonyl]-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

[00445] To a solution of N2-[(4-nitrophenyl)sulfonyl]-N1-(tetrahydro-2H-pyran-4-yl)glycinamide (7.00 g, 20.39 mmol) and 1,2-dibromoethane (17.57 mL, 204 mmol) in DMF (136 mL) was added potassium carbonate (28.2 g, 204 mmol). The mixture was heated to 60 °C. After 2.5 hours, the mixture was cooled and filtered through a pad of Celite®, washed with EtOAc (75 mL). The solvent was removed under reduced pressure. To the crude orange semi-solid was added EtOAc (25 mL) and 1 N HCl (25 mL), and the suspension was sonicated for 15 minutes. The precipitate was filtered to give 3.35 g of the title compound. The filtrate was concentrated and EtOAc (10 mL) was added. The suspension was sonicated for 15 minutes, and the precipitate filtered to give a second batch of the title compound 1.07 g. ES-LCMS m/z: 369.6 (M+1).

Step C

1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

[00446] To a suspension of potassium carbonate (5.83 g, 42.2 mmol) in acetonitrile (125 mL) at 50 °C was added thiophenol (3.10 mL, 30.1 mmol). After 45 minutes, 4-[(4-nitrophenyl)sulfonyl]-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone (4.45 g, 12.05 mmol) in DMF (25 mL) was added dropwise. After 2 hours at 50 °C, the mixture was cooled and filtered through a pad of Celite®. The solvent was removed under high vacuum. The crude was purified by silica gel chromatography [DCM, 5% MeOH in DCM, 10% MeOH in DCM] to give 1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone (1.6267 g, 8.83 mmol, 73.3 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.41 (dd, *J*=12.2, 2.2 Hz, 2 H), 1.70 (qd, *J*=12.4, 4.6 Hz, 2 H), 2.88 (t, *J*=5.4 Hz, 2 H), 3.11 - 3.21 (m, 2 H), 3.25 (s, 2 H), 3.30 - 3.52 (m, 3 H), 3.89 (dd, *J*=11.2, 4.5 Hz, 2 H), 4.48 (tt, *J*=12.1, 4.1 Hz, 1 H); ES-LCMS m/z: 185.55 (M+1).

Step D

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

[00447] To a solution of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (103 mg, 0.3 mmol), 1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone (66.3 mg, 0.360 mmol), N,N-diisopropylethylamine (210 µL, 1.200 mmol) in DMF (1.5 mL) was added HATU (120 mg, 0.315 mmol). After 30 minutes, the mixture was diluted with EtOAc (20 mL) and washed with 1 N HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography [80-100%EtOAc in n-hexanes] to give 4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone (131.9 mg, 0.254 mmol, 85 % yield) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.48 (m, 2 H), 1.62 - 1.84 (m, 2 H), 3.34 - 3.46 (m, 4 H), 3.76 - 4.04 (m, 4 H), 4.23 (s, 1 H), 4.35 - 4.59 (m, 2 H), 8.10 (s, 1 H), 9.01 (d, *J*=10.1 Hz, 1 H); ES-LCMS m/z: 509.2 (M+1).

EXAMPLE 131

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

(Compound 131)

[00448] The title compound (112 mg, 78%) was prepared by HATU coupling of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone in a manner analogous to that described herein.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.78 - 1.11 (m, 4 H), 1.48 (d, *J*=12.3 Hz, 2 H), 1.60 - 1.85 (m, 2 H), 2.15 - 2.30 (m, 1 H), 3.34 - 3.44 (m, 4 H), 3.76 - 3.95 (m, 3 H), 3.95 - 4.08 (m, 1 H), 4.23 (s, 1 H), 4.33 - 4.62 (m, 2 H), 7.60 (br. s., 1 H), 8.45 (d, *J*=4.3 Hz, 1 H); ES-LCMS m/z: 471.4 (M+1).

EXAMPLE 132

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone

(Compound 132)

[00449] The title compound was prepared by HATU coupling of 3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone in a manner analogous to that described herein. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.50 (br. s., 2 H), 1.72 (d, *J*=11.8 Hz, 2 H), 3.40 (br. s., 4 H), 3.80 - 3.96 (m, 3 H), 4.02 (t, *J*=4.4 Hz, 1 H), 4.24 (s, 1 H), 4.49 (s, 2 H), 8.22 (s, 1 H), 8.42 (br. s., 2 H), 8.84 (d, *J*=6.4 Hz, 1 H), 12.22 - 14.04 (m, 1 H); ES-LCMS MZ: 497.3 (M+1).

EXAMPLE 133

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone

(Compound 133)

[00450] To a solution of 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methyloxy)phenyl]-2-piperazinone (200 mg, 0.4 mmol) in anhydrous DCM (10 mL) at -78 °C under nitrogen was added boron tribromide (1 g, 4 mmol) dropwise. The mixture was allowed to stir at -78 °C for 30 minutes then warmed to room temperature for 2 hours. The reaction was quenched with saturated aqueous Na_2CO_3 and extracted with DCM. The combined organic solvent was dried (Na_2SO_4), filtered and concentrated. The crude product was purified by preparative TLC [petroleum ether: ethyl acetate (1:1 v/v)] to give the title compound (40 mg, 20%) as solid. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.65 - 3.83 (m, 2 H), 3.96 - 4.10 (m, 1 H), 4.10 - 4.24 (m, 1 H), 4.37 (s, 1 H), 4.61 (s, 1 H), 6.78 (d, J = 8 Hz, 2 H), 7.12 (d, J = 8 Hz, 2 H), 7.33 (s, 1 H), 7.84 (s, 1 H), 8.23 (s, 1 H), 8.57 (s, 1 H), 8.84 (s, 1 H), 9.52 (s, 1 H); ES-LCMS MZ: 504.8 (M+1).

EXAMPLE 134

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone

(Compound 134)

[00451] The title compound (60 mg, 64 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(2,3-difluorophenyl)-2-piperazinone. ^{1}H NMR (300 MHz, *d*-Chloroform) δ ppm 3.80 – 4.00 (m, 2 H), 4.18 (br. s., 1 H), 4.55 (br. s., 1 H), 4.64 (s, 1H), 4.91 (s, 1H), 6.76 (s, 1H), 7.00 – 7.25 (m, 3 H), 7.60 (s, 1H), 7.79 (s, 1 H), 7.86 (s, 1H), 8.36 (s, 1H); ES-LCMS MZ: 524.8.

EXAMPLE 135

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone

(Compound 135)

[00452] The title compound (70 mg, 75 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(2,3-difluorophenyl)-2-piperazinone. ^{1}H NMR (300 MHz, *d*-Chloroform) δ ppm 0.99 (d, J = 6.3 Hz, 6 H), 1.85-2.20 (m, 1 H), 2.61 (d, J = 6.3 Hz, 2H), 3.80 - 3.95 (m, 2H), 4.20 (br. s., 1 H), 4.53 (br. s., 1 H), 4.64 (s, 1H), 4.87 (s, 1H), 7.00 – 7.25 (m, 3 H), 7.52 (s, 1H), 8.00-8.10 (m, 1 H); ES-LCMS MZ: 514.9 (M+1).

EXAMPLE 136

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 136)

[00453] The title compound (1.936 g, 78%) was prepared by HATU coupling of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and piperazin-2-one in a manner similar to that described herein. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.83 - 0.95 (m, 2 H), 0.95 - 1.08 (m, 2 H), 2.14 - 2.28 (m, 1 H), 3.19 - 3.31 (m, 2 H), 3.74 - 3.97 (m, 2 H), 4.16 (s, 1 H), 4.36 (s, 1 H), 7.59 (s, 1 H), 8.13 (br. s., 1 H), 8.45 (s, 1 H); ES-LCMS MZ: 387.4 (M+1).

EXAMPLE 137

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclohexen-1-yl)-2-piperazinone

(Compound 137)

[00454] To a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone (98.4 mg, 0.203

mmol) in dichloromethane (DCM) (4.059 mL) at -78 °C was added (diethylamino)sulfur trifluoride (DAST) (0.054 mL, 0.406 mmol). After 2 hours, the mixture was diluted with DCM (20 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL), then brine (10 mL), dried ($MgSO_4$), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography (0-100% EtOAc/n-hex) to give the title compound as white powder (after lyophilization). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.77 - 0.95 (m, 2 H), 0.95 - 1.10 (m, 2 H), 1.56 - 1.78 (m, 2 H), 1.99 (s, 1 H), 2.08 - 2.27 (m, 4 H), 3.30 - 3.43 (m, 2 H), 3.78 (br. s., 0.5 H), 3.94 (br. s., 1 H), 4.03 - 4.14 (m, 0.5 H), 4.14 - 4.33 (m, 1 H), 4.35 - 4.60 (m, 2 H), 5.64 (s, 2 H), 7.60 (s, 1 H), 8.45 (br. s., 1 H); ES-LCMS m/z: 467.5 (M+1).

EXAMPLE 138

methyl (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetate

(Compound 138)

[00455] To a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone (152.2 mg, 0.394 mmol) and methyl chloroacetate (0.041 mL, 0.472 mmol) in DMF (1.312 mL) at room temperature was added sodium hydride (60%wt, 18.89 mg, 0.472 mmol) in one portion. After 1 hour, 10 uL of methyl chloroacetate was added. After another hour, the mixture was diluted with EtOAc (20 mL) and washed with saturated aqueous NH_4Cl (10 mL), then brine (10 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude was purified by silica gel chromatography [20-80% EtOAc in n-hex] to give methyl (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetate (69.1 mg, 0.148 mmol, 37.5 % yield) as white powder (after lyophilization). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.86 - 0.93 (m, 2 H), 0.97 - 1.06 (m, 2 H), 2.12 - 2.28 (m, 1 H), 3.50 (t, J=5.1 Hz, 2 H), 3.66 (d, J=2.5 Hz, 3 H), 3.93 (br. s., 1 H), 4.05 (br. s., 1 H), 4.13 - 4.21 (m, 2 H), 4.28 (s, 1 H), 4.54 (s, 1 H), 7.60 (s, 1 H), 8.46 (br. s., 1 H); ES-LCMS m/z: 459.0 (M+1).

EXAMPLE 139

(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetic acid

(Compound 139)

[00456] To a solution of methyl (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetate (35 mg,

0.076 mmol) in THF (6 mL) was added a solution of lithium hydroxide monohydrate (8.00 mg, 0.191 mmol) in water (2 mL). After 1.45 hours, THF was removed under reduced pressure. To the aqueous phase was added 1 N HCl (1 mL) which gave a precipitate. This was centrifuged to give (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetic acid (35 mg, 0.077 mmol, quantitative) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.81 - 0.95 (m, 2 H), 0.96 - 1.08 (m, 2 H), 2.15 - 2.27 (m, 1 H), 3.48 (br. s., 2 H), 3.92 (br. s., 1 H), 3.97 - 4.15 (m, 3 H), 4.27 (s, 1 H), 4.53 (s, 1 H), 7.60 (s, 1 H), 8.46 (br. s., 1 H), 12.82 (br. s., 1 H); ES-LCMS m/z: 445.0 (M+1).

EXAMPLE 140

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone

(Compound 140)

Step A

1-(4-hydroxyphenyl)-2-piperazinone hydrochloride

[00457] A suspension of 1-Boc-3-oxopiperazine (200 mg, 0.999 mmol), 4-bromophenol (190 mg, 1.099 mmol), potassium carbonate (276 mg, 1.998 mmol), copper(I) iodide (9.51 mg, 0.050 mmol) and trans-N,N'-dimethylcyclohexane-1,2-diamine (14.21 mg, 0.100 mmol) in 1,4-dioxane (3.995 mL) was heated at 100-115 °C for 5 days. A similar reaction was carried out under the same conditions in toluene (3.995 mL). Both reactions were combined and filtered through a pad of silica gel and washed with EtOAc (100 mL). The filtrate was washed with saturated aqueous NH_4Cl (20 mL), then brine (20 mL), dried ($MgSO_4$), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography [0-80% EtOAc/n-hex] to give 1,1-dimethylethyl 4-(4-hydroxyphenyl)-3-oxo-1-piperazinecarboxylate (84.3 mg, 0.288 mmol, 14.5 % yield) as off-white powder. ES-LCMS m/z: 293.3 (M+1). To a solution of 1,1-dimethylethyl 4-(4-hydroxyphenyl)-3-oxo-1-piperazinecarboxylate (81 mg, 0.277 mmol) in dichloromethane (DCM) (6 mL) was added a solution of hydrochloric acid (4 M, 3 mL, 12.00 mmol) in 1,4-dioxane. After 1.5 hours, the solvent was concentrated under reduced pressure to give 1-(4-hydroxyphenyl)-2-piperazinone hydrochloride (71.8 mg, quantitative) as beige powder. ES-LCMS m/z: 193.5 (M+1).

Step B

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone

[00458] The title compound (93.5 mg, 98 %) was prepared by HATU coupling of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(4-hydroxyphenyl)-2-piperazinone hydrochloride in a manner similar to that described herein. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.90 (d, J=5.0 Hz, 2 H), 0.95 - 1.11 (m, 2 H), 2.13 - 2.29 (m, 1 H), 3.71 (d, J=4.9 Hz, 2 H), 4.00 (br. s., 1 H), 4.15 (br. s., 1 H), 4.35 (s, 1 H), 4.59 (s, 1 H), 6.68 - 6.82 (m, 2 H), 7.09 - 7.17 (m, 2 H), 7.60 (s, 1 H), 8.46 (s, 1 H), 9.52 (d, J=3.8 Hz, 1 H); ES-LCMS m/z: 479.2 (M+1).

EXAMPLE 141

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone

(Compound 141)

Step A

1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone hydrochloride

[00459] To a suspension of 1-Boc-3-oxopiperazine (500 mg, 2.497 mmol), 4-bromo-2-fluorophenol (477 mg, 2.497 mmol), copper(I) iodide (23.78 mg, 0.125 mmol), trans-N,N'-dimethylcyclohexane-1,2-diamine (0.039 mL, 0.250 mmol) and potassium carbonate (690 mg, 4.99 mmol) was heated in 1,4-dioxane (9.988 mL) at 120 °C in a sealed tube for 2.5 days. The mixture was filtered through a pad of Celite® and washed with EtOAc (60 mL). The organic phase was washed with saturated aqueous NH_4Cl (15 mL), brine (15 mL), dried ($MgSO_4$), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography [20-70% EtOAc in n-hexanes) to give 1,1-dimethylethyl 4-(3-fluoro-4-hydroxyphenyl)-3-oxo-1-piperazinecarboxylate (108.8 mg, 0.351 mmol, 14% yield) as a beige solid. ES-LCMS m/z: 311.2 (M+1). To a solution of 1,1-dimethylethyl 4-(3-fluoro-4-hydroxyphenyl)-3-oxo-1-piperazinecarboxylate (105 mg, 0.338 mmol) in dichloromethane (DCM) (6 mL) was added a solution of hydrochloric acid (4 M, 3 mL, 12.00 mmol) in 1,4-dioxane at room temperature. After 3 hours, the solvent was concentrated under reduced pressure to give 1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone hydrochloride (106.6 mg, quantitative) as beige solid. This was used for the next step without further purification. ES-LCMS m/z: 211.2 (M+1).

Step B

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone

[00460] The title compound (32.8 mg, 98%) was prepared by HATU coupling of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone in a manner similar to that described herein. ^{1}H

NMR (400 MHz, DMSO-d_6) δ ppm 0.90 (q, J=5.2 Hz, 2 H), 0.95 - 1.09 (m, 2 H), 2.14 - 2.29 (m, 1 H), 3.64 - 3.84 (m, 2 H), 3.99 (d, J=5.4 Hz, 1 H), 4.16 (t, J=5.0 Hz, 1 H), 4.36 (s, 1 H), 4.61 (s, 1 H), 6.85 - 7.07 (m, 2 H), 7.14 - 7.29 (m, 1 H), 7.60 (s, 1 H), 8.46 (s, 1 H), 9.97 (br. s., 1 H); ES-LCMS m/z: 497.2 (M+1).

EXAMPLE 142

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone

(Compound 142)

[00461] The title compound (80 mg, 76 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(3,4-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.80-3.95 (m, 2 H), 4.06 (br. s., 1 H), 4.23 (br. s., 1 H), 4.43 (s, 1 H), 4.70 (s, 1 H), 7.20-7.40 (m, 2H), 7.40-7.65 (m, 2 H), 7.86 (s, 1H), 7.25 (s, 1H), 8.59 (s, 1H), 8.86 (s, 1H); ES-LCMS m/z: 524.8 (M+1).

EXAMPLE 143

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone

(Compound 143)

[00462] The title compound (100 mg, 44 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(3,5-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.85 – 4.00 (m, 2 H), 4.00 – 4.15 (m, 1 H), 4.15 - 4.30 (m, 1 H), 4.45 (s, 1 H), 4.72 (s, 1 H), 7.10 - 7.40 (m, 4 H), 7.87 (s, 1 H), 8.25 (s, 1 H), 8.59 (s, 1 H), 8.86 (s, 1 H); ES-LCMS m/z: 524.8 (M+1).

EXAMPLE 144

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone

(Compound 144)

[00463] The title compound (25 mg, 17 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(2,4-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.69 - 3.86 (m, 2 H),

3.98 - 4.28 (m, 2 H), 4.44 (s, 1 H), 4.71 (s, 1 H), 7.11 - 7.24 (m, 1 H), 7.34 (s, 1 H), 7.35 - 7.65 (m, 2 H), 7.85 (t, J=1.7 Hz, 1 H), 8.23 (s, 1 H), 8.57 (s, 1 H), 8.85 (s, 1 H); ES-LCMS m/z: 524.8 (M+1).

EXAMPLE 145

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone

(Compound 145)

[00464] The title compound (34 mg, 23 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(2,5-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.78 (br. s., 2 H), 4.06 (br. s., 1 H), 4.22 (br. s., 1 H), 4.45 (s, 1 H), 4.72 (s, 1 H), 7.18 - 7.56 (m, 4 H), 7.85 (s, 1 H), 8.23 (s, 1 H), 8.57 (s, 1 H), 8.85 (s, 1 H); ES-LCMS m/z: 524.8 (M+1).

EXAMPLE 146

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone

(Compound 146)

[00465] The title compound (42 mg, 51 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(2,4-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 0.91 (d, J=6.5 Hz, 6 H), 1.95 (s, 1 H), 2.64 (d, J=7.1 Hz, 2 H), 3.60 - 3.82 (m, 2 H), 4.06 (br. s., 1 H), 4.21 (br. s., 1 H), 4.44 (s, 1 H), 4.70 (s, 1 H), 7.18 (br. s., 1 H), 7.31 - 7.65 (m, 2 H), 7.86 (s, 1 H), 8.51 (br. s., 1 H); ES-LCMS m/z: 514.9 (M+1).

EXAMPLE 147

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone

(Compound 147)

[00466] The title compound (48 mg, 37 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(2,5-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 0.91 (d, J=6.6 Hz, 6 H), 1.83 - 2.07 (m, 1 H), 2.64 (d, J=7.1 Hz, 2 H), 3.77 (m, 2 H), 4.06 (m, 1 H), 4.22 (m, 1 H),

4.44 (s, 1 H), 4.71 (s, 1 H), 7.27 (m, 1 H), 7.48 (m, 2 H), 7.85 (s, 1 H), 8.50 (br. s., 1 H); ES-LCMS m/z: 514.9 (M+1).

EXAMPLE 148

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone

(Compound 148)

[00467] The title compound (60 mg, 45 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-(3,4-difluorophenyl)-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 0.91 (d, J=6.5 Hz, 6 H), 1.83 - 2.05 (m, 1 H), 2.64 (d, J=7.0 Hz, 2 H), 3.71 - 3.92 (m, 2 H), 3.95 - 4.08 (m, 1 H), 4.14 - 4.29 (m, 1 H), 4.40 (s, 1 H), 4.67 (s, 1 H), 7.20 - 7.35 (m, 1 H), 7.41 - 7.68 (m, 2 H), 7.85 (s, 1 H), 8.50 (br. s., 1 H); ES-LCMS m/z: 514.9 (M+1).

EXAMPLE 149

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-(methyloxy)phenyl]-2-piperazinone

(Compound 149)

[00468] The title compound (80 mg, 66 %) was prepared in a manner similar to that described in Example 125 with the use of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-[3-(methyloxy)phenyl]-2-piperazinone hydrochloride. ^{1}H NMR (300 MHz, DMSO- d_6) δ ppm 3.76 (s, 3 H), 3.77 - 3.91 (m, 2 H), 3.99 - 4.10 (m, 1 H), 4.14 - 4.27 (m, 1 H), 4.40 (s, 1 H), 4.66 (s, 1 H), 6.81 - 7.07 (m, 3 H), 7.25 - 7.39 (m, 2 H), 7.84 (s, 1 H), 8.23 (s, 1 H), 8.57 (s, 1 H), 8.84 (s, 1 H); ES-LCMS m/z: 518.8 (M+1).

EXAMPLE 150

4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 150)

[00469] A solution of 3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (65 mg, 0.222 mmol), 1-(1,3-thiazol-2-yl)-2-piperazinone hydrochloride (48.8 mg, 0.222 mmol), HATU (101 mg, 0.267 mmol) and DIPEA (0.116 mL, 0.666 mmol) in DMF (4 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed sequentially with 5% aqueous LiCl

twice and saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-50% EtOAc/hexanes) to give the title compound (70 mg, 69%) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.54 (br. s, 1 H), 7.93 (s, 1 H), 7.59 (d, *J*=3.5 Hz, 1 H), 7.37 (br. s, 1 H), 4.90 (s, 1 H), 4.59 (s, 1 H), 4.25 (br. s, 3 H), 4.10 (br. s, 1 H), 2.80 (q, *J*=7.5 Hz, 2 H), 1.26 (t, *J* = 7.5 Hz, 3 H).

EXAMPLE 151

4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 151)

[00470] A solution of 3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (65 mg, 0.222 mmol), 1-cyclopentyl-2-piperazinone hydrochloride (45.5 mg, 0.222 mmol), HATU (101 mg, 0.267 mmol) and DIPEA (0.116 mL, 0.666 mmol) in DMF (4 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed sequentially with 5% LiCl twice and saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-80% EtOAc/hexanes) to give the title compound (79 mg, 80%) as a white foam. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.08 (s, 0.5 H), 8.05 (s, 0.5 H), 7.54 (s, 1 H), 5.05-4.80 (m, 1 H), 4.60 (s, 1 H), 4.42 (s, 1 H), 4.31 (br. s, 1 H), 3.95 (br. s, 1 H), 3.50-3.30 (m, 2 H), 2.90-2.70 (m, 2 H), 2.00-1.40 (m, 8 H), 1.34 (t, *J*=7.4 Hz, 3 H).

EXAMPLE 152

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

(Compound 152)

Step A

methyl 3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00471] An aqueous solution of 3M K_3PO_4 (6.68 mL, 20.05 mmol) was added to a mixture of methyl 3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (3.0 g, 6.68 mmol) and 3-furanylboronic acid (0.785 g, 7.02 mmol) in acetonitrile (30 mL) under N_2 at room temperature. $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.273 g, 0.334 mmol) was then added. The reaction mixture was stirred at room temperature for 1 hour then heated at 50 ° C for 1 hour. The mixture was cooled to room temperature and the solvent was evaporated. The residue was dissolved in CH_2Cl_2, washed with water and brine, dried over

Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-1% $MeOH/CH_2Cl_2$) to give the title compound (2.06 g, 79%) as an off-white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.39 (s, 1 H) 7.85 (s, 1 H), 7.80 (s, 1 H), 7.58 (t, *J*=1.56 Hz, 1 H), 6.74 (d, *J*=0.78 Hz, 1 H), 4.01 (s, 3 H).

Step B

3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00472] A solution of 1 N NaOH (8.0 mL, 8.00 mmol) was added to a suspension of methyl 3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (1.0 g, 2.57 mmol) in THF (20 mL) and water (20 mL) at room temperature. The reaction mixture was stirred for 3 hours, acidified to pH ~ 2 with 1 N HCl, extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated to dryness to give 3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.96 g, 100 % yield) as a light yellow solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 13.37 (br. s, 1 H), 8.74 (s, 1 H), 8.58 (s, 1 H), 8.22 (s, 1 H), 7.86 (t, *J*=1.56 Hz, 1 H), 7.31 (d, 1 H).

Step C

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone

[00473] A solution of 3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (140 mg, 0.373 mmol), 1-cyclopentyl-2-piperazinone hydrochloride (80 mg, 0.392 mmol), HATU (170 mg, 0.448 mmol) and DIPEA (0.196 mL, 1.120 mmol) in DMF (4 mL) was maintained with stirring at room temperature for 3 hours. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-70% EtOAc/hexanes) to give a white solid, which was stirred with 1:1 hexanes:Et_2O containing 1% of MeOH for 1 hour. The solid was collected and washed with 1:1 hexanes:Et_2O containing 1% of MeOH and air dried to give the title compound (150 mg, 77 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.80-8.70 (m, 1 H), 8.56 (s, 1 H), 8.22 (s, 1 H), 7.85 (s, 1 H), 7.31 (s, 1 H), 4.90-4.70 (m, 1 H), 4.38 (s, 1 H), 4.22 (s, 1 H), 4.00-3.90 (m, 1 H), 3.90-3.80 (m, 1 H), 3.45-3.30 (m, 2 H), 1.80-1.40 (m, 8 H).

EXAMPLE 153

2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 153)

[00474] A mixture of 4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (100 mg, 0.190 mmol), copper(I) cyanide (68.2 mg, 0.761 mmol) in DMF (1.5 mL) was heated in microwave oven at 150 °C for 25 minutes. Upon cooling to room temperature, the mixture was diluted with EtOAc, filtered through a pad of Celite, washed with water twice and brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-60% EtOAc/hexanes) to give the title compound (55 mg, 61 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 9.08 (s, 0.5 H), 9,06 (s, 0.5 H), 8.63 (s, 1 H), 8.43 (s, 1 H), 7.86 (t, *J*=1.6 Hz, 1 H), 7.38 (d, *J*=1.3 Hz, 1 H), 4.85-4.70 (m, 1 H), 4.70 (s, 1 H), 4.35-4.26 (m, 1 H), 4.25 (s, 1 H), 3.90-3.80 (m, 1 H), 3.45-3.35 (m, 2 H), 1.80-1.45 (m, 8 H).

EXAMPLE 154

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 154)

[00475] A solution of 3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (130 mg, 0.347 mmol), 1-cyclobutyl-2-piperazinone hydrochloride (69.4 mg, 0.364 mmol), HATU (158 mg, 0.416 mmol) and DIPEA (0.182 mL, 1.040 mmol) in DMF (4 mL) was maintained with stirring at room temperature for 3 hours. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-45% EtOAc/CH_2Cl_2) to give a white solid, which was stirred with 1:1 hexanes:Et_2O containing 1% of MeOH for 1 hour. The solid was collected and washed with 1:1 hexanes:Et_2O containing 1% of MeOH and air dried to give the title compound (153 mg, 86 % yield) as an off-white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.80-8.70 (m, 1 H), 8.56 (s, 1 H), 8.22 (s, 1 H), 7.85 (s, 1 H), 7.31 (s, 1 H), 4.90-4.75 (m, 1 H), 4.37 (s, 1 H), 4.21 (s, 1 H), 4.00-3.95 (m, 1 H), 3.95-3.85 (m, 1 H), 3.55-3.40 (m, 2 H), 2.30-2.10 (m, 2 H), 2.05-1.95 (m, 2 H), 1.70-1.55 (m, 2 H).

EXAMPLE 155

2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 155)

[00476] A mixture of 4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone (100 mg, 0.196 mmol), copper(I) cyanide (70.1 mg, 0.782 mmol) in DMF (1.5 mL) was heated in microwave oven at 150 °C

for 20 minutes. Upon cooling to room temperature, the mixture was diluted with EtOAc, filtered through a pad of Celite, washed with water/brine twice and brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-55% EtOAc/hexanes) to give the title compound (69 mg, 77 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 9.08 (s, 0.5 H), 9,06 (s, 0.5 H), 8.63 (s, 1 H), 8.43 (s, 1 H), 7.86 (s, 1 H), 7.38 (s, 1 H), 4.90-4.80 (m, 1 H), 4.68 (s, 1 H), 4.35-4.25 (m, 1 H), 4.23 (s, 1 H), 3.95-3.85 (m, 1 H), 3.55-3.45 (m, 2 H), 2.30-2.10 (m, 2 H), 2.05-1.95 (m, 2 H), 1.70-1.60 (m, 2 H).

EXAMPLE 156

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone

(Compound 156)

Step A

N2-[(4-nitrophenyl)sulfonyl]-N1-(tetrahydro-2H-thiopyran-4-yl)glycinamide

[00477] A solution of N-[(4-nitrophenyl)sulfonyl]glycine (1.5 g, 5.76 mmol), tetrahydro-2H-thiopyran-4-ylamine (0.766 g, 6.34 mmol), HATU (2.63 g, 6.92 mmol) and DIPEA (3.02 mL, 17.29 mmol) in DMF (20 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed with 1 N HCl, water, 5% LiCl, saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated to the title compound (1.86 g, 90 % yield) as a yellowish brown solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.45-8.35 (m, 3 H), 8.05-8.00 (m, 2 H), 7.90 (d, *J*=7.9 Hz, 1 H), 3.52 (d, *J*=5.6 Hz, 2 H), 3.50-3.40 (m, 1 H), 2.60-2.55 (m, 4 H), 1.90-1.80 (m, 2 H), 1.45-1.35 (m, 2 H).

Step B

4-[(4-nitrophenyl)sulfonyl]-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone

[00478] To a solution of N2-[(4-nitrophenyl)sulfonyl]-N1-(tetrahydro-2H-thiopyran-4-yl)glycinamide (1.86 g, 5.17 mmol) in DMF (34.5 mL) was added potassium carbonate (7.15 g, 51.7 mmol) and 1,2-dibromoethane (4.46 mL, 51.7 mmol). The mixture was heated at 60 °C overnight, cooled, EtOAc was added and the mixture was filtered through a pad of Celite. The filtrate was washed with 1 N HCl, water, 5% LiCl and brine, dried over Na_2SO_4, filtered and concentrated to an orange solid, which was stirred with 1:1 EtOAc/Et_2O for 30 minutes. The solid was collected and washed with 1:1 EtOAc/Et_2O to give the title compound (0.905 g, 45.4 % yield) as beige solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.45-8.40 (m, 2 H), 8.10-8.05 (m, 2 H), 4.20-4.05 (m, 1 H), 3.66 (s, 2 H), 3.30-3.25 (m, 4 H), 2.75-2.65 (m, 2 H), 2.65-2.55 (m, 2 H), 1.75-1.60 (m, 4 H).

Step C

1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone

[00479] To a suspension of potassium carbonate (1.129 g, 8.17 mmol) in acetonitrile (24 mL) at 50 °C was added thiophenol (0.620 mL, 5.84 mmol). After 30 minutes, a suspension of 4-[(4-nitrophenyl)sulfonyl]-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone (0.9 g, 2.335 mmol) in DMF (8 mL) was added dropwise. After stirred at 50 °C for 3 hours, the mixture was cooled, diluted with CH_2Cl_2 and filtered through a pad of Celite. The solvent was removed under the reduced pressure. The residue was diluted with 50 mL of CH_2Cl_2 and loaded onto SCX columns (3 x 10 g) pretreated with MeOH then CH_2Cl_2. After flushing with 1:1 CH_2Cl_2/MeOH, the columns were eluted with 2 M NH_3 in MeOH. The filtrate was concentrated to dryness to give the title compound (255 mg, 54.5 % yield) as viscous brown oil. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 4.30-4.15 (m, 1 H), 3.20 (s, 2 H), 3.15-3.10 (m, 2 H), 2.85-2.80 (m, 2 H), 2.75-2.60 (m, 5 H), 1.85-1.70 (m, 4 H).

Step D

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone

[00480] A solution of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (150 mg, 0.454 mmol), 1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone (106 mg, 0.476 mmol), HATU (207 mg, 0.544 mmol) and DIPEA (0.158 mL, 0.907 mmol) in DMF (4 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-40% EtOAc/CH_2Cl_2) to give a light yellow solid, which was stirred with 1:1 hexanes:Et_2O containing 1% of MeOH for 1 hour. The solid was collected and washed with 1:1 hexanes:Et_2O containing 1% of MeOH and air dried to give the title compound (189 mg, 81 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.85-8.80 (m, 1 H), 8.55 (s, 1 H), 8.21 (s, 1 H), 7.83 (s, 1 H), 7.32 (s, 1 H), 4.45 (s, 1 H), 4.30-4.15 (m, 2 H), 4.00-3.95 (m, 1 H), 3.85-3.80 (m, 1 H), 3.45-3.30 (m, 2 H), 2.80-2.60 (m, 4 H), 1.90-1.70 (m, 4 H).

EXAMPLE 157

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone

(Compound 157)

[00481] Oxone (180 mg, 0.292 mmol) was added to a stirred solution of 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone (50 mg, 0.097 mmol) in methanol (4 mL), acetone (6 mL) and water (2 mL) at 0 °C. The reaction mixture was allowed to warm up to room temperature and stirred at room temperature overnight. water was added, and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over Na_2SO_4, filtered, concentrated to a white solid, which was triturated with 1:1 hexanes:Et_2O containing 1% of MeOH. The solid was collected and washed with 1:1 hexanes:Et_2O containing 1% of MeOH and air dried to give the title compound (52 mg, 98 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.85-8.80 (m, 1 H), 8.57 (s, 1 H), 8.23 (s, 1 H), 7.84 (s, 1 H), 7.33 (s, 1 H), 4.65-4.50 (m, 1 H), 4.49 (s, 1 H), 4.24 (s, 1 H), 4.05-3.95 (m, 1 H), 3.90-3.80 (m, 1 H), 3.45-3.30 (m, 4 H), 3.10-3.00 (m, 2 H), 2.25-2.10 (m, 2 H), 2.00-1.85 (m, 2 H).

EXAMPLE 158

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

(Compound 158)

Step A

methyl 6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00482] A mixture of methyl 6-bromo-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (1.500 g, 4.64 mmol), cyclopropylboronic acid (0.798 g, 9.29 mmol), potassium phosphate (3.05 g, 13.93 mmol), $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.190 g, 0.232 mmol) in 1,4-dioxane (40 mL) was degassed with N_2 and heated at 90 °C for 3 hours. The mixture was cooled to room temperature, diluted with EtOAc and water, filtered through a pad of Celite. The filtrate was transferred to a separatory funnel. The organic layer was separated, and the aqueous layer was further extracted with EtOAc. The combined EtOAc extract was washed with brine and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-45% EtOAc/hexanes) followed by trituration with 5% EtOAc/hexanes give the title compound (0.87 g, 66 % yield) as colorless crystals. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.21 (s, 1 H), 8.07 (s, 1 H), 7.38 (s, 1 H), 3.98 (s, 3 H), 2.00-1.95 (m, 1 H), 1.10-1.05 (m, 2 H), 1.80-1.75 (m, 2 H).

Step B

methyl 3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate

[00483] NBS (0.531 g, 2.96 mmol) was added to a solution of methyl 6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (0.8 g, 2.81 mmol) in 1,2-

dichloroethane (DCE) (25 mL). The reaction mixture was stirred at room temperature for 5 hours, diluted with CH_2Cl_2, washed with 5% aqueous $Na_2S_2O_3$, saturated $NaHCO_3$ and brine. The CH_2Cl_2 extract was dried over Na_2SO_4, filtered and concentrated to dryness to give the title compound (1.03 g, 100 % yield) as an off-white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.12 (s, 1 H), 7.43 (s, 1 H), 3.99 (s, 3 H), 2.10-2.00 (m, 1H), 1.15-1.05 (m, 2 H), 0.85-0.75 (m, 2 H).

Step C

3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00484] A solution of 1 N NaOH (8.8 mL, 8.80 mmol) was added to a solution of methyl 3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylate (1.04 g, 2.86 mmol) in THF (32 mL) and water (24 mL) at room temperature. The reaction mixture was stirred for 3 hours, acidified to pH ~ 2 with 1 N HCl, extracted with EtOAc twice. The combined organic extract was washed with brine, dried over Na_2SO_4, filtered and concentrated to dryness to give the title compound (1 g, 100 % yield) as a light yellow solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 13.29 (s, 1 H), 8.43 (s, 1 H), 7.57 (s, 1 H), 2.30-2.20 (m, 1H), 1.05-0.95 (m, 2 H), 0.95-0.90 (m, 2 H).

Step D

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone

[00485] A solution of 3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (120 mg, 0.344 mmol), 1-cyclobutyl-2-piperazinone hydrochloride (68.8 mg, 0.361 mmol), HATU (157 mg, 0.412 mmol) and DIPEA (0.180 mL, 1.031 mmol) in DMF (4 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na2SO4, filtered, concentrated and purified by silica gel chromatography (0-35% EtOAc/CH2Cl2) to yield a colorless oil, which solidified after standing at room temperature in 1:1 hexanes:Et2O containing 1% of MeOH. The mixture was then stirred for 1 hour. The solid was collected and washed with 1:1 hexanes:Et2O containing 1% of MeOH and air dried to give the product as a white solid, which seemed to be gummy. The material was redissolved with CH2Cl2, dried over Na2SO4 and concentrated to dryness. The residue was stirred with 1:2 hexanes:Et2O for 30 minutes and sonicated. The white solid was collected and washed with 1:1 hexanes:Et2O, air dried to give the title compound (92 mg, 55.2 % yield) as a white solid. The filtrate was concentrated to 1/5 of the liquid volume, and the white precipitate was collected and washed with hexanes, air dried to give additional title compound (49 mg, 29.4 % yield) as a white solid. 1H NMR (400 MHz, DMSO-d6) δ ppm 8.50-8.40 (m, 1 H), 7.58 (s, 1 H),

4.95-4.75 (m, 1 H), 4.35 (s, 1 H), 4.19 (s, 1 H), 4.00-3.80 (m, 2 H), 3.55-3.40 (m, 2 H), 2.30-2.05 (m, 3 H), 1.98 (br. s, 2 H), 1.70-1.55 (m, 2 H), 1.10-1.00 (m, 2 H), 1.00-0.80 (m, 2 H).

EXAMPLE 159

2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 159)

[00486] A mixture of 4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone (108 mg, 0.223 mmol), copper(I) cyanide (80 mg, 0.890 mmol) in DMF (2 mL) was heated in microwave oven at 140 °C for 20 minutes. Upon cooling to room temperature, the mixture was diluted with EtOAc, filtered through a pad of Celite, washed with water/brine twice and brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-50% EtOAc/hexanes) to give the title compound (70 mg, 73 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.72 (s, 0.5 H), 8.71 (s, 0.5 H), 7.79 (s, 0.5 H), 7.77 (s, 0.5 H), 4.95-4.75 (m, 1 H), 4.68 (s, 1 H), 4.35-4.25 (m, 1 H), 4.22 (s, 1 H), 3.95-3.85 (m, 1 H), 3.55-3.45 (m, 2 H), 2.35-2.10 (m, 3 H), 2.05-1.95 (m, 2 H), 1.70-1.55 (m, 2 H), 1.10-1.00 (m, 2 H), 1.00-0.90 (m, 2 H).

EXAMPLE 160

2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 160)

[00487] A mixture of 4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone (104 mg, 0.208 mmol), copper(I) cyanide (74.6 mg, 0.833 mmol) in DMF (2 mL) was heated in microwave oven at 135 °C for 20 minutes. Upon cooling to room temperature, the mixture was diluted with EtOAc, filtered through a pad of Celite, washed with water/brine twice, brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-40% EtOAc/hexanes) to give the title compound (75 mg, 81 % yield) as a white foam. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.72 (s, 1 H), 7.80-7.75 (m, 1 H), 4.85-4.70 (m, 1 H), 4.69 (s, 1 H), 4.35-4.25 (m, 1 H), 4.23 (s, 1 H), 3.90-3.80 (m, 1 H), 3.45-3.35 (m, 2 H), 2.35-2.25 (m, 1 H), 1.75-1.45 (m, 8 H), 1.10-1.00 (m, 2 H), 1.00-0.90 (m, 2 H).

EXAMPLE 161

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone

(Compound 161)

[00488] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (190 mg, 0.624 mmol), 1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone (146 mg, 0.655 mmol), HATU (285 mg, 0.748 mmol) and DIPEA (0.218 mL, 1.247 mmol) in DMF (5 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-40% EtOAc/CH_2Cl_2) to give a light yellow foam, which was stirred with 1:1 hexanes:Et_2O containing 1% of MeOH for 1.5 hours. The solid was collected and washed with 1:1 hexanes:Et_2O containing 1% of MeOH and air dried to give the title compound (240 mg, 79 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.45 (s, 1 H), 7.60 (s, 1 H), 4.45 (s, 1 H), 4.35-4.15 (m, 2 H), 3.99 (br. s, 1 H), 3.83 (br. s, 1 H), 3.45-3.30 (m, 2 H), 2.80-2.60 (m, 4 H), 2.30-2.15 (m, 1 H), 1.95-1.70 (m, 4 H), 1.05-0.95 (m, 2 H), 0.95-0.80 (m, 2 H).

EXAMPLE 162

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone

(Compound 162)

[00489] Oxone (356 mg, 0.579 mmol) was added to a stirred solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone (80.5 mg, 0.165 mmol) in methanol (7 mL), acetone (1 mL) and water (2 mL) at 0 °C. The reaction mixture was allowed to warm up to room temperature and stirred at room temperature overnight. water was added, and mixture was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over Na_2SO_4, filtered, concentrated to a white solid, which was triturated with 1:1 hexanes:Et_2O containing 1% of MeOH. The solid was collected and washed with 1:1 hexanes:Et_2O containing 1% of MeOH and air dried to give the title compound (70 mg, 82 % yield) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.50-8.40 (m, 1 H), 7.60 (s, 1 H), 4.65-4.50 (m, 1 H), 4.47 (s, 1 H), 4.22 (s, 1 H), 4.05-3.95 (m, 1 H), 3.90-3.80 (m, 1 H), 3.45-3.30 (m, 4 H), 3.10-3.00 (m, 2 H), 2.25-2.10 (m, 3 H), 1.95-1.80 (m, 2 H), 1.05-0.95 (m, 2 H), 0.95-0.85 (m, 2 H).

EXAMPLE 163

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

(Compound 163)

Step A

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone

[00490] A solution of 3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (140 mg, 0.401 mmol), 1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone (149 mg, 0.421 mmol), HATU (183 mg, 0.481 mmol) and DIPEA (0.140 mL, 0.802 mmol) in DMF (5 mL) was maintained with stirring at room temperature for 3.5 hours. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-50% EtOAc/hexanes) to give the title compound (285 mg, 96% pure, 99 % yield) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.20-8.10 (m, 1 H), 7.45-7.40 (m, 1 H), 4.57 (s, 1 H), 4.65-4.35 (m, 2 H), 4.30-4.20 (m, 1 H), 4.00-3.90 (m, 1 H), 3.70-3.55 (m, 1 H), 3.45-3.35 (m, 2 H), 2.10-1.95 (m, 3 H), 1.80-1.65 (m, 2 H), 1.60-1.40 (m, 4 H), 1.20-1.07 (m, 2 H), 1.06 (s, 21 H), 0.90-0.80 (m, 2 H).

Step B

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00491] To a solution of 4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-{[tris(1-methylethyl)silyl]oxy}cyclohexyl)-2-piperazinone (150 mg, 0.210 mmol) in THF (4 mL) in an ice bath was added 1.0 M TBAF in THF (0.315 mL, 0.315 mmol). The reaction mixture was allowed to warm up to room temperature and stirred at room temperature for 2 hours. The reaction mixture was poured into ethyl acetate and washed sequentially with saturated $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-40% acetone/CH_2Cl_2) to give the title compound (100 mg, 90 % yield) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.20-8.10 (m, 1 H), 7.43 (s, 1 H), 4.59 (s, 1 H), 4.58-4.40 (m, 2 H), 4.30-4.20 (m, 1 H), 4.00-3.90 (m, 1 H), 3.65-3.50 (m, 1 H), 3.45-3.35 (m, 2 H), 2.10-2.00 (m, 3 H), 1.80-1.65 (m, 2 H), 1.65-1.40 (m, 4 H), 1.20-1.10 (m, 2 H), 0.85-0.75 (m, 2 H).

EXAMPLE 164

6-cyclopropyl-2-{[4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 164)

[00492] A mixture of 4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone (78 mg, 0.147 mmol), copper(I) cyanide (52.8 mg, 0.589 mmol) in DMF (1.5 mL) was heated in microwave oven at 135 °C for 20 minutes. Upon cooling to room temperature, the mixture was diluted with EtOAc, filtered through a pad of Celite, washed with water/brine twice, brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-40% acetone/CH_2Cl_2) to give the title compound (55 mg, 79 % yield) as a white foam. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.35-8.25 (m, 1 H), 7.59 (s, 1 H), 4.88 (s, 1 H), 4.60-4.40 (m, 3 H), 4.05-3.95 (m, 1 H), 3.65-3.50 (m, 1 H), 3.45-3.35 (m, 2 H), 2.10-2.00 (m, 3 H), 1.80-1.65 (m, 2 H), 1.65-1.40 (m, 4 H), 1.25-1.15 (m, 2 H), 0.90-0.80 (m, 2 H).

EXAMPLE 165

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone

(Compound 165)

[00493] A solution of 3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (114 mg, 0.327 mmol), 1-(3-methylcyclobutyl)-2-piperazinone hydrochloride (66.8 mg, 0.327 mmol), HATU (143 mg, 0.376 mmol) and DIPEA (0.171 mL, 0.980 mmol) in DMF (4 mL) was maintained with stirring at room temperature overnight. The reaction mixture was poured into ethyl acetate and washed with 5% LiCl twice. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-70% EtOAc/hexanes) to yield a light yellow foam, which was stirred with 2:1 hexanes:Et_2O for 1 hour, sonicated and then stirred for additional 30 minutes. The white solid was collected and washed with 1:1 hexanes:Et_2O, air dried to give the title compound (127 mg, 78 % yield) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.16 (s, 0.5 H), 8.12 (s, 0.5 H), 7.47 (s, 0.5 H), 7.44 (s, 0.5 H), 5.30-5.15 (m, 0.5 H), 4.85-4.70 (m, 0.5 H), 4.57 (s, 1 H), 4.41 (s, 1 H), 4.27 (br. s, 1 H), 4.00 (br. s, 1 H), 3.60-3.40 (m, 2 H), 2.40-1.80 (m, 6 H), 1.25-1.05 (m, 5 H), 0.85-0.75 (m, 2 H).

EXAMPLE 166

6-cyclopropyl-2-{[4-(3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 166)

[00494] A mixture of 4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone (110 mg, 0.220 mmol), copper(I) cyanide (79 mg, 0.881 mmol) in DMF (2 mL) was heated in microwave oven at 135 °C for 20 minutes. Cooled to room temperature, the mixture was diluted with EtOAc, filtered through a pad of Celite, washed with water/brine twice, brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-55% EtOAc/hexanes) to give the title compound (70 mg, 71 % yield) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.31 (s, 0.5 H), 8.30 (s, 0.5 H), 7.59 (s, 0.5 H), 7.58 (s, 0.5 H), 5.35-5.20 (m, 0.5 H), 4.86 (s, 1 H), 4.85-4.70 (m, 0.5 H), 4.57 (br. s, 1 H), 4.43 (s, 1 H), 4.05-3.95 (m, 1 H), 3.60-3.45 (m, 2 H), 2.40-1.60 (m, 6 H), 1.25-1.10 (m, 3 H), 1.10-1.00 (m ,2 H), 0.90-0.80 (m, 2 H).

EXAMPLE 167

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone

(Compound 167)

Step A

(+/-)-(trans)-1,1-dimethylethyl 4-(2-hydroxycyclopentyl)-3-oxo-1-piperazinecarboxylate

[00495] Et_3N (1.175 mL, 8.43 mmol) was added to a solution of (+/-)- (trans)-2-aminocyclopentanol hydrochloride (1.160 g, 8.43 mmol) in methanol (20 mL), methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (1.5 g, 6.49 mmol) was then added. The mixture was stirred at room temperature for 15 minutes and $NaCNBH_4$ (0.611 g, 9.73 mmol) was added. The mixture was stirred overnight and then concentrated. The residue was diluted with 1 N NaOH and extracted with 5 % MeOH in DCM, The combined extracts were dried over Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (0-6 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (0.83 g, 45%) as a white foam. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.50 (q, *J*=8.06 Hz, 1 H), 4.03 - 4.21 (m, 3 H), 3.67 - 3.78 (m, 1 H), 3.52 - 3.62 (m, 1 H), 3.24 - 3.38 (m, 2 H), 2.73 - 3.06 (m, 1 H), 1.60 - 2.05 (m, 6 H), 1.47 (s, 9 H).

Step B

(+/-)-(Trans)-1-(2-hydroxycyclopentyl)-2-piperazinone trifluoroacetate (salt)

[00496] TFA (0.157 mL, 2.040 mmol) was added to a solution of (+/-)- (trans)-1,1-dimethylethyl 4-(2-hydroxycyclopentyl)-3-oxo-1-piperazinecarboxylate (58 mg, 0.204 mmol) in dichloromethane (1.0 mL) at room temperature. It was stirred for 2 hours and the mixture was then concentrated, co-evaporated with hexanes, dried under vacuum to give the title compound as a purple oil that was used without purification and assumed to be quantitative. 1H NMR (400 MHz, DMSO-d_6) δ ppm 9.26 (br. s., 2 H), 5.47 (dt, *J*=7.76, 5.29 Hz, 1 H), 4.65 (dd, *J*=14.73, 8.49 Hz, 1 H), 4.39 (q, *J*=8.46 Hz, 1 H), 4.05 (q, *J*=7.74 Hz, 1 H), 3.65 - 3.80 (m, 2 H), 3.46 (br. s., 1 H), 3.27 - 3.42 (m, 2 H), 1.38 - 1.96 (m, 6 H).

Step C

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone

[00497] Et_3N (0.041 mL, 0.293 mmol) was added to a mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (38.8 mg, 0.117 mmol), (+/-)-(trans)-1-(2-hydroxycyclopentyl)-2-piperazinone trifluoroacetate (salt) (35.0 mg, 0.117 mmol), EDC (27.0 mg, 0.141 mmol) and HOBT (21.56 mg, 0.141 mmol) in N,N-dimethylformamide(2.0 mL) at room temperature. The mixture was stirred overnight. After removal of the solvent under reduced pressure, the residue was dried under vacuum. Saturated $NaHCO_3$ was added and the mixture was extracted with 5 % MeOH in DCM. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-5 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (32 mg, 55%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.33-8.35 (m, 1 H), 7.86 (s, 1 H), 7.79 (s, 1 H), 7.60 (s, 1 H), 6.75 (s, 1 H), 4.64 - 4.89 (m, 1 H), 4.33 - 4.62 (m, 3 H), 4.08 - 4.26 (m, 2 H), 3.44 - 3.95 (m, 3 H), 1.94 - 2.06 (m, 2 H), 1.80 - 1.90 (m, 1 H), 1.67 - 1.79 (m, 3 H). ES-LCMS m/z: 497.3 (M+1).

EXAMPLE 168

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone

(Compound 168)

[00498] Et_3N (0.350 mL, 2.51 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (153 mg, 0.503 mmol), (+/-)-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone trifluoroacetate (salt) (150 mg, 0.503 mmol), EDC (116 mg, 0.604 mmol) and HOBT (92 mg, 0.604 mmol) in N,N-dimethylformamide (8.0 mL) at room temperature. The mixture was stirred overnight. After removal of the solvent under reduced pressure, the residue was dried under vacuum.

Saturated $NaHCO_3$ was added and the mixture was extracted with 5 % MeOH in DCM. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-5 % 2 M NH3 solution of MeOH in DCM) to give the title compound (125 mg, 53%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05-8.07 (m, 1 H), 7.42 (s, 1 H), 4.61 - 4.88 (m, 1 H), 4.33 - 4.61 (m, 3 H), 4.08 - 4.25 (m, 2 H), 3.40 - 3.92 (m, 3 H), 1.93 - 2.09 (m, 3 H), 1.80 - 1.89 (m, 1 H), 1.67 - 1.79 (m, 3 H), 1.09 - 1.16 (m, 2 H), 0.75 - 0.84 (m, 2 H). ES-LCMS m/z: 471.4 (M+1).

EXAMPLE 169

(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone

(Compound 169)

[00499] Et_3N (0.350 mL, 2.51 mmol) was added to a mixture of 6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (173 mg, 0.503 mmol), (+/-)-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone trifluoroacetate (salt) (150 mg, 0.503 mmol), EDC (116 mg, 0.604 mmol) and HOBT (92 mg, 0.604 mmol) in N,N-dimethylformamide (8.0 mL) at room temperature. The mixture was stirred overnight. After removal of the solvent under reduced pressure, the residue was dried under vacuum. Saturated $NaHCO_3$ was added and the mixture was extracted with 5 % MeOH in DCM. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-5 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (180 mg, 70%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.46-8.48 (m, 1 H), 7.75 (s, 1 H), 4.61 - 4.84 (m, 1 H), 4.34 - 4.61 (m, 3 H), 4.08 - 4.23 (m, 2 H), 3.41 - 3.94 (m, 3 H), 1.91 - 2.08 (m, 3 H), 1.82 - 1.89 (m, 1 H), 1.71 - 1.78 (m, 2 H). ES-LCMS m/z: 511.3 (M+1).

EXAMPLE 170

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone

(Compound 170)

Step A

1,1-dimethylethyl 4-(3-cyclopenten-1-yl)-3-oxo-1-piperazinecarboxylate

[00500] Et_3N (2.351 mL, 16.87 mmol) was added to a solution of 3-cyclopenten-1-amine hydrochloride (2.017 g, 16.87 mmol) in methanol (40 mL), followed by methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (3.0 g, 12.97 mmol). The

mixture was stirred at room temperature for 15 minutes and $NaCNBH_4$ (1.223 g, 19.46 mmol) was added. The mixture was stirred overnight and then concentrated. The residue was diluted with 1 N NaOH, and extracted with 5 % MeOH in DCM, The combined extracts were dried over Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (0-3 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (1.7 g, 49%) as a light-yellow solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.74 (s, 2 H), 5.49 (ddd, *J*=8.93, 4.68, 4.54 Hz, 1 H), 4.08 (s, 2 H), 3.59 (t, *J*=5.27 Hz, 2 H), 3.17 - 3.23 (m, 2 H), 2.70 (dd, *J*=15.80, 8.98 Hz, 2 H), 2.25 (dd, *J*=15.61, 3.71 Hz, 2 H), 1.47 (s, 9 H).

Step B

1-(3-cyclopenten-1-yl)-2-piperazinone trifluoroacetate

[00501] TFA (9.84 mL, 128 mmol) was added to a solution of 1,1-dimethylethyl 4-(3-cyclopenten-1-yl)-3-oxo-1-piperazinecarboxylate (1.7 g, 6.38 mmol) in dichloromethane (20 mL) at room temperature. It was stirred for 2 hours and the mixture was then concentrated, co-evaporated with hexanes, and dried under vacuum to give the title compound as purple oil that was used without purification and assumed to be quantitative. 1H NMR (400 MHz, DMSO-d_6) δ ppm 9.15 (br. s., 2 H), 5.76 (s, 2 H), 5.20 - 5.31 (m, 1 H), 3.72 (br. s., 2 H) 3.37 (br. s., 2 H), 3.26 (t, *J*=5.46 Hz, 2 H), 2.57 (dd, *J*=15.71, 8.88 Hz, 2 H), 2.29 (dd, *J*=15.51, 3.80 Hz, 2 H).

Step C

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone

[00502] Et_3N (2.213 mL, 15.88 mmol) was added to a mixture of 3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (1.050 g, 3.18 mmol), 1-(3-cyclopenten-1-yl)-2-piperazinone trifluoroacetate (0.89 g, 3.18 mmol), EDC (0.731 g, 3.81 mmol) and HOBT (0.584 g, 3.81 mmol) in N,N-dimethylformamide (30 mL) at room temperature. The mixture was stirred overnight. After removal of the solvent under reduced pressure, the residue was dried under vacuum. Saturated $NaHCO_3$ was added and the mixture was extracted with 5 % MeOH in DCM. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-30 % ethyl acetate in DCM) to give the title compound (0.59 g, 39%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.32-8.34 (m, 1 H), 7.86 (s, 1 H), 7.78 (s, 1 H), 7.60 (s, 1 H), 6.75 (s, 1 H), 5.77 (s, 2 H), 5.40 - 5.60 (m, 1 H), 4.66 (s, 1 H), 4.45 (s, 1 H), 4.33 (t, *J*=5.07 Hz, 1 H), 3.97 (t, *J*=5.37 Hz, 1 H), 3.38 (ddd, *J*=11.27, 5.51, 5.27 Hz, 2 H), 2.66 - 2.81 (m, 2 H), 2.31 (ddd, 2 H). ES-LCMS m/z: 479.4 (M+1).

EXAMPLE 171

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone

(Compound 171)

[00503] Et_3N (2.213 mL, 15.88 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.968 g, 3.18 mmol), 1-(3-cyclopenten-1-yl)-2-piperazinone trifluoroacetate (0.89 g, 3.18 mmol), EDC (0.731 g, 3.81 mmol) and HOBT (0.584 g, 3.81 mmol) in N,N-dimethylformamide (30 mL) at room temperature. The mixture was stirred overnight. After removal of the solvent under reduced pressure, the residue was dried under vacuum. Saturated $NaHCO_3$ was added and the mixture was extracted with 5 % MeOH in DCM. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-30 % ethyl acetate in DCM) to give the title compound (0.83 g, 58%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05-8.07 (m, 1 H), 7.42 (s, 1 H), 5.76 (s, 2 H), 5.40 - 5.58 (m, 1 H), 4.64 (s, 1 H), 4.44 (s, 1 H), 4.27 - 4.35 (m, 1 H), 3.91 - 3.98 (m, 1 H), 3.30 - 3.41 (m, 2 H), 2.65 - 2.78 (m, 2 H), 2.23 - 2.37 (m, 2 H), 2.00 - 2.08 (m, 1 H), 1.08 - 1.16 (m, 2 H), 0.80 (d, 2 H). ES-LCMS m/z: 453.4 (M+1).

EXAMPLE 172

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-trans-(3-hydroxycyclopentyl)-2-piperazinone

(Compound 172)

[00504] BH_3.THF (4.7 mL, 4.7 mmol) was added dropwise to a suspension of 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (450 mg, 0.940 mmol) in tetrahydrofuran (18 mL) at 0 ° C under N_2. The mixture was stirred at 0 ° C for 40 minutes and then was allowed to warm up to room temperature and stirred overnight to afford a clear yellow solution. A solution of $NaBO_3.4H_2O$ (795 mg, 5.17 mmol) in water (25 mL) was added. It was stirred for 30 minutes; brine was added, and the mixture was extracted with EtOAc. The combined extracts were washed with brine and dried over Na_2SO_4. The residue was purified by silica gel chromatography (0-5 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (320 mg, 69 %) as a light-yellow solid.

1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.32-35 (m, 1 H), 7.86 (s, 1 H), 7.78 (s, 1 H), 7.60 (s, 1 H), 6.75 (s, 1 H), 5.19 (ddd, *J*=17.95, 8.88, 8.68 Hz, 1 H), 4.60 - 4.72 (m, 1 H), 4.41 - 4.50 (m, 2 H), 4.28 - 4.40 (m, 1 H), 3.99 (q, *J*=5.27 Hz, 1 H), 3.47 (t, *J*=5.17 Hz,

1 H), 3.41 (t, *J*=4.98 Hz, 1 H), 2.02 - 2.19 (m, 2 H), 1.79 - 1.99 (m, 2 H), 1.59 - 1.74 (m, 2 H). ES-LCMS m/z: 453.4 (M+1). ES-LCMS m/z: 497.4 (M+1).

EXAMPLE 173

1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 173)

[00505] Diethylzinc (1.987 mL, 1.987 mmol) was dissolved in dichloromethane (3 mL) and cooled to 0 ° C under N_2. TFA (0.153 mL, 1.987 mmol) in dichloromethane (3 mL) was added very slowly (15 minutes) via syringe pump and the mixture was stirred for 20 minutes. Diiodomethane (0.160 mL, 1.987 mmol) in dichloromethane (3 mL) was then added very slowly (15 minutes) via syringe pump and the mixture was stirred for 20 minutes. 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (60 mg, 0.132 mmol) was added. The mixture was allowed to warm to room temperature and stirred for 3 days. The mixture was diluted with DCM and washed consecutively with saturated NH_4Cl and saturated $NaHCO_3$. The organic phase was dried (Na_2SO_4), filtered and evaporated. The residue was purified by Reverse-Phase HPLC (water:acetonitrile with 0.1% formic acid) to give the title compound as a mixture of cis/trans-isomers (41 mg, 66 %) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.04-8.07 (m, 1 H), 7.41 (s, 1 H), 4.65 - 5.43 (m, 1 H), 4.60 (s, 1 H), 4.38 - 4.45 (m, 1 H), 4.24 - 4.34 (m, 1 H), 3.89 - 3.97 (m, 1 H), 3.27 - 3.48 (m, 2 H), 1.74 - 2.29 (m, 5 H), 1.24 - 1.37 (m, 2 H), 1.07 - 1.17 (m, 2 H), 0.76 - 0.84 (m, 2 H), 0.30 - 0.45 (m, 2 H). ES-LCMS m/z: 467.4 (M+1).

EXAMPLE 174

1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

(Compound 174)

[00506] Diethylzinc (2.193 mL, 2.193 mmol) was dissolved in dichloromethane (3 mL) and cooled to 0 °C under N_2. TFA (0.169 mL, 2.193 mmol) in dichloromethane (3 mL) was added very slowly (15 minutes) via syringe pump and the mixture was stirred for 20 minutes. Diiodomethane (0.177 mL, 2.193 mmol) in dichloromethane (3 mL) was then added very slowly (15 minutes) via syringe pump and the mixture was stirred for 20 minutes. 4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (70 mg, 0.146 mmol) was added. The mixture was allowed to warm to room temperature and stirred overnight. The mixture was diluted with

DCM and washed consecutively with saturated NH_4Cl and saturated $NaHCO_3$. The organic phase was dried (Na_2SO_4), filtered and evaporated. The residue was purified by Reverse-Phase HPLC (water:acetonitrile with 0.1% formic acid) to give the title compound as a mixture of cis/trans-isomers (33 mg, 46 %) as a light-yellow solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.32-8.34 (m, 1 H) 7.86 (s, 1 H) 7.78 (s, 1 H) 7.60 (s, 1 H) 6.75 (s, 1 H) 4.66 - 5.44 (m, 1 H) 4.63 (s, 1 H) 4.38 - 4.46 (m, 1 H) 4.28 - 4.35 (m, 1 H) 3.90 - 3.99 (m, 1 H) 3.28 - 3.50 (m, 2 H) 1.87 - 2.49 (m, 2 H) 1.74 - 1.87 (m, 2 H) 1.25 - 1.37 (m, 2 H) 0.27 - 0.47 (m, 2 H). ES-LCMS m/z: 493.2 (M+1).

EXAMPLE 175

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-trans-(3-hydroxycyclopentyl)-2-piperazinone

(Compound 175)

[00507] BH_3.THF (3.97 mL, 3.97 mmol) was added dropwise to a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (600 mg, 1.325 mmol) in tetrahydrofuran (15 mL) at 0 °C under N_2. The mixture was stirred at 0 °C for 40 minutes and then was allowed to warm up to room temperature and stirred for 4 hours. A solution of $NaBO_3.4H_2O$ (652 mg, 4.24 mmol) in water (25 mL) was added. It was stirred for 30 minutes; brine was added, and the mixture was extracted with EtOAc. The combined extracts were washed with brine and dried over Na_2SO_4. The residue was purified by silica gel chromatography (0-5 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (430 mg, 69%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05-8.07 (m, 1 H), 7.42 (s, 1 H), 5.18 (ddd, *J*=17.80, 8.83, 8.68 Hz, 1 H), 4.63 (s, 1 H), 4.45 (br. s., 1 H), 4.43 (s, 1 H), 4.26 - 4.39 (m, 1 H), 3.90 - 4.04 (m, 1 H), 3.43 - 3.49 (m, 1 H), 3.40 (t, *J*=5.07 Hz, 1 H), 2.00 - 2.18 (m, 3 H), 1.79 - 1.97 (m, 2 H), 1.61 - 1.73 (m, 2 H), 1.08 - 1.17 (m, 2 H), 0.76 - 0.84 (m, 2 H). ES-LCMS m/z: 471.4 (M+1).

EXAMPLE 176

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone (Enantiomer 1)

(Compound 176)

[00508] The racemic (+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone (110 mg, Example 168) was purified by SFC (Supercritical Fluid Chromatography): (ADH-Chiral Technologies 10x250 mm, 5 µm column; Solvent/mobile phase: 70% MeOH / 30% CO_2, Rt = 5.00

minute). Upon separation, the individual enantiomers were further purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to give the title compound (22mg, 20% recovery) as a white solid. 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.06 (d, J=7.02 Hz, 1 H) 7.42 (s, 1 H) 4.33 - 4.87 (m, 4 H) 4.08 - 4.23 (m, 2 H) 3.39 - 3.91 (m, 3 H) 1.93 - 2.09 (m, 3 H) 1.80 - 1.89 (m, 1 H) 1.71 (d, J=4.88 Hz, 3 H) 1.08 - 1.17 (m, 2 H) 0.76 - 0.86 (m, 2 H). ES-LCMS m/z: 471.2 (M+1).

EXAMPLE 177

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone (Enantiomer 2)

(Compound 177)

[00509] The racemic (+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone (110 mg, Example 168) was purified by SFC (Supercritical Fluid Chromatography): (ADH-Chiral Technologies 10x250 mm, 5 µm column; Solvent/mobile phase: 70% MeOH / 30% CO_2, Rt = 7.23 minute). Upon separation, the individual enantiomers were further purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to give the title compound (22mg, 20% recovery) as a white solid. 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.06 (d, J=7.02 Hz, 1 H) 7.42 (s, 1 H) 4.33 - 4.86 (m, 4 H) 4.08 - 4.23 (m, 2 H) 3.20 - 3.92 (m, 3 H) 1.91 - 2.09 (m, 3 H) 1.84 (dd, J=6.24, 3.90 Hz, 1 H) 1.65 - 1.79 (m, 3 H) 1.09 - 1.16 (m, 2 H) 0.77 - 0.84 (m, 2 H). ES-LCMS m/z: 471.2 (M+1).

EXAMPLE 178

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone

(Compound 178)

Step A

(+/-)-N^1-[(cis)-2-hydroxycyclopentyl]-N^2-[(4-nitrophenyl)sulfonyl]glycinamide

[00510] DIPEA (2.274 mL, 13.02 mmol) was added to a mixture of N-[(4-nitrophenyl)sulfonyl]glycine (1.694 g, 6.51 mmol), (+/-)-(cis)-4-amino-3-hexanol hydrochloride (1.000 g, 6.51 mmol), EDC (1.498 g, 7.81 mmol) and HOBt (1.196 g, 7.81 mmol) in N,N-dimethylformamide (30 mL) at room temperature. The mixture was stirred overnight. After removal of the solvent under reduced pressure; EtOAc was added and the mixture was washed with water, saturated $NaHCO_3$ and brine. The organic phase was dried (Na_2SO_4), filtered, evaporated and dried in vacuo to give the title product (2.0g, 89 %) as a light-yellow solid which was pure enough for the next step without further

purification. 1H NMR (400 MHz, DMSO-d_6) δ ppm 8.40 (d, *J*=8.78 Hz, 2 H), 8.36 (br. s., 1 H), 8.04 (d, *J*=8.78 Hz, 2 H), 7.57 (d, *J*=7.61 Hz, 1 H), 4.69 (d, *J*=3.90 Hz, 1 H), 3.80 - 3.88 (m, 1 H), 3.69 (dd, *J*=7.80, 4.68 Hz, 1 H), 3.56 (s, 2 H), 1.60 - 1.75 (m, 3 H), 1.47 - 1.57 (m, 1 H), 1.33 - 1.47 (m, 2 H). ES-LCMS m/z: 344.2 (M+1).

Step B

(+/-)-1-[(cis)-2-hydroxycyclopentyl]-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone

[00511] A mixture of (+/-)-N1-[(cis)-2-hydroxycyclopentyl]-N2-[(4-nitrophenyl)sulfonyl]glycinamide (2.0 g, 5.82 mmol), 1,2-dibromoethane (4.42 mL, 51.3 mmol) and K_2CO_3 (7.08 g, 51.3 mmol) in N,N-dimethylformamide (40 mL) was heated to 60 °C and stirred overnight. After removal of the solvent, EtOAc was added and the mixture was washed with water and brine. The organic phase was dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-3 % 2 M NH3 solution of MeOH in DCM) to give the title compound (1.28 g, 60%) as a light-yellow solid. 1H NMR (400 MHz, DMSO-d_6) δ ppm 8.46 (d, *J*=8.98 Hz, 2 H), 8.10 (d, *J*=8.78 Hz, 2 H), 4.60 (d, *J*=3.90 Hz, 1 H), 4.13 - 4.23 (m, 1 H), 3.96 - 4.04 (m, 1 H), 3.77 (d, *J*=16.19 Hz, 1 H), 3.44 - 3.61 (m, 3 H), 3.36 (t, *J*=3.80 Hz, 1 H), 3.16 (ddd, *J*=11.85, 8.34, 3.61 Hz, 1 H), 1.66 - 1.85 (m, 3 H), 1.48 - 1.58 (m, 1 H), 1.35 - 1.47 (m, 2 H). ES-LCMS m/z: 370.1 (M+1).

Step C

(+/-)-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone

[00512] Benzenethiol (0.892 mL, 8.66 mmol) was added to a suspension of K_2CO_3 (1.676 g, 12.13 mmol) in acetonitrile (35 mL) at 50 °C. The mixture was stirred for 30 minutes, (+/-)-1-[(cis)-2-hydroxycyclopentyl]-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone (1.28 g, 3.47 mmol) in N,N-dimethylformamide (7 mL) was then added dropwise over 20 minutes. After 1 hour, the mixture was cooled to room temperature. The insoluble material was removed via filtration through a pad of Celite. The filtrate was concentrated and the residue was purified by silica gel chromatography (0-10 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (450 mg, 71 %) as a brown oil. 1H NMR (400 MHz, DMSO-d_6) δ ppm 4.60 (d, *J*=4.10 Hz, 1 H), 4.25 (ddd, *J*=12.00, 7.41, 4.78 Hz, 1 H), 4.09 (d, *J*=4.10 Hz, 1 H), 3.47 (dt, *J*=11.61, 4.63 Hz, 1 H), 3.25 (d, *J*=1.95 Hz, 2 H), 3.19 (ddd, *J*=11.85, 6.15, 6.00 Hz, 1 H), 2.85 (t, *J*=5.37 Hz, 2 H), 1.68 - 1.95 (m, 3 H), 1.51 - 1.60 (m, 1 H), 1.38 - 1.50 (m, 2 H).

Step D

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone

[00513] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (152 mg, 0.500 mmol), (+/-)-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone (92 mg, 0.5 mmol), EDC (115 mg, 0.600 mmol) and HOBT (92 mg, 0.600 mmol) in N,N-dimethylformamide (5.0 mL) was stirred overnight at room temperature. The mixture was stirred overnight. After removal off the solvent under reduced pressure the residue was dried under vacuum. Saturated $NaHCO_3$ was added and the mixture was extracted with 5 % MeOH in DCM. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-5 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (198 mg, 84%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.04-8.06 (m, 1 H), 7.41 (s, 1 H), 4.56 - 4.77 (m, 1 H), 4.30 - 4.55 (m, 3 H), 4.09 - 4.22 (m, 1 H), 3.49 - 3.89 (m, 2 H), 1.97 - 2.16 (m, 3 H), 1.75 - 1.96 (m, 3 H), 1.51 - 1.71 (m, 3 H), 1.12 (d, *J*=7.80 Hz, 2 H), 0.80 (d, *J*=4.49 Hz, 2 H). ES-LCMS m/z: 471.3 (M+1).

EXAMPLE 179

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3,4-dihydroxycyclopentyl)-2-piperazinone (Isomer 1)

(Compound 179)

[00514] A mixture of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (226 mg, 0.5 mmol) and AD-mix-beta (694 mg, 0.500 mmol) in tert-butanol (2.5 mL) and water (2.500 mL) was stirred overnight at room temperature. The mixture was diluted with EtOAc and sodium sulfite (1.0 eq) was added. The mixture was stirred for 20 minutes. The organic layer was separated, washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered and evaporated. The residue was purified by silica gel chromatography (0-8 % 2 M NH_3 solution of MeOH in DCM) to give two isomers. Isomer 1 was obtained as a white solid, 23 mg (9.5 %). 1H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (br. s., 1 H) 7.60 (s, 1 H) 4.77 - 4.96 (m, 1 H) 4.57 - 4.64 (m, 2 H) 4.43 (s, 1 H) 4.19 (s, 1 H) 3.99 (t, *J*=4.88 Hz, 1 H) 3.82 (d, *J*=5.46 Hz, 1 H) 3.75 (d, *J*=3.12 Hz, 2 H) 3.42 - 3.54 (m, 2 H) 2.16 - 2.26 (m, 1 H) 1.84 - 1.96 (m, 2 H) 1.48 - 1.62 (m, 2 H) 0.98 - 1.06 (m, 2 H) 0.86 - 0.93 (m, 2 H). ES-LCMS m/z: 487.1 (M+1).

EXAMPLE 180

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3,4-dihydroxycyclopentyl)-2-piperazinone (Isomer 2)

(Compound 180)

[00515] A mixture of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (226 mg, 0.5 mmol) and AD-mix-beta (694 mg, 0.500 mmol) in tert-butanol (2.5 mL) and water (2.500 mL) was stirred overnight at room temperature. The mixture was diluted with EtOAc and sodium sulfite (1.0 eq) was added. The mixture was stirred for 20 minutes. The organic layer was separated, washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered and evaporated. The residue was purified by silica gel chromatography (0-8 % 2 M NH_3 solution of MeOH in DCM) to give two isomers. Isomer 2 was obtained as a white solid, 178 mg (73 %). 1H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, *J*=5.07 Hz, 1 H) 7.60 (br. s., 1 H) 5.09 (dt, *J*=16.93, 8.41 Hz, 1 H) 4.49 (br. s., 2 H) 4.43 (s, 1 H) 4.19 (s, 1 H) 3.91 - 4.05 (m, 3 H) 3.79 - 3.87 (m, 1 H) 3.35 - 3.42 (m, 2 H) 2.16 - 2.27 (m, 1 H) 1.65 - 1.78 (m, 4 H) 0.97 - 1.06 (m, 2 H) 0.89 (q, *J*=5.07 Hz, 2 H). ES-LCMS m/z: 487.1 (M+1).

EXAMPLE 181

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-trans-(3-hydroxycyclopentyl)-2-piperazinone (Enantiomer 1)

(Compound 181)

[00516] Chiral separation of Example 175 was performed on a ChiralPak ODH column (250x10 mm i.d., 5um; Daicel Chemical Ind.; Osaka, Japan) under supercritical conditions maintained at 40 °C, 140 bar with methanol modified CO_2 (28%MeOH, 72% CO_2) delivered at a combined flow rate of 10mL/min on a Thar Discovery Series SFC system (Thar Instruments, Inc.; Pittsburgh, Pa). The enantiomers were detected using a Gilson selectable wavelength 151 UV-Vis detector at 280nm. Enantiomer 1 (125 mg, 42% recovery) was obtained as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.37 Hz, 1 H) 7.42 (s, 1 H) 5.18 (ddd, *J*=17.76, 8.78, 8.58 Hz, 1 H) 4.63 (s, 1 H) 4.39 - 4.49 (m, 2 H) 4.33 (q, *J*=5.01 Hz, 1 H) 3.97 (d, *J*=5.07 Hz, 1 H) 3.45 (t, *J*=4.68 Hz, 1 H) 3.40 (d, *J*=4.88 Hz, 1 H) 1.98 - 2.18 (m, 3 H) 1.79 - 1.97 (m, 2 H) 1.65 (d, *J*=5.85 Hz, 2 H) 1.07 - 1.16 (m, 2 H) 0.80 (d, *J*=4.88 Hz, 2 H). ES-LCMS m/z: 471.2 (M+1).

EXAMPLE 182

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-trans-(3-hydroxycyclopentyl)-2-piperazinone (Enantiomer 2)

(Compound 182)

[00517] Chiral separation of Example 175 was performed on a ChiralPak ODH column (250x10 mm i.d., 5um; Daicel Chemical Ind.; Osaka, Japan) under supercritical conditions maintained at 40 °C, 140 bar with methanol modified CO_2 (28%MeOH, 72%

CO_2) delivered at a combined flow rate of 10mL/min on a Thar Discovery Series SFC system (Thar Instruments, Inc.; Pittsburgh, Pa). The enantiomers were detected using a Gilson selectable wavelength 151 UV-Vis detector at 280nm. Enantiomer 2 (124 mg, 41% recovery) was obtained as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.17 Hz, 1 H) 7.42 (s, 1 H) 5.09 - 5.27 (m, 1 H) 4.63 (s, 1 H) 4.40 - 4.50 (m, 2 H) 4.33 (q, *J*=5.07 Hz, 1 H) 3.97 (q, *J*=4.68 Hz, 1 H) 3.45 (t, *J*=4.98 Hz, 1 H) 3.40 (d, *J*=5.07 Hz, 1 H) 1.98 - 2.19 (m, 3 H) 1.78 - 1.97 (m, 2 H) 1.65 (br. s., 2 H) 1.07 - 1.16 (m, 2 H) 0.80 (d, *J*=5.07 Hz, 2 H). ES-LCMS m/z: 471.2 (M+1).

EXAMPLE 183

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone

(Compound 183)

[00518] HATU (150 mg, 0.394 mmol) was added to a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (100 mg, 0.328 mmol), 1-cyclohexyl-2-piperazinone (71.8 mg, 0.394 mmol) and DIPEA (0.075 mL, 0.427 mmol) in DMF (2 mL) at room temperature under nitrogen. After 16 hours, the clear solution was poured slowly into an aqueous 1 N HCl solution (~15 mL) and stirred for 10 minutes at room temperature. The solid was filtered and dried under vacuum to give 105 mg of the desired product in ~90-95% purity. The crude material was purified by Reverse Phase HPLC (MeCN/water + 0.1% TFA) to give one batch of the title compound (9 mg, 0.018 mmol, 6% yield) and a second batch of the title compound (45 mg, 0.091 mmol, 28% yield) as white solids. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.46 (d, 1 H) 7.61 (br. s., 1 H) 4.44 (s, 1 H) 4.09 - 4.33 (m, 2 H) 4.00 (t, 1 H) 3.83 (t, 1 H) 3.24 - 3.48 (m, 2 H) 2.12 - 2.29 (m, 1 H) 1.76 (d, 2 H) 1.53 - 1.66 (m, 3 H) 1.45 (d, 2 H) 1.30 (d, 2 H) 0.98 - 1.21 (m, 3 H) 0.84 - 0.98 (m, 2 H). LCMS m/z 469.1 (M+1).

EXAMPLE 184

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone

(Compound 184)

[00519] HATU (150 mg, 0.394 mmol) was added to a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (100 mg, 0.328 mmol), 1-(1,3-thiazol-2-yl)-2-piperazinone HCl (79 mg, 0.361 mmol) and DIPEA (0.115 mL, 0.656 mmol) in DMF (2 mL) at room temperature under nitrogen. After 16 hours, the clear solution was poured slowly into an aqueous 1 N HCl solution (~15 mL) and stirred for

10 minutes at room temperature. The solid was filtered and dried under vacuum to give 105 mg of the desired product that was further purified by Reverse Phase HPLC (MeCN/water + 0.1% formic acid) to give the title compound (51 mg, 0.103 mmol, 31% yield) as a white powder. 1H NMR (400 MHz, DMSO-d_6) δ ppm 8.47 (s, 1 H) 7.53 - 7.67 (m, 2 H) 7.29 - 7.40 (m, 1 H) 4.89 (s, 1 H) 4.58 (s, 1 H) 4.25 (s, 3 H) 4.10 (d, 1 H) 2.16 - 2.29 (m, 1 H) 1.03 (dd, 2 H) 0.82 - 0.96 (m, 2 H). LCMS m/z 470.0 (M+1).

EXAMPLE 185

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-3-hydroxycyclopentyl]-2-piperazinone

(Compound 185)

Step A

(+/-)-3-azidocyclopentanone

[00520] Prepared according to the literature procedure described in *Organic Letters* **1999**, *7*, 1107. AcOH (25.1 mL, 438 mmol) was added to a solution of 2-cyclopenten-1-one (6 g, 73.1 mmol), triethylamine (2.037 mL, 14.62 mmol), and $TMSN_3$ (58.2 mL, 438 mmol) in DCM (300 mL) at room temperature. The solution was stirred for 16 hours (TLC shows a new slightly less polar spot). Silica gel was added and the solution was concentrated via rotary evaporation (note: blast shield used in case of explosion). The dry reaction mixture was purified on silica gel to give the desired product which contains ethyl acetate (note: product appears volatile so no further effort was taken to remove solvent).

Step B

(+/-)-1,1-dimethylethyl (3-oxocyclopentyl)carbamate

[00521] A mixture of (+/-)-3-azidocyclopentanone (7.5 g, 59.9 mmol), Pd-C (3.19 g, 3.00 mmol), and Boc_2O (15.31 mL, 65.9 mmol) in ethyl acetate (100 mL) was stirred at room temperature under H_2 (60 psig) for 4 hours. The vessel was carefully vented, purged with N_2, filtered through Celite and concentrated under reduced pressure. The crude product was purified on silica gel (hexanes/ethyl acetate) to give the title compound (3.02 g, 15.16 mmol, 25.3 % yield) as a white solid.

Step C

(+/-)-1,1-dimethylethyl [(cis)-3-hydroxycyclopentyl]carbamate and (+/-)-1,1-dimethylethyl [(trans)-3-hydroxycyclopentyl]carbamate

[00522] $NaBH_4$ (1.147 g, 30.3 mmol) was added as a solid to a solution of (+/-)-1,1-dimethylethyl (3-oxocyclopentyl)carbamate (3.02 g, 15.16 mmol) in EtOH (75 mL) at 0 °C. After stirring for 2.5 hours at 0 °C, saturated $NaHCO_3$ solution (~60 mL) was added slowly then the EtOH was removed under reduced pressure. The residual aqueous mixture was

extracted with ethyl acetate (2 x 125mL) and the combined organic layers were washed with water, brine, dried over $NaSO_4$, filtered and concentrated to give 3.1 g of a mixture of cis/trans isomers. The crude material was purified on silica gel (90:10 to 10:90 hexanes/ethyl acetate) to give (+/-)-1,1-dimethylethyl [(cis)-3-hydroxycyclopentyl]carbamate (1.35 g, 6.71 mmol, 44% yield) and (+/-)-1,1-dimethylethyl [(trans)-3-hydroxycyclopentyl]carbamate (1.43 g, 7.11 mmol, 47 % yield) as white powders. Literature reference p. 112 WO2005019221.

Step D

(+/-)-(cis)-3-aminocyclopentanol hydrochloride salt

[00523] 4 N HCl in dioxane (13.42 mL, 53.7 mmol) was added to a solution of (+/-)-1,1-dimethylethyl [(cis)-3-hydroxycyclopentyl]carbamate (1.35 g, 6.71 mmol) in 1,4-dioxane (13 mL) at 0 °C. After stirring for 1.5 hours under nitrogen, the solution was warmed to room temperature and stirred for 3 hours. The mixture (white solid formed) was concentrated under reduced pressure to give the title compound (0.93 g, 6.42 mmol, 96 % yield) as a white powder.

Step E

(+/-)-N^1-[(cis)-3-hydroxycyclopentyl]-N^2-[(4-nitrophenyl)sulfonyl]glycinamide

[00524] HATU (3.08 g, 8.11 mmol) was added to a solution of (+/-)-(cis)-3-aminocyclopentanol HCl (0.93 g, 6.76 mmol), N-[(4-nitrophenyl)sulfonyl]glycine (1.759 g, 6.76 mmol) and DIPEA (3.54 mL, 20.27 mmol) in DMF (30 mL) at room temperature. After 4 hours, water (200 mL) and ethyl acetate (250 mL) were added. The aqueous layer was separated and extracted again with ethyl acetate (250 mL). The combined organic layers were washed with water, brine, dried over $MgSO_4$, filtered and concentrated to give an orange oil. The crude product was purified on silica gel (30% hexanes/EtOAc) to give the title compound (1.45 g, 4.14 mmol, 61% yield) as a white solid.

Step F

(+/-)-1-[(cis)-3-hydroxycyclopentyl]-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone

[00525] A mixture of (+/-)-N1-[(cis)-3-hydroxycyclopentyl]-N2-[(4-nitrophenyl)sulfonyl]glycinamide (1.45 g, 4.22 mmol), 1,2-dibromoethane (3.64 mL, 42.2 mmol) and K_2CO_3 (5.84 g, 42.2 mmol) in DMF (20 mL) were heated to 60 °C with stirring under nitrogen for 16 hours. Water (200 mL) and ethyl acetate (200 mL) were added. The aqueous layer was separated and extracted again with ethyl acetate (150 mL). The combined organic layers were washed with water, brine, dried over $MgSO_4$, filtered and concentrated to give an orange solid. The crude material was recrystallized from hot EtOH to give the desired product in ca. 80% purity. This was recombined with the EtOH

filtrate and purified on silica gel (70% EtOAc/hex - 100% EtOAc) to give the title compound (0.84 g, 2.251 mmol, 53% yield) as a white solid.

Step G

(+/-)-1-[(cis)-3-hydroxycyclopentyl]-2-piperazinone

[00526] A suspension of thiophenol (0.820 mL, 7.96 mmol) and K_2CO_3 (0.786 g, 5.69 mmol) in MeCN (25 mL) was heated to 50 °C. After stirring for 30 minutes, a solution of (+/-)-1-[(cis)-3-hydroxycyclopentyl]-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone (0.84 g, 2.274 mmol) in DMF (4 mL) was added dropwise. The red/orange mixture was stirred for 4 hours then cooled to room temperature and filtered thru Celite washing with MeCN. The orange solution was concentrated under reduced pressure and absorbed onto a small plug of silica gel. DCM was used to wash away the non-polar organic impurities then the compound was eluted off with 15% MeOH/DCM to give the title compound (0.26 g, 1.411 mmol, 62% yield) as a pale yellow solid.

Step H

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-3-hydroxycyclopentyl]-2-piperazinone

[00527] HATU (0.644 g, 1.693 mmol) was added to a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.430 g, 1.411 mmol), (+/-)-1-[(cis)-3-hydroxycyclopentyl]-2-piperazinone (0.26 g, 1.411 mmol) and DIPEA (0.493 mL, 2.82 mmol) in DMF (10 mL) at room temperature. After 4 hours, water (200 mL) and ethyl acetate (250 mL) were added. The aqueous layer was separated and extracted again with ethyl acetate (250 mL). The combined organic layers were washed with water, brine, dried over $MgSO_4$, filtered and concentrated to give an orange oil. The crude product was purified on silica gel (30% hexanes/EtOAc) to give the title compound (0.56 g, 1.130 mmol, 80% yield) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05 (d, 1 H) 7.41 (s, 1 H) 4.56 - 4.68 (m, 1 H) 4.47 (s, 1 H) 4.20 - 4.44 (m, 3 H) 3.87 - 4.06 (m, 1 H) 3.53 - 3.64 (m, 2 H) 2.97 - 3.13 (m, 1 H) 2.18 - 2.32 (m, 1 H) 1.98 - 2.09 (m, 2 H) 1.77 - 1.98 (m, 2 H) 1.61 - 1.77 (m, 2 H) 1.07 - 1.16 (m, 2 H) 0.75 - 0.83 (m, 2 H). LCMS m/z: 471.3 (M+1).

EXAMPLE 186

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone

(Compound 186)

[00528] 3-Chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (35 mg, 0.11 mmol) and 1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone

hydrochloride (25.6 mg, 0.109 mmol) were dissolved in dimethylformamide (3 mL) before *N*-ethyl-*N*-(1-methylethyl)-2-propanamine (0.095 mL, 0.55 mmol) was added, followed by N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (45.6 mg, 0.120 mmol). The mixture was stirred for 2 hours, diluted with ethyl acetate, washed with brine, washed with 5% lithium chloride, and concentrated. The residue was purified by reverse phase HPLC to give the title compound (25 mg; 46%). ^{1}H NMR (METHANOL-d_4) δ ppm 8.28 - 8.46 (m, 1 H), 7.63 - 7.85 (m, 1 H), 4.51 - 4.63 (m, 1 H), 4.21 - 4.44 (m, 2 H), 4.03 - 4.19 (m, 1 H), 3.87 - 4.03 (m, 1 H), 3.38 - 3.58 (m, 3 H), 2.52 - 2.74 (m, 2 H), 1.83 - 2.10 (m, 4 H), 1.53 - 1.75 (m, 4 H), 1.30 - 1.47 (m, 2 H), 0.95 (d, 6 H). ES-LCMS m/z: 501, 503 (M+1).

EXAMPLE 187

6-cyclopropyl-2-{[4-(cis-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 187)

[00529] The title compound (19 mg) was obtained from the mixture of cis and trans isomers (Example 166) after chromatographic separation on a Chiralcel OJH column (250x10 mm i.d., 5um; Daicel Chemical Ind.; Osaka, Japan) under supercritical conditions maintained at 40 °C, 140 bar with methanol modified CO_2 (10% MeOH, 90% CO_2) delivered at a combined flow rate of 10mL/min on a Thar Discovery SFC system (Thar Instruments, Inc., Pittsburgh, PA). The isomers were detected using a Gilson 151 UV/Vis detector (Gilson, Inc., Middleton, WI) at 254 nm. ^{1}H NMR (400 MHz, DMSO-*d*6) δ ppm 8.75-8.70 (m, 1 H), 7.80-7.75 (m, 1 H), 4.75 - 4.60 (m, 2 H), 4.35-4.25 (m, 1 H), 4.21 (s, 1 H), 3.95-3.85 (m, 1 H), 3.55-3.45 (m, 2 H), 2.35 - 2.20 (m, 1 H), 2.20-2.10 (m, 2 H), 2.05-1.90 (m, 1 H), 1.80-1.65 (m, 2 H), 1.10-1.00 (m, 5 H), 1.00-0.90 (m, 2 H).

EXAMPLE 188

6-cyclopropyl-2-{[4-(trans-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

(Compound 188)

[00530] The title compound (17.5 mg) was obtained from the mixture of cis and trans isomers (Example 166) as described in Example 187. ^{1}H NMR (400 MHz, DMSO-*d*6) δ ppm 8.75-8.70 (m, 1 H), 7.80-7.75 (m, 1 H), 5.15-5.00 (m, 1 H), 4.67 (s, 1 H), 4.35-4.25 (m, 1 H), 4.22 (s, 1 H), 3.95-3.85 (m, 1 H), 3.55-3.45 (m, 2 H), 2.45-2.15 (m, 4 H), 1.80-1.65 (m, 2 H), 1.15 (d, *J*=7.1 Hz, 3 H), 1.10-1.00 (m, 2 H), 1.00-0.90 (m, 2 H).

EXAMPLE 189

1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone (Isomer 1)

(Compound 189)

[00531] Separation of a cis/trans mixture of 1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone (Example 173) was achieved on an (S,S) Whelk-O column (250x10 mm i.d., 5um; Regis Technologies, Morton Grove, Il) under supercritical conditions maintained at 40 °C, 140 bar with methanol modified CO_2 (38%MeOH, 62% CO_2) delivered at a combined flow rate of 10ml/min on a Thar Discovery Series SFC system (Thar Instruments, Inc.; Pittsburgh, Pa). The isomers were detected using a Gilson selectable wavelength 151 UV-Vis detector at 280nm. The early eluting isomer was obtained as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05 (d, 1 H) 7.41 (s, 1 H) 4.67 - 4.86 (m, 1 H) 4.60 (s, 1 H) 4.41 (s, 1 H) 4.23 - 4.35 (m, 1 H) 3.93 (t, 1 H) 3.35 - 3.50 (m, 2 H) 1.98 - 2.11 (m, 1 H) 1.86 - 1.97 (m, 2 H) 1.72 - 1.85 (m, 2 H) 1.27 - 1.36 (m, 2 H) 1.07 - 1.17 (m, 2 H) 0.75 - 0.85 (m, 2 H) 0.30 - 0.45 (m, 2 H).

EXAMPLE 190

1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone (Isomer 2)

(Compound 190)

[00532] The title compound was obtained from the separation of the mixture of cis- and trans-isomers as described in Example 189. The late eluting isomer was isolated as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05 (d, 1 H) 7.41 (s, 1 H) 5.17 - 5.47 (m, 1 H) 4.60 (s, 1 H) 4.40 (s, 1 H) 4.28 (t, 1 H) 3.92 (t, 1 H) 3.32 (ddd, 2 H) 2.11 - 2.35 (m, 2 H) 1.94 - 2.12 (m, 1 H) 1.19 - 1.40 (m, 4 H) 1.02 - 1.19 (m, 2 H) 0.87 - 1.02 (m, 1 H) 0.69 - 0.87 (m, 2 H) 0.13 (q, 1 H).

EXAMPLE 191

(Compound 191)

(5*S*)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

[00533] Racemic 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone was purified by chiral reverse phase HPLC using a ChiralPak AD-H 30X250mm column that was eluted with 70% hexane /

30% isopropanol. Run time was 18 minutes and fractions were triggered by threshold at 254 nm. Fractions were concentrated to give the title compound. ^{1}H NMR (CHLOROFORM-*d*) □ ppm ^{1}H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 8.00 - 8.11 (m, 1 H), 7.40 (s, 1 H), 5.45 (m, 0.5 H), 4.97 - 5.20 (m, 1.5 H), 4.70 - 4.92 (m, 1 H), 4.19 (d, 0.5 H), 3.96 (d, 0.5 H), 3.58 - 3.72 (m,1 H), 3.31 (d, 1 H), 1.96 - 2.23 (m, 5 H), 1.65 - 1.79 (m, 2 H), 1.31 - 1.41 (m, 3 H), 1.06 - 1.15 (m, 2 H), 0.74 - 0.85 (m, 2 H). MS (ESI) m/z 455, 457 (MH^+).

EXAMPLE 192

(Compound 192)

(5*R*)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone

[00534] Racemic 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone was purified by chiral reverse phase HPLC using a ChiralPak AD-H 30X250mm column that was eluted with 70% hexane / 30% isopropanol. Run time was 18 minutes and fractions were triggered by threshold at 254 nm. Fractions were concentrated to give the title compound. ^{1}H NMR (CHLOROFORM-*d*) □ ppm ^{1}H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 8.00 - 8.11 (m, 1 H), 7.40 (s, 1 H), 5.45 (m, 0.5 H), 4.97 - 5.20 (m, 1.5 H), 4.70 - 4.92 (m, 1 H), 4.19 (d, 0.5 H), 3.96 (d, 0.5 H), 3.58 - 3.72 (m,1 H), 3.31 (d, 1 H), 1.96 - 2.23 (m, 5 H), 1.65 - 1.79 (m, 2 H), 1.31 - 1.41 (m, 3 H), 1.06 - 1.15 (m, 2 H), 0.74 - 0.85 (m, 2 H). MS (ESI) m/z 455, 457 (MH^+).

EXAMPLE 193

(Compound 193)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-(hydroxymethyl)-2-piperazinone

Step A

1,1-dimethylethyl 4-[(cyclobutylamino)methyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate

[00535] 3-(1,1-dimethylethyl) 4-methyl 2,2-dimethyl-1,3-oxazolidine-3,4-dicarboxylate (2.0 g, 7.7 mmol) in toluene was cooled to -78 °C. Diisobutylaluminium hydride (13.11 ml, 13.11 mmol) was added dropwise so that the internal temperature did not go above -70 °C. The mixture was stirred for 3 hours and then quenched with drop-wise addition of methanol so that the internal temperature did not go above -70 °C. The

reaction was poured into iced 1M hydrochloric acid and extracted 3 times with ethyl acetate. The combined organic layers were washed 2 times with brine, dried over sodium sulfate, and concentrated. The residue, 1,1-dimethylethyl 4-formyl-2,2-dimethyl-1,3-oxazolidine-3-carboxylate, was dissolved in 1,2-dichloroethane (20 mL). Cyclobutylamine (1.99 mL, 23.3 mmol) and acetic acid (0.444 mL, 7.76 mmol) were added, followed by sodium triacetoxyborohydride (4.9 g, 23.3 mmol). The mixture was stirred at room temperature for 4 hours, quenched with saturated sodium bicarbonate, and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated to give the title compound (2.27 g, >99%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 3.86 – 3.93 (2 H, m), 3.79 – 3.86 (1 H, m), 3.63 – 3.79 (1 H, m), 3.06 – 3.20 (1 H, m), 2.53 – 2.69 (1 H, m), 2.26 – 2.44 (1 H, m), 2.01 – 2.15 (2 H, m), 1.51 – 1.70 (4 H, m), 1.44 (3 H, s), 1.33 – 1.43 (12 H, m).

Step B

1,1-dimethylethyl 4-{[(bromoacetyl)(cyclobutyl)amino]methyl}-2,2-dimethyl-1,3-oxazolidine-3-carboxylate

[00536] 1,1-dimethylethyl 4-[(cyclobutylamino)methyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (732 mg, 2.57 mmol) and N,N-diisopropylethylamine (1.35 mL, 7.72 mmol) in dichloromethane (25 mL) were cooled to 5 °C in an ice bath before bromoacetyl bromide (0.246 mL, 2.83 mmol) was added. The mixture was stirred for 1 hour. The mixture was diluted with additional dichloromethane, quenched with saturated sodium bicarbonate, and extracted 2 times with dichloromethane. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 20% ethyl acetate in dichloromethane. Fractions were concentrated to give the title compound (390 mg, 37%). MS (ESI) m/z = 405, 407 (MH^+) and 427, 429 (MNa^+).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-(hydroxymethyl)-2-piperazinone

[00537] 1,1-dimethylethyl 4-{[(bromoacetyl)(cyclobutyl)amino]methyl}-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (390 mg, 0.96 mmol) was stirred in dichloromethane (2 mL) and trifluoroacetic acid (2 mL) for 2 hours. The mixture was concentrated thoroughly and the residue dissolved in dichloromethane (2 mL). Potassium carbonate (1060 mg, 7.68 mmol) was added and the mixture stirred for 1 hour. N,N-Diisopropylethylamine (0.838 mL, 4.80 mmol) was added and the mixture stirred for 2 hours. The mixture was quenched with water and extracted 3 times with dichloromethane. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue

was dissolved in N,N-dimethylformamide (5 mL) before 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (220 mg, 0.722 mmol) and N,N-diisopropylethylamine (0.504 mL, 2.89 mmol) were added. 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.571 mL, 0.961 mmol) was added drop-wise and the mixture stirred for 2 hours. The mixture was quenched with water and extracted 2 times with ethyl acetate. The combined ethyl acetate layers were washed with brine, washed with 5% lithium chloride, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 100% ethyl acetate in dichloromethane. Fractions were concentrated to give the title compound (95 mg, 28%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 8.38 - 8.51 (m, 1 H), 7.53 - 7.67 (m, 1 H), 5.10 - 5.23 (m, 0.5 H), 4.76 - 4.96 (m, 1.5 H), 4.61 - 4.75 (m, 1 H), 4.51 - 4.60 (m, 0.5 H), 4.28 - 4.41 (m, 0.5 H), 4.06 - 4.20 (m, 0.5 H), 3.75 - 3.86 (m, 0.5 H), 3.64 - 3.75 (m, 0.5 H), 3.49 - 3.64 (m, 2 H), 3.37 - 3.49 (m, 1.5 H), 2.08 - 2.29 (m, 3 H), 1.87 - 2.08 (m, 2 H), 1.54 - 1.72 (m, 2 H), 0.96 - 1.06 (m, 2 H), 0.90 (m, 2 H). MS (ESI) m/z 471, 473 (MH^+).

EXAMPLE 194

(Compound 194)

1-[(1*R*,3*s*,5*S*)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

[00538] Methyl 3-chloro-6-(1*H*-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylate (796 mg, 1.848 mmol) was slurried in methanol (10 mL) and water (10 mL) before sodium hydroxide (1M) (5.54 mL, 5.54 mmol) was added. The mixture was stirred for 2 hours and concentrated. The residue was co-evaporated with toluene 2 times to help remove water. The residue was dissolved in N,N-dimethylformamide (2 mL) before 1-[(1*R*,3*s*,5*S*)-bicyclo[3.1.0]hex-3-yl]-2-piperazinone hydrochloride (100 mg, 0.461 mmol) and N,N-diisopropylethylamine (0.322 mL, 1.85 mmol) were added. 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.549 mL, 0.923 mmol) was added dropwise and the mixture stirred for 2 hours. The mixture was quenched with water and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5% lithium chloride, dried over sodium sulfate, and concentrated. The residue was purified by silica gel chromatography eluting with a gradient of 0% to 10% methanol in dichloromethane. Fractions were concentrated and the residue purified by reverse phase HPLC to give the title compound (6.0 mg, 2.6%). ^{1}H NMR (400 MHz, METHANOL-d_4) □ ppm 9.49 - 9.66 (m, 1 H), 9.18 - 9.33 (m, 1 H), 8.22 - 8.32 (m, 1 H), 8.09 - 8.20 (m, 1 H), 7.74 - 7.90 (m, 1 H),

4.50 - 4.72 (m, 2 H), 4.27 - 4.42 (m, 1 H), 4.09 - 4.19 (m, 1 H), 3.90 - 4.00 (m, 1 H), 3.40 - 3.53 (m, 2 H), 1.75 - 1.97 (m, 4 H), 1.26 - 1.44 (m, 2 H), 0.34 - 0.53 (m, 1 H), 0.19 - 0.33 (m, 1 H). MS (ESI) m/z 493, 495 (MH^+).

EXAMPLE 195

(Compound 195)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(*trans*-4-hydroxycyclohexyl)-5-methyl-2-piperazinone

Step A

1,1-dimethylethyl {2-[(trans-4-hydroxycyclohexyl)amino]-1-methyl-2-oxoethyl}carbamate

[00539] To a solution of *N*-{[(1,1-dimethylethyl)oxy]carbonyl}alanine (2.0 g, 11 mmol) in N,N-dimethylformamide (50 mL) was added *trans*-4-aminocyclohexanol hydrochloride (1.8 g, 12 mmol), and N,N-diisopropylethylamine (5.5 mL, 32 mmol), followed by dropwise addition of 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (7.54 mL, 12.7 mmol). The mixture was stirred for 2 hours, quenched with water, and extracted with ethyl acetate. The organic phase was washed with brine, washed with 5% lithium chloride, dried over sodium sulfate and concentrated to give the title compound (1.1 g, 36 %). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 7.47 - 7.65 (m, 1 H), 6.69 - 6.88 (m, 1 H), 4.41 - 4.66 (m, 1 H), 3.82 - 3.96 (m, 1 H), 3.39 - 3.51 (m, 1 H), 1.79 (br. s., 2 H), 1.70 (br. s., 2 H), 1.30 - 1.40 (m, 9 H), 1.14 - 1.24 (m, 5 H), 1.11 (d, 3 H).

Step B

N^1-(trans-4-{[(1,1-dimethylethyl)(dimethyl)silyl]oxy}cyclohexyl)-N^2-{[(1,1-dimethylethyl)oxy]carbonyl}alaninamide

[00540] To a mixture of 1,1-dimethylethyl {2-[(*trans*-4-hydroxycyclohexyl)amino]-1-methyl-2-oxoethyl}carbamate (1.1 g, 3.8 mmol), imidazole (0.523 g, 7.68 mmol), and *N,N-dimethyl-4-pyridinamine* (0.047 g, 0.38 mmol) in N,N-dimethylformamide (25 mL) was added tert-butyldimethylchlorosilane (0.695 g, 4.61 mmol). The mixture was stirred for 4 hours and diluted with 100 mL of ethyl acetate. The mixture was washed with 10% citric acid, washed with brine, washed with 5% lithium chloride, dried over sodium sulfate, and concentrated to give the title compound (1.4 g, 91%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 7.47 - 7.68 (m, 1 H), 6.62 - 6.90 (m, 1 H), 3.81 - 3.98 (m, 1 H), 3.52 - 3.63 (m, 1 H), 3.39 - 3.52 (m, 1 H), 1.66 - 1.87 (m, 4 H), 1.36 (s, 9 H), 1.15 - 1.31 (m, 4 H), 1.12 (d, 3 H), 0.85 (s, 9 H), 0.03 (s, 6 H).

Step C

1,1-dimethylethyl {2-[(trans-4-{[(1,1-dimethylethyl)(dimethyl)silyl]oxy}cyclohexyl)amino]-1-methylethyl}carbamate

[00541] To a 5 °C slurry of N^1-(*trans*-4-{[(1,1-dimethylethyl)(dimethyl)silyl]oxy}cyclohexyl)-N^2-{[(1,1-dimethylethyl)oxy]carbonyl}alaninamide (1.4 g, 3.5 mmol) in tetrahydrofuran (8.74 ml) and toluene (8.74 ml) was added sodium bis(2-methoxyethoxy)aluminumhydride (3.20 ml, 10.5 mmol) slowly dropwise. The mixture was allowed to warm to room temperature and then heated to 35 °C for 16 hours. The mixture was cooled in an ice-bath and carefully quenched with 5M sodium hydroxide at such a rate to keep internal temperature below 20 °C. The mixture was stirred for 20 minutes at room temperature before 30 mL of toluene was added. The layers were separated and the organic phase washed 2 times with 10 mL of 5M sodium hydroxide before being dried over sodium sulfate and concentrated. The resulting oil solidified upon standing. LC-MS analysis showed incomplete reaction. The material was subject to the same reaction conditions as just described, except that the mixture was heated to 40 °C for 16 hours. The mixture was cooled to 5 °C and quenched slowly with 5M sodium hydroxide. The mixture was allowed to warm to room temperature and stirred for 30 minutes, extracted 2 times with toluene and the combined organic layers washed with 5M sodium hydroxide, washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 5% methanol in dichloromethane to give the title compound (1.0 g, 74%). MS (ESI) m/z 388 (MH^+).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-5-methyl-2-piperazinone

[00542] 1,1-dimethylethyl {2-[(*trans*-4-{[(1,1-dimethylethyl)(dimethyl)silyl]oxy}cyclohexyl)amino]-1-methylethyl}carbamate (1.0 g, 2.6 mmol) and N,N-diisopropylethylamine (1.8 mL, 10 mmol) in dichloromethane (25 mL) were cooled to 5 °C in an ice bath before bromoacetyl bromide (0.28 mL, 3.2 mmol) was added. The mixture was stirred for 15 minutes and then allowed to warm to room temperature. The mixture was diluted with dichloromethane, washed with saturated sodium bicarbonate, washed with brine, dried over sodium sulfate, and concentrated. The residue was taken up in N,N-dimethylformamide (25 mL) and cesium carbonate (6.0 g, 18 mmol) added. The mixture was stirred at room temperature for 3 days. The mixture was diluted with water and extracted 2 times with ethyl acetate. The combined organic layers were dried over sodium sulfate and concentrated. The residue was dissolved in 20 mL of dichloromethane and 20

mL of trifluoroacetic acid was added. The mixture was stirred for 2 hours and concentrated, diluted with saturated sodium bicarbonate and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate and concentrated. The residue was dissolved in N,N-dimethylformamide (3 mL) before 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (200 mg, 0.66 mmol) and N,N-diisopropylethylamine (0.573 mL, 3.28 mmol) were added. 1-Propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.586 mL, 0.985 mmol) was added dropwise and the mixture stirred for 4 hours. The mixture was diluted with water and extracted 2 times with ethyl acetate. The combined organic layers were washed with brine, washed with 5% lithium chloride, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 5% methanol in dichloromethane to give the title compound (25 mg, 7.6%). ^{1}H NMR (400 MHz, METHANOL-d_4) □ ppm 8.22 - 8.46 (m, 1 H), 7.46 - 7.66 (m, 1 H), 4.89 - 5.05 (m, 1 H), 4.55 - 4.78 (m, 1 H), 4.12 - 4.54 (m, 2.5 H), 3.76 - 4.00 (m, 0.5 H), 3.37 - 3.65 (m, 3 H), 2.06 - 2.20 (m, 1 H), 1.86 - 2.07 (m, 3 H), 1.48 - 1.79 (m, 2 H), 1.17 - 1.48 (m, 6 H), 1.01 - 1.11 (m, 2 H), 0.84 (m, 2 H). MS (ESI) m/z 499, 501 (MH^+).

EXAMPLE 196

(Compound 196)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3-oxocyclopentyl)-2-piperazinone

[00543] 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(+/- cis)-3-hydroxycyclopentyl]-2-piperazinone (racemic mixture of +/- cis) (530 mg, 1.1 mmol) was dissolved in dichloromethane (10 mL) and Dess-Martin periodinane (716 mg, 1.69 mmol) was added. The mixture was stirred for 2 hours. An additional amount of Dess-Martin reagent (200 mg) was added and the mixture stirred for 1 hour. The mixture was quenched with saturated sodium bicarbonate and extracted 2 times with dichloromethane. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 50% acetone in dichloromethane to give the title compound (485 mg, 87%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 8.45 (d, 1 H), 7.60 (s, 1 H), 4.81 - 5.08 (m, 1 H), 4.49 (s, 1 H), 4.24 (d, 1 H), 4.05 (d, 1 H), 3.87 (d, 1 H), 3.38 - 3.57 (m, 2 H), 2.37 (d, 1 H), 2.15 - 2.34 (m, 4 H), 1.95 - 2.10 (m, 2 H), 0.97 - 1.07 (m, 2 H), 0.79 - 0.92 (m, 2 H). MS (ESI) m/z 469, 471 (MH^+).

EXAMPLE 197

(Compound 197)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(cyclobutylmethyl)-2-piperazinone

Step A

1-cyclobutylmethanamine hydrochloride

[00544] Borane-tetrahydrofuran complex (1M in tetrahydrofuran) (68.8 mL, 68.8 mmol) was added slowly dropwise over 15 minutes to a solution of cyclobutanecarbonitrile (4.65 g, 57.3 mmol) in tetrahydrofuran (15 mL). The mixture was heated at reflux for 16 hours and then cooled to room temperature. Methanol (75 mL) was added slowly dropwise over 15 minutes. The mixture was cooled to 5 °C in an ice bath before gaseous hydrogen chloride was bubbled into the mixture for 30 minutes. The mixture was allowed to warm to room temperature and then refluxed for 90 minutes. The mixture was allowed to cool to room temperature and concentrated. The residue was co-evaporated 2 times with methanol and concentrated. Ethyl ether was added and solids were collected by filtration and taken up in hot isopropanol, filtered, and hot acetonitrile added to the filtrate. Solids formed upon cooling and were collected by filtration. The solids were dried under vacuum to give the title compound (1.1 g, 16%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 8.08 (br. s., 2 H), 2.79 (d, 2 H), 2.51 - 2.62 (m, 1 H), 1.94 - 2.08 (m, 2 H), 1.65 - 1.90 (m, 4 H).

Step B

1,1-dimethylethyl 4-(cyclobutylmethyl)-3-oxo-1-piperazinecarboxylate

[00545] To a solution methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (1.4 g, 5.9 mmol) in methanol (25 ml) was added sodium sulfate (5.2 g, 37 mmol), 1-cyclobutylmethanamine hydrochloride (0.79 g, 6.5 mmol) and N,N-diisopropylethylamine (1.1 ml, 6.5 mmol). The mixture was stirred for 20 minutes before sodium borohydride (0.27 g, 7.1 mmol) was added portion-wise in order to control frothing. The mixture was stirred at room temperature for 18 hours, quenched with saturated sodium bicarbonate, and extracted with ethyl acetate. The organic phase was washed with brine, dried over sodium sulfate, and concentrated to give the title compound (1.35 g, 86%). MS (ESI) m/z = 269 (MH^+).

Step C

1-(cyclobutylmethyl)-2-piperazinone hydrochloride

[00546] 1,1-dimethylethyl 4-(cyclobutylmethyl)-3-oxo-1-piperazinecarboxylate (1.3 g, 4.8 mmol) was dissolved in tetrahydrofuran (10 mL) before hydrogen chloride (4M in

dioxane) (9.7 mL, 39 mmol) was added. The mixture was stirred for 2 hours, concentrated, and the residue dried under vacuum. The reaction was not complete. The residue was re-dissolved in 4M hydrogen chloride in dioxane (9.7 mL, 39 mmol) and stirred overnight at room temperature. The mixture was concentrated and the residue dried under vacuum to give the title compound (1.0 g, 99%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 9.89 (br. s., 2 H), 3.61 - 3.68 (m, 2 H), 3.46 - 3.52 (m, 2 H), 3.38 (d, 2 H), 3.27 - 3.35 (m, 1 H), 2.52 - 2.60 (m, 1 H), 1.91 - 2.05 (m, 2 H), 1.76 - 1.90 (m, 2 H), 1.61 - 1.76 (m, 2 H).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclobutylmethyl)-2-piperazinone

[00547] 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (115 mg, 0.377 mmol) was dissolved in N,N-dimethylformamide (4 mL) before 1-(cyclobutylmethyl)-2-piperazinone hydrochloride (93 mg, 0.453 mmol), N,N-diisopropylethylamine (0.264 mL, 1.510 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (172 mg, 0.453 mmol) were added sequentially. The mixture was stirred for 2 hours, quenched with brine, extracted 2 times with ethyl acetate, and concentrated. The residue was purified by silica gel chromatography eluting with a gradient of 0% to 50% ethyl acetate in dichloromethane. Fractions were concentrated and the residue dissolved in ethyl acetate. Hexanes were added until the mixture was cloudy and the mixture was concentrated. The residue was slurried in hexanes and solids were collected by filtration to give the title compound (85 mg, 50%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 8.45 (d, 1 H), 7.59 (s, 1 H), 4.42 (s, 1 H), 4.20 (s, 1 H), 3.98 (t, 1 H), 3.85 (t, 1 H), 3.35 - 3.43 (m, 4 H), 2.52 - 2.61 (m, 1 H), 2.15 - 2.28 (m, 1 H), 1.91 - 2.03 (m, 2 H), 1.76 - 1.89 (m, 2 H), 1.69 (d, 2 H), 0.97 - 1.05 (m, 2 H), 0.86 - 0.92 (m, 2 H). MS (ESI) m/z 455, 457 (MH^+).

EXAMPLE 198

(Compound 198)

4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone

[00548] To a mixture of 3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (2.7 g, 9.0 mmol), 1-(trans-4-hydroxycyclohexyl)-2-piperazinone hydrochloride (2.12 g, 9.03 mmol), and N,N-diisopropylethylamine (7.88 mL, 45.1 mmol) in N,N-dimethylformamide (50 mL) was added 1-propanephosphonic acid cyclic anhydride,

50 wt. % solution in ethyl acetate (8.05 mL, 13.5 mmol) dropwise. The mixture was stirred for 4 hours, diluted with water, and extracted 4 times with ethyl acetate. The combined organic layers were washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by silica gel chromatography eluting with a gradient of 0% to 5% methanol in dichloromethane to give the title compound (3.2 g, 74%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 8.90 - 9.11 (m, 1 H), 8.07 (s, 1 H), 4.43 - 4.77 (m, 1 H), 4.38 (s, 1 H), 4.08 - 4.26 (m, 2 H), 3.95 (t, 1 H), 3.82 (t, 1 H), 3.28 - 3.41 (m, 3 H), 1.85 (d, 2 H), 1.42 - 1.65 (m, 4 H), 1.13 - 1.33 (m, 2 H). MS (ESI) m/z 479, 481 (MH^+).

EXAMPLE 199

(Compound 199)

1-[(1*R*,3*s*,5*S*)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

[00549] To 3-chloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (48.8 mg, 0.185 mmol) in N,N-dimethylformamide (2 mL) at 5 °C was added 1-[(1*R*,3*s*,5*S*)-bicyclo[3.1.0]hex-3-yl]-2-piperazinone hydrochloride (40 mg, 0.185 mmol) and N,N-diisopropylethylamine (0.161 mL, 0.923 mmol). 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.165 mL, 0.277 mmol) was added drop-wise. The reaction was stirred for 2 hours and the reaction mixture injected directly onto a reverse phase HPLC column to give the title compound (50 mg, 64%). ^{1}H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 8.22 - 8.46 (1 H, m), 7.67 (1 H, d), 7.11 (1 H, t), 4.63 - 4.90 (1 H, m), 4.58 (1 H, s), 4.40 (1 H, s), 4.23 - 4.34 (1 H, m), 3.93 (1 H, t), 3.42 (2 H, dt), 1.85 - 1.96 (2 H, m), 1.72 - 1.85 (2 H, m), 1.21 - 1.37 (2 H, m), 0.25 - 0.46 (2 H, m). MS (ESI) m/z 427, 429 (MH^+).

EXAMPLE 200

(Compound 200)

1-[(1*R*,3*s*,5*S*)-bicyclo[3.1.0]hex-3-yl]-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

[00550] To 3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (55.2 mg, 0.185 mmol) in N,N-dimethylformamide (2 mL) at 5 °C was added 1-[(1*R*,3*s*,5*S*)-bicyclo[3.1.0]hex-3-yl]-2-piperazinone hydrochloride (40 mg, 0.19 mmol) and N,N-diisopropylethylamine (0.161 mL, 0.923 mmol). 1-propanephosphonic acid cyclic

anhydride, 50 wt. % solution in ethyl acetate (0.165 mL, 0.277 mmol) was added drop-wise. The reaction was stirred for 2 hours and the reaction mixture injected directly onto a reverse phase HPLC column to give the title compound (50 mg, 64%). ^{1}H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 8.35 (1 H, dd), 7.64 (1 H, s), 4.62 - 4.87 (1 H, m), 4.58 (1 H, s), 4.39 (1 H, s), 4.19 - 4.30 (1 H, m), 3.84 - 4.01 (1 H, m), 3.30 - 3.57 (2 H, m), 1.90 (2 H, ddd), 1.70 - 1.84 (2 H, m), 1.24 - 1.35 (2 H, m), 0.27 - 0.48 (2 H, m). MS (ESI) m/z = 461, 463 (MH^+).

EXAMPLE 201

(Compound 201)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(2*r*,3a*R*,6a*S*)-5-*syn*-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

Step A

5,5-dimethyltetrahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'(3'H)-one

[00551] A solution of tetrahydro-2,5(1*H*,3*H*)-pentalenedione (3.0 g, 21.7 mmol), neopentyl glycol (2.3 g, 4.3 mmol) and TsOH.H_2O (0.8 g, 4.3 mmol) in benzene (108 mL) was heated under reflux in a Dean-Stark trap overnight. Diethyl ether was added and the mixture was washed with 10% NaOH, water, and brine, dried ($MgSO_4$), filtered, and evaporated. The residue was purified by silica gel chromatography (0-50% EtOAc/hexs) to provide the title compound (2.1 g, 44%) as a white solid.

Step B

(3a'R,6a'S)-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'-ol

[00552] $NaBH_4$ (0.39 g, 10.4 mmol) was added to a -45 °C solution of 5,5-dimethyltetrahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'(3'*H*)-one (1.2 g, 5.2 mmol) in EtOH (14.6 mL). The reaction mixture was stirred for 2 hours at this temperature and allowed to warm slowly to room temperature. The reaction mixture was evaporated and CH_2Cl_2 and sat'd $NaHCO_3$ were added. The aqueous phase was extracted with CH_2Cl_2. The organic phases were combined, dried (Na_2SO_4), filtered, and evaporated. The residue was purified by silica gel chromatography (0-50% EtOAc/hexs) to provide the title compound (0.47 g, 40%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.23 (quin, *J*=5.9 Hz, 1 H), 3.51 (s, 2 H), 3.48 (s, 2 H), 2.49 - 2.60 (m, 2 H), 2.23 (dd, *J*=13.5, 9.3 Hz, 2 H), 2.05 - 2.15 (m, 2 H), 1.92 (dd, *J*=13.5, 5.2 Hz, 2 H), 1.53 (ddd, *J*=13.1, 5.6, 5.4 Hz, 2 H), 0.97 (s, 6 H).

Step C

(3a'R,6a'S)-5'-azido-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalene]

[00553] MsCl (0.19 mL, 2.5 mmol) was added to a solution of (3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-ol (0.47 g, 2.1 mmol) and DIPEA (0.73 mL, 4.2 mmol) in CH_2Cl_2 (10.4 mL). The reaction mixture was stirred for 30 minutes and sat'd $NaHCO_3$ was added. The solution was extracted with CH_2Cl_2 and the organic layer was dried (Na_2SO_4), filtered, and evaporated to provide a yellow solid. The solid was stirred in a solution of NaN_3 (0.54 g, 8.4 mmol) in DMF (10 mL). The reaction mixture was stirred at room temperature for 2 hours and heated at 45 °C overnight. Water was added and the solution was extracted with 10% CH_2Cl_2 in hexanes. The organic layer was dried (Na_2SO_4), filtered and evaporated. The residue was passed through a short pad of silica gel eluting with 10% EtOAc/hexs to provide the title compound (0.49 g, 94%) as a clear oil. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.03 (quin, *J*=5.1 Hz, 1 H), 3.48 (s, 2 H), 3.47 (s, 2 H), 2.61 - 2.75 (m, 2 H), 2.15 - 2.26 (m, 2 H), 1.90 (ddd, *J*=13.3, 8.3, 5.1 Hz, 2 H), 1.60 - 1.74 (m, 4 H), 0.97 (s, 6 H).

Step D

1,1-dimethylethyl 4-[(3a'R,6a'S)-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl]-3-oxo-1-piperazinecarboxylate

[00554] A solution of (3a'*R*,6a'*S*)-5'-azido-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalene] (0.49 g, 2.0 mmol) and catalytic Pd/C (5%) in MeOH (8 mL) was stirred under an atmospheric pressure of hydrogen for 1 hour. The reaction mixture was filtered through celite and evaporated to provide the amine as an oil. The title compound was obtained (0.55 g, 68%) from the above amine and methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (0.5 g, 2.2 mmol) following a previously described procedure. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.03 - 5.21 (m, 1 H), 4.08 (s, 2 H), 3.60 (t, *J*=5.1 Hz, 2 H), 3.48 (d, *J*=4.9 Hz, 4 H), 3.25 (t, *J*=5.1 Hz, 2 H), 2.54 - 2.68 (m, 2 H), 2.40 (dd, *J*=13.1, 8.6 Hz, 2 H), 1.64 - 1.75 (m, 2 H), 1.50 - 1.64 (m, 4 H), 1.47 (s, 9 H), 0.96 (s, 6 H).

Step E

1,1-dimethylethyl 4-[(2r,3aR,6aS)-5-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate

[00555] A solution of 1,1-dimethylethyl 4-[(3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl]-3-oxo-1-piperazinecarboxylate (0.55 g, 1.3 mmol) and $TsOH.H_2O$ (0.13 g, 0.67 mmol) in acetone (13 mL) and water (0.25 mL) was stirred at room temperature for 4 hours. Sat'd $NaHCO_3$ was added and the solution was extracted with EtOAc (3x). The organic layers were combined, dried (Na_2SO_4), filtered, and evaporated to give the ketone as a clear oil. This ketone was dissolved in MeOH (13 mL) and cooled to 0 °C. $NaBH_4$ (0.10 g, 2.68 mmol) was added and the reaction mixture was

stirred for 1 hour. The solution was evaporated and taken up in EtOAc and sat'd $NaHCO_3$. The aqueous phase was extracted with EtOAc (3x) and the organic layers were combined, dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (50-100% EtOAc/hexs) to afford the title compound (0.34 g, 79%) as a white foam. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.08 - 5.24 (m, 1 H), 3.99 - 4.11 (m, 3 H), 3.59 (t, *J*=5.2 Hz, 2 H), 3.24 (t, *J*=5.2 Hz, 2 H), 2.39 - 2.54 (m, 2 H), 2.13 - 2.28 (m, 2 H), 1.76 (s, 1 H), 1.65 - 1.75 (m, 2 H), 1.57 - 1.64 (m, 2 H), 1.47 (s, 9 H), 1.24 - 1.36 (m, 2 H).

Step F

1,1-dimethylethyl 3-oxo-4-{(2r,3aR,6aS)-5-[(phenylcarbonyl)oxy]octahydro-2-pentalenyl}-1-piperazinecarboxylate

[00556] DIAD (0.07 mL, 0.36 mmol) was added dropwise to a 0 °C solution of 1,1-dimethylethyl 4-[(2*r*,3a*R*,6a*S*)-5-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (0.091 g, 0.28 mmol), triphenylphosphine (0.095 g, 0.36 mmol), and benzoic acid (0.051 g, 0.42 mmol) in THF (2.8 mL). The reaction mixture was stirred at room temperature for 2 hours and evaporated to dryness. The residue was purified by silica gel chromatography (0-50% EtOAc/hexs) to afford the title compound (0.099 g, 83%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.98 (d, *J*=7.8 Hz, 2 H), 7.50 - 7.56 (m, 1 H), 7.41 (t, *J*=7.7 Hz, 2 H), 5.47 (br. s., 1 H), 4.93 - 5.05 (m, 1 H), 4.08 (s, 2 H), 3.60 (t, *J*=5.1 Hz, 2 H), 3.26 (t, *J*=5.1 Hz, 2 H), 2.76 - 2.88 (m, 2 H), 2.25 (dd, *J*=14.1, 7.2 Hz, 2 H), 1.68 - 1.82 (m, 2 H), 1.55 - 1.67 (m, 4 H), 1.46 (s, 9 H).

Step G

1,1-dimethylethyl 4-[(2r,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate

[00557] A solution of 1,1-dimethylethyl 3-oxo-4-{(2*r*,3a*R*,6a*S*)-5-[(phenylcarbonyl)oxy]octahydro-2-pentalenyl}-1-piperazinecarboxylate (0.099 g, 0.23 mmol) in 1M NaOH (0.5 mL, 0.5 mmol) and MeOH (0.5 mL) was heated at 55 °C for 1.5 hour and diluted with EtOAc and water. The aqueous phase was extracted with EtOAc and the organic phases were combined, dried (Na_2SO_4), filtered and evaporated. The residue was passed through a short plug of silica gel, eluting with EtOAc to provide the title compound (0.076 g, 98%) as a white foam. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.85 - 5.00 (m, 1 H), 4.39 (br. s., 1 H), 4.05 (s, 2 H), 3.58 (t, *J*=5.2 Hz, 2 H), 3.24 (t, *J*=5.1 Hz, 2H), 2.70 - 2.82 (m, 2 H), 1.96 (dd, *J*=13.5, 6.7 Hz, 2 H), 1.82 (br. s., 1 H), 1.63 - 1.77 (m, 2 H), 1.39 - 1.56 (m, 13 H).

Step H

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

[00558] A solution of 1,1-dimethylethyl 4-[(2*r*,3a*R*,6a*S*)-5-*syn*-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (0.076 g, 0.23 mmol) in CH_2Cl_2 (2.3 mL) and 4N HCl/dioxane (0.58 mL, 2.3 mmol) was stirred at room temperature overnight and evaporated to dryness to provide the amine as a white solid that was used without further purification. The title compound (0.045 g, 77%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (0.029 g, 0.11 mmol) and the above amine (0.038 g, 0.12 mmol) using a previously described procedure. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.41 - 8.48 (m, 1 H), 7.60 (br. s., 1 H), 4.63 - 4.83 (m, 1 H), 4.44 (s, 1 H), 4.32 (br. s., 1 H), 4.20 (s, 1 H), 4.15 (br. s., 1 H), 3.99 (t, *J*=4.7 Hz, 1 H), 3.82 (t, *J*=4.9 Hz, 1 H), 3.33 (d, *J*=3.6 Hz, 2 H), 2.62 (br. s., 2 H), 2.15 - 2.28 (m, 1 H), 1.67 - 1.86 (m, 4H), 1.35 (dd, *J*=11.4, 6.1 Hz, 2 H), 1.25 (dd, *J*=11.7, 5.4 Hz, 2 H), 0.98 - 1.06 (m, 2 H), 0.89 (q, *J*=5.1 Hz, 2 H). ES-LCMS m/z: 511 (M+1).

EXAMPLE 202

(Compound 202)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(2*r*,3a*R*,6a*S*)-5-*anti*-hydroxy-5-methyloctahydro-2-pentalenyl]-2-piperazinone

[00559] A solution of 1,1-dimethylethyl 4-[(2*r*,3a*R*,6a*S*)-5-*anti*-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (0.24 g, 0.75 mmol) in CH_2Cl_2 (7.5 mL) and 4N HCl/dioxane (1.9 mL, 7.5 mmol) was stirred at room temperature overnight and evaporated to dryness to provide the amine as a white solid that was used without further purification. The title compound (0.33 g, 87%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (0.23 g, 0.75 mmol) and the above amine (0.17 g, 0.75 mmol) using a previously described procedure. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.45 (br. s., 1 H), 7.60 (s, 1 H), 4.85 - 5.04 (m, 1 H), 4.61 (t, *J*=4.8 Hz, 1 H), 4.45 (s, 1 H), 4.22 (s, 1 H), 3.99 (t, *J*=4.8 Hz, 1 H), 3.73 - 3.88 (m, 2 H), 3.26 - 3.41 (m, 2 H), 2.34 (d, *J*=6.0 Hz, 2 H), 2.16 - 2.28 (m, 1 H), 1.96 - 2.09 (m, 2 H), 1.63 - 1.77 (m, 2 H), 1.41 (dd, *J*=11.4, 6.2 Hz, 2 H), 0.97 - 1.15 (m, 4 H), 0.85 - 0.94 (m, 2 H). ES-LCMS m/z: 511 (M+1).

EXAMPLE 203

(Compound 203)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(2*s*,3a*R*,6a*S*)-5-*anti*-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

Step A

(3a'R,6a'S)-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl benzoate

[00560] DIAD (0.44 mL, 2.3 mmol) was added dropwise to a 0 °C solution of (3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-ol (0.47 g, 2.06 mmol), triphenylphosphine (0.59 g, 2.26 mmol) and benzoic acid (0.30 g, 2.47 mmol) in THF (20 mL). The mixture was stirred at 0 °C for 5 hours, diluted with water and extracted with EtOAc. The organic phase was dried (Na_2SO_4), filtered, evaporated and purified by silica gel chromatography (0-40% EtOAc/hexs) to afford the title compound (0.45 g, 66%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.96 - 8.04 (m, 2 H), 7.50 - 7.57 (m, 1 H), 7.42 (t, *J*=7.7 Hz, 2 H), 5.48 - 5.54 (m, 1 H), 3.49 (s, 4H), 2.71 - 2.85 (m, 2 H), 2.23 (dd, *J*=13.4, 8.9 Hz, 2 H), 2.06 - 2.17 (m, 2 H), 1.70 - 1.86 (m, 4 H), 0.97 (s, 6 H).

Step B

(3a'R,6a'S)-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'-ol

[00561] A solution of (3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl benzoate (0.45 g, 1.35 mmol) in MeOH (2mL) and 1M NaOH (2 mL, 2 mmol) was heated at 60 °C for 2 hours. The reaction mixture was diluted with water and extracted with EtOAc. The organic phase was dried (Na_2SO_4), filtered, evaporated and purified by silica gel chromatography (0-50% EtOAc/hexs) to afford the title compound (0.27 g, 88%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.43 (quin, *J*=4.5 Hz, 1 H), 3.48 (s, 2 H), 3.47 (s, 2 H), 2.65 - 2.77 (m, 2 H), 2.24 (dd, *J*=13.3, 8.9 Hz, 2 H), 1.76 - 1.88 (m, 2 H), 1.57 - 1.71 (m, 4 H), 0.97 (s, 6 H).

Step C

(3a'R,6a'S)-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl azide

[00562] MsCl (0.11 mL, 1.43 mmol) was added to a solution of (3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-ol (0.27 g, 1.19 mmol) and DIPEA (0.42 mL, 2.38 mmol) in CH_2Cl_2 (6 mL). The reaction mixture was stirred for 30 minutes and sat'd $NaHCO_3$ was added. The solution was extracted with CH_2Cl_2 (3x) and the organic phases were combined, dried ($NaSO_4$), filtered, and evaporated to give a light yellow solid. The residue was dissolved in DMF (10 mL) and NaN_3 (0.31 g, 4.8 mmol) was added, and the reaction mixture was stirred at room temperature for 2 hours and at 45 °C overnight. Water was added and the solution was extracted with 9:1 hex:CH_2Cl_2. The

organic phases were combined, dried (Na_2SO_4), filtered, evaporated and purified by silica gel chromatography (10% EtOAc/hexs) to afford the title compound (0.29 g, 98%) as a clear oil. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 3.72 - 3.83 (m, 1 H), 3.49 (s, 2 H), 3.48 (s, 2 H), 2.44 - 2.60 (m, 2 H), 2.22 (dd, *J*=13.3, 8.7 Hz, 2 H), 2.07 - 2.18 (m, 2 H), 1.79 (dd, *J*=13.2, 5.5 Hz, 2 H), 1.50 - 1.60 (m, 2 H), 0.97 (s, 6 H).

Step D

1,1-dimethylethyl 4-[(3a'R,6a'S)-5,5-dimethylhexahydro-1'H-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl]-3-oxo-1-piperazinecarboxylate

[00563] The title compound (0.41 g, 86%) was obtained from (3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl azide (0.29 g, 1.17 mmol) following a previously described procedure. 1H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 4.79 - 4.92 (m, *J*=12.3, 12.3, 6.5, 6.2 Hz, 1 H), 4.08 (s, 2 H), 3.59 (t, *J*=5.1 Hz, 2 H), 3.51 (s, 2 H), 3.48 (s, 2 H), 3.24 (t, *J*=5.0 Hz, 2 H), 2.47 - 2.60 (m, 2 H), 2.00 - 2.11 (m, 2 H), 1.90 - 2.00 (m, 2 H), 1.87 (dd, *J*=13.2, 2.0 Hz, 2 H), 1.38 - 1.52 (m, 11 H), 0.98 (s, 6 H).

Step E

1,1-dimethylethyl 4-[(2s,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (endo alcohol isomer) and 1,1-dimethylethyl 4-[(2s,3aR,6aS)-5-anti-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (exo alcohol isomer).

[00564] A solution of 1,1-dimethylethyl 4-[(3a'*R*,6a'*S*)-5,5-dimethylhexahydro-1'*H*-spiro[1,3-dioxane-2,2'-pentalen]-5'-yl]-3-oxo-1-piperazinecarboxylate (0.41 g, 1.0 mmol) and $TsOH.H_2O$ (0.096 g, 0.50 mmol) in acetone (10 mL) and water (0.20 mL) was stirred at room temperature for 5 hours. Sat'd $NaHCO_3$ was added and the solution was extracted with EtOAc (3x). The organic layers were combined, dried (Na_2SO_4), filtered, and evaporated to give the ketone as a white solid. This ketone was dissolved in MeOH (10 mL) and cooled to 0 °C. $NaBH_4$ (0.076 g, 2.0 mmol) was added and the reaction mixture was stirred for 3 hours. The solution was evaporated and taken up in EtOAc and sat'd $NaHCO_3$. The aqueous phase was extracted with EtOAc (3x) and the organic layers were combined, dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (60-100% EtOAc/hexs) to afford the endo alcohol isomer (0.18 g, 55%) as the major compound and the exo alcohol isomer (0.033 g, 10%) as the minor compound. Major isomer: 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.78 - 4.91 (m, *J*=12.3, 12.3, 6.5, 6.2 Hz, 1 H), 4.38 (quin, *J*=4.5 Hz, 1 H), 4.06 (s, 2 H), 3.56 (t, *J*=5.2 Hz, 2 H), 3.27 (t, *J*=5.1 Hz, 2 H), 2.43 - 2.55 (m, 2 H), 1.91 - 2.02 (m, 4 H), 1.87 (s, 1 H), 1.51 - 1.66 (m, 4 H), 1.45 (s, 9 H). Minor isomer: 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 4.75 - 4.91 (m, *J*=12.3, 12.3, 6.3, 6.1 Hz, 1 H), 4.41 (quin, *J*=5.2 Hz, 1 H), 4.07 (s, 2 H),

3.60 (t, *J*=5.2 Hz, 2 H), 3.24 (t, *J*=5.1 Hz, 2 H), 2.55 - 2.69 (m, 2 H), 1.95 - 2.06 (m, 2 H), 1.75 - 1.86 (m, 2 H), 1.59 - 1.73 (m, 4 H), 1.46 (s, 9 H), 1.13 - 1.24 (m, 2 H).

Step F

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-anti-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

[00565] A solution of 1,1-dimethylethyl 4-[(2*s*,3a*R*,6a*S*)-5-*anti*-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (exo alcohol isomer) (0.033 g, 0.10 mmol) in CH_2Cl_2 (1.0 mL) and 4N HCl/dioxane (0.26 mL, 1.0 mmol) was stirred at room temperature overnight and evaporated to dryness to provide the amine as a white solid that was used without further purification. The title compound (0.34 g, 65%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (0.034 g, 0.11 mmol) and the above amine (0.10 mmol) using a previously-described procedure. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.41 - 8.49 (m, 1 H), 7.60 (br. s., 1 H), 4.48 - 4.64 (m, 1 H), 4.38 - 4.47 (m, 2 H), 4.16 - 4.27 (m, 2 H), 4.00 (d, *J*=4.5 Hz, 1 H), 3.82 (t, *J*=4.6 Hz, 1 H), 3.35 - 3.40 (m, 2 H), 2.45 (d, *J*=2.2 Hz, 2 H), 2.16 - 2.28 (m, 1 H), 1.82 (d, *J*=3.6 Hz, 2 H), 1.42 - 1.65 (m, 4 H), 1.24 (d, *J*=3.2 Hz, 2 H), 1.02 (d, *J*=7.9 Hz, 2 H), 0.90 (d, *J*=5.1 Hz, 2 H). ES-LCMS m/z: 511 (M+1).

EXAMPLE 204

(Compound 204)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(2*s*,3a*R*,6a*S*)-5-*syn*-hydroxyoctahydro-2-pentalenyl]-2-piperazinone

[00566] A solution of 1,1-dimethylethyl 4-[(2*s*,3a*R*,6a*S*)-5-*syn*-hydroxyoctahydro-2-pentalenyl]-3-oxo-1-piperazinecarboxylate (endo alcohol isomer) (0.040 g, 0.12 mmol) in CH_2Cl_2 (1.2 mL) and 4N HCl/dioxane (0.31 mL, 1.2 mmol) was stirred at room temperature overnight and evaporated to dryness to provide the amine as a white solid that was used without further purification. The title compound (0.54 g, 86%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (0.041 g, 0.14 mmol) and the above amine (0.12 mmol) using a previously-described procedure. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.45 (m, 1 H), 7.60 (br. s., 1 H), 4.58 - 4.74 (m, 1 H), 4.47 - 4.58 (m, 1 H), 4.44 (s, 1 H), 4.20 (s, 1 H), 4.11 (br. s., 1 H), 4.00 (br. s., 1 H), 3.83 (br. s., 1 H), 3.33 (s, 2 H), 2.34 (d, *J*=3.0 Hz, 2 H), 2.16 - 2.26 (m, 1 H), 1.74 - 1.89 (m, 4 H), 1.51 - 1.66 (m, 2H), 1.34 - 1.48 (m, 2 H), 0.97 - 1.08 (m, 2 H), 0.82 - 0.94 (m, 2 H). ES-LCMS m/z 511 (M+1).

EXAMPLE 205

(Compound 205)

1-[(1*R*,5*S*,6*r*)-bicyclo[3.1.0]hex-6-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone

Step A

1,5□-bicyclo[3.1.0]hex-2-ene-6□-carbaldehyde

[00567] mCPBA (20 g, 87 mmol) was added in portions over 2 hours to a 0 °C solution of norbornadiene (11.5 mL, 113 mmol) in CH_2Cl_2 (300 mL). After 3 hours at room temperature, the suspension was filtered. The organic layer was washed with ice cold 5% $NaHCO_3$ solution and ice cold water, dried ($MgSO_4$), filtered, evaporated to provide the endo aldehyde as a clear oil. The oil was taken up in MeOH (100 mL) and NaOMe (7g, 130 mmol) was added. The mixture was heated under reflux for 24 hours, diluted with water (150 mL), and extracted with Et_2O. The organic layer was washed with water, brine, dried ($MgSO_4$), filtered through a pad of silica gel, rinsed with Et_2O, and evaporated to provide the title compound (5.2 g, 55%) as a dark brown oil. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 9.34 (d, *J*=4.6 Hz, 1 H), 5.98 (dd, *J*=5.4, 2.1 Hz, 1 H), 5.59 - 5.64 (m, 1 H), 2.72 - 2.82 (m, 1 H), 2.62 (dt, *J*=4.2, 2.1 Hz, 1 H), 2.50 (dd, *J*=18.9, 2.0 Hz, 1 H), 2.39 (td, *J*=6.3, 3.1 Hz, 1 H), 1.25 - 1.31 (m, 1 H).

Step B.

1,5□-bicyclo[3.1.0]hex-2-ene-6□-carboxylic acid

[00568] A solution of silver nitrate (27.6 g, 162 mmol) in water (70 mL) was added to a solution of 1,5□-bicyclo[3.1.0]hex-2-ene-6□-carbaldehyde (5.2 g, 48 mmol) in EtOH (30 mL). 2M NaOH solution (128 mL, 256 mmol) was added dropwise to the reaction mixture and the solution was stirred in the dark for 4 hours. The reaction mixture was filtered, washed with water and extracted with Et_2O. The aqueous layer was acidified to pH 1 with conc. HCl and extracted with Et_2O (3x). The organic layer was washed with water, dried ($MgSO_4$), filtered, and evaporated to provide the title compound (4.0 g, 67%) as a yellow solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 11.09 (br. s., 1 H), 5.91 - 5.98 (m, 1 H), 5.54 - 5.64 (m, 1 H), 2.72 (dd, *J*=18.4, 6.5 Hz, 1 H), 2.41 - 2.56 (m, 2 H), 2.23 - 2.36 (m, 1 H), 0.90 - 1.05 (m, 1 H).

Step C

1,1-dimethylethyl 1,5□-bicyclo[3.1.0]hex-2-en-6□-ylcarbamate

[00569] Triethylamine (3.7 mL, 26.6 mmol) and ethyl chloroformate (2.6 mL, 27.1 mmoL) were slowly added to a 0°C solution of 1,5□-bicyclo[3.1.0]hex-2-ene-6□-carboxylic acid (3.0 g, 24.2 mmol) in CH_2Cl_2 (60 mL). After 15 mins, the reaction mixture was

evaporated to dryness and the residue was taken up in acetone (30 mL) and cooled to 0 °C. A 0 °C solution of sodium azide (3.14 g, 48.3 mmol) in water (16 mL) was added and the solution was stirred for 15 mins, diluted with water and extracted with EtOAc. The organic layer was dried ($MgSO_4$), filtered, and evaporated to dryness. The dark brown oil was taken up in toluene (60 mL), and tBuOH (9 mL) and the solution was heated under reflux for 24 hours. After evaporation, the residue was purified by silica gel chromatography (0-30% EtOAc/hexs) to provide the title compound (0.8 g, 17%) as an off-white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.80 - 5.93 (m, 1 H), 5.37 - 5.52 (m, 1 H), 4.72 (br. s., 1 H), 2.55 - 2.67 (m, 1 H), 2.37 - 2.48 (m, 1H), 2.02 (d, *J*=5.9 Hz, 1 H), 1.86 (br. s., 1 H), 1.67 (t, *J*=6.5 Hz, 1 H), 1.45 (s, 9 H).

Step D

1,1-dimethylethyl 4-bicyclo[3.1.0]hex-2-en-6-yl-3-oxo-1-piperazinecarboxylate

[00570] A solution of 1,1-dimethylethyl 1,5□-bicyclo[3.1.0]hex-2-en-6□-ylcarbamate (0.80 g, 4.1 mmol) in TFA (3 mL) and CH_2Cl_2 (6 mL) was stirred at room temperature for 1h. Aqueous $NaHCO_3$ was added and the solution was extracted with EtOAc. The organic phase was dried (Na_2SO_4), filtered and evaporated to provide the amine which was used without further purification. A solution of the amine, methyl *N*-{[(1,1-dimethylethyl)oxy]carbonyl}-*N*-(2-oxoethyl)glycinate (0.95 g, 4.1 mmol) and sodium sulfate (4.1 g, 28.7 mmol) in MeOH (11.5 mL) was stirred for 1 hour. $NaBH_4$ (0.17 g, 4.5 mmol) was added and after another 2 hours, NaH (0.26 g, 6.6 mmol) was added and the mixture was stirred for an additional 2 hours before addition of citric acid and EtOAc. The solution was extracted with EtOAc and organic layers were combined, dried (Na_2SO_4), evaporated and the residue was purified by silica gel chromatography (0-60% EtOAc/hexanes) to provide the title compound (0.26 g, 0.94 mmol) as a yellow oil.

Step E

1,1-dimethylethyl 4-bicyclo[3.1.0]hex-6-yl-3-oxo-1-piperazinecarboxylate

[00571] A solution of 1,1-dimethylethyl 4-bicyclo[3.1.0]hex-2-en-6-yl-3-oxo-1-piperazinecarboxylate (0.26 g, 0.94 mmol) and catalytic PtO_2 in EtOAc (10 mL) was stirred under a 20 psi hydrogen atmosphere for 2 hours 15 mins. The reaction mixture was filtered through Celite and evaporated to provide the title compound as a light yellow oil (0.27 g, quant).

Step F

1-bicyclo[3.1.0]hex-6-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

[00572] A solution of 1,1-dimethylethyl (1*R*,5*S*,6*r*)-bicyclo[3.1.0]hex-6-ylcarbamate (0.066 g, 0.24 mmoL) and TFA (0.25 mL, 3.2 mmol) in CH_2Cl_2 (0..5 mL) was stirred at

room temperature for 1h. The mixture was evaporated to dryness to provide the crude amine which was used without further purification. 1-Propanephosphonic acid cyclic anhydride (0.21 mL of a 50% solution in EtOAc, 0.35 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (0.066 g, 0.24 mmol), the above amine (0.24 mmol) and DIPEA (0.25 mL, 1.4 mmol) in DMF (1.6 mL). The reaction mixture as stirred at room temperature overnight, diluted with methylene chloride and washed with 0.5 M sodium carbonate. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was purified by reverse phase HPLC (acetonitrile/water with 0.1% formic acid) to afford the title compound (0.044 g, 40%) as a white solid. 1H NMR (400 MHz, DMSO-*d*6) δ ppm 8.42 - 8.47 (m, 1 H), 7.59 (br. s., 1 H), 4.40 (s, 1 H), 4.16 (s, 1 H), 3.97 (t, *J*=5.0 Hz, 1 H), 3.82 (t, *J*=5.1 Hz, 1 H), 3.32 (d, *J*=4.2 Hz, 2 H), 2.41 (s, 1 H), 2.17 - 2.27 (m, 1 H), 1.74 - 1.84 (m, 2 H), 1.61 - 1.74 (m, 2 H), 1.46 - 1.59 (m, 3 H), 0.97 - 1.14 (m, 3 H), 0.84 - 0.93 (m, 2 H). ES-LCMS m/z 467 (M+1).

EXAMPLE 206

(Compound 206)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone

Step A

N^1-(1-methyl-5-oxo-3-pyrrolidinyl)-N^2-[(4-nitrophenyl)sulfonyl]glycinamide

[00573] A solution of N-[(4-nitrophenyl)sulfonyl]glycine (1.5 g, 5.76 mmol), 4-amino-1-methyl-2-pyrrolidinone hydrochloride (1.005 g, 6.34 mmol), HATU (2.63 g, 6.92 mmol) and DIPEA (3.02 mL, 17.29 mmol) in N,N-dimethylformamide (DMF) (20 mL) was stirred at room temperature for 5 hours. The reaction mixture was poured into ethyl acetate and washed with 1N HCl, water, 5% aqueous LiCl, saturated aqueous $NaHCO_3$ and brine. The acid wash was further extracted with EtOAc (7 x 50 mL). All organic layers were combined and washed with saturated $NaHCO_3$ and dried over Na_2SO_4, filtered and concentrated. The solid was collected and washed with EtOAc to yield N^1-(1-methyl-5-oxo-3-pyrrolidinyl)-N^2-[(4-nitrophenyl) sulfonyl] glycinamide (1.11 g) as a creamy white solid. The filtrate was concentrated, and the precipitated solid was collected and washed with EtOAc and Et_2O to give additional product (0.24 g) as a creamy white solid. Two more iterations of concentration of the filtrate, precipitation and washing with EtOAc and Et_2O, gave an additional 0.20 g of the product. The overall yield for the reaction was 75%. MS (ESI) m/z 357 (M+1).

Step B

1-(1-methyl-5-oxo-3-pyrrolidinyl)-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone

[00574] To a solution of N^1-(1-methyl-5-oxo-3-pyrrolidinyl)-N^2-[(4-nitrophenyl)sulfonyl]glycinamide (1.34 g, 3.76 mmol) in N,N-dimethylformamide (DMF) (25 mL) was added potassium carbonate (4.16 g, 30.1 mmol) and 1,2-dibromoethane (2.63 mL, 30.1 mmol). The mixture was heated at 60 °C overnight, cooled and EtOAc was added. The mixture was filtered through a pad of Celite. The filtrate was washed with 0.5 N HCl/brine, then brine and dried over Na_2SO_4, filtered and concentrated to an orange solid, which was stirred with 1:1 EtOAc/Et_2O for 30 minutes. The solid was collected and washed with 1:1 EtOAc/Et_2O to give 1-(1-methyl-5-oxo-3-pyrrolidinyl)-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone (1.05 g, 73%) as a light yellow solid. MS (ESI) m/z 383 (M+1).

Step C

1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone

[00575] To a suspension of potassium carbonate (1.328 g, 9.61 mmol) in acetonitrile (24 mL) at 50 °C was added thiophenol (0.729 mL, 6.86 mmol). After 30 minutes, a suspension of 1-(1-methyl-5-oxo-3-pyrrolidinyl)-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone (1.05 g, 2.75 mmol) in N,N-Dimethylformamide (DMF) (8 mL) was added dropwise. After stirring at 50 °C for 3 hours, the mixture was cooled, diluted with CH_2Cl_2 and filtered through a pad of celite. The filtrate was concentrated under reduced pressure. The residue was diluted with 55 mL of CH_2Cl_2, then loaded onto SCX columns (2 x 10 g) pretreated with MeOH then CH_2Cl_2. After flushing with 1:1 CH_2Cl_2/MeOH, the column was eluted with 2N NH_3 in MeOH. The filtrate was concentrated to give 1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone (418 mg, 77%) as a brown viscous oil. MS (ESI) m/z = 198 (M+1).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone

[00576] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (120 mg, 0.394 mmol), 1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone (117 mg, 0.591 mmol) and DIPEA (0.206 mL, 1.182 mmol) in N,N-dimethylformamide (DMF) (3 mL) was stirred for 15 minutes, then cooled in an ice bath. 1-Propanephosphonic acid cyclic anhydride (50% wt% in EtOAc, 0.352 mL, 0.591 mmol) was added dropwise. The reaction mixture was stirred for 1.5 hour. The reaction mixture was then dropwise added to water (20 mL) and extracted with EtOAc. The combined organic extract was washed with 5% LiCl and brine, dried over Na_2SO_4, filtered,

concentrated and purified by silica gel chromatography (0-6 % MeOH/CH_2Cl_2) to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone (180 mg, 94%) as a white foam. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.10 - 8.05 (m, 1 H), 7.43 (s, 1 H), 5.50 - 5.30 (m, 1 H), 4.80 - 4.64 (m, 1 H), 4.58 - 4.24 (m, 2 H), 4.10 - 3.95 (m, 1 H), 3.80 - 3.63 (m, 1 H), 3.55 - 3.25 (m, 3 H), 2.90 (s, 3 H), 2.80 - 2.65 (m, 1 H), 2.50 - 2.40 (m, 1 H), 2.08 - 2.00 (m, 1 H), 1.20 - 1.10 (m, 2 H), 0.86 - 0.80 (m, 2 H). ES-LCMS m/z 484 (M+1).

EXAMPLE 207

(Compound 207)

1-[(endo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo [1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

Step A

1,1-dimethylethyl 4-(endo)-bicyclo[2.2.1]hept-2-yl-3-oxo-1-piperazinecarboxylate

[00577] A mixture of 2-aminonorbornane hydrochloride (0.274 g, 2.439 mmol), DIPEA (0.426 mL, 2.439 mmol) and sodium sulfate (1.732 g, 12.19 mmol) was stirred in MeOH (8 mL) for 2 hours, then $NaBH_4$ (0.093 g, 2.439 mmol) was added in portions. The mixture was stirred for 2 hours then 60% NaH dispersion in oil (0.163 g, 4.06 mmol) was added in portions. After 2 hours, aqueous citric acid (10% by wt.) was added slowly to adjust the pH to about 5. The mixture was extracted with EtOAc. The combined organic extract was washed with brine and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-45 % EtOAc/Hexanes) to give 1,1-dimethylethyl 4-(endo)-bicyclo[2.2.1]hept-2-yl-3-oxo-1-piperazine carboxylate (0.39 g, 65%) as a white solid. ES-LCMS m/z 295 (M+1).

Step B

(endo)-1-bicyclo[2.2.1]hept-2-yl-2-piperazinone hydrochloride

[00578] A mixture of 1,1-dimethylethyl 4-(endo)-bicyclo[2.2.1]hept-2-yl-3-oxo-1-piperazinecarboxylate (388 mg, 1.318 mmol), 4*M* HCl in 1,4-dioxane (5 mL, 20.00 mmol) and 1,4-dioxane (7 mL) was stirred at room temperature overnight. The reaction mixture was concentrated to dryness under reduced pressure to give (endo)-1-bicyclo[2.2.1]hept-2-yl-2-piperazinone hydrochloride (308 mg) as a light brown solid, which was used without further purification. ES-LCMS m/z 195 (M+1).

Step C

1-[(endo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

[00579] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (90 mg, 0.295 mmol), (endo)-1-bicyclo[2.2.1]hept-2-yl-2-piperazinone hydrochloride (95 mg, 0.414 mmol) and DIPEA (0.206 mL, 1.182 mmol) in N,N-Dimethylformamide (DMF) (2.5 mL) was stirred at room temperature for 15 minutes, then cooled in an ice bath. 1-Propanephosphonic acid cyclic anhydride (50% wt% in EtOAc, 0.246 mL, 0.414 mmol) was added dropwise. The reaction mixture was stirred for 2 hours and then diluted with EtOAc. The mixture was washed with water, 5% LiCl and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-75 % EtOAc/Hexanes) to give 1-[(endo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone (136 mg, 96%) as a white foam. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.50 - 8.40 (m, 1 H), 7.60 (s, 1 H), 4.60 - 4.05 (m, 4 H), 3.90 - 3.57 (m, 1 H), 3.56 - 3.38 (m, 1.52 H), 2.44 - 2.40 (m, 0.48 H), 2.30 - 2.15 (m, 2 H), 1.75 - 1.62 (m, 1 H), 1.60 - 1.20 (m, 8 H), 1.08 - 0.98 (m, 2 H), 0.94 - 0.82 (m, 2 H). ES-LCMS m/z 481 (M+1).

EXAMPLE 208

(Compound 208)

1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo [1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

Step A

2-[(trans)-bicyclo[3.1.0]hex-3-yl]-1H-isoindole-1,3(2H)-dione

[00580] DIAD (8.11 mL, 41.7 mmol) was added to a solution of (cis)-bicyclo[3.1.0]hexan-3-ol (3.15 g, 32.1 mmol), 1H-isoindole-1,3(2H)-dione (6.14 g, 41.7 mmol), and triphenylphosphine (10.94 g, 41.7 mmol) in THF (300 mL) at 0 °C. The reaction was warmed to room temperature and stirred overnight. Water (25 mL) and EtOAc (50 mL) were added. The organic layer was separated, washed with brine, dried over $MgSO_4$, filtered and concentrated to give a yellow solid. The material was purified on silica gel (hexanes/EtOAc) to give 2-[(trans)-bicyclo[3.1.0]hex-3-yl]-1H-isoindole-1,3(2H)-dione (5.5 g, 24.20 mmol, 75%) as a white solid.

Step B

(trans)-bicyclo[3.1.0]hexan-3-amine hydrochloride

[00581] Hydrazine monohydrate (5.50 mL, 112 mmol) was added to a suspension of 2-[(trans)-bicyclo[3.1.0]hex-3-yl]-1H-isoindole-1,3(2H)-dione (5.1 g, 22.44 mmol) in EtOH (200 mL) and the mixture was heated at reflux for 16 hours. The mixture was cooled to room temperature and Et_2O (50 mL) was added. The solid was filtered off and

the filtrate was concentrated (note: amine appears to be volatile). Et_2O (30 mL) was added and again the solid was filtered off. The filtrate was concentrated then EtOH (20 mL) and Et_2O (20 mL) were added. The solvents were removed under vacuum in an attempt to remove excess hydrazine, then HCl in 1,4-dioxane (4*M*, 5mL) was added. The mixture was concentrated to dryness and used without further purification in the next step.

Step C

1,1-dimethylethyl 4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinecarboxylate

[00582] A mixture of (trans)-bicyclo[3.1.0]hex-3-ylamine hydrochloride (1.098 g, 8.22 mmol), methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (1.9 g, 8.22 mmol), Hunig's base (1.579 mL, 9.04 mmol), and sodium sulfate (7.00 g, 49.3 mmol) was stirred in MeOH (30 mL) for 2 hours, then $NaBH_4$ (0.342 g, 9.04 mmol) was added in portions over ca. 10 minutes. The mixture was stirred for 2 hours then 60% NaH dispersion in oil (0.624 g, 15.61 mmol) was added in portions over ca. 10 min. After 2 hours, aqueous citric acid (30% by wt., 50 mL) was added slowly and the mixture was filtered through Celite and washed with MeOH. The filtrate was concentrated under reduced pressure to remove MeOH and the remaining aqueous layer was extracted with ethyl acetate (2 x 150 mL). The organic layers were combined, washed with saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered and concentrated. The product was purified on silica gel (hexanes/ethyl acetate) to give 1,1-dimethylethyl 4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinecarboxylate (1.67 g, 5.96 mmol, 73%) as a white solid.

Step D

1-[(trans)-bicyclo[3.1.0]hex-3-yl]-2-piperazinone hydrochloride

[00583] To a solution of 1,1-dimethylethyl 4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinecarboxylate (1.67 g, 5.96 mmol) in DCM (30 mL) was added 4*M* HCl in 1,4-dioxane (14.89 mL, 59.6 mmol). The solution was stirred for 16 hours then the solvent was removed under reduced pressure to give the title compound as a white solid that was used without further purification.

Step E

1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo [1,2-a] pyridin-2-yl]carbonyl}-2-piperazinone

[00584] A solution of 3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (110 mg, 0.315 mmol), 1-[(trans)-bicyclo[3.1.0]hex-3-yl]-2-piperazinone hydrochloride (102 mg, 0.473 mmol) and DIPEA (0.220 mL, 1.260 mmol) in N,N-Dimethylformamide (DMF) (2.5 mL) was stirred at room temperature for 15 minutes, then cooled in an ice bath. 1-Propanephosphonic acid cyclic anhydride (50% wt% in

EtOAc, 0.281 mL, 0.473 mmol) was added dropwise. The reaction mixture was stirred for 1.5 hour and then diluted with EtOAc. The mixture was washed with water, 5% LiCl and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by Prep SFC method (40%MeOH/CO_2, 140bars, 40 °C, 10mL/min, 220nm, WhelkO column, 1.9mg/inj.) to give 1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone (72 mg, 45%) as a white solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.20 - 8.05 (m, 1 H), 7.42 (s, 1 H), 4.85 - 4.65 (m, 1 H), 4.56 (s, 1 H), 4.41 (s, 1 H), 4.30 - 4.20 (m, 1 H), 4.00 - 3.90 (m, 1 H), 3.50 - 3.35 (m, 2 H), 2.10 - 2.00 (m, 1 H), 1.98 - 1.70 (m, 4 H), 1.40 - 1.18 (m, 2 H), 1.17 - 1.04 (m, 2 H), 0.85 - 0.75 (m, 2 H), 0.44 - 0.30 (m, 2 H). ES-LCMS m/z 511, 513 (M+1).

EXAMPLE 209

(Compound 209)

2-({4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinyl}carbonyl)-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile

[00585] A mixture of 1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone (61 mg, 0.119 mmol), copper(I) cyanide (42.7 mg, 0.477 mmol) in N,N-dimethylformamide (DMF) (1.5 mL) was heated in microwave oven at 135 °C for 20 minutes. Cooled to room temperature, the reaction mixture was diluted with EtOAc and filtered through a pad of Celite. The filtrate was washed with water/brine twice, brine, and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-50 % EtOAc/Hexanes) to give 2-({4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinyl}carbonyl)-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile (51 mg, 93%) as a white foam. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.35 - 8.25 (m, 1 H), 7.58 (s, 1 H), 4.90 - 4.65 (m, 2 H), 4.58 - 4.45 (m, 1 H), 4.43 (s, 1 H), 4.04 - 3.95 (m, 1 H), 3.50 - 3.35 (m, 2 H), 2.10 - 2.00 (m, 1 H), 1.98 - 1.70 (m, 4 H), 1.40 - 1.28 (m, 2 H), 1.25 - 1.24 (m, 2 H), 0.95 - 0.80 (m, 2 H), 0.45 - 0.34 (m, 2 H). ES-LCMS m/z 458 (M+1).

EXAMPLE 210

(Compound 210)

1-[(exo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

Step A

1,1-dimethylethyl 4-(exo)-bicyclo[2.2.1]hept-2-yl-3-oxo-1-piperazinecarboxylate

[00586] A mixture of exo-2-amino-norbornane (0.175 g, 1.557 mmol), methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (0.3 g, 1.297 mmol) and sodium sulfate (1.106 g, 7.78 mmol) was stirred in MeOH (5 mL) for 2 hours, then $NaBH_4$ (0.059 g, 1.557 mmol) was added in portions. The mixture was stirred for 2 hours then 60% NaH dispersion in oil (0.104 g, 2.59 mmol) was added in portions. After 2 hours, aqueous citric acid (10% by wt.) was added slowly to adjust pH to about 5. The mixture was extracted with EtOAc. The combined organic extract was washed with brine and dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-45% EtOAc/Hexanes) to give 1,1-dimethylethyl 4-(exo)-bicyclo[2.2.1]hept-2-yl-3-oxo-1-piperazinecarboxylate (270 mg, 71%) as a white solid. ES-LCMS m/z 295 (M+1).

Step B

(exo)-1-bicyclo[2.2.1]hept-2-yl-2-piperazinone hydrochloride

[00587] A mixture of 1,1-dimethylethyl 4-(exo)-bicyclo[2.2.1]hept-2-yl-3-oxo-1-piperazinecarboxylate (270 mg, 0.917 mmol), 4*M* HCl in 1,4-dioxane (3 mL, 12.00 mmol) and 1,4-dioxane (5 mL) was stirred at room temperature overnight. The reaction mixture was concentrated dryness to give (exo)-1-bicyclo[2.2.1]hept-2-yl-2-piperazinone hydrochloride (213 mg, 100%) as an off-white solid, which was used without further purification. ES-LCMS m/z 195 (M+1).

Step C

1-[(exo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone

[00588] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (72 mg, 0.236 mmol), (exo)-1-bicyclo[2.2.1]hept-2-yl-2-piperazinone hydrochloride (71.6 mg, 0.307 mmol) and DIPEA (0.165 mL, 0.945 mmol) in N,N-dimethylformamide (DMF) (2 mL) was stirred at room temperature for 15 minutes, then cooled in an ice bath. 1-Propanephosphonic acid cyclic anhydride (50% wt% in EtOAc, 0.197 mL, 0.331 mmol) was added dropwise. The reaction mixture was stirred for 2 hours and then diluted with EtOAc. The mixture was washed with water, 5% LiCl and brine. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-75 % EtOAc/Hexanes) to give 1-[(exo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone (105 mg, 92%) as a white foam. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.50 - 8.40 (m, 1 H), 7.60 (s, 1 H), 4.50 - 4.35 (m, 1 H), 4.33 - 4.08 (m, 2 H), 4.05 - 3.74 (m, 2

H), 3.50 - 3.33 (m, 3 H), 2.30 - 2.18 (m, 3 H), 1.75 - 1.60 (m, 1 H), 1.57 - 1.40 (m, 4 H), 1.30 - 1.05 (m, 2 H), 1.04 - 1.00 (m, 2 H), 0.95 - 0.85 (m, 2 H). ES-LCMS m/z 481 (M+1).

EXAMPLE 211

(Compound 211)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(methyloxy)cyclohexyl]-2-piperazinone

[00589] Sodium hydride (60% oil dispersion) (0.036 g, 0.0009 mol) was added to a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone (0.269 g, 0.00055 mol) in DMF (3 mL) at room temperature, followed by methyl iodide (0.304 mL, 0.0049 mol). The mixture was stirred at room temperature overnight. The reaction was quenched with water and the mixture was extracted with ethyl acetate. The organic layers were combined and washed with water and brine, dried over sodium sulfate and concentrated. Half of the residue was purified by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) to afford 24 mg of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.47 (d, 1 H) 7.62 (m, 1 H) 4.45 (s, 1 H) 4.11 - 4.34 (m, 2 H) 3.92 - 4.09 (m, 1 H) 3.84 (t, 1 H) 3.39 - 3.54 (m, 2 H) 3.24 (s, 3 H) 2.92 - 3.15 (m, 1 H) 2.16 - 2.29 (m, 1 H) 1.95 - 2.14 (m, 2 H) 1.44 - 1.69 (m, 4 H) 1.11 - 1.31 (m, 2 H) 1.00 - 1.11 (m, 2 H) 0.83 - 0.96 (m, 2 H). MS (ESI) m/z 499 (M+1).

EXAMPLE 212

(Compound 212)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-fluorocyclobutyl)-2-piperazinone

Step A

1,1-dimethylethyl (3-fluorocyclobutyl)carbamate

[00590] A solution of 3-fluorocyclobutanecarboxylic acid (1.00 g, 0.0085 mol), diphenylphosphoryl azide (2.74 mL, 0.013 mol) and triethylamine (2.360 mL, 0.017 mol) in tert-butanol (20 mL) was heated at reflux overnight. Saturated aqueous sodium bicarbonate was added followed by evaporation of most of the tert-butanol under reduced pressure. The resulting suspension was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate and concentrated to give the title compound (1.14 g, 71%) as a white solid.

Step B

(3-fluorocyclobutyl)amine hydrochloride

[00591] A mixture of 1,1-dimethylethyl (3-fluorocyclobutyl)carbamate (1.10 g, 0.0058 mol) and 4N HCl in dioxane (20 mL, 0.658 mol) was stirred at room temperature for 1 hour. The solvent was evaporated to give a white solid which was triturated with diethyl ether and dried under vacuum to afford the title compound (0.756 g, 93%).

Step C

N^1-(3-fluorocyclobutyl)-N^2-[(4-nitrophenyl)sulfonyl]glycinamide

[00592] HATU (1.31 g, 0.0034 mol) was added to a mixture of N-[(4-nitrophenyl)sulfonyl]glycine (0.746 g, 0.0029 mol), (3-fluorocyclobutyl)amine hydrochloride (0.360 g, 0.0029 mmol) and DIPEA (1.50 mL, 0.0086 mol) in DMF (50 mL). The mixture was stirred at room temperature overnight. Ethyl acetate and water were subsequently added. The organic layer was washed with water and brine and dried over sodium sulfate. The solvent was evaporated to give the desired product (0.613 g, 64%) as a yellow solid. MS (ESI) m/z 331 (M+1).

Step D

1-(3-fluorocyclobutyl)-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone

[00593] A mixture of N^1-(3-fluorocyclobutyl)-N^2-[(4-nitrophenyl)sulfonyl]glycinamide (0.605 g, 0.00183 mol) and potassium carbonate (1.262 g, 0.0091 mol) in DMF (10 mL) was heated at 60 °C for 30 min. 1,2-Dibromoethane (0.79 mL, 0.0091 mol) was added and heating was continued overnight. Ethyl acetate and water were added to the reaction mixture. The aqueous layer was back extracted with ethyl acetate and the combined organic layers were washed with water and brine, dried over sodium sulfate and concentrated to afford the title compound (0.556 g, 85%) as a brown oil. MS (ESI) m/z 358 (M+1).

Step E

1-(3-fluorocyclobutyl)-2-piperazinone

[00594] Thiophenol (0.40 mL, 0.00385 mol) was added to a suspension of potassium carbonate (0.746 g, 0.0054 mol) in acetonitrile (30 mL) at 50 °C. After 30 min, 1-(3-fluorocyclobutyl)-4-[(4-nitrophenyl)sulfonyl]-2-piperazinone (0.551 g, 0.00154 mol) in acetonitrile (10 mL) was added dropwise. The mixture was heated at 50 °C for one hour. The reaction mixture was cooled to room temperature and filtered through Celite. The solvent was evaporated and the residue was purified on a short silica gel plug eluted with 0-10% methanol:DCM to give the title compound (0.189 g, 71%). MS(ESI) m/z 173 (M+1).

Step F

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-fluorocyclobutyl)-2-piperazinone

[00595] A mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.303 g, 0.00099 mol), 1-(3-fluorocyclobutyl)-2-piperazinone (0.171 g, 0.00099 mol), DIPEA (0.520 mL, 0.0029 mol) and HATU (0.453 g, 0.00119 mol) in DMF (4 mL) was stirred at room temperature. The reaction mixture was diluted with ethyl acetate and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified by silica gel chromatography with DCM:methanol to give the desired compound (0.288 g, 63%) as a mixture of cis and trans isomers. The title (trans) compound (0.114 g, 22%) was isolated by SFC. ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 8.16 - 8.40 (m, 1 H) 7.57 (s, 1 H) 4.97 - 5.33 (m, 2 H) 4.45 - 4.60 (m, 1 H) 4.33 (s, 1 H) 4.16 (t, *J*=5.27 Hz, 1 H) 3.86 - 4.06 (m, 1 H) 3.48 - 3.59 (m, 2 H) 2.54 - 2.77 (m, 2 H) 2.33 - 2.52 (m, 2 H) 1.95 - 2.24 (m, 1 H) 0.97 - 1.18 (m, 2 H) 0.62 - 0.91 (m, 2 H). MS(ESI) m/z 459 (M+1).

EXAMPLE 213

(Compound 213)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-3-fluorocyclobutyl)-2-piperazinone

[00596] The title (cis) compound (0.019 g, 4%) was isolated by SFC from the isomeric mixture from Example 212, Step F. ^{1}H NMR (400 MHz, methanol-d_4) δ ppm 8.30 (d, *J*=3.12 Hz, 1 H) 7.57 (s, 1 H) 4.88 and 4.72 (m, 1 H) 4.56 (s, 1 H) 4.27 - 4.45 (m, 2 H) 4.15 (t, 1 H) 3.97 - 4.06 (m, 1 H) 3.56 (t, 2 H) 2.54 - 2.75 (m, 2 H) 2.26 - 2.50 (m, 2 H) 2.00 - 2.18 (m, 1 H) 0.98 - 1.14 (m, 2 H) 0.74 - 0.90 (m, 2 H). ES-LCMS m/z 459 (M+1).

EXAMPLE 214

(Compound 214)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-ethyl-2-piperazinone

Step A

1,1-dimethylethyl {1-[(cyclobutylamino)carbonyl]propyl}carbamate

[00597] To a solution of 2-({[(1,1-dimethylethyl)oxy]carbonyl}amino)butanoic acid (4.0 g, 20 mmol) in N,N-dimethylformamide (100 mL) was added cyclobutylamine (1.9 mL,

22 mmol), N,N-diisopropylethylamine (10.3 mL, 59.0 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (8.23 g, 21.7 mmol). The mixture was stirred for 2 hours, quenched with water, and extracted 2 times with ethyl acetate.The combined organic layers were washed with brine, washed with 5% lithium chloride, dried over sodium sulfate and concentrated. The residue was slurried in ethyl ether, stirred for 30 minutes, and the solids collected by filtration. The product was purified by passing through a silica gel plug, and eluting with 25% ethyl acetate in dichloromethane to give the title compound (3.1 g, 62%). ^{1}H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 6.00 - 6.39 (m, 1 H), 4.85 - 5.19 (m, 1 H), 4.27 - 4.53 (m, 1 H), 3.78 - 4.03 (m, 1 H), 2.26 - 2.46 (m, 2 H), 1.78 - 1.96 (m, 3 H), 1.52 - 1.78 (m, 3 H), 1.45 (s, 9 H), 0.94 (t, 3 H).

Step B

1,1-dimethylethyl {1-[(cyclobutylamino)methyl]propyl}carbamate

[00598] To a 5 °C slurry of 1,1-dimethylethyl {1-[(cyclobutylamino)carbonyl]-propyl}carbamate (3.12 g, 12.17 mmol) in tetrahydrofuran (30.4 ml) and toluene (30.4 ml) was added Red-Al (11.1 ml, 36.5 mmol) slowly drop-wise. The mixture was allowed to warm to room temperature and then heated to 35 °C for 16 hours. The mixture was cooled in an ice-bath and carefully quenched with 5M sodium hydroxide, which was added at such a rate as to keep the internal temperature below 20 °C. The mixture was stirred for 20 minutes at room temperature before 30 mL of toluene was added. The layers were separated and the organic phase washed 2 times with 10 mL of 5M sodium hydroxide. The organic phase was dried over sodium sulfate and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 10% 2M ammonia/isopropanol in dichloromethane to give the title compound (1.7 g, 59%). ^{1}H NMR (400 MHz, CHLOROFORM-*d*) □ ppm 4.51 - 4.79 (m, 1 H), 3.94 - 4.16 (m, 1 H), 3.44 - 3.64 (m, 1 H), 3.14 - 3.32 (m, 1 H), 2.57 (d, 2 H), 2.20 (d, 2 H), 1.56 - 1.75 (m, 4 H), 1.47 - 1.56 (m, 2 H), 1.21 (d, 9 H), 0.92 (t, 3 H).

Step C

1,1-dimethylethyl (1-{[(chloroacetyl)(cyclobutyl)amino]methyl}propyl)carbamate

[00599] A solution of 1,1-dimethylethyl {1-[(cyclobutylamino)methyl]propyl}carbamate (440 mg, 1.82 mmol) in ethyl acetate (5.0 mL) and 1M sodium bicarbonate (5.0 mL, 5.0 mmol) was cooled to 5 °C in an ice bath before chloroacetyl chloride (0.22 mL, 2.7 mmol) was added. The mixture was slowly allowed to warm to room temperature, stirred for 3 hours, and then extracted 2 times with ethyl acetate. The combined organic layers were washed with saturated sodium bicarbonate,

washed with brine, dried over sodium sulfate, and concentrated to give the title compound (530 mg, 92%) as a clear oil. MS (ESI) m/z 319, 321 (MH^+).

Step D

1,1-dimethylethyl 4-cyclobutyl-2-ethyl-5-oxo-1-piperazinecarboxylate

[00600] 1,1-dimethylethyl (1-{[(chloroacetyl)(cyclobutyl)amino]methyl}propyl)carbamate (530 mg, 1.7 mmol) was dissolved in N,N-dimethylformamide (10 mL) and cooled to 5 °C in an ice bath before cesium carbonate (1.1 g, 3.3 mmol) was added. The mixture was allowed to warm to room temperature and stirred overnight. The mixture was quenched with water and extracted 3 times with ethyl acetate. The combined organic layers were washed with 5% lithium chloride, washed with brine, dried over sodium sulfate, and concentrated to give the title compound (430 mg, 91%). MS (ESI) m/z = 283 (MH^+).

Step E

1-cyclobutyl-5-ethyl-2-piperazinone trifluoroacetate

[00601] 1,1-dimethylethyl 4-cyclobutyl-2-ethyl-5-oxo-1-piperazinecarboxylate (430 mg, 1.52 mmol) was dissolved in dichloromethane (5 mL) before trifluoroacetic acid (5.00 mL) was added. The mixture was stirred for 3 hours and concentrated. The residue was co-evaporated 2 times with toluene to help remove any remaining trifluoroacetic acid. Concentration gave the title compound (490 mg, >99%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 9.07 - 9.49 (m, 2 H), 4.71 - 4.94 (m, 1 H), 3.74 (s, 2 H), 3.63 (dd, 1 H), 3.39 - 3.55 (m, 1 H), 3.25 (dd, 1 H), 2.22 (dt, 2 H), 1.90 - 2.04 (m, 2 H), 1.56 - 1.80 (m, 4 H), 0.99 (t, 3 H).

Step F

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-ethyl-2-piperazinone

[00602] 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (77 mg, 0.252 mmol) was dissolved in N,N-dimethylformamide (2.0 mL) before N,N-diisopropylethylamine (220 µl, 1.26 mmol), 1-cyclobutyl-5-ethyl-2-piperazinone trifluoroacetate (82 mg, 0.25 mmol), and N-[(dimethylamino)(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methylidene]-N-methylmethanaminium hexafluorophosphate (HATU) (115 mg, 0.302 mmol) were added sequentially. The reaction mixture was quenched with water and extracted with ethyl acetate. The organic phase was washed with brine and concentrated. The residue was purified by silica chromatography eluting with a gradient of 0% to 100% ethyl acetate in dichloromethane to give the title compound (63 mg, 53%). ^{1}H NMR (400 MHz, DMSO-d_6) □ ppm 8.46 (s, 1 H), 7.60 (s, 1 H), 4.79 - 5.05 (m, 1 H), 4.62 - 4.77 (m, 1 H), 4.48 (m, 1 H), 3.94 - 4.10 (d, 0.5 H), 3.72 (d, 0.5 H), 3.40 - 3.57 (m, 2 H), 2.17 - 2.28 (m, 1 H), 2.13 (br. s., 2 H), 1.88 - 2.04 (m, 2 H), 1.56 - 1.75 (m, 3 H), 1.40 -

1.57 (m, 1 H), 0.98 - 1.06 (m, 2 H), 0.84 - 0.97 (m, 3 H), 0.79 (t, 2 H). MS (ESI) m/z = 469, 471 (MH^+).

EXAMPLE 215

(Compound 215)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(hydroxymethyl)cyclohexyl]-2-piperazinone

Step A

(trans-4-aminocyclohexyl)methanol hydrochloride

[00603] HCl (4N in dioxane) (3.5 mL, 0.014 mol) was added to a solution of 1,1-dimethylethyl [*trans*-4-(hydroxymethyl)cyclohexyl]carbamate (0.622 g,0.0027 mol) in DCM (10 mL). The mixture was stirred at room temperature for 2 hours. The solvent was evaporated to give the crude title compound (0.449 g). MS (ESI) m/z 130 (M+1).

Step B

1,1-dimethylethyl 4-[trans-4-(hydroxymethyl)cyclohexyl]-3-oxo-1-piperazinecarboxylate

[00604] The title compound (0.335 g, 48%) was obtained as a white foam from methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (0.520 g, 0.0022 mol) and (*trans*-4-aminocyclohexyl)methanol hydrochloride (0.447 g, 0.0027 mol) by a previously described procedure.

Step C

[00605] 1-[trans-4-(hydroxymethyl)cyclohexyl]-2-piperazinone hydrochloride
The title compound was obtained as a white solid (0.263 g, 100%) by treating 1,1-dimethylethyl 4-[*trans*-4-(hydroxymethyl)cyclohexyl]-3-oxo-1-piperazinecarboxylate (0.330 g, 0.00106 mol) with 4N HCl in dioxane by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.84 (br. s., 2 H) 4.20 (t, 1 H) 3.62 - 3.73 (m, 2 H) 3.40 - 3.52 (m, 2 H) 3.29 - 3.39 (m, 2 H) 3.22 (d, 2 H) 1.81 (d, 2 H) 1.39 - 1.63 (m, 4 H) 1.21 - 1.37 (m, 1 H) 0.86 - 1.08 (m, 2 H).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(hydroxymethyl)cyclohexyl]-2-piperazinone

[00606] The title compound (0.025 g, 18%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.085 g, 0.00028 mmol), 1-[*trans*-4-(hydroxymethyl)cyclohexyl]-2-piperazinone hydrochloride (0.069 g, 0.00028 mol) and HATU (0.127 g, 0.00033 mol) by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, 1 H) 7.48 - 7.67 (m, 1 H) 4.32 -

4.54 (m, 2 H) 4.09 - 4.29 (m, 3 H) 3.99 (m., 1 H) 3.82 (m, 1 H) 3.16 - 3.24 (m, 3 H) 2.15 - 2.28 (m, 1 H) 1.79 (d, 2 H) 1.38 - 1.64 (m, 4 H) 1.29 (br. s., 1 H) 0.93 - 1.08 (m, 4 H) 0.90 (d, 2 H). MS (ESI) m/z 499 (M+1).

EXAMPLE 216

(Compound 216)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone (Isomer 1)

Step A

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

[00607] Pyridinium chlorochromate (0.333 g, 0.00155 mol) was added to a suspension of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone (0.500 g, 0.00103 mol) in DCM (20 mL). The mixture was stirred at room temperature overnight. Diethyl ether was added and the mixture was filtered through Celite. The solvent was evaporated and the residue was purified by silica gel chromatography to give the desired product (0.350 g, 70%) as a white foam. MS (ESI) m/z = 483 (M+1).

Step B

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone (Isomer 1)

[00608] Methylmagnesium chloride (3.0 M in THF) (0.595 mL, 0.00179 mol) was added to a -78 °C solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone (0.345 g, 0.000714 mol) in THF (5 mL). The reaction mixture was warmed to room temperature and stirred for 2 hours. Saturated aqueous ammonium chloride (1 mL) was added and the mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine and concentrated. The crude mixture of isomers was subjected to silica gel chromatography with DCM:methanol followed by reverse phase HPLC (acetonitrile:water with 0.1% formic acid) gave the title compound (0.012 g, 3%). ^{1}H NMR (400 MHz, chloroform-*d*) δ ppm 8.06 (d, *J*=8.60 Hz, 1 H) 7.32 - 7.54 (m, 1 H) 4.62 (s, 1 H), 4.36 - 4.56 (m, 1 H), 4.42 (m, 1H) 4.22 - 4.38 (m, 1 H) 3.87 - 4.06 (m, 1 H) 3.36 - 3.59 (m, 2 H) 1.96 - 2.19 (m, 1 H) 1.81 - 1.95 (m, 2 H) 1.37 - 1.79 (m, 6 H) 1.17 - 1.37 (m, 3 H) 1.12 (d, *J*=7.43 Hz, 2 H) 0.80 (d, 2 H). MS (ESI) m/z 499 (M+1).

EXAMPLE 217

(Compound 217)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone (Isomer 2)

[00609] The title compound (0.013 g, 4%) was isolated from the mixture of isomers in Example 216, Step B. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, 1 H) 7.42 (s, 1 H) 4.59 - 4.68 (m, 1 H) 4.44 - 4.57 (m, 1 H) 4.43 (s, 2 H) 4.33 (t, 1 H) 3.92 - 4.02 (m, 1 H) 3.38 - 3.49 (m, 2 H) 1.99 - 2.13 (m, 1 H) 1.74 - 1.88 (m, 2 H) 1.52 - 1.75 (m, 6 H) 1.30 (s, 3 H) 1.05 - 1.18 (m, 2 H) 0.80 (d, 2 H). MS (ESI) m/z 499 (M+1).

EXAMPLE 218

(Compound 218)

(+/-)-trans-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxycyclohexyl)-2-piperazinone (racemic)

Step A

1-[trans-2-hydroxycyclohexyl]-2-piperazinone hydrochloride

[00610] trans-2-Aminocyclohexanol hydrochloride (0.316 g, 0.00208 mol) was treated with methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (0.482 g, 0.00208 mol) and sodium borohydride by a previously described procedure. The crude product was dissolved in DCM and treated with 4N HCl in dioxane at room temperature overnight. The solvent was evaporated to give the title compound (0.280 g, 86%) as a beige foam. MS (ESI) m/z 199 (M+1).

Step B

(+/-)-trans-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxycyclohexyl)-2-piperazinone (racemic)

[00611] The title compound (0.246 g, 41%) was obtained from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.363 g, 1.193 mmol), and *trans*-1-(2-hydroxycyclohexy)]-2-piperazinone hydrochloride (0.280 g, 1.193 mmol) by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.35 (s, 1 H) 7.61 (s, 1 H) 4.32 - 4.59 (m, 2 H) 3.91 - 4.26 (m, 1 H) 3.82 (br. s., 1 H) 3.28 - 3.64 (m, 4 H) 2.10 - 2.29 (m, 1 H) 1.84 - 1.98 (m, 1 H) 1.33 - 1.73 (m, 4 H) 1.11 - 1.38 (m, 3 H) 0.96 - 1.11 (m, 2 H) 0.74 - 0.96 (m, 2 H). MS (ESI) m/z 485 (M+1).

EXAMPLE 219

(Compound 219)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone (Enantiomer 1)

[00612] The title compound (0.079 g) was isolated from the racemic mixture from Example 218 by SFC as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, 1 H) 7.41 - 7.68 (m, 1 H) 4.70 (d, 1 H) 4.53 and 4.35 (m, 1 H) 4.26 - 4.41 (m, 1 H) 4.15 - 4.27 (m, 2 H) 3.94 and 3.79 (m, 1 H) 3.34 - 3.54 (m, 2 H) 2.08 - 2.30 (m, 1 H) 1.90 (br. s., 1 H) 1.32 - 1.70 (m, 4 H) 1.11 - 1.31 (m, 3 H) 1.02 (d, *J*=8.00 Hz, 2 H) 0.76 - 0.95 (m, 2 H). MS (ESI) m/z 485 (M+1).

EXAMPLE 220

(Compound 220)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone (Enantiomer 2)

[00613] The title compound (0.085 g) was isolated from the racemic mixture from Example 218 by SFC as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, 1 H) 7.41 - 7.68 (m, 1 H) 4.70 (d, 1 H) 4.53 and 4.35 (m, 1 H) 4.26 - 4.41 (m, 1 H) 4.15 - 4.27 (m, 2 H) 3.94 and 3.79 (m, 1 H) 3.34 - 3.54 (m, 2 H) 2.08 - 2.30 (m, 1 H) 1.90 (br. s., 1 H) 1.32 - 1.70 (m, 4 H) 1.11 - 1.31 (m, 3 H) 1.02 (d, *J*=8.00 Hz, 2 H) 0.76 - 0.95 (m, 2 H). MS (ESI) m/z 485 (M+1).

EXAMPLE 221

(Compound 221)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methylamino)cyclohexyl]-2-piperazinone

Step A

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone

[00614] Dess-Martin periodinane (0.656 g, 0.00155 mol) was added to a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone (0.500 g, 0.00103 mol) in DCM (30 mL). The mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with DCM

and washed with saturated aqueous sodium bicarbonate, dried over sodium sulfate and concentrated. Chromatography on silica gel with methanol:DCM provided the title compound (0.380 g, 76%). MS (ESI) m/z = 483 (M+1).

Step B

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methylamino)cyclohexyl]-2-piperazinone

[00615] To a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone (0.360 g, 0.00075 mol) in methanol (10 mL) was added sodium sulfate (0.635 g, 0.0045 mol) and methylamine (2M in THF) (1.1 mL,0.0022 mol). The mixture was stirred at room temperature for 1 hour before sodium borohydride (0.034 g, 0.00089 mol) was added. After 1 hour, most of the methanol was evaporated, and the residue was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over sodium sulfate and concentrated to give the title compound (0.354 g, 91%) as a mixture of isomers (90:10). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, 1 H) 7.36 - 7.67 (m, 1 H) 4.43 (s, 1 H) 4.10 - 4.32 (m, 2 H) 3.96 - 4.00 (m, 1 H) 3.82 (t, 1 H) 3.34 - 3.42 (m, 2 H) 2.24 (s, 3 H) 2.11 - 2.25 (m, 2 H) 1.87 - 1.96 (m, 2 H) 1.44 - 1.60 (m, 4 H) 0.95 - 1.11 (m, 4 H) 0.81 - 0.94 (m, 2 H). MS (ESI) m/z 498 (M+1).

EXAMPLE 222

(Compound 222)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone

Step A

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclohexen-1-yl)-2-piperazinone

[00616] A mixture of *trans*-4-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)cyclohexyl methanesulfonate (0.902 g, 0.0016 mol) and DBU (0.338 mL, 0.0022 mol) in dioxane (5 mL) was heated at reflux for 24 hours. The reaction mixture was diluted with ethyl acetate, washed with 1N aqueous HCl, saturated sodium bicarbonate and water. The organic layer was dried over sodium sulfate and concentrated. Silica gel chromatography gave the title compound (0.194 g, 26%) as a white foam. MS (ESI) m/z 467 (M+1).

Step B

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone

[00617] A mixture of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclohexen-1-yl)-2-piperazinone (0.178 g, 0.00038 mol), AD-mix-beta (0.530 g), t-butanol (2.5 mL) and water (2.5 mL) was stirred at room temperature overnight.The reaction mixture was diluted with ethyl acetate. Sodium sulfite (0.048 g, 0.00038 mol) was added and the mixture was stirred at room temperature for 20 min. The organic layer was washed with saturated aqueous sodium bicarbonate, dried over sodium sulfate and concentrated to a white foam containing a mixture of diastereomers. Reverse phase HPLC gave the title compound (0.067 g, 35%) as a 70:30 mixture of enantiomers. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (s, 1 H) 7.60 (s, 1 H) 4.57 (d,1 H) 4.44 (s, 1 H) 4.26 - 4.34 (m, 1 H) 4.17 - 4.23 (m, 1 H) 3.91 - 4.01 (m, 1 H) 3.79 - 3.88 (m, 1 H) 3.63 - 3.73 (m, 1 H) 3.41 - 3.52 (m, 1 H) 2.17 - 2.28 (m, 1 H) 1.59 - 1.84 (m, 4 H) 1.31 - 1.48 (m, 2 H) 1.14 - 1.26 (m, 1 H) 0.97 - 1.07 (m, 2 H) 0.83 - 0.94 (m, 2 H). MS (ESI) m/z 501 (M+1).

EXAMPLE 223

(Compound 223)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone

[00618] The title compound (0.033 g, 17%) was obtained from the mixture of diastereomers in Example 222, Step B, as a 90:10 mixture of enantiomers. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.35 - 8.60 (m, 1 H) 7.59 (s, 1 H) 4.54 - 4.80 (m, 1 H) 4.32 - 4.52 (m, 3 H) 4.11 - 4.28 (m, 1 H) 3.88 - 4.10 (m, 1 H) 3.63 - 3.90 (m, 2 H) 2.10 - 2.28 (m, 1 H) 1.36 - 1.79 (m, 7 H) 1.03 (s, 2 H) 0.76 - 0.96 (m, 2 H). MS (ESI) m/z 501 (M+1).

EXAMPLE 224

(Compound 224)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-methylcyclohexyl)-2-piperazinone

Step A

1-(trans-4-methylcyclohexyl)-2-piperazinone hydrochloride

[00619] The title compound (0.110 g, 89%) was obtained by reaction of methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (0.216 g, 0.00093 mol) and (*trans*-4-methylcyclohexyl)amine (0.106 g, 0.00093 mol) with sodium borohydride and sodium hydride, followed by treatment with 4N HCl in dioxane by previously described procedures. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.61 (br. s., 2 H) 4.03 - 4.40 (m, 1 H) 3.67 (s, 2 H) 3.42 (m, 3 H) 1.72 (m, 2 H) 1.39 - 1.60 (m, 4 H) 1.20 - 1.41 (m, 1 H) 0.93 - 1.16 (m, 2 H) 0.87 (m, 3 H).

Step B

*4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-*methylcyclohexyl)-2-piperazinone

[00620] The title compound (0.060, 74%) was obtained as a white foam from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.060 g, 0.00020 mmol) and 1-(*trans*-4-methylcyclohexyl)-2-piperazinone hydrochloride (0.046 g, 0.00020 mol) by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.29 - 8.68 (m, 1 H) 7.43 - 7.78 (m, 1 H) 4.36 - 4.55 (m, 1 H) 4.11 - 4.31 (m, 2 H) 3.91 - 4.06 (m, 1 H) 3.71 - 3.92 (m, 1 H) 3.36 - 3.45 (m, 1 H) 2.62 - 2.73 (m, 1 H) 2.04 - 2.28 (m, 1 H) 1.63 - 1.85 (m, 2 H) 1.40 - 1.62 (m, 4 H) 1.22 - 1.40 (m, 1 H) 0.94 - 1.12 (m, 4 H) 0.75 - 0.94 (m, 5 H). MS (ESI) m/z 483 (M+1).

EXAMPLE 225

(Compound 225)

4-[(3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

Step A

methyl 6,8-dibromoimidazo[1,2-a]pyridine-2-carboxylate

[00621] The title compound (0.554 g, 63%) was obtained from 3,5-dibromo-2-pyridinamine (0.665 g, 0.0026 mol) and methyl bromopyruvate (0.281 mL, 0.0026 mol) using a previously described procedure. MS (ESI) m/z 334 (M+2).

Step B

methyl 6,8-dibromo-3-chloroimidazo[1,2-a]pyridine-2-carboxylate

[00622] A mixture of methyl 6,8-dibromoimidazo[1,2-a]pyridine-2-carboxylate (0.540 g, 0.00162 mol) and N-chlorosuccinimide (0.216 g, 0.00162 mol) in DMF (20 mL) was heated at 50 °C for 1 hour. The reaction mixture was diluted with ethyl acetate and water. The organic layer was washed with water and brine, dried over sodium sulfate and concentrated to give the title compound (540 mg, 91%). MS (ESI) m/z 368 (M+2).

Step C

methyl 3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridine-2-carboxylate

[00623] The title compound (0.090 g, 47%) was obtained from methyl 6,8-dibromo-3-chloroimidazo[1,2-a]pyridine-2-carboxylate (0.534 g, 0.00144 mol) and cyclopropylboronic acid by a previously described procedure. MS (ESI) m/z 291 (M+1).

Step D

3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridine-2-carboxylic acid

[00624] 1M aqueous NaOH (0.805 mL, 0.000805 mol) was added to a solution of methyl 3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridine-2-carboxylate (0.078 g, 0.00027 mol) in THF (2 mL). The mixture was stirred at room temperature for 1 hour, then acidified with 1N aqueous HCl and extracted with ethyl acetate.The organic layer was dried over sodium sulfate and concentrated to give the title compound (0.074 g, quant.). MS (ESI) m/z 277 (M+1).

Step E

4-[(3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00625] The title compound (0.088 g, 74%) was obtained from 3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridine-2-carboxylic acid (0.070 g, 0.00025 mol) and 1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone hydrochloride (0.0594 g, 0.00025 mol) by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.97 (s, 1 H) 6.60 - 6.83 (m, 1 H) 4.44 - 4.67 (m, 2 H) 4.18 (s, 2 H) 4.01 - 4.12 (m, 1 H) 3.81 (m, 1 H) 3.34 - 3.45 (m, 2 H) 2.39 (m, 1 H) 2.00 - 2.15 (m, 1 H) 1.85 (m, 2 H) 1.52 (m, 4 H) 1.00 - 1.34 (m, 7 H) 0.87 - 1.00 (m, 2 H) 0.67 - 0.86 (m, 2 H). MS (ESI) m/z 457 (M+1).

EXAMPLE 226

(Compound 226)

4-{[3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

Step A

methyl 6-bromo-3-chloro-8-({[4-(methyloxy)phenyl]methyl}oxy)imidazo[1,2-a]pyridine-2-carboxylate

[00626] The title compound (2.48 g, 71%) was obtained from methyl 6-bromo-8-({[4-(methyloxy)phenyl]methyl}oxy)imidazo[1,2-a]pyridine-2-carboxylate (3.21 g, 0.0082 mol) and N-chlorosuccinimide by a previously described procedure. MS (ESI) m/z 425 (M+1).

Step B

methyl 3-chloro-6-cyclopropyl-8-({[4-(methyloxy)phenyl]methyl}oxy)imidazo[1,2-a]pyridine-2-carboxylate

[00627] The title compound (0.300 g, 34%) was obtained from methyl 6-bromo-3-chloro-8-({[4-(methyloxy)phenyl]methyl}oxy)imidazo[1,2-a]pyridine-2-carboxylate (0.981 g, 0.0023 mmol) and cyclopropylboronic acid (0.198 g, 2.305 mmol) by a previously described procedure. MS (ESI) m/z 387 (M+1).

Step C

methyl 3-chloro-6-cyclopropyl-8-hydroxyimidazo[1,2-a]pyridine-2-carboxylate

[00628] Trifluoroacetic acid (1 mL, 0.013 mol) was added to a solution of methyl 3-chloro-6-cyclopropyl-8-({[4-(methyloxy)phenyl]methyl}oxy)imidazo[1,2-a]pyridine-2-carboxylate (0.244 g, 0.00063 mol) in DCM (1.5 mL). The mixture was stirred at room temperature for 1 hour. The solvent was evaporated and the residue was purified by silica gel chromatography to give the title compound (0.168 g, quant.). MS (ESI) m/z= 267 (M+1).

Step D

methyl 3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridine-2-carboxylate

[00629] Sodium hydride (60% oil dispersion) (0.028 g, 0.00070 mol) was added to a solution of methyl 3-chloro-6-cyclopropyl-8-hydroxyimidazo[1,2-a]pyridine-2-carboxylate (0.170 g, 0.00064 mol) in THF, followed by addition of methyl iodide (0.120 mL, 0.0019 mol). The mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over sodium sulfate and concentrated to give the crude title compound (0.116 g, 65%) which was carried further without additional purification. MS (ESI) m/z 281 (M+1).

Step E

3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridine-2-carboxylic acid

[00630] The title compound (0.063 g, 57%) was obtained as an off-white solid by treatment of methyl 3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridine-2-carboxylate (0.116 g, 0.00041 mol) with aqueous sodium hydroxide by a previously described procedure. MS (ESI) m/z 267 (M+1).

Step F

4-{[3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00631] The title compound (0.031 g, 29%) was obtained as an off-white solid from 3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridine-2-carboxylic acid (0.061 g, 0.00023 mol) and 1-(trans-4-hydroxycyclohexyl)-2-piperazinone hydrochloride (0.054 g,

0.00023 mol) by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.81 (s, 1 H) 6.50 (s, 1 H) 4.47 - 4.70 (m, 2 H) 4.16 (s, 2 H) 4.01 - 4.10 (m, 1 H) 3.96 (s, 3 H) 3.72 - 3.85 (m, 1 H) 3.33 - 3.46 (m, 2 H) 2.02 - 2.22 (m, 1 H) 1.75 - 1.94 (m, 2 H) 1.51 (m, 4 H) 1.12 - 1.35 (m, 2 H) 0.89 - 1.06 (m, 2 H) 0.70 - 0.89 (m, 2 H). MS (ESI) m/z 447 (M+1).

EXAMPLE 227

(Compound 227)

4-{[3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

Step A

methyl 3-chloro-6-cyclopropyl-8-hydroxyimidazo[1,2-a]pyridine-2-carboxylate

[00632] The title compound (0.380 g, 98%) was obtained by treatment of 3-chloro-6-cyclopropyl-8-({[4-(methyloxy)phenyl]methyl}oxy)imidazo[1,2-a]pyridine-2-carboxylate (0.563 g, 0.00145 mol) with TFA by a previously described procedure. MS (ESI) m/z 267 (M+1).

Step B

methyl 3-chloro-6-cyclopropyl-8-{[(trifluoromethyl)sulfonyl]oxy}imidazo[1,2-a]pyridine-2-carboxylate

[00633] N-phenyltrifluoromethylsulfonimide (0.509 g, 0.00142 mol) was added to a cold solution of methyl 3-chloro-6-cyclopropyl-8-hydroxyimidazo[1,2-a]pyridine-2-carboxylate (0.380 g, 0.00142 mol) in DCM (8 mL). The mixture was allowed to warm to room temperature and stirred overnight. The mixture was diluted with DCM, washed with water, dried over sodium sulfate and concentrated. Purification by silica gel chromatography gave the title compound (0.425 g, 75%). MS (ESI) m/z 399 (M+1).

Step C

methyl 3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridine-2-carboxylate

[00634] A mixture of methyl 3-chloro-6-cyclopropyl-8-{[(trifluoromethyl)sulfonyl]oxy}-imidazo[1,2-a]pyridine-2-carboxylate (0.417 g, 0.00105 mol),potassium isopropenyltrifluoroborate (0.186 g, 0.00125 mol), triethylamine (0.729 mL, 0.0052 mol) and [1,1'-bis(diphenylphosphino)-ferrocene]dichloropalladium(II), complex with dichloromethane (0.085 g, 0.000105 mol) in n-propanol (20 mL) was heated at 80 °C for 2 hours. The solvent was evaporated and the residue taken up in ethyl acetate and filtered through Celite. The filtrate was evaporated and the residue was purified by silica gel

chromatography to give the title compound, in 80% purity (0.177 g, 58%) as a colorless oil. MS (ESI) m/z 291 (M+1).

Step D

3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridine-2-carboxylic acid

[00635] The title compound (0.157 g, 96%) was obtained as a light yellow solid by treatment of methyl 3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridine-2-carboxylate (0.172 g, 0.00059 mol) with aqueous sodium hydroxide by a previously described procedure. MS (ESI) m/z 277 (M+1).

Step E

4-{[3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00636] The title compound (0.155 g, 64%) was obtained from 3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.146 g, 0.00053 mol) and 1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone hydrochloride (0.124 g, 0.00053 mol) by a previously described procedure. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.66 - 8.01 (m, 1 H) 6.89 - 7.10 (m, 1 H) 6.13 - 6.39 (m, 1 H) 5.40 - 5.62 (m, 1 H) 4.62 - 4.88 (m, 1 H) 4.37 - 4.57 (m, 2 H) 4.27 - 4.37 (m, 1 H) 3.85 - 4.01 (m, 1 H) 3.45 - 3.65 (m, 1 H) 3.32 - 3.47 (m, 2 H) 2.28 (s, 3 H) 2.04 (s, 2 H) 1.91 - 2.01 (m, 1 H) 1.78 - 1.88 (m, 1 H) 1.64 - 1.80 (m, 2 H) 1.37 - 1.64 (m, 4 H) 0.97 - 1.11 (m, 2 H) 0.74 (m, 2 H). MS (ESI) m/z 457 (M+1).

EXAMPLE 228

(Compound 228)

4-[(8-acetyl-3-chloro-6-cyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone

[00637] The title compound (0.015 g, 12%) was isolated as a pale yellow solid as a by-product of the hydrogenation of 4-{[3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(*trans*-4-hydroxycyclohexyl)-2-piperazinone (0.153 g, 0.00033 mol) at 50 psi with diphenyl disulfide (0.00073 g, 0.000033 mol) and 10% palladium on carbon (0.035 g, 0.000033 mol) in ethanol (15 mL) by a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.26 - 8.69 (m, 1 H) 7.37 - 7.79 (m, 1 H) 4.55 (s, 2 H) 4.20 (s, 2 H) 4.08 (m, 1 H) 3.72 - 3.89 (m, 1 H), 3.35 (m, 2H), 2.89 (s, 3 H) 2.08 - 2.30 (m, 1 H) 1.86 (m, 2 H) 1.41 - 1.66 (m, 4 H) 1.10 - 1.32 (m, 2 H) 0.93 - 1.13 (m, 2 H) 0.58 - 0.91 (m, 2 H). MS (ESI) m/z 459 (M+1).

EXAMPLE 229

(Compound 229)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(5-methyl-2-thienyl)-2-piperazinone

Step A

1,1-dimethylethyl 4-(5-methyl-2-thienyl)-3-oxo-1-piperazinecarboxylate

[00638] A solution of 1-Boc-3-piperazinone (500mg, 2.5mmol), 5-bromo-2-methylthiophene (402 mg, 2.27 mmol), CuI (21.6 mg, 0.114 mmol), dimethylethylenediamine (20 mg, 0.227 mmol) and K_2CO_3 (627 mg, 4.5 mmol) in dry toluene (10 mL) was heated at 110 °C overnight. The reaction mixture was diluted with EtOAc (40mL) and filtered off. The filtrate was concentrated and the residue was purified with silica gel chromatography (PE:EA= 1:1) to give the title compound (220 mg, 33%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 6.59-6.57 (m, 1H), 6.49 (d, 1H), 4.31 (s, 2H), 3.84 (s, 4H), 2.45 (s, 3H), 1.51 (s, 9H).

Step B

1-(5-methyl-2-thienyl)-2-piperazinone hydrochloride salt

[00639] A solution of 1,1-dimethylethyl 4-(5-methyl-2-thienyl)-3-oxo-1-piperazinecarboxylate (220 mg, 0.74 mmol) in 4N HCl in dioxane (10mL) was stirred at room temperature for 1 hour. The solvent was removed by evaporation and the residue was washed with petroleum ether (60 mL) to give the title compound (160 mg, 93%) as a white solid.

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-2-thienyl)-2-piperazinone

[00640] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridine-2-carboxylic acid (109 mg, 0.36 mmol) and TBTU (138 mg, 0.43 mmol) in dry DMF (5 mL) was stirred at room temperature for 10 min. To this solution was added 1-(5-methyl-2-thienyl)-2-piperazinone hydrochloride salt (100 mg, 0.43 mmol) and DIPEA (116 mg, 0.9 mmol). The reaction mixture was stirred at room temperature for 2 hours, diluted with water (20mL), and extracted with EtOAc (30mL x 3). The combined organic layer was washed with brine (40mL x 2), dried (Na_2SO_4), evaporated, and purified by silica gel chromatography (PE:EA=1:1) to give the title compound (100 mg, 57%) as a light yellow solid. ^{1}H NMR (300MHz, $CDCl_3$) δ= 8.06 (s, 1H), 7.43 (s, 1H), 6.55-6.51 (m, 2H), 4.94 (s, 1H), 4.63 (s, 1H), 4.53 (t, 1H), 4.16 (t, 1H), 4.04-3.95 (m, 2H), 2.42 (s, 3H), 2.07-2.01 (m, 1H), 1.15-1.10 (m, 2H), 0.83-0.78 (m, 2H). LCMS (*m/z*, ES^+) 483 (M+1).

EXAMPLE 230

(Compound 230)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(5-methyl-3-thienyl)-2-piperazinone

Step A

1,1-dimethylethyl 4-(5-methyl-3-thienyl)-3-oxo-1-piperazinecarboxylate

[00641] A solution of 1-Boc-3-piperazinone (500mg, 2.5mmol), 4-bromo-2-methylthiophene (400 mg, 2.26 mmol), CuI (22 mg, 0.115 mmol), dimethylethylenediamine (20 mg, 0.227 mmol) and K_2CO_3 (624 mg, 4.5 mmol) in dry toluene (20 mL) was heated at 110°C overnight. The reaction mixture was diluted with EtOAc (40 mL) and filtered off. The filtrate was concentrated and the residue was purified with silica gel chromatography. (PE:EA= 1:1) to give the title compound (266 mg, 42%) as a white solid.

Step B

1-(5-methyl-3-thienyl)-2-piperazinone hydrochloride salt

[00642] A solution of 1,1-dimethylethyl 4-(5-methyl-3-thienyl)-3-oxo-1-piperazinecarboxylate (266 mg, 0.898 mmol) in 4N HCl in dioxane (10 mL) was stirred at room temperature for 1 hour. The solvent was removed by evaporation and the residue was washed with petroleum ether (60 mL) to give the title compound (200 mg, 96%) as a white solid.

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-3-thienyl)-2-piperazinone

[00643] A solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (218 mg, 0.72 mmol) and TBTU (276 mg, 0.86 mmol) in dry DMF (10 mL) was stirred at room temperature for 10 min. To this solution was added 1-(5-methyl-3-thienyl)-2-piperazinone hydrochloride salt (200 mg, 0.86 mmol) and DIPEA (232 mg, 1.8 mmol). The reaction mixture was stirred at room temperature for 2 hours, diluted with water (40 mL), and extracted with EtOAc (30 mL x 3). The combined organic phase was washed with brine (40 mL x 2), dried (Na_2SO_4), evaporated and purified with silica gel chromatography (PE:EA=1:1) to give the title compound (110 mg, 32%) as a white solid. ^{1}H NMR (300MHz, $CDCl_3$) δ= 8.08 (s, 1H), 7.45 (s, 1H), 7.05-7.00 (m, 2H), 4.83 (s, 1H), 4.59 (s, 1H), 4.48 (t, 1H), 4.14 (t, 1H), 3.98-3.91 (m, 2H), 2.49 (s, 3H), 2.06 (m, 1H), 1.16-1.11 (m, 2H), 0.82 (m, 2H). LCMS (m/z, ES^+) 483 (M+1).

EXAMPLE 231

(Compound 231)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

Step A

1,1-dimethylethyl 3-oxo-4-(3-thienyl)-1-piperazinecarboxylate

[00644] A solution of 1-Boc-3-piperazinone (600 mg, 3.0 mmol), 3-bromothiophene (978 mg, 6.0 mmol), CuI (29 mg, 0.15 mmol), dimethylethylenediamine (26mg, 0.30mmol) and K_2CO_3 (828 mg, 6.0 mmol) in dry toluene (20 mL) was heated at 110°C overnight. The reaction mixture was diluted with EtOAc (40 mL) and filtered off. The filtrate was concentrated and the residue was purified with silica gel chrom (PE:EA= 3:1) to give the title compound (600mg, 71%) as a white solid. ^{1}H NMR (300MHz, $CDCl_3$) δ= 7.31-7.30 (m, 3H), 4.25 (s, 2H), 3.79 (s, 4H), 1.49 (s, 9H).

Step B

1-(3-thienyl)-2-piperazinone hydrochloride salt

[00645] The title compound (400 mg, 86%) was obtained from 1,1-dimethylethyl 3-oxo-4-(3-thienyl)-1-piperazinecarboxylate (600 mg, 2.1 mmol) by a previously described procedure.

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone

[00646] The title compound (109 mg, 48%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (146 mg, 0.48 mmol), TBTU (160 mg, 0.50 mmol), 1-(5-methyl-3-thienyl)-2-piperazinone hydrochloride salt (110 mg, 0.5 mmol) and DIPEA (310 mg, 2.4 mmol) by a previously described procedure. ^{1}H NMR (300MHz, $CDCl_3$) δ= 8.09 (d, 1H), 7.45 (s, 1H), 7.35 (t, 3H), 4.87(s,1H), 4.61(s, 1H), 4.51(t, 1H), 4.16(s, 3H), 2.05(d, 1H), 1.14(d, 2H), 0.83(t, 2H). LCMS (*m/z*, ES^+) 469 (M+1).

EXAMPLE 232

(Compound 232)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone

Step A

1,1-dimethylethyl 3-oxo-4-(2-thienyl)-1-piperazinecarboxylate

[00647] The title compound (230 mg, 27%) was obtained as a white solid from 1-Boc-3-piperazinone (600 mg, 3.0 mmol), 2-bromothiophene (978 mg, 6.0 mmol), CuI (29 mg, 0.15 mmol), dimethylethylenediamine (26 mg, 0.30 mmol) and K_2CO_3 (828 mg, 6.0 mmol) by a previously described procedure. ^{1}H NMR (300MHz, CDCl3) δ= 6.99 (dd, 1H, *J*=1.3Hz, 5.6Hz), 6.91 (dd, 1H, *J*=3.9Hz, 5.6Hz), 6.68 (m, 1H), 4.31 (s, 2H), 3.87-3.83 (m, 4H), 1.49 (s, 9H).

Step B

1-(2-thienyl)-2-piperazinone hydrochloride salt

[00648] The title compound (200 mg, 86%) was obtained from 1,1-dimethylethyl 3-oxo-4-(2-thienyl)-1-piperazinecarboxylate (300 mg, 1.1 mmol) by a previously described procedure.

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone

[00649] The title compound (100 mg, 44%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (145 mg, 0.48 mmol), TBTU (160 mg, 0.50 mmol), 1-(2-thienyl)-2-piperazinone hydrochloride salt (109 mg, 0.5 mmol) and DIPEA (310 mg, 2.4 mmol) by a previously described procedure. ^{1}H NMR (300MHz, $CDCl_3$) δ= 8.10 (s, 1H), 7.46 (s, 1H), 7.02 (s, 1H), 6.95 (t, 1H), 6.75(s,1H), 5.02(s,1H), 4.68(s, 1H), 4.59(s, 1H), 4.12(t,3H), 2.06(s, 1H), 1.14(d, 2H), 0.84(t, 2H). LCMS (m/z, ES^+) 469 (M+1).

EXAMPLE 233

(Compound 233)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone

Step A

1,1-dimethylethyl 4-[5-(methyloxy)-2-pyridinyl]-3-oxo-1-piperazinecarboxylate

[00650] To a suspension of 1-Boc-3-oxopiperazine (500 mg, 2.497 mmol), 2-bromo-5-methoxypyridine (470 mg, 2.497 mmol), copper(I) iodide (23.78 mg, 0.125 mmol), *trans*-N,N'-dimethylcyclohexane-1,2-diamine (0.039 mL, 0.250 mmol) and potassium carbonate (690 mg, 4.99 mmol) in 1,4-dioxane (10 mL) was heated to 120 °C for 4 days. The mixture was filtered through a pad of Celite and washed

with EtOAc (50 mL). The filtrate was washed with saturated aqueous NH_4Cl (15 mL), then brine (15 mL), dried ($MgSO_4$), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography (30-70% EtOAc in hexanes) to give 1,1-dimethylethyl 4-[5-(methyloxy)-2-pyridinyl]-3-oxo-1-piperazinecarboxylate (642.4 mg, 2.090 mmol, 84 %) as a white solid. MS(ESI) m/z: 308.3 (MH^+).

Step B

1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone hydrochloride

[00651] To a solution of 1,1-dimethylethyl 4-[5-(methyloxy)-2-pyridinyl]-3-oxo-1-piperazinecarboxylate (323 mg, 1.051 mmol) in dichloromethane (10 mL) at room temperature was added a solution of 4 M hydrogen chloride in 1,4-dioxane (10 mL, 40.0 mmol). After 2.5 hours, the solvent was removed under reduced pressure and dried under high vacuum to give 1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone hydrochloride (374.9 mg, quantitative) as hygroscopic solid. MS(ESI) m/z: 208.3 (MH^+).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone

[00652] To a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (180 mg, 0.591 mmol), 1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone hydrochloride (216 mg, 0.886 mmol), N,N-diisopropylethylamine (0.516 mL, 2.95 mmol) in DMF (3 mL) at room temperature was added HATU (236 mg, 0.620 mmol). After 1 hour, the mixture was diluted with EtOAc (60 mL), and washed with saturated aqueous $NaHCO_3$ (25 mL), then brine (25 mL), dried (Na_2SO_4), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography [30-90% EtOAc in hexanes] to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone (214.7 mg, 0.426 mmol, 72%) as white powder (after lyophilization). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 0.86 - 0.96 (m, 2 H), 0.97 - 1.07 (m, 2 H), 2.16 - 2.28 (m, 1 H), 3.83 (s, 3 H), 3.94 - 4.09 (m, 3 H), 4.10 - 4.18 (m, 1 H), 4.43 (s, 1 H), 4.69 (s, 1 H), 7.43 - 7.52 (m, 1 H), 7.60 (s, 1 H), 7.74 (dd, *J*=16.3, 9.0 Hz, 1 H), 8.16 (t, *J*=3.1 Hz, 1 H), 8.47 (s, 1 H); MS(ESI) m/z: 494.0 (MH^+).

EXAMPLE 234

(Compound 234)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone

Step A

1,1-dimethylethyl 4-[6-(methyloxy)-3-pyridinyl]-3-oxo-1-piperazinecarboxylate

[00653] The title compound (640.6 mg, 83%) was obtained as white solid from 1-Boc-3-oxopiperazine and 5-bromo-2-methoxypyridine using a similar procedure to that described in Example 233, Step A. MS(ESI) m/z: 308.5 (MH^+).

Step B

1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone hydrochloride

[00654] The title compound (305.8 mg, quant.) was obtained as white solid from 1,1-dimethylethyl 4-[6-(methyloxy)-3-pyridinyl]-3-oxo-1-piperazinecarboxylate using a similar procedure to that described in Example 233, Step B. MS(ESI) m/z: 207.8 (MH^+).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone

[00655] The title compound (296 mg, 70%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone hydrochloride using a similar procedure to that described in Example 233, Step C. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 0.84 - 0.96 (m, 2 H), 0.96 - 1.07 (m, 2 H), 2.15 - 2.28 (m, 1 H), 3.79 (dt, *J*=14.1, 5.3 Hz, 2 H), 3.85 (s, 3 H), 4.00 - 4.08 (m, 1 H), 4.21 (t, *J*=5.0 Hz, 1 H), 4.40 (s, 1 H), 4.66 (s, 1 H), 6.82 - 6.92 (m, 1 H), 7.60 (s, 1 H), 7.73 (ddd, *J*=8.5, 5.4, 2.7 Hz, 1 H), 8.14 - 8.23 (m, 1 H), 8.47 (s, 1 H); MS(ESI) m/z: 494.1 (MH^+).

EXAMPLE 235

(Compound 235)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone

Step A

1,1-dimethylethyl 4-[2-fluoro-4-(methyloxy)phenyl]-3-oxo-1-piperazinecarboxylate

[00656] The title compound (642.1 mg, 79%) was obtained as white solid from 1-Boc-3-oxopiperazine and 4-bromo-3-fluoroanisole using a similar procedure to that described in Example 233, Step A. MS(ESI) m/z: 325.2 (MH^+).

Step B

1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone hydrochloride

[00657] The title compound (367.4 mg, quant.) was obtained as semi-solid from 1,1-dimethylethyl 4-[2-fluoro-4-(methyloxy)phenyl]-3-oxo-1-piperazinecarboxylate using a similar procedure to that described in Example 233, Step B. MS(ESI) m/z: 225.2 (MH^+).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone

[00658] The title compound (355.6 mg, 83%) was obtained as white powder from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid and 1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone hydrochloride using a similar procedure to that described in Example 233, Step C. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 0.84 - 0.96 (m, 2 H), 0.97 - 1.08 (m, 2 H), 2.15 - 2.28 (m, 1 H), 3.62 - 3.75 (m, 2 H), 3.78 (s, 3 H), 4.01 - 4.10 (m, 1 H), 4.18 (t, *J*=5.0 Hz, 1 H), 4.41 (s, 1 H), 4.67 (s, 1 H), 6.83 (d, *J*=8.8 Hz, 1 H), 6.90 - 7.01 (m, 1 H), 7.36 (td, *J*=8.9, 4.3 Hz, 1 H), 7.60 (s, 1 H), 8.47 (s, 1 H); MS(ESI) m/z: 511.1 (MH^+).

EXAMPLE 236

(Compound 236)

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile

Step A

1,1-dimethylethyl 4-(3-cyanophenyl)-3-oxo-1-piperazinecarboxylate

[00659] The title compound (400 mg, 53%) was obtained as a white solid from 1-Boc-3-piperazinone (532 mg, 2.6 mmol), 3-iodobenzonitrile (580 mg, 2.5 mmol), CuI (24 mg, 0.13 mmol), dimethylethylenediamine (22 mg, 0.25 mmol) and K_2CO_3 (690 mg, 5.0 mmol) by a previously described procedure. ^1H NMR (300MHz, CDCl3) δ= 7.63 (m, 1H), 7.55 (m, 1H), 7.53 (m, 1H), 4.25 (s, 2H), 3.81-3.73 (m, 4H), 1.48 (s, 9H).

Step B

3-(2-oxo-1-piperazinyl)benzonitrile hydrochloride salt

[00660] The title compound (180 mg, 81%) was obtained as a white solid from 1,1-dimethylethyl 4-(3-cyanophenyl)-3-oxo-1-piperazinecarboxylate (280 mg, 0.93 mmol) by a previously described procedure.

Step C

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile

[00661] The title compound (100 mg, 46%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (145 mg, 0.48 mmol), TBTU (154 mg, 0.48 mmol), 3-(2-oxo-1-piperazinyl)benzonitrile hydrochloride salt (108 mg, 0.45 mmol) and DIPEA (238 mg, 1.82 mmol) by a previously described procedure. ^{1}H NMR (300MHz, $CDCl_3$) δ= 8.08 (s, 1H), 7.68 (d, 1H), 7.63-7.7.53 (m, 3H), 7.43(s,1H), 4.90(s,1H), 4.61(s, 1H), 4.53(t, 1H), 4.16(q, 1H), 3.97(t,1H), 3.92(t, 1H), 2.05(m, 1H), 1.13(q, 2H), 0.84(m, 2H). LCMS (*m/z*, ES^+) 488 (M+1).

EXAMPLE 237

(Compound 237)

2-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile

Step A

1,1-dimethylethyl 4-(2-cyanophenyl)-3-oxo-1-piperazinecarboxylate

[00662] The title compound (430 mg, 48%) was obtained as a white solid from 1-Boc-3-piperazinone (630 mg, 3.15 mmol), 2-bromobenzonitrile (546 mg, 3.0 mmol), CuI (29 mg, 0.15 mmol), dimethylethylenediamine (27 mg, 0.3 mmol) and K_2CO_3 (828 mg, 6.0 mmol) by a previously described procedure. ^{1}H NMR (300MHz, $CDCl_3$) δ= 7.77 (dt, 1H, *J*=3Hz, 6Hz), 7.76 (dd, 1H, *J*=3Hz, 6Hz), 7.48 (dt, 1H, *J*=3Hz, 6Hz), 7.40 (dd, 1H, *J*=3Hz, 6Hz), 4.34 (s, 2H), 3.91-3.88 (m, 2H), 3.79-3.75 (m, 2H), 1.53 (s, 9H).

Step B

2-(2-oxo-1-piperazinyl)benzonitrile hydrochloride salt

[00663] The title compound (280 mg, 81%) was obtained from 1,1-dimethylethyl 4-(2-cyanophenyl)-3-oxo-1-piperazinecarboxylate (430 mg, 1.4 mmol) by a previously described procedure.

Step C

2-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile

[00664] The title compound (60 mg, 49%) was obtained as a white solid from 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (81 mg, 0.27 mmol), TBTU (86 mg, 0.27 mmol), 2-(2-oxo-1-piperazinyl)benzonitrile hydrochloride salt (60 mg, 0.25 mmol) and DIPEA (135 mg, 1.0 mmol) by a previously described procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.08 (s, 1H), 7.77(d, 1H), 7.69(d, 1H), 7.50-7.42(m,3H), 4.92(s,1H), 4.66(s, 1H), 4.57(s, 1H), 4.25(q, 1H), 3.96(t, 1H), 3.90(d, 1H), 2.03(q, 1H), 1.13(m, 2H), 0.82(q, 2H). LCMS (m/z, ES^+) = 488 (M+1).

EXAMPLE 238

(Compound 238)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluoro-4-hydroxyphenyl)-2-piperazinone

[00665] 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone (143 mg, 0.280 mmol) was co-evaporated with benzene (2 x 4 mL). The white solid was dissolved in DCM (2.8 mL) and cooled to -78 °C. After 5 minutes, boron tribromide (0.212 mL, 2.239 mmol) was added dropwise. After 1 hour, the dry-ice bath was replaced by an ice-water bath. After 5 hours, the mixture was diluted with DCM (50 mL) and saturated aqueous $NaHCO_3$ (20 mL) was added. The aqueous phase was separated and extracted with DCM (30 mL). The combined organic phases were washed with brine (30 mL), dried (Na_2SO_4), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography [40-100% EtOAc in hexanes] to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluoro-4-hydroxyphenyl)-2-piperazinone (45.4 mg, 0.090 mmol, 32%) as white powder (after lyophilization). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.83 - 0.95 (m, 2 H), 0.95 - 1.08 (m, 2 H), 2.17 - 2.29 (m, 1 H), 3.66 (m, 2 H), 4.02 (m, 1 H), 4.16 (t, *J*=5.0 Hz, 1 H), 4.39 (s, 1 H), 4.64 (s, 1 H), 6.54 - 6.72 (m, 2 H), 7.14 - 7.30 (m, 1 H), 7.60 (s, 1 H), 8.46 (s, 1 H), 10.05 (s, 1 H); MS(ESI) m/z: 497.1 (MH^+).

EXAMPLE 239

(Compound 239)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-hydroxy-2-pyridinyl)-2-piperazinone

[00666] To a suspension of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone (193.4 mg, 0.392 mmol) in DCM (3.62 mL) at -78 °C was added boron tribromide (0.296 mL, 3.13 mmol) dropwise. After 1 hour, the dry-ice acetone bath was switched to an ice-water bath. After 30 minutes, DCM (5 mL) was added to help dissolve the compound. After 4 hours, the mixture was stored in a fridge for 2 days. The mixture was placed in ice-water bath and DCM (10 mL) was added. After 4.5 hours, the mixture was diluted with DCM (50 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL). The organic layer was separated and aqueous phase extracted with EtOAc (50 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated. The residue was absorbed on silica gel and purified by silica gel chromatography [50-100% EtOAc in hexanes] to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-hydroxy-2-pyridinyl)-2-piperazinone (28.5 mg, 0.058 mmol, 15%) as a white solid (after lyophilization). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.86 - 0.94 (m, 2 H), 0.98 - 1.07 (m, 2 H), 2.16 - 2.28 (m, 1 H), 3.90 - 4.06 (m, 3 H), 4.08 - 4.16 (m, 1 H), 4.41 (s, 1 H), 4.66 (s, 1 H), 7.23 (td, *J*=8.0, 2.9 Hz, 1 H), 7.54 - 7.65 (m, 2 H), 7.97 (t, *J*=3.1 Hz, 1 H), 8.47 (s, 1 H), 9.97 (m, *J*=4.7 Hz, 1 H); MS(ESI) m/z: 480.2 (MH^+).

EXAMPLE 240

(Compound 240)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxo-1,6-dihydro-3-pyridinyl)-2-piperazinone

[00667] To a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone (102.7 mg, 0.208 mmol) in 1,2-dichloroethane (20.5 mL) at room temperature was added iodotrimethylsilane (0.283 mL, 2.080 mmol). After 45 minutes, the mixture was heated to 70 °C. After 6 hours, MeOH (1 mL) was added carefully and the mixture was stirred at 50 °C overnight. The mixture was diluted with DCM (100 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL), brine (50 mL), dried (Na_2SO_4), filtered and concentrated to give a dark green solid. The crude material was purified on preparative HPLC (10-90% ACN gradient, 0.1% formic acid) to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxo-1,6-dihydro-3-pyridinyl)-2-piperazinone (35.8 mg, 0.071 mmol, 34%) as off-white powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.85 - 0.94 (m, 2 H), 0.98 - 1.06 (m, 2 H), 2.12 - 2.29 (m, 1 H), 3.60 - 3.77 (m, 2 H), 3.99 (t, *J*=5.1 Hz, 1 H), 4.15 (t, *J*=5.0

Hz, 1 H), 4.34 (s, 1 H), 4.61 (s, 1 H), 6.29 - 6.38 (m, 1 H), 7.40 - 7.48 (m, 1 H), 7.48 - 7.55 (m, 1 H), 7.60 (s, 1 H), 8.47 (s, 1 H), 11.66 (br. s., 1 H); MS(ESI) m/z: 480.2 (MH^+).

EXAMPLE 241

(Compound 241)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[*trans*-3-(hydroxymethyl)cyclobutyl]-2-piperazinone

Step A

(trans-3-aminocyclobutyl)methanol hydrochloride

[00668] To a solution of *tert*-butyl *trans*-3-hydroxymethylcyclobutylcarbamate (994 mg, 4.94 mmol) in DCM (10 mL) was added a solution of 4 M hydrogen chloride in 1,4-dioxane (9.88 mL, 39.5 mmol). After 1 hour, 50 minutes, the solvent was removed under reduced pressure to give (*trans*-3-aminocyclobutyl)methanol hydrochloride (808.2 mg) as white solid. This was used in the next step without further purification. MS(ESI) m/z: 203.1 (2M+1).

Step B

1,1-dimethylethyl 4-[trans-3-(hydroxymethyl)cyclobutyl]-3-oxo-1-piperazinecarboxylate

[00669] A solution of methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (1142 mg, 4.94 mmol), (*trans*-3-aminocyclobutyl)methanol hydrochloride (0.8 g crude weight from previous step), N,N-diisopropylethylamine (0.863 mL, 4.94 mmol) and sodium sulfate (4210 mg, 29.6 mmol) was stirred in methanol (25 mL). After 40 minutes, sodium borohydride (187 mg, 4.94 mmol) was added. After 50 minutes, sodium hydride (395 mg, 9.88 mmol) was added to the mixture. After 2 hours, 30% citric acid (25 mL) was added to the mixture and the salt filtered through a short pad of Celite. The solvent was removed under reduced pressure. The crude material was extracted with EtOAc (150 mL), and washed with saturated $NaHCO_3$ (50 mL), brine (50 mL), dried (Na_2SO_4), filtered and concentrated. The residue was absorbed on silica gel and purified by silica gel chromatography [0-5% MeOH in EtOAc] to give 1,1-dimethylethyl 4-[*trans*-3-(hydroxymethyl)cyclobutyl]-3-oxo-1-piperazinecarboxylate (634.4 mg, 2.231 mmol, 45%) as white solid. MS(ESI) m/z: 285.2 (MH^+).

Step C

1-[trans-3-(hydroxymethyl)cyclobutyl]-2-piperazinone hydrochloride

[00670] To a solution of 1,1-dimethylethyl 4-[trans-3-(hydroxymethyl)cyclobutyl]-3-oxo-1-piperazinecarboxylate (109.5 mg, 0.385 mmol) in DCM (3 mL) was added a solution of a solution of 4 M hydrogen chloride in 1,4-dioxane (0.770 mL, 3.08 mmol) and the

reaction mixture was stirred for 1 hour 45 minutes. The solvent was removed under reduced pressure to give 1-[*trans*-3-(hydroxymethyl)cyclobutyl]-2-piperazinone hydrochloride (90.8 mg, 0.411 mmol, quantitative yield) as white solid. MS(ESI) m/z: 185.5 (MH^+).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-3-(hydroxymethyl)cyclobutyl]-2-piperazinone

[00671] To a solution of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (80 mg, 0.263 mmol), 1-[*trans*-3-(hydroxymethyl)cyclobutyl]-2-piperazinone hydrochloride (87 mg, 0.394 mmol) (HCl), N,N-diisopropylethylamine (0.183 mL, 1.050 mmol) in DMF (1.3 mL) at 0 °C was added dropwise a solution of 1-propanephosphonic acid cyclic anhydride in EtOAc (50% wt) (0.188 mL, 0.315 mmol). After 20 minutes, water (15 mL) was added to the mixture and extracted with EtOAc (50 mL). The organic phase was separated and washed with brine (15 mL), dried (Na_2SO_4), filtered and concentrated. The residue was absorbed on silica gel and purified by silica gel chromatography [0-5%MeOH in EtOAc] to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-3-(hydroxymethyl)cyclobutyl]-2-piperazinone (98.5 mg, 0.205 mmol, 78 %) as white solid (after lyophilization). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.78 - 0.95 (m, 2 H), 0.96 - 1.07 (m, 2 H), 1.76 - 1.95 (m, 2 H), 2.11 - 2.37 (m, 4 H), 3.40 - 3.61 (m, 4 H), 3.88 (t, *J*=5.1 Hz, 1 H), 4.05 (t, *J*=4.9 Hz, 1 H), 4.19 (s, 1 H), 4.43 (s, 1 H), 4.64 (t, *J*=5.3 Hz, 1 H), 4.88 - 5.09 (m, 1 H), 7.54 - 7.66 (m, 1 H), 8.40 - 8.50 (m, 1 H); MS(ESI) m/z: 471.2 (MH^+).

EXAMPLE 242

(Compound 242)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxybicyclo[3.1.0]hex-3-yl)-2-piperazinone

Step A

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxy-3-cyclopenten-1-yl)-2-piperazinone

[00672] A suspension of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (868.4 mg, 1.918 mmol) and selenium dioxide (213 mg, 1.918 mmol) in THF (16 mL) and 1,2-dimethoxyethane (8 mL) was degassed in a sealed tube and heated at 70 °C for 16 hours. The mixture was cooled, filtered through a pad of Celite, and the solvent was removed under reduced pressure.

The residue was absorbed on silica gel and purified by silica gel chromatography [0-3%MeOH in EtOAc] to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxy-3-cyclopenten-1-yl)-2-piperazinone (186.5 mg, 0.398 mmol, 21%, 77% pure by UV 254 nm) as yellow film. MS(ESI) m/z: 469.3 (MH^+). Starting material (316 mg, 36%, 88% pure by UV 254 nm) was recovered.

Step B

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-*hydroxybicyclo[3.1.0]hex-3-yl)-2-piperazinone*

[00673] A solution of 1 M diethylzinc in hexanes (5.89 mL, 5.89 mmol) was added to DCM (7 mL) at 0 °C. A solution of TFA (0.454 mL, 5.89 mmol) in DCM (7 mL) was added dropwise to the mixture. The mixture was allowed to stir for 20 minutes. Diiodomethane (0.475 mL, 5.89 mmol) in DCM (7 mL) was added dropwise over 30 minutes and the mixture was allowed to stir for 20 minutes. 4-{[3-Chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxy-3-cyclopenten-1-yl)-2-piperazinone (184 mg, 0.392 mmol) in DCM (4 mL) was added dropwise. The mixture was allowed to slowly warm to room temperature overnight. The reaction mixture was diluted with DCM (100 mL), and washed successively with saturated aqueous NH_4Cl (25 mL), saturated aqueous $NaHCO_3$ (25 mL), brine (25 mL), dried (Na_2SO_4), filtered and concentrated. The crude was absorbed on silica gel and purified by silica gel chromatography [0-3% MeOH in DCM, then 30% MeOH in DCM]. Combined fractions were concentrated to give 150 mg of foam. This was further purified by preparative HPLC (3 injections) [10-60% ACN gradient (12 minutes run), 10-50% ACN gradient (20 minutes run), 10-40% ACN gradient (20 minutes run)]. The combined fractions were lyophilized to give 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxybicyclo[3.1.0]hex-3-yl)-2-piperazinone (54.6 mg, 0.102 mmol, 26%) as a white powder. MS(ESI) m/z: 483.3 (MH^+).

EXAMPLE 243

(Compound 243)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone (enantiomer 1)

and

EXAMPLE 244

(Compound 244)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone (enantiomer 2)

[00674] The enantiomers (50 mg) were separated by super-critical fluid chromatography (SFC) (ADH column, 10 x 250 mm, 10 mL/min, 20% MeOH in CO_2, 140 bar, 40 °C, 10 mL/min) to give two enantiomers.

[00675] Enantiomer 1: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone [14.4 mg, >95%ee, MS(ESI) m/z: 483.2 (MH^+)] and

[00676] Enantiomer 2: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone [13.8 mg, >95%ee, MS(ESI) m/z: 483.1 (MH^+)].

[00677] NMR data for Enantiomer 1: 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.35 (m, 1 H), 0.60 (d, *J*=3.4 Hz, 1 H), 0.85 - 0.95 (m, 2 H), 0.98 - 1.07 (m, 2 H), 1.19 - 1.30 (m, 1 H), 1.30 - 1.46 (m, 1 H), 1.64 - 1.77 (m, 1 H), 1.77 - 1.92 (m, 1 H), 2.14 - 2.27 (m, 1 H), 3.35 - 3.47 (m, 2 H), 3.54 - 3.67 (m, 0.5 H), 3.78 (dt, *J*=13.3, 4.1 Hz, 0.5 H), 3.97 - 4.25 (m, 2.5 H), 4.33 (d, *J*=17.7 Hz, 1 H), 4.36 - 4.47 (m, 1 H), 4.56 (d, *J*=17.5 Hz, 0.5 H), 4.79 (dd, *J*=8.0, 5.7 Hz, 1 H), 7.55 - 7.65 (m, 1 H), 8.40 - 8.52 (m, 1 H).

EXAMPLE 245

(Compound 245)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone (enantiomer 1)

and

EXAMPLE 246

(Compound 246)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone (enantiomer 2)

Step A

1,1-dimethylethyl 4-(3-cyclopenten-1-yl)-3-oxo-1-piperazinecarboxylate

[00678] Et_3N (2.351 mL, 16.87 mmol) was added to a solution of 3-cyclopenten-1-amine hydrochloride (2.017 g, 16.87 mmol) in methanol (40 mL). Methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (3.0 g, 12.97 mmol) was added and the mixture was stirred at room temperature for 15 min. $NaCNBH_3$ (1.223 g, 19.46 mmol) was added and the mixture was stirred overnight and concentrated. The residue was diluted with 1 N NaOH and extracted with 5 % MeOH in DCM, The combined extracts were dried over Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (0-3 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (1.7 g, 49%) as a light-yellow solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.74 (s, 2 H), 5.49 (ddd, *J*=8.93, 4.68, 4.54 Hz, 1 H), 4.08 (s, 2 H), 3.59 (t, *J*=5.27 Hz, 2 H), 3.17 - 3.23 (m, 2 H), 2.70 (dd, *J*=15.80, 8.98 Hz, 2 H), 2.25 (dd, *J*=15.61, 3.71 Hz, 2 H), 1.47 (s, 9 H).

Step B

1-(3-cyclopenten-1-yl)-2-piperazinone trifluoroacetate

[00679] TFA (9.84 mL, 128 mmol) was added to a solution of 1,1-dimethylethyl 4-(3-cyclopenten-1-yl)-3-oxo-1-piperazinecarboxylate (1.7 g, 6.38 mmol) in dichloromethane (20 mL) at room temperature. The mixture was stirred for 2 hours and then concentrated, co-evaporated with hexanes, and dried under vacuum to give the title compound as a purple oil which was used without further purification. 1H NMR (400 MHz, DMSO-d_6) δ ppm 9.15 (br. s., 2 H) 5.76 (s, 2 H) 5.20 - 5.31 (m, *J*=8.78, 8.78, 4.39, 4.19 Hz, 1 H) 3.72 (br. s., 2 H) 3.37 (br. s., 2 H) 3.26 (t, *J*=5.46 Hz, 2 H) 2.57 (dd, *J*=15.71, 8.88 Hz, 2 H) 2.29 (dd, *J*=15.51, 3.80 Hz, 2 H).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone

[00680] Et_3N (2.213 mL, 15.88 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (0.968 g, 3.18 mmol), 1-(3-cyclopenten-1-yl)-2-piperazinone trifluoroacetate (0.89 g, 3.18 mmol), EDC (0.731 g, 3.81 mmol) and HOBT (0.584 g, 3.81 mmol) in N,N-dimethylformamide (30 mL) at room temperature. The mixture was stirred overnight. The solvent was removed by evaporation, sat'd $NaHCO_3$ was added and the solution was extracted with 5 % MeOH in DCM. The combined organic extract was dried (Na_2SO_4), filtered and evaporated. The residue was purified by silica gel chromatography (0-30 % ethyl acetate in DCM) to give the title compound (0.83 g, 58%) as a white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05-8.07 (m, 1 H), 7.42 (s, 1 H), 5.76 (s, 2 H), 5.40 - 5.58 (m, 1 H), 4.64 (s, 1 H), 4.44 (s, 1 H), 4.27 - 4.35 (m, 1 H), 3.91 - 3.98 (m, 1 H), 3.30 - 3.41 (m, 2 H), 2.65 - 2.78

(m, 2 H), 2.23 - 2.37 (m, 2 H), 2.00 - 2.08 (m, 1 H), 1.08 - 1.16 (m, 2 H), 0.80 (d, 2 H). ES-LCMS: m/z 453.4 (M+1).

Step D

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone

[00681] BH_3.THF (3.97 mL, 3.97 mmol) was added dropwise to a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (600 mg, 1.325 mmol) in tetrahydrofuran (15 mL) at 0 ° C under N_2. The mixture was stirred at 0 ° C for 40 minutes and allowed to warm up to room temperature and stirred for 4 hours. A solution of $NaBO_3.4H_2O$ (652 mg, 4.24 mmol) in water (25 mL) was added and the reaction mixture was stirred for 30 minutes, diluted with brine, and extracted with EtOAc. The combined extracts were washed with brine, dried (Na_2SO_4), evaporated, and purified by silica gel chromatography (0-5 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (430 mg, 69%) as a racemic mixture. The racemic 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone was purified by SFC (Supercritical Fluid Chromatography).

[00682] Enantiomer 1 (ChiralPak ODH column, 250x10 mm i.d., 5um; Daicel Chemical Ind.; Osaka, Japan; Solvent/mobile phase: 72 % MeOH/28 % CO_2, Flow rate = 10 mL/min. Rt = 5.45 minute): white solid (125 mg, 42 %). 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.37 Hz, 1 H) 7.42 (s, 1 H) 5.18 (ddd, *J*=17.76, 8.78, 8.58 Hz, 1 H) 4.63 (s, 1 H) 4.39 - 4.49 (m, 2 H) 4.33 (q, *J*=5.01 Hz, 1 H) 3.97 (d, *J*=5.07 Hz, 1 H) 3.45 (t, *J*=4.68 Hz, 1 H) 3.40 (d, *J*=4.88 Hz, 1 H) 1.98 - 2.18 (m, 3 H) 1.79 - 1.97 (m, 2 H) 1.65 (d, *J*=5.85 Hz, 2 H) 1.07 - 1.16 (m, 2 H) 0.80 (d, *J*=4.88 Hz, 2 H). ES-LCMS: m/z 471.2 (M+1).

[00683] Enantiomer 2 (ChiralPak ODH column, 250x10 mm i.d., 5um; Daicel Chemical Ind.; Osaka, Japan; Solvent/mobile phase: 72 % MeOH/28 % CO_2, Flow rate = 10 mL/min. Rt = 6.85 minute): white solid (124 mg, 41 %). 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.17 Hz, 1 H) 7.42 (s, 1 H) 5.09 - 5.27 (m, 1 H) 4.63 (s, 1 H) 4.40 - 4.50 (m, 2 H) 4.33 (q, *J*=5.07 Hz, 1 H) 3.97 (q, *J*=4.68 Hz, 1 H) 3.45 (t, *J*=4.98 Hz, 1 H) 3.40 (d, *J*=5.07 Hz, 1 H) 1.98 - 2.19 (m, 3 H) 1.78 - 1.97 (m, 2 H) 1.65 (br. s., 2 H) 1.07 - 1.16 (m, 2 H) 0.80 (d, *J*=5.07 Hz, 2 H). ES-LCMS: m/z 471.2 (M+1).

EXAMPLE 247

(Compound 247)

Ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate (isomer 1)

and

EXAMPLE 248

(Compound 248)

Ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate (isomer 2)

[00684] 2-(ethyloxy)-2-oxoethanediazonium (0.231 mL, 2.208 mmol) was added to a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (100 mg, 0.221 mmol) and $Pd(OAc)_2$ (4.96 mg, 0.022 mmol) in tetrahydrofuran (2.0 mL) at 0 °C . It was stirred for 1 hour at 0 °C and then allowed to warm up to room temperature. The mixture was stirred for 3 days, diluted with DCM, washed with saturated $NaHCO_3$, and dried over Na_2SO_4. It was filtered and evaporated. The residue was purified by silica gel chromatography (0-5 % MeOH in DCM) to give the title compound as a white solid (110 mg, 92 %) which was an isomeric mixture and was isolated by reverse phase HPLC (water:acetonitrile with 0.1% formic acid).

[00685] Isomer 1: white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.37 Hz, 1 H) 7.42 (s, 1 H) 4.67 - 4.87 (m, 1 H) 4.63 (s, 1 H) 4.41 (s, 1 H) 4.32 (t, *J*=4.98 Hz, 1 H) 4.11 (qd, *J*=7.06, 2.24 Hz, 2 H) 3.95 (t, *J*=5.27 Hz, 1 H) 3.44 (t, *J*=4.98 Hz, 1 H) 3.39 (t, *J*=5.27 Hz, 1 H) 1.99 - 2.11 (m, 3 H) 1.84 - 1.97 (m, 4 H) 1.66 (d, *J*=14.05 Hz, 1 H) 1.26 (td, *J*=7.07, 3.61 Hz, 3 H) 1.07 - 1.16 (m, 2 H) 0.77 - 0.84 (m, 2 H). ES-LCMS: m/z 539.3 (M+1).

[00686] Isomer 2: white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.95 Hz, 1 H) 7.41 (s, 1 H) 4.85 - 4.99 (m, 1 H) 4.59 (s, 1 H) 4.39 (s, 1 H) 4.30 (t, *J*=5.07 Hz, 1 H) 4.16 (quin, *J*=7.07 Hz, 2 H) 3.96 (t, *J*=5.37 Hz, 1 H) 3.52 (t, *J*=5.17 Hz, 1 H) 3.47 (t, *J*=5.37 Hz, 1 H) 2.28 (ddd, *J*=13.85, 8.68, 5.17 Hz, 2 H) 1.92 - 2.13 (m, 5 H) 1.62 (t, *J*=8.29 Hz, 1 H) 1.30 (q, *J*=7.22 Hz, 3 H) 1.07 - 1.15 (m, 2 H) 0.77 - 0.84 (m, 2 H).). ES-LCMS: m/z 539.3 (M+1).

EXAMPLE 249

(Compound 249)

Ethyl 3-(4-{[6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate (isomer 1)

and

EXAMPLE 250

(Compound 250)

Ethyl 3-(4-{[6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate (isomer 2)

[00687] $NaBH_4$ (16.15 mg, 0.427 mmol) was added to a solution of ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate (92 mg, 0.171 mmol) in methanol (2.0 mL) at 0 °C. The reaction mixture was allowed warm up to room temperature, stirred for 2 hours, evaporated, and purified by reverse HPLC (water:acetonitrile with 0.1% formic acid).

[00688] Isomer 1: white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.09 - 8.22 (m, 1 H) 8.08 (br. s., 1 H) 7.36 (s, 1 H) 4.95 (s, 1 H) 4.79 (d, *J*=7.80 Hz, 1 H) 4.61 - 4.70 (m, 2 H) 4.37 - 4.45 (m, 1 H) 4.04 - 4.15 (m, 2 H) 3.94 (d, *J*=4.29 Hz, 2 H) 3.41 - 3.49 (m, 1 H) 3.37 (d, *J*=4.68 Hz, 1 H) 1.98 - 2.10 (m, 2 H) 1.84 - 1.98 (m, 4 H) 1.26 (t, *J*=7.12 Hz, 3 H) 1.02 - 1.11 (m, 2 H) 0.71 - 0.78 (m, 2 H). ES-LCMS: m/z 505.4 (M+1).

[00689] Isomer 2: white solid. 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.09 - 8.22 (m, 1 H) 8.02 - 8.09 (m, 1 H) 7.35 (s, 1 H) 4.85 - 5.01 (m, 2 H) 4.65 (t, *J*=4.78 Hz, 1 H) 4.38 (s, 1 H) 4.10 - 4.21 (m, 2 H) 3.95 (br. s., 1 H) 3.52 (t, *J*=4.78 Hz, 1 H) 3.46 (d, *J*=4.68 Hz, 1 H) 2.21 - 2.33 (m, 2 H) 2.01 - 2.12 (m, 2 H) 1.88 - 2.01 (m, 3 H) 1.62 (t, *J*=8.29 Hz, 1 H) 1.30 (t, *J*=7.02 Hz, 3 H) 1.03 - 1.11 (m, 2 H) 0.71 - 0.78 (m, 2 H). ES-LCMS: m/z 505.4 (M+1).

.

EXAMPLE 251

(Compound 251)

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylic acid

[00690] NaOH (4.06 mL, 4.06 mmol) was added to a solution of ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate (730 mg, 1.354 mmol) in tetrahydrofuran

(8.0 mL) and water (8.00 mL) at room temperature. The mixture was stirred for 6 hour and was then acidified to pH=1 with HCl (5 N), extracted with EtOAC. The combined extracts were dried over Na_2SO_4, filtered and evaporated. The residue was purified by silica gel chromatography (0-3 % MeOH in EtOAC with 0.1 % of formic acid) to give the title compound as a yellow foam (350 mg, 51 %) which was an isomeric mixture. One isomer was obtained as a white solid after purification by reverse HPLC (30% MeCN in H_2O). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.09 (br. s., 1 H) 8.45 (d, *J*=7.02 Hz, 1 H) 7.60 (d, *J*=4.88 Hz, 1 H) 4.96 - 5.14 (m, 1 H) 4.40 (s, 1 H) 4.17 (s, 1 H) 4.01 (t, *J*=4.88 Hz, 1 H) 3.83 (t, *J*=4.98 Hz, 1 H) 3.39 - 3.47 (m, 1 H) 2.22 (t, *J*=4.39 Hz, 1 H) 1.81 - 2.08 (m, 6 H) 1.50 - 1.61 (m, 1 H) 1.10 - 1.30 (m, 1 H) 1.02 (d, *J*=8.19 Hz, 2 H) 0.89 (d, *J*=5.07 Hz, 2 H). ES-LCMS: m/z 511.3 (M+1).

EXAMPLE 252

(Compound 252)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(hydroxymethyl)bicyclo[3.1.0]hex-3-yl]-2-piperazinone

[00691] BH_3.THF (0.411 mL, 0.411 mmol) was added to a solution of 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylic acid (70 mg, 0.137 mmol, isomeric mixture) in tetrahydrofuran (3.0 mL) at 0 °C. The mixture was stirred for 6 hours, and additional BH_3.THF (0.411 mL, 0.411 mmol) was added. The mixture was stirred overnight and quenched with aq. NaOH (1 N). The pH was adjusted to 10 and the aqueous layer was extracted with EtOAc. The aqueous phase was acidified to pH=1 with HCl (5 N), and extracted with EtOAc. The organic extracts were dried over Na_2SO_4, filtered and evaporated. The residue was purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to give the title compound (one isomer) as a white solid (9 mg, 13 %). 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=10.15 Hz, 1 H) 7.42 (s, 1 H) 4.66 - 5.13 (m, 1 H) 4.62 (s, 1 H) 4.41 (s, 1 H) 4.26 - 4.37 (m, 1 H) 3.90 - 4.01 (m, 1 H) 3.47 - 3.82 (m, 1 H) 3.35 - 3.46 (m, 3 H) 1.92 - 2.09 (m, 3 H) 1.77 - 1.89 (m, 2 H) 1.27 (br. s., 2 H) 1.07 - 1.20 (m, 3 H) 0.75 - 0.85 (m, 2 H). ES-LCMS: m/z 497.3 (M+1).

EXAMPLE 253

(Compound 253)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(6,6-difluorobicyclo[3.1.0]hex-3-yl)-2-piperazinone (isomer 1)

and

EXAMPLE 254

(Compound 254)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(6,6-difluorobicyclo[3.1.0]hex-3-yl)-2-piperazinone (isomer 2)

[00692] A solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (120 mg, 0.265 mmol) in diglyme (3 mL) was heated at 160 °C with vigorous stirring. Sodium chloro(difluoro)acetate (1.32 g, 8.48 mmol) was added portion wise over 4 hours. The reaction mixture was cooled to room temperature and then diluted with water, brine and EtOAc. Next, the solution was filtered through a pad of Celite. The organic layer was subsequently separated and then dried over Na_2SO_4, filtered, concentrated and purified by silica gel chromatography (0-75 % EtOAc/Hexane) to give the desired product (87 mg) as a brown oil. The product was then further purified by reverse HPLC (30% CH_3CN/H_2O to 90% CH_3CN/H_2O with 0.1% formic acid) to afford the two isomers of the title compound.

[00693] Isomer 1: white solid. 30 mg. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.76 Hz, 1 H) 7.42 (s, 1 H) 4.84 - 5.00 (m, 1 H) 4.64 (s, 1 H) 4.41 (s, 1 H) 4.33 (t, *J*=5.07 Hz, 1 H) 3.97 (t, *J*=5.27 Hz, 1 H) 3.49 (t, *J*=5.07 Hz, 1 H) 3.43 (t, *J*=5.27 Hz, 1 H) 1.99 - 2.28 (m, 7 H) 1.07 - 1.18 (m, 2 H) 0.75 - 0.86 (m, 2 H). ES-LCMS: m/z 503.3 (M+1).

[00694] Isomer 2: white solid. 7.5 mg. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=7.80 Hz, 1 H) 7.42 (s, 1 H) 5.29 - 5.54 (m, 1 H) 4.63 - 4.68 (m, 1 H) 4.42 (s, 1 H) 4.27 - 4.34 (m, 1 H) 3.95 (t, *J*=5.37 Hz, 1 H) 3.34 - 3.44 (m, 2 H) 2.21 (d, *J*=8.39 Hz, 2 H) 2.04 (dd, *J*=9.17, 3.71 Hz, 3 H) 1.70 (t, *J*=12.19 Hz, 2 H) 1.08 - 1.16 (m, 2 H) 0.76 - 0.83 (m, 2 H). ES-LCMS: m/z 503.2 (M+1).

EXAMPLE 255

(Compound 255)

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carbonitrile

Step A

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxamide

[00695] EDC (135 mg, 0.705 mmol) was added to a mixture of 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylic acid (120 mg, 0.235 mmol) and HOBT (108 mg, 0.705 mmol) in N,N-dimethylformamide (2.0 ml) under N_2 at room temperature. The reaction mixture was stirred for 30 minutes and ammonium hydroxide (0.154 ml, 3.95 mmol) was added. The mixture was stirred for 2 days at room temperature, evaporated and the residue was purified by reverse HPLC HPLC (water:acetonitrile with 0.1% formic acid) to give the title compound as a white solid (80 mg, 67 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.45 (d, *J*=5.85 Hz, 1 H) 7.60 (d, *J*=4.68 Hz, 1 H) 7.35 (br. s., 1 H) 6.73 (br. s., 1 H) 4.49 - 5.04 (m, 1 H) 4.36 - 4.47 (m, 1 H) 4.18 (d, *J*=18.15 Hz, 1 H) 3.98 (br. s., 1 H) 3.81 (br. s., 1 H) 2.22 (br. s., 1 H) 1.98 - 2.11 (m, 1 H) 1.81 - 1.97 (m, 2 H) 1.72 - 1.81 (m, 1 H) 1.39 - 1.71 (m, 3 H) 1.02 (d, *J*=7.80 Hz, 2 H) 0.90 (d, *J*=4.88 Hz, 2 H). ES-LCMS: m/z 510.1 (M+1).

Step B

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carbonitrile

[00696] TFAA (0.023 mL, 0.165 mmol) was added to a mixture of 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxamide (70 mg, 0.137 mmol) and pyridine (0.022 mL, 0.275 mmol) in tetrahydrofuran (2.0 mL) at 0 °C. The reaction mixture was allowed warm up to room temperature and stirred overnight. The solution was concentrated and the residue was purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to afford the title compound as a white solid (38 mg, 56 %). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.06 (d, J=8.78 Hz, 1 H) 7.42 (s, 1 H) 4.52 - 4.77 (m, 2 H) 4.38 - 4.42 (m, 1 H) 4.28 - 4.35 (m, 1 H) 3.90 - 4.04 (m, 1 H) 3.46 - 3.58 (m, 1 H) 3.32 - 3.46 (m, 1 H) 2.29 - 2.51 (m, 1 H) 2.16 - 2.29 (m, 1 H) 1.88 - 2.15 (m, 5 H) 1.31 - 1.53 (m, 1 H) 1.08 - 1.16 (m, 2 H) 0.76 - 0.83 (m, 2 H). ES-LCMS: m/z 492.2 (M+1).

EXAMPLE 256

(Compound 256)

(trans)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone

Step A

(trans)-ethyl 3-oxabicyclo[3.1.0]hexane-6-carboxylate

[00697] 2-(Ethyloxy)-2-oxoethanediazonium (8.79 mL, 84 mmol) in THF(40 mL) was added by a syringe pump (over 50 hours) to a solution of 2,5-dihydrofuran (5.16 mL, 70 mmol) and rhodium(II) acetate dimer (1.547 g, 3.50 mmol) in dichloromethane (250 mL) at room temperature. The reaction mixture was then filtered through a pad of Celite and evaporated. The residue was purified by silica gel chromatography (0-25% EtOAc in hexane) to give the title compound as a colorless oil (5.5 g, 50 %). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 4.14 (q, J=7.09 Hz, 2 H) 3.93 (d, J=8.59 Hz, 2 H) 3.75 (d, J=8.39 Hz, 2 H) 2.16 (br. s., 2 H) 1.61 (t, J=3.02 Hz, 1 H) 1.27 (t, J=7.12 Hz, 3 H).

Step B

(trans)-3-oxabicyclo[3.1.0]hexane-6-carboxylic acid

[00698] A solution of LiOH (1.528 g, 36.4 mmol) in water (30 mL) was added to a solution of (trans)-ethyl 3-oxabicyclo[3.1.0]hexane-6-carboxylate (5.17 g, 33.1 mmol) in methanol (80 mL) at room temperature under nitrogen. The mixture was stirred overnight and partially concentrated to remove the MeOH. It was cooled in an ice bath, and HCl in dioxane (4 N) was added to adjust the pH to 5. The mixture was concentrated and extracted with EtOAc (3x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give the desired product (2.89 g, 68 %) as a white solid which required no further purification. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 3.96 (d, J=8.78 Hz, 2 H) 3.77 (d, J=8.78 Hz, 2 H) 2.24 (br. s., 2 H) 1.62 (t, 1 H).

Step C

(trans)-1,1-Dimethylethyl 3-oxabicyclo[3.1.0]hex-6-ylcarbamate

[00699] A mixture of (trans)-3-oxabicyclo[3.1.0]-hexane-6-carboxylic acid (2.85 g, 22.24 mmol), diphenyl azidophosphate (5.27 mL, 24.47 mmol) and TEA (6.51 mL, 46.7 mmol) in tert-butanol (150 mL) was heated under reflux for 2 days. The solution was concentrated and the residue was dissolved in EtOAc, and washed with 1N HCl solution, saturated $NaHCO_3$ and brine, and dried over Na_2SO_4. The residue was purified by silica gel chromatography (0-40% EtOAc in hexane) to give the title compound as a white solid (0.71 g, 16 %). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 4.66 (br. s., 1 H) 3.97 (d, J=8.39 Hz, 2 H) 3.71 (d, J=8.39 Hz, 2 H) 2.40 (br. s., 1 H) 1.77 (br. s., 2 H) 1.45 (s, 9 H).

Step D

(trans)-3-oxabicyclo[3.1.0]hex-6-ylamine hydrochloride

[00700] HCl (17.8 ml, 586 mmo, 4 N in 1,4-dioxane) was added to a solution of 1,1-dimethylethyl 3-oxabicyclo[3.1.0]hex-6-ylcarbamate (710 mg, 3.56 mmol) in 1,4-dioxane (18 mL) under nitrogen at room temperature. The reaction mixture was stirred overnight and then concentrated to dryness to give the title compound as a white solid which was used without purification and assumed to be quantitative. ^{1}H NMR (400 MHz,

METHANOL-d_4) δ ppm 3.94 (d, *J*=8.78 Hz, 2 H) 3.69 (d, *J*=8.78 Hz, 2 H) 2.37 (s, 1 H) 2.05 (d, *J*=0.98 Hz, 2 H).

Step E

(trans)-1,1-dimethylethyl 4-(3-oxabicyclo[3.1.0]hex-6-yl)-3-oxo-1-piperazinecarboxylate

[00701] To a solution of methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (0.745 g, 3.22 mmol) in methanol (16 mL) was added sodium sulfate (2.74 g, 19.32 mmol) followed by (trans)-3-oxabicyclo[3.1.0]hex-6-ylamine hydrochloride (0.480 g, 3.54 mmol) and DIPEA (0.675 mL, 3.86 mmol). The mixture was stirred for 1 hour and $NaBH_4$ (0.146 g, 3.86 mmol) was added portion wise in order to control effervescence. After 2 hours, NaH (0.258 g, 6.44 mmol) was added portion wise. The mixture was stirred for 2 hours, evaporated and the residue was dissolved EtOAc. The solution was filtered through a pad of celite and diluted with 10 % citric acid. The organic layer was separated and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by silica gel chromatography (0-4 % 2 M NH_3 solution of MeOH in DCM) to give the title compound (0.55 g, 60 %) as a white solid. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 4.00 - 4.08 (m, 4 H) 3.76 (d, J=8.39 Hz, 2 H) 3.62 (t, J=5.37 Hz, 2 H) 3.32 (t, J=5.37 Hz, 2 H) 2.52 (br. s., 0 H) 1.94 (s, 2 H) 1.47 (s, 9 H). ES-LCMS: m/z 283.2 (M+1).

Step F

(trans)-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone hydrochloride

[00702] HCl (9.65 mL, 38.6 mmol, 4.0 M in 1,4-dioxane) was added to a solution of (trans)-1,1-dimethylethyl 4-(3-oxabicyclo[3.1.0]hex-6-yl)-3-oxo-1-piperazinecarboxylate (545 mg, 1.93 mmol) in 1,4-dioxane (10 mL) under N_2 at room temperature. The reaction mixture was stirred for 6 hours and then concentrated to dryness to give the title compound as a white solid which was used without purification and assumed to be quantitative. ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 3.96 (s, 1 H) 3.94 (s, 1 H) 3.74 - 3.80 (m, 2 H) 3.62 - 3.72 (m, 3 H) 3.50 - 3.57 (m, 2 H) 3.41 - 3.49 (m, 2 H) 2.46 (s, 1 H) 2.02 (s, 2 H).

Step G

(trans)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone

[00703] DIPEA (0.112 mL, 0.643 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (49 mg, 0.161 mmol) and (trans)-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone hydrochloride (35.2 mg, 0.161 mmol) in N,N-dimethylformamide (2.0 mL) at room temperature under nitrogen. The

mixture was stirred for 30 minutes at room temperature and cooled to 0 °C. 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.144 mL, 0.241 mmol) was added. The mixture was allowed to warm up to room temperature and stirred for 1 hour. Saturated $NaHCO_3$ was added and the solution was extracted with EtOAc, washed with 5 % aqueous LiCl, dried over Na_2SO_4, filtered, evaporated and purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to afford the title compound (58 mg, 77 %) as a white solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=8.59 Hz, 1 H) 7.42 (s, 1 H) 4.64 (s, 1 H) 4.40 (s, 1 H) 4.30 (t, *J*=4.98 Hz, 1 H) 4.05 (t, *J*=9.07 Hz, 2 H) 3.99 (t, *J*=5.37 Hz, 1 H) 3.72 - 3.81 (m, 2 H) 3.53 (t, *J*=4.98 Hz, 1 H) 3.46 (t, *J*=5.37 Hz, 1 H) 2.55 (d, *J*=9.17 Hz, 1 H) 2.01 - 2.09 (m, 1 H) 1.97 (d, *J*=17.17 Hz, 2 H) 1.08 - 1.16 (m, 2 H) 0.76 - 0.84 (m, 2 H). ES-LCMS: m/z 469.2 (M+1).

EXAMPLE 257

(Compound 257)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-[(1*R*,3*R*)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone

Step A

1,1-dimethylethyl [(1R,3R)-3-(hydroxymethyl)cyclopentyl]methylcarbamate

[00704] Ethyl chloroformate (0.197 mL, 2.055 mmol) was added to a stirred solution of (1R,3R)-3-[{[(1,1-dimethylethyl)oxy]carbonyl}(methyl)amino]cyclopentanecarboxylic acid (500 mg, 2.055 mmol) and TEA (0.301 mL, 2.158 mmol) in dry THF(5.0 mL) at 0 °C. The reaction mixture was stirred for 30 minutes at 0 °C and filtered. The filtrate was slowly added to a stirred suspension of $NaBH_4$ (233 mg, 6.17 mmol) in 20 % aqueous THF (5.0 mL) at 10 °C. The mixture was stirred for another 30 minutes at the same temperature and then acidified with 1N HCl to pH = 4. The mixture was extracted with EtOAc (3x) and the combined organic layers were washed with 2N NaOH (2x), water (2x) and brine, and dried over Na_2SO_4. Evaporation afforded the title compound (465 mg, 99 %) as a white solid which was used without purification. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 4.50 (br. s., 1 H) 3.97 (br. s., 1 H) 3.52 (d, J=6.83 Hz, 2 H) 2.26 (ddd, J=14.88, 7.80, 7.56 Hz, 1 H) 1.98 - 2.09 (m, 1 H) 1.82 - 1.92 (m, 1 H) 1.66 - 1.76 (m, 1 H) 1.55 - 1.65 (m, 2 H) 1.44 (s, 9 H) 1.23 - 1.42 (m, 2 H).

Step B

[(1R,3R)-3-(methylamino)cyclopentyl]methanol hydrochloride

[00705] HCl (9.65 mL, 38.6 mmol, 4.0 M in 1,4-dioxane) was added to a solution of 1,1-dimethylethyl 4-(3-oxabicyclo[3.1.0]hex-6-yl)-3-oxo-1-piperazinecarboxylate (545 mg,

1.930 mmol) in 1,4-dioxane (10 mL). The reaction mixture was stirred for 6 hours, concentrated and dried in vacuo to give the desired product as a sticky oil which was used without purification and assumed to be quantitative. ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 3.63 (s, 2 H) 3.54 - 3.62 (m, 1 H) 3.43 (qd, J=10.68, 6.44 Hz, 2 H) 3.28 (dt, J=3.22, 1.71 Hz, 2 H) 2.31 (ddd, J=14.84, 7.32, 7.13 Hz, 1 H) 2.07 - 2.17 (m, 1 H) 1.92 (dddd, J=12.55, 8.25, 8.01, 4.20 Hz, 1 H) 1.70 - 1.87 (m, 2 H) 1.54 - 1.66 (m, 1 H) 1.33 - 1.47 (m, 1 H).

Step C

1,1-dimethylethyl 4-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-3-oxo-1-piperazinecarboxylate

[00706] To a solution of methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (358 mg, 1.55 mmol) in methanol (10 mL) was added sodium sulfate (1.32 g, 9.30 mmol) followed by [(1R,3R)-3-(methylamino)cyclopentyl]methanol hydrochloride (282 mg, 1.705 mmol) and DIPEA (0.325 mL, 1.860 mmol). The mixture was stirred for 1 hour before $NaBH_4$ (70.4 mg, 1.860 mmol) was added portion wise in order to control effervescence. A mild exotherm was observed. After 2 hours, NaH (124 mg, 3.10 mmol) was added portion wise in order to control effervescence. The mixture was stirred for 2 hour. Most of the solvent was removed off and the residue was diluted with EtOAC. It was then filtered through a pad of Celite and the filtrate treated with 10 % citric acid. The organic layer was separated and the aqueous phase was extracted with EtOAC. The combined extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by silica gel chromatography (0-4 % MeOH in DCM) to give the title compound (66 mg, 14%) as a colorless sticky oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.02 (quin, *J*=8.63 Hz, 1 H) 4.01 - 4.15 (m, 2 H) 3.57 - 3.69 (m, 2 H) 3.55 (d, *J*=6.63 Hz, 2 H) 3.28 (t, *J*=5.17 Hz, 2 H) 2.27 (ddd, *J*=15.02, 7.80, 7.61 Hz, 1 H) 1.86 - 1.98 (m, 2 H) 1.69 (t, *J*=8.00 Hz, 2 H) 1.51 - 1.59 (m, 1 H) 1.47 (s, 9 H) 1.24 - 1.37 (m, 1 H). ES-LCMS: m/z 299.2 (M+1).

Step D

1-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone hydrochloride

[00707] HCl (1.106 mL, 4.42 mmol, 4.0 M in 1,4-dioxane) was added to a solution of 1,1-dimethylethyl 4-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-3-oxo-1-piperazinecarboxylate (66 mg, 0.221 mmol) in 1,4-dioxane (1.0 mL) at room temperature. The mixture was stirred for 4 hours and concentrated to give the desired product as a white solid which was used without purification and assumed quantitative. ES-LCMS: m/z 197.8 (M-1).

Step E

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone

[00708] DIPEA (0.077 mL, 0.440 mmol) was added to a mixture of 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (33.5 mg, 0.110 mmol) and 1-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone hydrochloride (25.8 mg, 0.110 mmol) in N,N-dimethylformamide (1.0 mL) at room temperature. The mixture was stirred for 30 minutes at room temperature and cooled to 0 °C. 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.098 mL, 0.165 mmol) was added and the reaction mixture was stirred at room temperature for 1 hour and diluted with saturated $NaHCO_3$. The solution was extracted with EtOAc, washed with 5 % aqueous LiCl, dried over Na_2SO_4, filtered, evaporated, and purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to afford the title compound (38 mg, 71 %) as a white solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.56 Hz, 1 H) 7.42 (s, 1 H) 4.91 - 5.10 (m, 1 H) 4.63 (d, *J*=4.88 Hz, 1 H) 4.21 - 4.51 (m, 2 H) 3.87 - 4.06 (m, 1 H) 3.52 - 3.60 (m, 2 H) 3.40 - 3.51 (m, 2 H) 2.30 (dt, *J*=14.98, 7.44 Hz, 1 H) 2.00 - 2.10 (m, 1 H) 1.88 - 1.99 (m, 2 H) 1.72 (q, *J*=8.00 Hz, 2 H) 1.51 - 1.61 (m, 1 H) 1.25 - 1.40 (m, 1 H) 1.08 - 1.17 (m, 2 H) 0.75 - 0.84 (m, 2 H). ES-LCMS: m/z 485.2 (M+1).

EXAMPLE 258

(Compound 258)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(5-oxo-3-pyrrolidinyl)-2-piperazinone

Step A

1,1-dimethylethyl 3-oxo-4-(5-oxo-3-pyrrolidinyl)-1-piperazinecarboxylate

[00709] The title compound (296 mg, 32 %) was prepared from methyl N-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(2-oxoethyl)glycinate (768 mg, 3.32 mmol), sodium sulfate (2.829 g, 19.92 mmol), 4-amino-2-pyrrolidinone hydrochloride (499 mg, 3.65 mmol), DIPEA (0.696 mL, 3.98 mmol), $NaBH_4$ (151 mg, 3.98 mmol) and NaH (398 mg, 9.96 mmol) following a previously described procedure. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.87 (br. s., 1 H) 5.42 - 5.55 (m, 1 H) 4.12 (s, 2 H) 3.60 - 3.79 (m, 3 H) 3.27 - 3.40 (m, 3 H) 2.67 (dd, *J*=17.76, 9.37 Hz, 1 H) 2.38 (dd, *J*=17.76, 5.07 Hz, 1 H) 1.48 (s, 9 H). ES-LCMS: m/z 284.2 (M+1).

Step B

1-(5-oxo-3-pyrrolidinyl)-2-piperazinone hydrochloride

[00710] HCl (5.22 mL, 20.89 mmol, 4.0 M in 1,4-dioxane) was added to a solution of 1,1-dimethylethyl 3-oxo-4-(5-oxo-3-pyrrolidinyl)-1-piperazinecarboxylate (296 mg, 1.045 mmol) in 1,4-dioxane (5.0 mL) at room temperature. The mixture was stirred for 4 hours and concentrated to give the desired product as a white solid which was used without purification and assumed to be quantitative. ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 5.15 (td, *J*=8.54, 4.59 Hz, 1 H) 3.85 (s, 2 H) 3.72 (dd, *J*=11.12, 8.19 Hz, 1 H) 3.65 (s, 2 H) 3.59 - 3.64 (m, 1 H) 3.52 - 3.58 (m, 2 H) 3.41 - 3.48 (m, 1 H) 2.69 (dd, *J*=17.66, 9.46 Hz, 1 H) 2.44 - 2.53 (m, 1 H) 1.59 (s, 1 H).

Step C

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-oxo-3-pyrrolidinyl)-2-piperazinone

[00711] The title compound (40 mg, 74 %) was isolated as a white solid from DIPEA (0.080 mL, 0.460 mmol), 3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxylic acid (35 mg, 0.115 mmol), 1-(5-oxo-3-pyrrolidinyl)-2-piperazinone hydrochloride (25.2 mg, 0.115 mmol) and 1-propanephosphonic acid cyclic anhydride, 50 wt. % solution in ethyl acetate (0.103 mL, 0.172 mmol) using a previously described procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.46 (br. s., 1 H) 7.72 (d, J=5.66 Hz, 1 H) 7.60 (s, 1 H) 5.16 (ddd, J=9.17, 4.49, 4.29 Hz, 1 H) 4.49 (d, J=1.56 Hz, 1 H) 4.23 (d, J=2.73 Hz, 1 H) 4.00 - 4.11 (m, 1 H) 3.79 - 3.95 (m, 1 H) 3.35 - 3.53 (m, 3 H) 3.23 (dd, J=10.24, 3.61 Hz, 1 H) 2.36 - 2.47 (m, 1 H) 2.17 - 2.35 (m, 2 H) 0.98 - 1.07 (m, 2 H) 0.86 - 0.93 (m, 2 H). ES-LCMS: m/z 470.2 (M+1).

EXAMPLE 259

(Compound 259)

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxabicyclo[3.1.0]hex-3-yl)-2-piperazinone

[00712] *m*-CPBA (269 mg, 1.091 mmol) was added in portions to a mixture of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone (380 mg, 0.839 mmol) and sodium bicarbonate (113 mg, 1.343 mmol) in dichloromethane (10 mL) at room temperature. The mixture was stirred overnight and filtered. The filtrate was washed with saturated Na_2SO_3, 10 % $NaHCO_3$ and water, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel chromatography (0-100 % EtOAc in hexane) to give the title compound (248 mg, 63 %) as a white solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.06 (d, *J*=9.17 Hz, 1 H) 7.42 (s, 1 H) 5.32 - 5.52 (m, 0.5 H) 4.62 (d, *J*=11.51 Hz, 1 H) 4.56 (t, 0.5 H) 4.41 (s, 1 H) 4.22 -

4.36 (m, 1 H) 3.86 - 4.02 (m, 1 H) 3.56 (d, *J*=3.12 Hz, 2 H) 3.35 - 3.54 (m, 2 H) 2.21 - 2.38 (m, 2 H) 1.82 - 2.08 (m, 2 H) 1.08 - 1.17 (m, 2 H) 0.76 - 0.84 (m, 2 H). ES-LCMS: m/z 469.2 (M+1).

EXAMPLE 260

(Compound 260)

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3,4-dihydroxycyclopentyl]-2-piperazinone

and

EXAMPLE 261

(Compound 261)

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-fluoro-4-hydroxycyclopentyl]-2-piperazinone

[00713] HF-pyridine (0.073 mL, 0.843 mmol) was added to a solution of 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxabicyclo[3.1.0]hex-3-yl)-2-piperazinone (238 mg, 0.508 mmol) in dichloromethane (4.0 mL) at 0 °C. The mixture was stirred for 2 hours at this temperature and diluted with water (10 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 5 mL). The combined organic extracts were dried over Na_2SO_4, filtered, evaporated, and purified by reverse phase HPLC (water:acetonitrile with 0.1% formic acid) to afford (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3,4-dihydroxycyclopentyl]-2-piperazinone (12 mg, 4.9 %) and (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-fluoro-4-hydroxycyclopentyl]-2-piperazinone (4.0 mg, 1.6 %).

[00714] (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3,4-dihydroxycyclopentyl]-2-piperazinone: ^{1}H NMR (400 MHz, DMSO-d_6) d ppm 8.45 (br. s., 1 H) 7.60 (s, 1 H) 4.99 - 5.19 (m, 1 H) 4.89 (br. s., 1 H) 4.73 (br. s., 1 H) 4.43 (d, *J*=4.29 Hz, 1 H) 4.12 - 4.27 (m, 1 H) 4.03 (q, *J*=7.15 Hz, 1 H) 3.73 - 3.99 (m, 4 H) 3.44 (d, *J*=4.88 Hz, 1 H) 2.18 - 2.27 (m, 1 H) 2.13 (td, *J*=9.22, 4.59 Hz, 1 H) 1.77 - 1.91 (m, 1 H) 1.60 (t, *J*=10.44 Hz, 1 H) 1.31 - 1.43 (m, 1 H) 0.98 - 1.07 (m, 2 H) 0.87 - 0.93 (m, 2 H). ES-LCMS: m/z 487.2 (M+1).

[00715] (+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-fluoro-4-hydroxycyclopentyl]-2-piperazinone: ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 8.33 (s, 1 H) 7.60 (s, 1 H) 5.09 (ddd, *J*=16.49, 8.10, 7.80 Hz, 1 H)

4.77 (br. s., 1 H) 4.59 (s, 1 H) 4.37 (d, *J*=3.71 Hz, 1 H) 3.89 - 4.25 (m, 3 H) 3.51 - 3.63 (m, 2 H) 2.36 (dd, *J*=14.83, 8.19 Hz, 1 H) 2.04 - 2.23 (m, 3 H) 1.66 (ddd, *J*=10.54, 7.02, 3.32 Hz, 1 H) 1.05 - 1.14 (m, 2 H) 0.80 - 0.90 (m, 2 H). ES-LCMS: m/z 489.2 (M+1).

Administration and Formulation

[00716] The chemical entities provided herein may inhibit viral replication by inhibiting the enzymes involved in replication, such as the non-structural proteins including RNA dependent RNA polymerase. They may also inhibit other enzymes utilized in the activity or proliferation of viruses in the *Flaviviridae* family, such as HCV. The chemical entities are administered at a therapeutically effective dosage, *e.g.*, a dosage sufficient to provide treatment for the disease.

[00717] In another embodiment, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of a compound of Formula (I) or a pharmaceutically acceptable salt thereof.

[00718] The compounds of the present invention can also be supplied in the form of a pharmaceutically acceptable salt. The terms "pharmaceutically acceptable salt" refer to salts prepared from pharmaceutically acceptable inorganic and organic acids and bases.

[00719] Pharmaceutically acceptable inorganic bases include metallic ions. More preferred metallic ions include, but are not limited to, appropriate alkali metal salts, alkaline earth metal salts and other physiological acceptable metal ions. Salts derived from inorganic bases include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc, and the like and in their usual valences. Exemplary salts include aluminum, calcium, lithium, magnesium, potassium, sodium and zinc. Particularly preferred are the ammonium, calcium, magnesium, potassium, and sodium salts.

[00720] Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, including in part, trimethylamine, diethylamine, N, N'-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine (N-methylglucamine) and procaine; substituted amines including naturally occurring substituted amines; cyclic amines; quaternary ammonium cations; and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine,

morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

[00721] Illustrative pharmaceutically acceptable acid addition salts of the compounds of the present invention can be prepared from the following acids, including, without limitation formic, acetic, propionic, benzoic, succinic, glycolic, gluconic, lactic, maleic, malic, tartaric, citric, nitic, ascorbic, glucuronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, hydrochloric, hydrobromic, hydroiodic, isocitric, trifluoroacetic, pamoic, propionic, anthranilic, mesylic, oxalacetic, oleic, stearic, salicylic, p-hydroxybenzoic, nicotinic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, phosphoric, phosphonic, ethanesulfonic, benzenesulfonic, pantothenic, toluenesulfonic, 2-hydroxyethanesulfonic, sulfanilic, sulfuric, salicylic, cyclohexylaminosulfonic, algenic, β-hydroxybutyric, galactaric and galacturonic acids. Preferred pharmaceutically acceptable salts include the salts of hydrochloric acid and trifluoroacetic acid.

All of the above salts can be prepared by those skilled in the art by conventional means from the corresponding compound of the present invention. For example, the pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. The salt may precipitate from solution and be collected by filtration or may be recovered by evaporation of the solvent. The degree of ionisation in the salt may vary from completely ionised to almost non-ionised. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p.1418, the disclosure of which is hereby incorporated by reference only with regards to the lists of suitable salts.

[00722] The compounds of the invention may exist in both unsolvated and solvated forms. The term 'solvate' is used herein to describe a molecular complex comprising the compound of the invention and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when said solvent is water. Pharmaceutically acceptable solvates include hydrates and other solvates wherein the solvent of crystallization may be isotopically substituted, *e.g.* D_2O, d_6-acetone, d_6-DMSO.

[00723] Compounds of formula (I) containing one or more asymmetric carbon atoms can exist as two or more stereoisomers. Where a compound of formula (I) contains an alkenyl or alkenylene group or a cycloalkyl group, geometric *cis*/*trans* (or Z/E) isomers

are possible. Where the compound contains, for example, a keto or oxime group or an aromatic moiety, tautomeric isomerism ('tautomerism') can occur. It follows that a single compound may exhibit more than one type of isomerism.

[00724] Included within the scope of the claimed compounds present invention are all stereoisomers, geometric isomers and tautomeric forms of the compounds of formula (I), including compounds exhibiting more than one type of isomerism, and mixtures of one or more thereof. Also included are acid addition or base salts wherein the counterion is optically active, for example, D-lactate or L-lysine, or racemic, for example, DL-tartrate or DL-arginine.

[00725] *Cis/trans* isomers may be separated by conventional techniques well known to those skilled in the art, for example, chromatography and fractional crystallisation.

[00726] Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC).

[00727] Alternatively, the racemate (or a racemic precursor) may be reacted with a suitable optically active compound, for example, an alcohol, or, in the case where the compound of formula (I) contains an acidic or basic moiety, an acid or base such as tartaric acid or 1-phenylethylamine. The resulting diastereomeric mixture may be separated by chromatography and/or fractional crystallization and one or both of the diastereoisomers converted to the corresponding pure enantiomer(s) by means well known to a skilled person.

[00728] Chiral compounds of the invention (and chiral precursors thereof) may be obtained in enantiomerically-enriched form using chromatography, typically HPLC, on a resin with an asymmetric stationary phase and with a mobile phase consisting of a hydrocarbon, typically heptane or hexane, containing from 0 to 50% isopropanol, typically from 2 to 20%, and from 0 to 5% of an alkylamine, typically 0.1% diethylamine. Concentration of the eluate affords the enriched mixture.

[00729] Mixtures of stereoisomers may be separated by conventional techniques known to those skilled in the art. [see, for example, "Stereochemistry of Organic Compounds" by E L Eliel (Wiley, New York, 1994).]

[00730] The present invention includes all pharmaceutically acceptable isotopically-labelled compounds of formula (I) wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number usually found in nature.

[00731] Examples of isotopes suitable for inclusion in the compounds of the invention include isotopes of hydrogen, such as ^{2}H and ^{3}H, carbon, such as ^{11}C, ^{13}C and ^{14}C, chlorine, such as ^{36}Cl, fluorine, such as ^{18}F, iodine, such as ^{123}I and ^{125}I, nitrogen, such as ^{13}N and ^{15}N, oxygen, such as ^{15}O, ^{17}O and ^{18}O, phosphorus, such as ^{32}P, and sulphur, such as ^{35}S.

[00732] Certain isotopically-labelled compounds of formula (I), for example, those incorporating a radioactive isotope, are useful in drug and/or substrate tissue distribution studies. The radioactive isotopes tritium, *i.e.* ^{3}H, and carbon-14, *i.e.* ^{14}C, are particularly useful for this purpose in view of their ease of incorporation and ready means of detection.

[00733] Substitution with heavier isotopes such as deuterium, *i.e.* ^{2}H, may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements, and hence may be preferred in some circumstances.

[00734] Isotopically-labelled compounds of formula (I) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations using an appropriate isotopically-labelled reagents in place of the non-labelled reagent previously employed.

[00735] The compounds of the present invention may be administered as prodrugs. Thus, certain derivatives of compounds of formula (I) which may have little or no pharmacological activity themselves can, when administered into or onto the body, be converted into compounds of formula (I) having the desired activity, for example, by hydrolytic cleavage. Such derivatives are referred to as 'prodrugs'.

[00736] Administration of the chemical entities described herein can be *via* any of the accepted modes of administration for agents that serve similar utilities including, but not limited to, orally, sublingually, subcutaneously, intravenously, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonarilly, vaginally, rectally, or intraocularly. In some embodiments, oral or parenteral administration is used.

[00737] Pharmaceutical compositions or formulations include solid, semi-solid, liquid and aerosol dosage forms, such as, e.g., tablets, capsules, powders, liquids, suspensions, suppositories, aerosols or the like. The chemical entities can also be administered in sustained or controlled release dosage forms, including depot injections, osmotic pumps, pills, transdermal (including electrotransport) patches, and the like, for prolonged and/or timed, pulsed administration at a predetermined rate. In certain embodiments, the compositions are provided in unit dosage forms suitable for single administration of a precise dose.

[00738] The chemical entities described herein can be administered either alone or more typically in combination with a conventional pharmaceutical carrier, excipient or the like (e.g., mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, sodium crosscarmellose, glucose, gelatin, sucrose, magnesium carbonate, and the like). If desired, the pharmaceutical composition can also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, solubilizing agents, pH buffering agents and the like (e.g., sodium acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine oleate, and the like). Generally, depending on the intended mode of administration, the pharmaceutical composition will contain about 0.005% to 95%; in certain embodiments, about 0.5% to 50% by weight of a chemical entity. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Easton, Pennsylvania.

[00739] In certain embodiments, the compositions will take the form of a pill or tablet and thus the composition will contain, along with the active ingredient, a diluent such as lactose, sucrose, dicalcium phosphate, or the like; a lubricant such as magnesium stearate or the like; and a binder such as starch, gum acacia, polyvinylpyrrolidine, gelatin, cellulose, cellulose derivatives or the like. In another solid dosage form, a powder, marume, solution or suspension (e.g., in propylene carbonate, vegetable oils or triglycerides) is encapsulated in a gelatin capsule.

[00740] Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, etc. at least one chemical entity and optional pharmaceutical adjuvants in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) to form a solution or suspension. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, as emulsions, or in solid forms suitable for dissolution or suspension in liquid prior to injection. The percentage of chemical entities contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the chemical entities and the needs of the subject. However, percentages of active ingredient of 0.01% to 10% in solution are employable, and will be higher if the composition is a solid which will be subsequently diluted to the above percentages. In certain embodiments, the composition will comprise from about 0.2 to 2% of the active agent in solution.

[00741] Pharmaceutical compositions of the chemical entities described herein may also be administered to the respiratory tract as an aerosol or solution for a nebulizer, or as a microfine powder for insufflation, alone or in combination with an inert carrier such as

lactose. In such a case, the particles of the pharmaceutical composition have diameters of less than 50 microns, in certain embodiments, less than 10 microns.

[00742] In general, the chemical entities provided will be administered in a therapeutically effective amount by any of the accepted modes of administration for agents that serve similar utilities. The actual amount of the chemical entity, i.e., the active ingredient, will depend upon numerous factors such as the severity of the disease to be treated, the age and relative health of the subject, the potency of the chemical entity used, the route and form of administration, and other factors. The drug can be administered more than once a day, such as once or twice a day.

[00743] Therapeutically effective amounts of the chemical entities described herein may range from approximately 0.01 to 200 mg per kilogram body weight of the recipient per day; such as about 0.01-100 mg/kg/day, for example, from about 0.1 to 50 mg/kg/day. Thus, for administration to a 70 kg person, the dosage range may be about 7-3500 mg per day.

[00744] In general, the chemical entities will be administered as pharmaceutical compositions by any one of the following routes: oral, systemic (e.g., transdermal, intranasal or by suppository), or parenteral (e.g., intramuscular, intravenous or subcutaneous) administration. In certain embodiments, oral administration with a convenient daily dosage regimen that can be adjusted according to the degree of affliction may be used. Compositions can take the form of tablets, pills, capsules, semisolids, powders, sustained release formulations, solutions, suspensions, elixirs, aerosols, or any other appropriate compositions. Another manner for administering the provided chemical entities is inhalation.

[00745] The choice of formulation depends on various factors such as the mode of drug administration and bioavailability of the drug substance. For delivery *via* inhalation the chemical entity can be formulated as liquid solution, suspensions, aerosol propellants or dry powder and loaded into a suitable dispenser for administration. There are several types of pharmaceutical inhalation devices-nebulizer inhalers, metered dose inhalers (MDI) and dry powder inhalers (DPI). Nebulizer devices produce a stream of high velocity air that causes the therapeutic agents (which are formulated in a liquid form) to spray as a mist that is carried into the patient's respiratory tract. MDIs typically are formulation packaged with a compressed gas. Upon actuation, the device discharges a measured amount of therapeutic agent by compressed gas, thus affording a reliable method of administering a set amount of agent. DPI dispenses therapeutic agents in the form of a free flowing powder that can be dispersed in the patient's inspiratory air-stream during breathing by the device. In order to achieve a free flowing powder, the therapeutic agent is

formulated with an excipient such as lactose. A measured amount of the therapeutic agent is stored in a capsule form and is dispensed with each actuation.

[00746] Recently, pharmaceutical compositions have been developed for drugs that show poor bioavailability based upon the principle that bioavailability can be increased by increasing the surface area i.e., decreasing particle size. For example, U.S. Patent No. 4,107,288 describes a pharmaceutical formulation having particles in the size range from 10 to 1,000 nm in which the active material is supported on a cross-linked matrix of macromolecules. U.S. Patent No. 5,145,684 describes the production of a pharmaceutical formulation in which the drug substance is pulverized to nanoparticles (average particle size of 400 nm) in the presence of a surface modifier and then dispersed in a liquid medium to give a pharmaceutical formulation that exhibits remarkably high bioavailability.

[00747] The compositions are comprised of, in general, at least one chemical entity described herein in combination with at least one pharmaceutically acceptable excipient. Acceptable excipients are non-toxic, aid administration, and do not adversely affect the therapeutic benefit of the at least one chemical entity described herein. Such excipient may be any solid, liquid, semi-solid or, in the case of an aerosol composition, gaseous excipient that is generally available to one of skill in the art.

[00748] Solid pharmaceutical excipients include starch, cellulose, talc, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, magnesium stearate, sodium stearate, glycerol monostearate, sodium chloride, dried skim milk and the like. Liquid and semisolid excipients may be selected from glycerol, propylene glycol, water, ethanol and various oils, including those of petroleum, animal, vegetable or synthetic origin, e.g., peanut oil, soybean oil, mineral oil, sesame oil, etc. Liquid carriers, for injectable solutions, include water, saline, aqueous dextrose, and glycols.

[00749] Compressed gases may be used to disperse a chemical entity described herein in aerosol form. Inert gases suitable for this purpose are nitrogen, carbon dioxide, etc. Other suitable pharmaceutical excipients and their formulations are described in Remington's Pharmaceutical Sciences, edited by E. W. Martin (Mack Publishing Company, 18th ed., 1990).

[00750] The amount of the chemical entity in a composition can vary within the full range employed by those skilled in the art. Typically, the composition will contain, on a weight percent (wt%) basis, from about 0.01-99.99 wt% of at least one chemical entity described herein based on the total composition, with the balance being one or more suitable pharmaceutical excipients. In certain embodiments, the at least one chemical entity described herein is present at a level of about 1-80 wt%. Representative

pharmaceutical compositions containing at least one chemical entity described herein are described below.

[00751] In another embodiment, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the *Flaviviridae* family of viruses, which method comprises administering to a mammal that has been diagnosed with said viral infection or is at risk of developing said viral infection a compound described herein. In another embodiment, the virus is hepatitis C virus.

[00752] In another embodiment, the method for treating a viral infection in a mammal mediated at least in part by a virus in the *Flaviviridae* family of viruses further comprises administration of a therapeutically effective amount of one or more agents active against hepatitis C virus. In another embodiment, the agent is an inhibitor of HCV protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV replicase, HCV NS5A protein, or inosine 5'-monophosphate dehydrogenase. In another embodiment, the agent is interferon. In another embodiment, the agent is ribavirin. In yet another embodiment, the agent(s) is a combination of interferon and ribavirin that is administered either simultaneously or sequentially.

[00753] In addition, the chemical entities described herein can be co-administered with, and the pharmaceutical compositions can include, other medicinal agents, pharmaceutical agents, adjuvants, and the like. Suitable medicinal and pharmaceutical agents include therapeutically effective amounts of one or more agents active against HCV. In some embodiments, the agent active against HCV is an inhibitor of HCV protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV replicase, HCV NS5A protein, or inosine 5'-monophosphate dehydrogenase.

[00754] Active agents against HCV include ribavirin, levovirin, viramidine, thymosin alpha-1, an inhibitor of NS3 serine protease, and inhibitor of inosine monophosphate dehydrogenase, interferon-alpha, either alone or in combination with ribavirin or levovirin. In some embodiments, the additional agent active against HCV is interferon-alpha or pegylated interferon-alpha alone or in combination with ribavirin or levovirin. In some embodiments, the agent active against hepatitis C virus is interferon.

[00755] The above other therapeutic agents, when employed in combination with the chemical entities described herein, may be used, for example, in those amounts indicated in the Physicians' Desk Reference (PDR) or as otherwise determined by one of ordinary skill in the art.

[00756] Additionally, the present specification is directed to a pharmaceutical composition comprising a therapeutically effective amount of at least one chemical entity

described herein in combination with a therapeutically effective amount of another active agent against RNA-dependent RNA virus and, in particular, against HCV. Agents active against HCV include, but are not limited to, ribavirin, levovirin, viramidine, thymosin alpha-1, an inhibitor of HCV NS3 serine protease, or an inhibitor of inosine monophosphate dehydrogenase, interferon-alpha pegylated interferon-alpha (peginterferon-alpha), a combination of interferon-alpha and ribavirin, a combination of peginterferon-alpha and ribavirin, a combination of interferon-alpha and levovirin, and a combination of peginterferon-alpha and levovirin. Interferon-alpha includes, but is not limited to, recombinant interferon-alpha2a (such as ROFERON interferon available from Hoffman-LaRoche, Nutley, NJ), interferon-alpha2b (such as Intron-A interferon available from Schering Corp., Kenilworth, New Jersey, USA), a consensus interferon, and a purified interferon-alpha product. For a discussion of ribavirin and its activity against HCV, see J.O. Saunders and S.A. Raybuck, "Inosine Monophosphate Dehydrogenase: Consideration of Structure, Kinetics and Therapeutic Potential," *Ann.* Rep. Med. Chem., 2:201-210 (2000).

[00757] The following examples serve to more fully describe the manner of making and using the above-described invention. It is understood that these examples in no way serve to limit the true scope of the invention, but rather are presented for illustrative purposes.

BIOLOGICAL EXAMPLES

EXAMPLE 262

ANTI-HEPATITIS C ACTIVITY

[00758] Compounds can exhibit anti-hepatitis C activity by inhibiting viral and host cell targets required in the replication cycle. A number of assays have been published to assess these activities. A general method that assesses the gross increase of HCV virus in culture is disclosed in U.S. Patent No. 5,738,985 to Miles, *et al.* *In vitro* assays have been reported in Ferrari, *et al.*, *J. of Vir.*, 73:1649-1654, 1999; Ishii, *et al.*, *Hepatology*, 29:1227-1235, 1999; Lohmann *et al.*, *J. of Bio. Chem.*, 274:10807-10815, 1999; and Yamashita, *et al.*, *J. of Bio. Chem.*, 273:15479-15486, 1998.

Replicon Assay

[00759] Two cell lines were used for screening of compounds for inhibiting HCV RNA replication (genoytype 1a and 1b). Genotype 1a replicon cells, are a Huh-7 derived cell line bearing the genotype 1a H77 NS3-5B bicistronic subgenomic replicon. *See, Blight, et al., J Virol.* (2003) 77(5): 3181–3190.

[00760] The genotype 1a replicon contains several adaptive mutations (NS4B Q31H, NS5A K68R, NS5A S232I), the luciferase gene and encodes for neomycin resistance. The genotype 1b replicon, also refered to as the ET replicon, is stably transfected with RNA transcripts harboring a I_{389}luc-ubi-neo/NS3-3'/ET replicon with firefly luciferase-ubiquitin-neomycin phosphotransferase fusion protein and EMCV-IRES driven NS3-5B polyprotein containing the cell culture adaptive mutations (E1202G; T1280I; K1846T) *See, Kreiger, et al., Journal of Virology* 75:4614-4624 (2001). Both cell lines were grown in DMEM, supplemented with 10% fetal calf serum, 2 mM Glutamine, Penicillin (100 IU/mL)/Streptomycin (100 µg/mL), 1x nonessential amino acids, and 250 µg/mL G418 ("Geneticin"). They were all available through Life Technologies (Bethesda, Md.). The cells were plated at 0.5 x 10^4 cells/well in 384 well plates containing compounds. The final concentration of compounds ranged between 0.1 nM to 50 µM and the final DMSO concentration of 0.5%.

[00761] Luciferase activity was measured 48 hours later by adding a Steady glo (Promega, Madison, Wis.). Percent inhibition of replication data was plotted relative to no compound control. Under the same condition, cytotoxicity of the compounds was determined using cell titer glo (Promega, Madison, Wis). EC_{50} values were determined from a 10 point dose response curve using 2-4 fold serial dilutions for each compound, which spans a concentration range of at least a 1000 fold. Replicon EC_{50} values, the concentration of compound required to inhibit 50% of the assay response, were calculated by curve fitting data to the Hill equation, using a non-linear least-squares curve-fitting program. The software tested the data for quality and rejected compounds with high and low activity before fitting the equation below.

$$y = a + [(b-a) / (1 + (10^x/10^c)^d)]$$

where y = response, *a*= minimum response (i.e. no inhibition), b= maximum response, x=compound concentration, c=EC_{50}, and d=Hill coefficient. If the data fit did not meet quality control criteria, six secondary models with different levels of data constraint were used. Analysis was performed using an XC50 module and BioAssay Enterprise (Cambridge Soft).

[00762] Further, compounds of the present disclosure, which were tested against more than one genotype of HCV replicon, were found to have similar inhibitory properties.

[00763] As detailed in Table 3 below, the compounds tested were found to exhibit EC_{50} percent inhibition values at a specific concentration, such as, 10 µM, for example,

which can also be derived from the equation above. Therefore, in certian aspects, the compounds of Formula (I) will exhibit a % inhibition of at least 80 % at the aforesaid 10 μM. In other aspects, the % inhibition is at least 50 % at 10 μM. In still other aspects, the % inhibition is at least 10 % at 10 μM.

[00764] As also detailed in Table 3 below, the compounds tested were found to exhibit EC_{50} values of about 60,000 nM or less, or about 25,000 nM or less. In other embodiments, the compounds will exhibit EC_{50} values of about 10,000 nM or less. In still other embodiments, the compounds will exhibit EC_{50} values of about 5,000 nM or less. In some embodiments, the compounds will exhibit EC_{50} values of about 1,000 nM or less, and in other embodiments, the compounds will exhibit EC_{50} values of about 500 nM or less, and in still further embodiments, about 100 nM or less, in some embodiments, about 50 nM or less, and in some embodiments, about 10 nM or less. Finally, in still further embodiments, the compounds will exhibit EC_{50} values of about 1 nM or less.

[00765] In some embodiment, after testing, certain compounds of Table 1 were found to demonstrate EC_{50} values as indicated in Table 3 for genotype 1a and 1b next to each compound reference number.

Table 3

Compound Number (*From Table 1*)	**HCV Genotype 1A Replicon EC_{50} (μM)**	**HCV Genotype 1B Replicon EC_{50} (μM)**
1	0.7807	0.7989
2	28.18	50.11
3	0.5433	0.1396
4	27.54	30.19
5	18.407	50.118
6	0.2073	0.2213
7	0.0143	0.0042
8	0.3758	0.7852
9	0.0989	0.1303
10	5.308	21.134
11	2.818	4.073
12	7.244	0.8222
13	18.83	4.265

14	0.1274	0.0254
15	0.4677	0.1758
16	0.4121	1.3335
17	0.5689	7.5858
18	0.4519	0.1000
19	1.640	0.9120
20	0.6607	0.3467
21	0.0020	0.0008
22	1.288	3.126
23	2.398	2.691
24	0.0822	0.1202
25	0.0023	0.0020
26	0.1349	0.0631
27	0.0290	0.0297
28	0.0724	0.0337
29	1.949	1.717
30	3.589	5.011
31	0.1820	0.2089
32	0.6457	0.0851
33	0.1738	0.0603
34	1.096	0.8913
35	0.0288	0.2371
36	5.011	3.090
37	0.0148	0.0025
38	0.0359	0.0891
39	0.0006	0.0136
40	0.0186	0.0305
41	0.0225	0.0138
42	0.1059	0.1820
43	0.0010	0.0090
44	0.0081	0.0827

45	0.0776	0.0684
46	0.0087	0.0114
47	0.0135	0.0396
48	0.0008	0.0100
49	0.0025	0.0226
50	0.0008	0.0033
51	0.0834	0.0750
52	1.029	0.8775
53	0.2010	0.1626
54	0.0036	0.0008
55	0.0075	0.0011
56	0.0031	0.0009
57	5.011	4.226
58	0.0072	0.0135
59	0.0063	0.0055
60	0.0011	0.0040
61	0.9977	0.3990
62	0.0468	0.0214
63	0.0495	0.0407
64	0.0219	0.2917
65	0.2371	5.011
66	0.0750	0.0871
67	0.0129	0.0072
68	0.0631	0.2265
69	0.1479	0.0385
70	0.0902	0.0078
71	0.0881	0.0229
72	5.011	5.011
73	0.0603	0.0569
74	0.1841	0.1161
75	0.3589	0.2427

76	0.0610	0.0355
77	0.0085	0.0030
78	0.0219	0.0168
79	0.0684	0.0091
80	0.2541	0.0750
81	0.0048	0.0018
82	0.7015	0.3451
83	2.180	0.6622
84	0.0908	0.0169
85	0.0955	0.0121
86	0.6397	0.0962
87	0.4710	0.0484
88	0.0509	0.0135
89	0.0121	0.0045
90	0.0149	0.0035
91	0.1766	0.0688
92	0.1268	0.0162
93	0.1126	0.0182
94	0.0030	0.0006
95	0.0053	0.0004
96	0.2518	0.0220
97	0.0032	0.0007
98	0.0126	0.0070
99	0.0126	0.0252
100	0.0076	0.0026
101	0.0165	0.0016
102	0.0781	0.0929
103	0.1308	0.1009
104	0.5559	0.4315
105	1.318	2.065
106	0.0181	0.0053

107	0.0041	0.0014
108	0.4294	0.1626
109	0.4467	0.5559
110	0.1175	0.1549
111	0.2917	0.5129
112	5.011	5.011
113	0.0016	0.0029
114	0.0006	0.0025
115	0.0250	0.0268
116	0.0088	0.0120
117	-	-
118	0.0347	0.0108
119	0.0432	0.0066
120	0.1109	0.0317
121	0.0055	0.0043
122	0.0676	0.5495
123	0.0240	0.0257
124	0.0028	0.0017
125	5.011	2.344
126	0.0039	0.0009
127	0.0011	0.0006
128	0.2679	0.5781
129	1.000	1.131
130	0.2294	0.2621
131	0.0250	0.0186
132	0.1287	0.3432
133	0.0026	0.0117
134	0.0410	0.0217
135	0.3639	0.1483
136	5.011	1.000
137	0.0083	0.0009

138	3.976	0.3300
139	5.011	5.011
140	0.0035	0.0083
141	0.0097	0.0168
142	1.174	1.659
143	2.951	0.5370
144	0.1928	0.5689
145	0.1349	0.0422
146	1.412	4.265
147	0.9550	0.6166
148	5.011	5.011
149	2.541	4.036
150	3.672	2.238
151	0.0150	0.0029
152	0.0032	0.0012
153	0.0029	0.0012
154	0.0166	0.0041
155	0.0062	0.0024
156	0.0451	0.0559
157	0.3780	0.0060
158	0.0069	0.0021
159	0.0028	0.0016
160	0.0027	0.0010
161	0.0450	0.0469
162	1.663	3.115
163	0.0009	0.0078
164	0.0011	0.0072
165	0.0059	0.0017
166	0.0022	0.0010
167	0.0628	0.0249
168	0.0129	0.0074

169	0.0956	0.0405
170	0.0036	0.0027
171	0.0066	0.0018
172	0.0241	0.0239
173	0.0002	0.0001
174	0.0003	0.0001
175	0.0228	0.0120
176	0.0560	0.0217
177	0.0071	0.0039
178	0.2145	0.0630
179	0.1881	0.2979
180	0.2907	0.1702
181	0.0128	0.0075
182	0.0521	0.0362
183	0.0065	0.0018
184	0.6918	0.8810
185	0.0493	0.0304
186	0.0016	0.0628
187	0.0057	0.0012
188	0.0025	0.0017
189	-	-
190	-	-
191	0.2518	0.0210
192	0.0032	0.0010
193	0.2218	0.0592
194	0.0360	0.0288
195	0.0008	0.0040
196	0.0047	0.0093
197	0.1259	0.0251
198	0.0126	0.0631
199	0.0501	0.0158

200	0.0025	0.0010
201	0.0662	0.0197
202	0.5012	0.3660
203	0.1155	0.4721
204	0.5012	0.5012
205	0.0158	0.0158
206	0.1029	0.0307
207	0.0249	0.0123
208	0.0002	0.0001
209	0.0001	0.0000
210	0.0431	0.0284
211	0.0062	0.0257
212	0.0068	0.0051
213	0.0137	0.0086
214	0.1000	0.0398
215	0.1932	0.0291
216	0.0585	0.0546
217	0.0027	0.0277
218	0.1293	0.0324
219	0.4121	0.0775
220	0.0897	0.0206
221	0.0403	0.1901
222	0.0592	0.0517
223	0.1003	0.1297
224	0.0063	0.0501
225	0.0008	0.0050
226	0.0631	0.2512
227	0.0002	0.0013
228	0.0040	0.0316
229	0.2518	0.2973
230	0.6707	0.1194

231	0.0290	0.0087
232	0.1160	0.0146
233	0.2344	0.0646
234	0.2301	0.0236
235	0.0058	0.0110
236	0.0798	0.2714
237	0.3565	0.0250
238	0.0017	0.0042
239	0.0471	0.0439
240	0.1585	0.1000
241	0.0040	0.0100
242	0.0022	0.0008
243	-	-
244	-	-
247	0.3902	0.2585
248	0.3960	0.1958
249	0.0766	0.0331
250	0.0853	0.0210
251	0.0746	0.0261
252	0.0788	0.0350
253	0.0012	0.0014
254	0.0056	0.0073
255	0.0032	0.0200
256	0.1995	0.1585
257	0.0079	0.0501
258	0.0794	0.1259
259	0.0251	0.0079
260	0.1000	0.1000
261	0.0158	0.0316

Formulation Examples

[00766] The following are representative pharmaceutical formulations containing a compound of Formula (I) or a pharmaceutically acceptable salt thereof.

EXAMPLE 263

Tablet formulation

[00767] The following ingredients are mixed intimately and pressed into single scored tablets.

Ingredient	Quantity per tablet (mg)
compound	400
cornstarch	50
croscarmellose sodium	25
lactose	120
magnesium stearate	5

EXAMPLE 264

Capsule formulation

[00768] The following ingredients are mixed intimately and loaded into a hard-shell gelatin capsule.

Ingredient	Quantity per capsule (mg)
compound	200
Lactose, spray-dried	148
magnesium stearate	2

EXAMPLE 265

Suspension formulation

[00769] The following ingredients are mixed to form a suspension for oral administration.

Ingredient	Amount
compound	1.0 g
fumaric acid	0.5 g
sodium chloride	2.0 g
methyl paraben	0.15 g
propyl paraben	0.05 g
granulated sugar	25.0 g

sorbitol (70% solution)	13.00 g
Veegum K (Vanderbilt Co.)	1.0 g
flavoring	0.035 mL
colorings	0.5 mg
distilled water	q.s. (quantity sufficient) to l00 mL

EXAMPLE 266

Injectable formulation

[00770] The following ingredients are mixed to form an injectable formulation.

Ingredient	Amount
compound	0.2 mg-20 mg
sodium acetate buffer solution,	0.4 M 2.0 mL
HCl (1 N) or NaOH (1 N)	q.s. to suitable pH
water (distilled, sterile)	q.s. to 20 mL

EXAMPLE 267

Suppository Formulation

[00771] A suppository of total weight 2.5 g is prepared by mixing the compound with Witepsol® H-15 (triglycerides of saturated vegetable fatty acid; Riches-Nelson, Inc., New York), and has the following composition:

Ingredient	Amount
compound	500 mg
Witepsol® H-15	balance

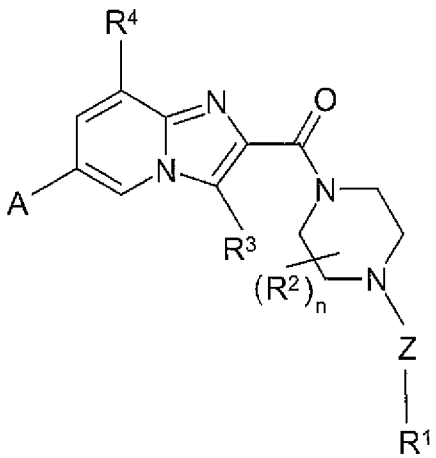
[00772] Although the invention has been shown and described above with reference to some embodiments, those skilled in the art will readily appreciate that the specific experiments detailed are only illustrative of the invention. It should be understood that various modifications can be made without departing from the spirit of the invention.

[00773] For example, for claim construction purposes, it is not intended that the claims set forth hereinafter be construed in any way narrower than the literal language thereof, and it is thus not intended that exemplary embodiments from the specification be read into the claims. Accordingly, it is to be understood that the present invention has been described by way of illustration and not limitations on the scope of the claims. Accordingly, the invention is limited only by the following claims. All publications, issued patents, patent applications, books and journal articles, cited in this application are each herein incorporated by reference in their entirety.

WHAT IS CLAIMED IS:

1. A compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or $(C_1$-$C_3)$alkylene;

A is selected from the group consisting of hydrogen, halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkenyl, $(C_1$-$C_6)$alkynyl, $(C_3$-$C_{14})$cycloalkyl, aryl, hydroxyl, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, $-SO_2N(R^6)_2$, $-C(O)NR^6R^6$, $-OR^7$, $-R^6R^7$, $-SO_2R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$, $-alkylR^9R^6$, $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, $(C_2$-$C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O, $(C_2$-$C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{10};

R^1 is selected from the group consisting of hydrogen, halo, cyano, hydroxyl, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkenyl, $(C_1$-$C_6)$alkynyl, $-C(O)N(R^6)_2$, $-R^9R^6$, $-SO_2N(R^6)_2$, $-SO_2R^6$, $(C_3$-$C_{14})$cycloalkyl, $(C_3$-$C_{14})$cycloalkenyl, aryl, $(C_2$-$C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2$-$C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{11};

R^2 is independently selected from the group consisting of oxo, $(C_1$-$C_6)$alkyl, $(C_3$-$C_{14})$cycloalkyl, $-alkylR^8$, and aryl, or optionally two R^2 alkyl groups, together with any intervening atoms, form a spiro or fused $(C_3$-$C_{14})$cycloalkyl ring;

R^3 is selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_{14})$cycloalkyl, halo, $-alkylR^8$, and cyano;

R^4 is selected from the group consisting of hydrogen, hydroxyl, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, (C_3-C_{14})cycloalkyl, aryl, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, $-alkyl(R^5)_mR^6$, $-alkylR^9R^6$, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-SO_2N(R^6)_2$, $-C(O)NR^6R^6$, $-OR^7$, $-R^6R^7$, $-SO_2R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$, $-alkylR^9R^6$, $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O; wherein said alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclic is optionally substituted with one to three R^{10};

R^5 is halo;

R^6 is independently selected from the group consisting of hydrogen and (C_1-C_6)alkyl;

R^7 is (C_3-C_{14})cycloalkyl;

R^8 is hydroxyl;

R^9 is carboxyl;

R^{10} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, hydroxyl, oxo, carboxyl, cyano, halo, $-C(O)NH_2$, $-SO_2NH_2$, $-SR^6$, $-S(O)R^6$, $-S(O)_2R^6$, $-S(O)_2NR^6R^6$, $-NR^6R^6$, $-NR^6C(O)NR^6R^6$, $-NR^6C(S)NR^6R^6$, $-NR^6S(O)_2R^6$ $-NR^6C(O)OR^6$, $-NR^6C(O)R^6$, $-C(NR^6)NR^6R^6$, $-C(O)NR^6R^6$, $-C(O)OR^6$, $-C(O)R^6$, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O;

R^{11} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkenyl, (C_1-C_6)alkynyl, hydroxyl, $-NR^6C(O)R^6$, $-OC(O)R^6$, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, halo, $-C(O)N(R^6)_2$, $-SO_2N(R^6)_2$, $-SO_2R^6$, oxo, $-alkylR^8$, $-alkylR^9$, $-alkylR^9R^6$, (C_3-C_{14})cycloalkyl, aryl, (C_2-C_6)heterocyclic having 1-3 heteroatoms selected from S, N and O, and (C_2-C_6)heteroaryl having 1-3 heteroatoms selected from S, N, and O; or optionally two R^{11} groups, together with any intervening atoms, form a fused (C_3-C_{14})cycloalkyl ring or a fused (C_2-C_6)heterocyclic ring having 1-3 heteroatoms selected from S, N and O; wherein said fused cycloalkyl or heterocyclic ring is optionally substituted with one to three R^{12};

R^{12} is independently selected from the group consisting of (C_1-C_6)alkyl, (C_1-C_6)alkoxy, oxo, halo, hydroxyl, carboxyl, cyano, $-OR^6(R^5)_m$, $-R^6(R^5)_m$, and $-NR^6R^6$;

m is an integer from 1 to 3; and

n is zero or an integer from 1 to 4.

2. The compound according to any of the preceding claims, wherein Z is a bond.

3. The compound according to any of the preceding claims, wherein A is selected from the group consisting of $(C_1$-$C_6)$alkyl, halo, $-OR^6$, $-OR^7$, $-$alkoxy$(R^5)_m$, $(C_3$-$C_{14})$cycloalkyl, $-R^6(C_3$-$C_{14})$cycloalkyl, $(C_2$-$C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2$-$C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O.

4. The compound according to any of the preceding claims, wherein A is selected from the group consisting of hydrogen, bromo, fluoro, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, cyclopropylmethyl, cyclopropyloxy, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, thienyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl.

5. The compound according to any of the preceding claims, wherein A is selected from the group consisting of ethyl, butyl, propyl, bromo, chloro, methoxy, ethoxy, propoxy, cyclopropyl, furanyl, pyrazolyl, tetrahydrofuranyl, and difluoromethoxy.

6. The compound according to any of the preceding claims, wherein A is selected from the group consisting of isobutyl, ethyl, ethoxy, cyclopropyl, furanyl, pyrazolyl, and difluoromethoxy.

7. The compound according to any of the preceding claims, wherein A is selected from the group consisting of furanyl and cyclopropyl.

8. The compound according to any of the preceding claims, wherein A is cyclopropyl.

9. The compound according to any of the preceding claims, wherein A is furanyl.

10. The compound according to any of the preceding claims, wherein R^1 is selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_{14})$cycloalkyl, aryl, $(C_2$-$C_6)$heterocyclic having 1-3 heteroatoms selected from S, N and O, and $(C_2$-$C_6)$heteroaryl having 1-3 heteroatoms selected from S, N, and O.

11. The compound according to any of the preceding claims, wherein R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, acetate, thiazolyl, cyclopropyl, cyclobutyl, bicyclohexyl, bicyclopentyl, bicyclooctyl, cyclohexyl, cyclopentyl, cyclopentenyl, cyclohexenyl, cycloheptyl, oxabicyclohexyl, phenyl, benzyl, pyridyl, pyridinyl, pyrrolidinyl, piperidinyl, thiophenyl, pyrazolyl, octahydropentalenyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl,

and thienyl.

12. The compound according to any of the preceding claims, wherein R^1 is (C_3-C_{14})cycloalkyl.

13. The compound according to any of the preceding claims, wherein R^1 is selected from the group consisting of cyclohexyl, cyclobutyl, cyclopentyl, and bicyclohexyl.

14. The compound according to any of the preceding claims, wherein R^1 is substituted with one or two R^{11}.

15. The compound according to any of the preceding claims, wherein R^1 is substituted with one R^{11}.

16. The compound according to any of the preceding claims, wherein R^2 is selected from the group consisting of hydrogen, oxo, and (C_1-C_6)alkyl.

17. The compound according to any of the preceding claims, wherein R^2 is selected from the group consisting of hydrogen, oxo, and methyl.

18. The compound according to any of the preceding claims, wherein R^2 is oxo.

19. The compound according to any of the preceding claims, wherein R^3 is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, halo, cyano, –alkylR^8, and (C_3-C_{14})cycloalkyl.

20. The compound according to any of the preceding claims, wherein R^3 is selected from the group consisting of hydrogen, methyl, ethyl, chloro, bromo, cyano, hydroxymethyl, and cyclopropyl.

21. The compound according to any of the preceding claims, wherein R^3 is selected from the group consisting of chloro and cyano.

22. The compound according to any of the preceding claims, wherein R^3 is chloro.

23. The compound according to any of the preceding claims, wherein R^4 is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkenyl, $–OR^6(R^5)_m$, $–R^6(R^5)_m$, $–alkyl(R^5)_mR^6$.

24. The compound according to any of the preceding claims, wherein R^4 is selected from the group consisting of trifluoromethyl, ethyl, and isopropylene.

25. The compound according to any of the preceding claims, wherein R^4 is trifluoromethyl.

26. The compound according to any of the preceding claims, wherein R^{11} is selected from the group consisting of hydroxyl, oxo, $–OC(O)R^6$, –alkylR^8, $–R^6(R^5)_m$, halo, (C_1-C_6)alkyl, and (C_1-C_6)alkoxy.

27. The compound according to any of the preceding claims, wherein R^{11} is selected from the group consisting of hydroxyl, oxo, hydroxymethyl, acetate, fluoro,

trifluoromethyl, methoxy, and methyl.

28. The compound according to any of the preceding claims, wherein R^{11} is hydroxyl.

29. The compound according to any of the preceding claims, wherein R^{11} is absent.

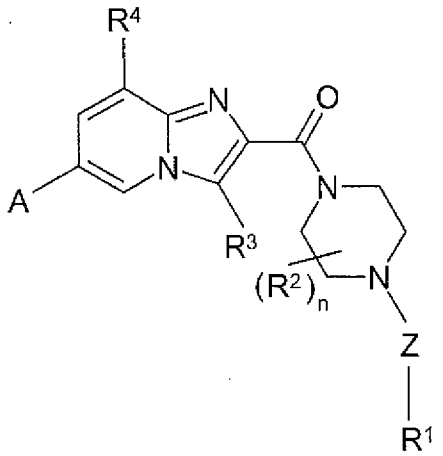
30. The compound according to any of the preceding claims, wherein m is three.

31. The compound according to any of the preceding claims, wherein m is two.

32. The compound according to any of the preceding claims, wherein n is zero.

33. A compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or methylene;

A is selected from the group consisting of hydrogen, bromo, fluoro, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, cyclopropylmethyl, cyclopropyloxy, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl;

R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, thiazolyl, cyclopropyl, cyclobutyl, bicyclohexyl, bicyclopentyl, bicyclooctyl, cyclohexyl, cyclopentyl, cycloheptyl, phenyl, benzyl, pyridyl, pyrrolidinyl, piperidinyl, thiophenyl, pyrazolyl, tetrahydrofuranyl, tetrahydropyranyl, thienyl, cyclopentenyl, and cyclohexenyl, wherein R^1 is optionally substituted with one to two R^{11};

R^2 is independently selected from the group consisting of hydrogen, oxo, methyl, ethyl, cyclopropyl, hydroxymethyl, and phenyl, or optionally two R^2 groups, together with any intervening atoms, form a spiro or fused cyclopropyl ring;

R^3 is selected from the group consisting of hydrogen, chloro, bromo, fluoro, and cyano;

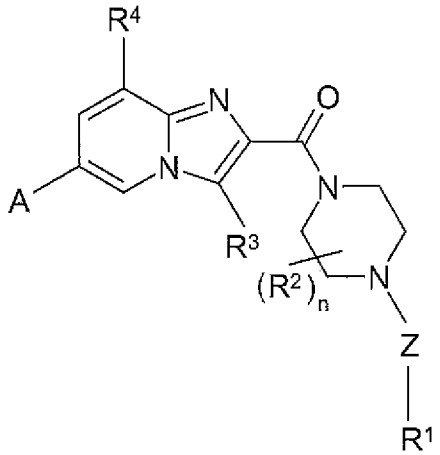
R^4 is selected from the group consisting of hydrogen, methyl, ethyl, isopropyl, dimethylamino, methylamino, isopropylene, methoxy, ethoxy, cyclopropyl, chloro, fluoro, bromo, difluoroethyl, and trifluoromethyl;

R^{11} is independently selected from the group consisting of methyl, methoxy, trifluoromethyl, fluoro, oxo, hydroxyl, hydroxymethyl, and acyloxy; and

n is zero or an integer from 1 to 4.

34. A compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or $(C_1$-$C_3)$alkylene;

A is selected from the group consisting of hydrogen, halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, haloalkoxy, $(C_3$-$C_{14})$cycloalkyl, aryl, $(C_2$-$C_6)$heteroaryl with 1-3 heteroatoms selected from S, N, and O, and $(C_2$-$C_6)$heterocyclic with 1-3 heteroatoms selected from N and O;

R^1 is selected from the group consisting of hydrogen, halo, cyano, carboxyl, hydroxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_{14})$cycloalkyl, aryl, $(C_3$-$C_6)$heterocyclic with 1-2 heteroatoms selected from S and O, and $(C_3$-$C_6)$heteroaryl with 1-2 heteroatoms selected from S, N, and O; wherein R^1 is optionally substituted with one to three R^{11};

R^2 is independently selected from the group consisting of hydrogen, oxo, methyl, and aryl;

R^3 is selected from the group consisting of hydrogen, halo, and cyano;

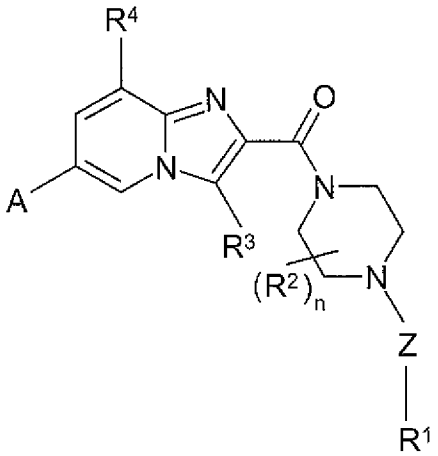
R^4 is selected from the group consisting of hydrogen, isopropylene, and haloalkyl;

R^{11} is independently selected from the group consisting of alkyl, alkoxy, haloalkyl, halo, oxo, hydroxyl, acyloxy; and

n is zero or an integer from 1 to 4.

35. A compound of Formula (I):

(I)



or a pharmaceutically acceptable salt thereof, wherein:

Z is optionally a bond or methylene;

A is selected from the group consisting of hydrogen, bromo, chloro, iodo, methyl, ethyl, propyl, butyl, pentyl, cyclopropyl, methoxy, ethoxy, propoxy, difluoromethoxy, pyrazolyl, furanyl, pyrrolyl, triazolyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, and imidazolyl;

R^1 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, cyano, carboxyl, thiazolyl, cyclopropyl, cyclobutyl, cyclohexyl, cyclopentyl, cycloheptyl, phenyl, benzyl, pyridyl, thiophenyl, tetrahydrofuranyl, tetrahydropyranyl, thienyl, cyclopentenyl, and cyclohexenyl, wherein R^1 is optionally substituted with one to two R^{11};

R^2 is independently selected from the group consisting of hydrogen, oxo, methyl, and phenyl;

R^3 is selected from the group consisting of hydrogen, chloro, bromo, and cyano;

R^4 is selected from the group consisting of hydrogen, isopropylene, and trifluoromethyl;

R^{11} is independently selected from the group consisting of methyl, methoxy, trifluoromethyl, fluoro, oxo, hydroxyl, and acyloxy; and

n is zero or an integer from 1 to 2.

36. A compound selected from the group consisting of:

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone,

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-phenyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-methyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(phenylmethyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-(trifluoromethyl)phenyl]-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-2-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-pyridinyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-pyridinyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopropyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cycloheptyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylethyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-methyl-1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-4-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3,3-dimethyl-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-3-methyl-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4,4-difluorocyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-oxocyclohexyl)-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclobutyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-3-methylcyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-methylcyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2,6-piperazinedione,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-3-hydroxycyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone,

trans-4-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)cyclohexyl acetate,

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-propyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,

4-{[6-butyl-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

(+/-)-4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(ethyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(3-pyridinyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

(+/-)-4-{[3-chloro-6-(tetrahydro-3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-[(1-methylethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

1-cyclopentyl-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-(tetrahydro-2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone ,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(methyloxy)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-(1-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone,
1-butyl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-propyl-2-piperazinone,
4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-butyl-2-piperazinone,
(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(+/-)-1-cyclobutyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methylpropyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclopropylmethyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-5-methyl-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-6-methyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
4-{[3-chloro-6-[(difluoromethyl)oxy]-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(3-thienyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(2-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrrol-3-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(2H-1,2,3-triazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
4-{[3-chloro-6-(1H-pyrrol-2-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,
1-cyclohexyl-4-{[6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,
4-{[3-chloro-6-(1-methylethyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorophenyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-ethylpropyl)-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-methylpropyl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-3-furanyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dimethylethyl)-2-piperazinone,

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-difluorocyclopentyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,3-dimethylcyclobutyl)-2-piperazinone,

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,2-difluorocyclopentyl)-2-piperazinone ,

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,

4-{[3-bromo-6-iodo-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone,

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methyloxy)phenyl]-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-hydroxyphenyl)-2-piperazinone,

4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,

4-{[3-chloro-6-(1H-pyrazol-4-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,3-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclohexen-1-yl)-2-piperazinone,

methyl (4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetate,

(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)acetic acid,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxyphenyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluoro-4-hydroxyphenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,5-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2,5-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3,4-difluorophenyl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-(methyloxy)phenyl]-2-piperazinone,

4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,

4-{[3-chloro-6-ethyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclopentyl-2-piperazinone,

2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

4-{[3-bromo-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,

2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone,

4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone,

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone,

2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

2-[(4-cyclopentyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(tetrahydro-2H-thiopyran-4-yl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-piperazinone,

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

6-cyclopropyl-2-{[4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-methylcyclobutyl)-2-piperazinone,

6-cyclopropyl-2-{[4-(3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone,

(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone,
(+/-)-4-{[6-bromo-3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-cyclopenten-1-yl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone,
(cis/trans mixture)-1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
(cis/trans mixture)-1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-(3-furanyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-2-hydroxycyclopentyl]-2-piperazinone ,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(cis)-2-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-(3,4-dihydroxycyclopentyl)-2-piperazinone ,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(trans)-3-hydroxycyclopentyl]-2-piperazinone ,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclohexyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1,3-thiazol-2-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-(2-methylpropyl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
6-cyclopropyl-2-{[4-(cis-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
6-cyclopropyl-2-{[4-(trans-3-methylcyclobutyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(5S)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
(5R)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-methyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-(hydroxymethyl)-2-piperazinone,
1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-6-(1H-imidazol-1-yl)-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-5-methyl-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxocyclopentyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cyclobutylmethyl)-2-piperazinone,
4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3-chloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
1-[(1R,3s,5S)-bicyclo[3.1.0]hex-3-yl]-4-{[3,6-dichloro-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2r,3aR,6aS)-5-anti-hydroxy-5-methyloctahydro-2-pentalenyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-anti-hydroxyoctahydro-2-pentalenyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(2s,3aR,6aS)-5-syn-hydroxyoctahydro-2-pentalenyl]-2-piperazinone,
1-[(1R,5S,6r)-bicyclo[3.1.0]hex-6-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(1-methyl-5-oxo-3-pyrrolidinyl)-2-piperazinone,

1-[(endo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

1-[(trans)-bicyclo[3.1.0]hex-3-yl]-4-{[3-bromo-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

2-({4-[(trans)-bicyclo[3.1.0]hex-3-yl]-3-oxo-1-piperazinyl}carbonyl)-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,

1-[(exo)-bicyclo[2.2.1]hept-2-yl]-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(methyloxy)cyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-fluorocyclobutyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-cyclobutyl-5-ethyl-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-4-(hydroxymethyl)cyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxy-4-methylcyclohexyl)-2-piperazinone,

(+/-)-trans-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-2-hydroxycyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[4-(methylamino)cyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S,4R)-3,4-dihydroxycyclohexyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-methylcyclohexyl)-2-piperazinone,

4-[(3-chloro-6,8-dicyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(methyloxy)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(1-methylethenyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-[(8-acetyl-3-chloro-6-cyclopropylimidazo[1,2-a]pyridin-2-yl)carbonyl]-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-2-thienyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-methyl-3-thienyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-thienyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-thienyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[5-(methyloxy)-2-pyridinyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(methyloxy)-3-pyridinyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[2-fluoro-4-(methyloxy)phenyl]-2-piperazinone,

3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile,

2-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)benzonitrile,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-fluoro-4-hydroxyphenyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-hydroxy-2-pyridinyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxo-1,6-dihydro-3-pyridinyl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[trans-3-(hydroxymethyl)cyclobutyl]-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(2-hydroxybicyclo[3.1.0]hex-3-yl)-2-piperazinone,

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone (Enantiomer 1),

4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S/R,2S/R,3S/R,5S/R)-2-hydroxybicyclo[3.1.0]hex-3-yl]-2-piperazinone (Enantiomer 2),
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-hydroxycyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1S,3S)-3-hydroxycyclopentyl]-2-piperazinone,
ethyl 3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate,
ethyl 3-(4-{[6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylate,
3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carboxylic acid,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[6-(hydroxymethyl)bicyclo[3.1.0]hex-3-yl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6,6-difluorobicyclo[3.1.0]hex-3-yl)-2-piperazinone,
3-(4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-2-oxo-1-piperazinyl)bicyclo[3.1.0]hexane-6-carbonitrile,
(Trans)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(3-oxabicyclo[3.1.0]hex-6-yl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[(1R,3R)-3-(hydroxymethyl)cyclopentyl]-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(5-oxo-3-pyrrolidinyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(6-oxabicyclo[3.1.0]hex-3-yl)-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3,4-dihydroxycyclopentyl]-2-piperazinone,
(+/-)-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-[3-fluoro-4-hydroxycyclopentyl]-2-piperazinone,
or a pharmaceutically acceptable salt thereof.

37. The compound according to claim 35, wherein the compound is selected from the group consisting of
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone,
1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-

2-yl]carbonyl}-2-piperazinone,
6-cyclopropyl-2-{[4-(4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
2-[(4-cyclobutyl-3-oxo-1-piperazinyl)carbonyl]-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile, and
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-1-cyclobutyl-2-piperazinone;
or a pharmaceutically acceptable salt thereof.

38. The compound according to claim 36, wherein the compound is selected from the group consisting of
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone,
6-cyclopropyl-2-{[4-(trans-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
6-cyclopropyl-2-{[4-(cis-4-hydroxycyclohexyl)-3-oxo-1-piperazinyl]carbonyl}-8-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile,
4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone, and
1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone,
or a pharmaceutically acceptable salt thereof.

39. The compound according to claim 37, wherein the compound is 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(4-hydroxycyclohexyl)-2-piperazinone, or a pharmaceutically acceptable salt thereof.

40. The compound according to claim 38, wherein the compound is 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(trans-4-hydroxycyclohexyl)-2-piperazinone, or a pharmaceutically acceptable salt thereof.

41. The compound according to claim 39, wherein the compound is 4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]carbonyl}-1-(cis-4-hydroxycyclohexyl)-2-piperazinone, or a pharmaceutically acceptable salt thereof.

42. The compound according to claim 40, wherein the compound is 1-bicyclo[3.1.0]hex-3-yl-4-{[3-chloro-6-cyclopropyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl]carbonyl}-2-piperazinone, or a pharmaceutically acceptable salt thereof.

43. A pharmaceutical composition comprising a pharmaceutically acceptable

diluent and a therapeutically effective amount of a compound of any preceding claim.

44. A method for treating a viral infection in a mammal mediated at least in part by a virus in the *Flaviviridae* family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of any one of claims 1 to 41.

45. The method of claim 43, wherein said virus is hepatitis C virus.

46. The method of claim 44, further comprising administration of a therapeutically effective amount of one or more agents active against hepatitis C virus.

47. The method of claim 45, wherein said agent active against hepatitis C virus is an inhibitor of HCV protease, HCV polymerase, HCV helicase, HCV entry, HCV assembly, HCV egress, HCV replicase, HCV NS5A protein, or inosine 5'-monophosphate dehydrogenase.

48. The method of claim 45, wherein said agent active against hepatitis C virus is interferon in combination with ribavirin.

49. The method of claim 45, wherein said agent active against hepatitis C virus is interferon.