(12) STANDARD PATENT (11) Application No. **AU 2019265134 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Azabenzimidazole compounds and pharmaceutical

(51) International Patent Classification(s)
C07D 471/04 (2006.01) ***A61K 31/551*** (2006.01)
A61K 31/437 (2006.01) ***A61P 3/10*** (2006.01)
A61K 31/444 (2006.01) ***A61P 13/02*** (2006.01)
A61K 31/4545 (2006.01) ***A61P 13/10*** (2006.01)
A61K 31/46 (2006.01) ***A61P 27/06*** (2006.01)
A61K 31/496 (2006.01) ***A61P 43/00*** (2006.01)
A61K 31/497 (2006.01) ***C07D 519/00*** (2006.01)

(21) Application No: **2019265134** (22) Date of Filing: **2019.05.07**

(87) WIPO No: **WO19/216294**

(30) Priority Data

(31) Number	(32) Date	(33) Country
2018-089867	**2018.05.08**	**JP**

(43) Publication Date: **2019.11.14**
(44) Accepted Journal Date: **2024.02.29**

(71) Applicant(s)
Nippon Shinyaku Co., Ltd.

(72) Inventor(s)
OIKAWA, Kouya;HIRAI, Sho;WAKITA, Kazuhiko;FUJIBAYASHI, Akiko

(74) Agent / Attorney
Spruson & Ferguson, GPO Box 3898, Sydney, NSW, 2001, AU

(56) Related Art
WO 2014/128465 A1
WO 2012/080236 A1
WO 2012/080230 A1
JP 2012031152 A
WO 2009/092764 A1
WO 2007/039297 A1

(12) 特許協力条約に基づいて公開された国際出願

(19) 世界知的所有権機関
国際事務局

(43) 国際公開日
2019年11月14日(14.11.2019)

WIPO | PCT

(10) 国際公開番号
WO 2019/216294 A1

(51) 国際特許分類:
C07D 471/04 (2006.01)　*A61K 31/551* (2006.01)
A61K 31/437 (2006.01)　*A61P 3/10* (2006.01)
A61K 31/444 (2006.01)　*A61P 13/02* (2006.01)
A61K 31/4545 (2006.01)　*A61P 13/10* (2006.01)
A61K 31/46 (2006.01)　*A61P 27/06* (2006.01)
A61K 31/496 (2006.01)　*A61P 43/00* (2006.01)
A61K 31/497 (2006.01)　*C07D 519/00* (2006.01)

(21) 国際出願番号：　PCT/JP2019/018201

(22) 国際出願日：　2019年5月7日(07.05.2019)

(25) 国際出願の言語：　日本語

(26) 国際公開の言語：　日本語

(30) 優先権データ：
特願 2018-089867　2018年5月8日(08.05.2018)　JP

(71) 出願人:日本新薬株式会社(**NIPPON SHINYAKU CO., LTD.**) [JP/JP]; 〒6018550 京都府京都市南区吉祥院西ノ庄門口町１４番地 Kyoto (JP).

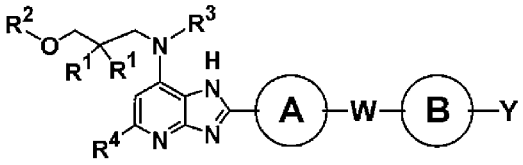
(72) 発明者:及川 幸也(**OIKAWA Kouya**); 〒6018550 京都府京都市南区吉祥院西ノ庄門口町１４番地 日本新薬株式会社内 Kyoto (JP). 平井 祥(**HIRAI Sho**); 〒6018550 京都府京都市南区吉祥院西ノ庄門口町１４番地 日本新薬株式会社内 Kyoto (JP). 脇田 和彦(**WAKITA Kazuhiko**); 〒6018550 京都府京都市南区吉祥院西ノ庄門口町１４番地 日本新薬株式会社内 Kyoto (JP). 藤林 明子(**FUJIBAYASHI Akiko**); 〒6018550 京都府京都市南区吉祥院西ノ庄門口町１４番地 日本新薬株式会社内 Kyoto (JP).

(74) 代理人: 中村 文胤 (**NAKAMURA Ayatsugu**); 〒6018550 京都府京都市南区吉祥院西ノ庄門口町１４番地 日本新薬株式会社知的財産部 Kyoto (JP).

(81) 指定国(表示のない限り、全ての種類の国内保護が可能): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,

(54) **Title:** AZABENZIMIDAZOLE COMPOUNDS AND PHARMACEUTICAL

(54) 発明の名称： アザベンゾイミダゾール化合物及び医薬



[1]

(57) **Abstract:** The purpose of the present invention is to provide compounds having an M3 PAM action. Examples of the present invention include azabenzimidazole compounds represented, for example, by formula [I], and pharmacologically acceptable salts thereof. These compounds have M3 PAM activity. In addition, because these compounds have M3 PAM activity, these compounds are useful as agents for the prevention or treatment of dysuria and/or urine storage disorder in underactive bladder, hypotonic bladder, acontractile bladder, detrusor hypoactivity, and neurogenic bladder.

(57) 要約：本発明の目的は、Ｍ３ ＰＡＭ作用を有する化合物を提供することにある。 本発明として、例えば次の式［１］で表されるアザベンゾイミダゾール化合物又はその医薬上許容される塩を挙げることができる。本発明化合物は、Ｍ３ ＰＡＭ活性を有している。また、本発明化合物はＭ３ ＰＡＭ活性を有することから、低活動膀胱、低緊張性膀胱、無収縮膀胱、排尿筋低活動及び神経因性膀胱における排尿障害や蓄尿障害の予防剤又は治療剤として有用である。

WO 2019/216294 A1

［続葉有］

HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) 指定国(表示のない限り、全ての種類の広域保護が可能): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), ユーラシア (AM, AZ, BY, KG, KZ, RU, TJ, TM), ヨーロッパ (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

添付公開書類:

一　国際調査報告（条約第21条(3)）

AZABENZIMIDAZOLE COMPOUNDS AND PHARMACEUTICAL

Technical Field

[0001]

The present invention relates to a pharmaceutical composition containing a novel azabenzimidazole compound, or a pharmaceutically acceptable salt thereof, or a solvate thereof as an active ingredient.

Background Art

[0002]

Acetylcholine (ACh) is a neurotransmitter, which is released from the terminals of parasympathetic nerves and motor nerves and transmits nerve stimulation with binding to the acetylcholine receptor (AChR). Acetylcholine receptors are classified into G protein-coupled muscarinic receptors and ion channel-type nicotine receptors. Muscarinic receptors are classified into five subtypes, M1 to M5. It has been reported that subtype M3 muscarinic receptors, which may be hereinafter referred to as "M3 receptors", are expressed mainly in bladder, gastrointestinal tract, pupil, salivary gland, lacrimal gland, etc., and involved in contraction of bladder, gastrointestinal tract and pupil, and secretion of saliva and tear (see Non-Patent Documents 1 and 2).

[0003]

A compound having an action of enhancing M3 receptor signal is expected to be useful as a protective or therapeutic agent for bladder/urethral diseases, gastrointestinal diseases, oral diseases, ocular diseases, etc. (see Non-Patent Documents 3-6).

Prior Art Documents

Non-Patent Documents

[0004]

Non-Patent Document 1: Pharmacological Reviews, 1998, Vol.50, No. 2, p.279-290

Non-Patent Document 2: British Journal of Pharmacology, 2006, Vol.148, no. 5, p. 565-578

Non-Patent Document 3: Arabian Journal of Urology, 2013, Vol.11, No. 4, p.319-330

Non-Patent Document 4: Clinics in Colon and Rectal Surgery., 2012, Vol.25, p.12-19

Non-Patent Document 5: Expert Opinion on Pharmacotherapy, 2009, Vol.10, No. 16, p.2663-2777
Non-Patent Document 6: Journal of Inflammation, 2017, Nov 21, 14:26
Non-Patent Document 7: Trends in Pharmacological Sciences, 2017, Vol.38, No. 9, p.837-847
Non-Patent Document 8: Nature, 2012, Vol.482, p.552-556

Summary of Invention

[0005]

Regarding G protein-coupled receptors, many structures of allosteric sites, which are different from orthosteric sites to which endogenous agonists bind, have been reported, and these allosteric sites are attracting attention in recent years (Non-patent Document 7). Some ligands to allosteric sites can alter the structure of a receptor so as to increase the affinity between an endogenous agonist and the receptor, whereby its signal in the presence of the endogenous agonist stimulation to the receptor can be enhanced. Such ligands that bind to an allosteric site and enhance the signal from a receptor caused by an endogenous agonist are herein referred to as Positive Allosteric Modulator (PAM). That is, a Positive Allosteric Modulator is a ligand that enhances the signal of an agonist by binding to an allosteric site, which is different from an orthosteric site to which the endogenous agonist binds.

[0006]

For M3 receptor, allosteric sites, which are different from orthosteric sites to which endogenous agonists (acetylcholine and muscarin) bind, have been reported in recent years (see Non-Patent Document 8). M3 receptor PAM (hereinafter referred to as "M3 PAM") is considered to be able to enhance the signal dependent on endogenous agonist stimulation to the M3 receptor. Therefore, M3 PAM can enhance the signal level of M3 receptor under more physiological conditions, and is expected to be promising for the treatment of diseases involving M3 receptor.

[0007]

An aspect of the present invention is to provide a compound having a M3 PAM activity.

[0008]

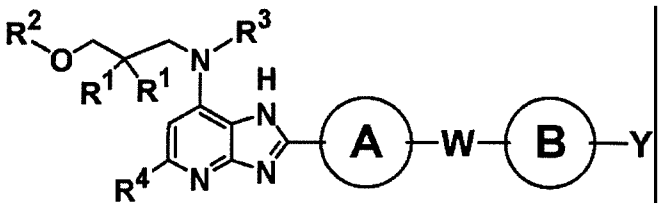
As a result of intensive studies, the inventors discovered that an azabenzimidazole compound represented by the formula [1] or a pharmaceutically acceptable salt thereof, or a solvate thereof, which may be herein referred to as "the present compound", has a M3 PAM activity.

[0009]

That is, disclosed herein are the following (Item 1) to (Item 4).

(Item 1)

An azabenzimidazole compound of the formula [1]:



[11

wherein:

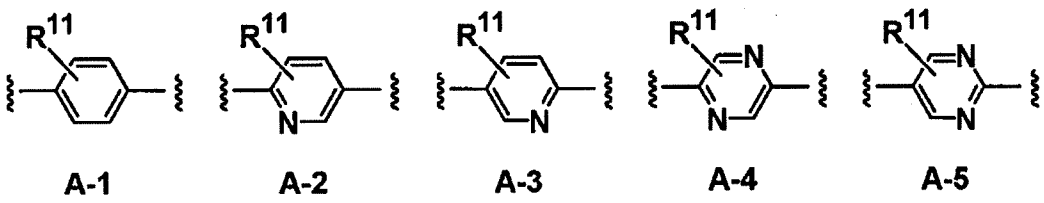
R^1 is a hydrogen atom or alkyl, or two R^1 are taken together with adjacent carbon atom to form a 3- to 7-membered cycloalkyl or an oxygen-containing non-aromatic heterocycle;

R^2 is a hydrogen atom, alkyl, cycloalkyl, alkyl substituted with cycloalkyl, or alkoxyalkyl;

R^3 is a hydrogen atom, alkyl, or alkoxyalkyl;

R^4 is pyridyl optionally substituted with one or two groups selected from the group consisting of alkyl, trihaloalkyl, alkoxy, cyano and cycloalkyl, or phenyl optionally substituted with 1 to 3 groups selected from the group consisting of trihaloalkyl, halogen, alkoxy and cycloalkyl;

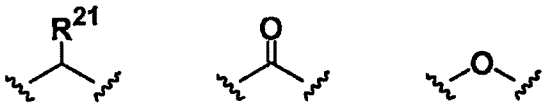
A is a group of the formula A-1, A-2, A-3, A-4, or A-5:



A-1 A-2 A-3 A-4 A-5

wherein the bond on the left side of each group is attached to the 2-position of the azabenzimidazole in the formula [1], and the bond on the right side is attached to W in the formula [1], and R^{11} is a group selected from a hydrogen atom, halogen, alkyl, alkoxy or nitro;

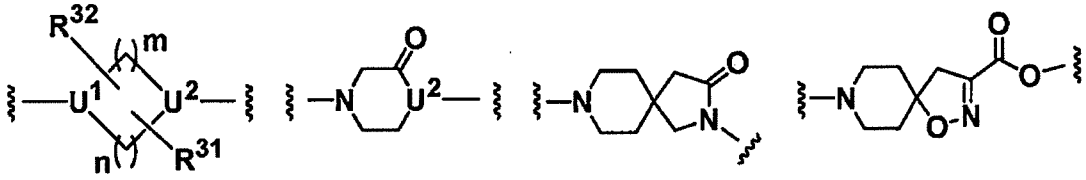
W is a bond, or a group of the formula W-1, W-2, or W-3:



W-1 W-2 W-3

wherein R^{21} is a hydrogen atom or alkyl;

B is a group of the formula B-1, B-2, B-3, or B-4:



B-1 B-2 B-3 B-4

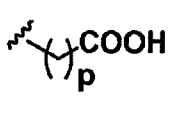
wherein

the bond on the left side of each group is attached to W in the formula [1],

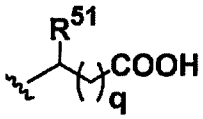
the bond on the right side is attached to Y in the formula [1],

U^1 is a nitrogen atom or CR^{41}, and U^2 is a nitrogen atom, or CR^{42}, and R^{41} and R^{42} are independently a hydrogen atom, alkyl, halogen or a hydroxyl group, m and n are independently 1, 2 or 3, and R^{31} and R^{32} are independently a hydrogen atom, alkyl, halogen or alkoxyalkyl, or R^{31} and R^{32} are taken together with adjacent carbon atom to form an alkylene bridge, provided that R^{31} and R^{32} substitute at any substitutable position other than U^1 and U^2;

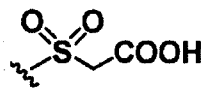
Y is a hydrogen atom, or a group of any one the formula Y-1 to Y-4, Y-11 to Y-16:



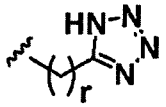
Y-1



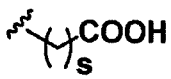
Y-2



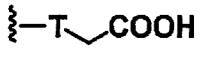
Y-3



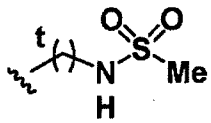
Y-4



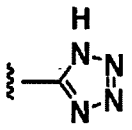
Y-11



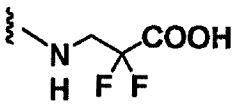
Y-12



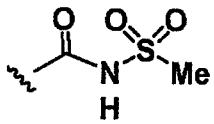
Y-13



Y-14



Y-15



Y-16

wherein

R^{51} is alkyl; p is 1, 2, or 3; q is 0, 1, or 2; r is 1, 2, or 3; T is O, S, SO_2, or NR^{61} wherein R^{61} is a hydrogen atom or alkyl; s is 0, 1, 2, or 3; and t is 0 or 1,

with the proviso that

(a) when W is a bond,

if B is B-1 or B-2 and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4,

if B is B-1 or B-2 and U^2 is CR^{42} wherein R^{42} is as defined above, then U^1 is a nitrogen atom and Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, and

if B is B-3 or B-4, then Y is a hydrogen atom;

(b) when W is W-1,

if B is B-1, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4, and

if B is B-1, U^1 is a nitrogen atom, and U^2 is CR^{42} wherein R^{42} is as defined above, then Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16;

(c) when W is W-2,

if B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4,

if B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is CR^{42} wherein R^{42} is as defined above, then Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, and

if B is B-3 or B-4, then Y is a hydrogen atom; and

(d) when W is W-3,

if B is B-1, U^1 is CR^{41} wherein R^{41} is as defined above, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

(Item 2)
A pharmaceutical composition comprising the azabenzimidazole compound according to Item 1 or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

(Item 3)
An M3 PAM comprising the azabenzimidazole compound according to Item 1 or Item 2 or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

(Item 4)
A prophylactic or therapeutic agent for voiding and/or storage disorders in bladder/urethral diseases, glaucoma or diabetes in which the M3 receptor is involved, comprising the azabenzimidazole compound according to any one of Items 1 to 3 or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

Effect of Invention

[0010]
A compound having a M3 PAM activity is provided by the invention.

Description of Embodiments

[0011]
The definitions of the terms as used herein are as follows.

[0012]
"Halogen" refers to a fluorine atom, a chlorine atom, a bromine atom, or an iodine atom.

[0013]
"Alkyl" includes, for example, a straight or a branched alkyl having 1 to 10 carbon atoms, preferably 1 to 8 carbon atoms, more preferably 1 to 6 carbon atoms, specifically, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, sec-pentyl, 1-ethylpropyl, 1,2-dimethylpropyl, tert-pentyl, 2-methylbutyl, isopentyl, neopentyl, n-hexyl, sec-hexyl, 1-ethylbutyl, isohexyl,

neohexyl, 1,1-dimethylbutyl, texyl, 2-ethylbutyl, 1,2,2-trimethylpropyl, 2,2-dimethylbutyl, n-heptyl, isoheptyl, n-octyl, isooctyl, and the like.

[0014]
Example of the alkyl moiety of "alkoxyalkyl" and "alkyl substituted with cycloalkyl" includes the aforementioned "alkyl".

[0015]
"Trihaloalkyl" refers to the above "alkyl" substituted with three of the above "halogen". Specific examples include trifluoromethyl, trichloromethyl, trifluoroethyl, and the like.

[0016]
"Alkoxy" refers to a group in which the above "alkyl" is attached to an oxygen atom and includes a straight or a branched alkoxy having 1 to 8 carbon atoms, preferably 1 to 6 carbon atoms, specifically, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentyloxy, n-hexyloxy, n-heptyloxy, and n-octyloxy, and the like.

[0017]
Examples of the alkoxy moiety of "alkoxyalkyl" include the aforementioned "alkoxy".

[0018]
"Alkylene" includes alkylene having a straight or a branched divalent hydrocarbon group having 1 to 6 carbon atoms. Specific examples include methylene, ethylene, and propylene.

[0019]
"Cycloalkyl" includes a mono-, di- or tri-cyclic saturated hydrocarbon group having 3 to 10 carbon atoms. A monocyclic cycloalkyl having 3 to 6 carbon atoms is preferred. Specific examples include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, bicyclo[2.1.0]pentyl, bicyclo[2.2.1]heptyl, and bicyclo[2.2.2]octyl.

[0020]

Examples of the cycloalkyl moiety of "alkyl substituted with cycloalkyl" include the aforementioned "cycloalkyl".

[0021]
Examples of "oxygen-containing non-aromatic heterocycle" include a 3- to 8-membered non-aromatic heterocyclic group, more preferably 5- to 7-membered non-aromatic heterocyclic group, containing an oxygen atom and carbon atoms as ring-constituting atoms. Specific examples include oxolanyl (1-oxolanyl, 2-oxolanyl), oxanyl (1-oxanyl, 2-oxanyl, 3-oxanyl), oxepanyl (1-oxepanyl, 2-oxepanyl, 3-oxepanyl), and the like.

[0022]
Each symbol in the formula [1] is described below.

[0023]
In the formula [1], R^1 is a hydrogen atom or alkyl, or two R^1 are taken together with adjacent carbon atom to form a 3- to 7-membered cycloalkyl or an oxygen-containing non-aromatic heterocycle.

[0024]
The "alkyl" for R^1 is preferably methyl, ethyl, n-propyl and n-butyl, more preferably methyl and ethyl.

[0025]
The "cycloalkyl" for R^1 is preferably cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, more preferably cyclobutyl, cyclopentyl and cyclohexyl.

[0026]
The "oxygen-containing non-aromatic heterocycle" for R^1 is preferably 1-oxanyl, 2-oxanyl and 3-oxanyl, more preferably 3-oxanyl.

[0027]
In the formula [1], R^2 is preferably a hydrogen atom, alkyl, cycloalkyl, alkyl substituted with cycloalkyl, or alkoxyalkyl.

[0028]
The "alkyl" for R^2 is preferably methyl, ethyl, n-propyl, n-butyl and

n-pentyl, more preferably methyl, ethyl, n-propyl and n-butyl.

[0029]
The "cycloalkyl" for R^2 is preferably cyclopropyl or cyclobutyl.

[0030]
The cycloalkyl of "alkyl substituted with cycloalkyl" for R^2 is preferably cyclobutyl or cyclopentyl, more preferably cyclobutyl.

[0031]
The alkyl of "alkyl substituted with cycloalkyl" for R^2 is preferably methyl or ethyl, more preferably methyl.

[0032]
The alkoxy of "alkoxyalkyl" for R^2 is preferably methoxy, ethoxy, n-propoxy and isopropoxy, more preferably methoxy and ethoxy.

[0033]
The alkyl of "alkoxyalkyl" for R^2 is preferably methyl, ethyl and propyl, more preferably methyl and ethyl.

[0034]
In the formula [1], R^3 is a hydrogen atom, alkyl, cycloalkyl, alkyl substituted with cycloalkyl, or alkoxyalkyl.

[0035]
The "alkyl" for R^3 is preferably methyl, ethyl and n-propyl, more preferably methyl and ethyl.

[0036]
The alkyl of "alkoxyalkyl" for R^3 is preferably methyl, ethyl and propyl, more preferably methyl and ethyl.

[0037]
The alkoxy of "alkoxyalkyl" for R^3 is preferably methoxy and ethoxy, more preferably methoxy.

[0038]
In the formula [1], R^4 is pyridyl optionally substituted with one or

two groups selected from the group consisting of alkyl, trihaloalkyl, alkoxy, cyano and cycloalkyl, or phenyl optionally substituted with 1 to 3 groups selected from the group consisting of trihaloalkyl, halogen, alkoxy and cycloalkyl.

[0039]
The "alkyl" in pyridyl optionally substituted with one or two alkyls according to R^4 is preferably methyl, ethyl or n-propyl.

[0040]
The "trihaloalkyl" in pyridyl optionally substituted with one or two trihaloalkyl according to R^4 is preferably trifluoromethyl.

[0041]
The "alkoxy" in pyridyl optionally substituted with one or two alkoxy according to R^4 is preferably methoxy, ethoxy, n-propoxy, or n-butoxy, more preferably ethoxy.

[0042]
The "cycloalkyl" in pyridyl optionally substituted with one or two cycloalkyl according to R^4 is preferably cyclopropyl or cyclobutyl, more preferably cyclopropyl.

[0043]
The "trihaloalkyl" in phenyl optionally substituted with 1 to 3 trihaloalkyl according to R^4 is preferably trifluoromethyl.

[0044]
The "halogen" in phenyl optionally substituted with 1 to 3 halogens according to R^4 is preferably a chlorine atom, a bromine atom or a fluorine atom, more preferably a fluorine atom.

[0045]
The "alkoxy" in phenyl optionally substituted with 1 to 3 alkoxy according to R^4 is preferably methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, more preferably methoxy and ethoxy.

[0046]
The "cycloalkyl" optionally substituted on phenyl according to R^4 is

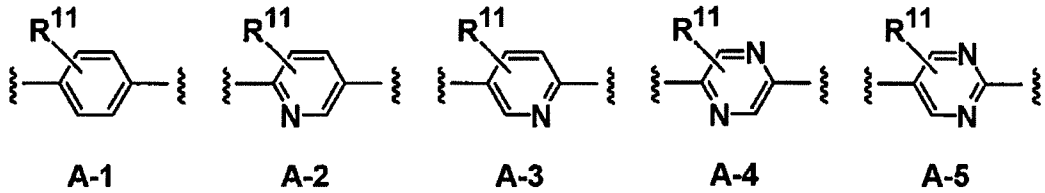
preferably cyclopropyl or cyclobutyl, more preferably cyclopropyl.

[0047]

R^4 is preferably pyridyl substituted with one group selected from the group consisting of alkyl, trihaloalkyl, alkoxy, cyano and cycloalkyl, and trihaloalkyl.

[0048]

In the formula [1], A is a group of the formula A-1, A-2, A-3, A-4, or A-5:



A-1 A-2 A-3 A-4 A-5

[0049]

In the formula [1], R^{11} is a group selected from a hydrogen atom, halogen, alkyl, alkoxy and nitro.

[0050]

The "halogen" for R^{11} is preferably a chlorine atom, a bromine atom and a fluorine atom, more preferably a chlorine atom and a fluorine atom.

[0051]

The "alkyl" for R^{11} is preferably methyl, ethyl and n-propyl, more preferably methyl and ethyl.

[0052]

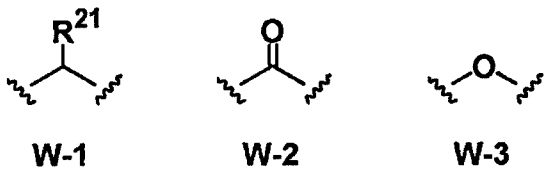
The "alkoxy" for R^{11} is preferably methoxy and ethoxy, more preferably methoxy.

[0053]

In the formula [1], A is preferably A-4.

[0054]

In the formula [1], W is selected from a bond, or W-1, W-2 or W-3:



W-1 W-2 W-3

[0055]

R^{21} in W-1 is a group selected from a hydrogen atom or alkyl.

[0056]

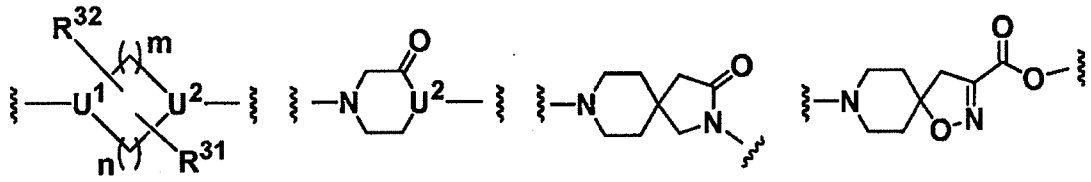
The "alkyl" for R^{21} is preferably methyl or ethyl, more preferably methyl.

[0057]

W in the formula [1] is preferably a bond.

[0058]

B is selected from B-1, B-2, B-3 or B-4:



B-1 B-2 B-3 B-4

wherein the bond on the left side of each of B-1 to B-4 is attached to W in the formula [1], and the bond on the right side is attached to Y in the formula [1].

[0059]

U^1 represents a nitrogen atom or CR^{41}, and U^2 represents a nitrogen atom or CR^{42} .

[0060]

R^{41} and R^{42} each independently represent a hydrogen atom, alkyl, halogen, or a hydroxyl group.

[0061]

The "alkyl" according to R^{41} and R^{42} is preferably methyl and ethyl,

more preferably methyl.

[0062]
m and n are each 1, 2 or 3.

[0063]
R^{31} and R^{32} are each independently a hydrogen atom, alkyl, halogen or alkoxyalkyl, or R^{31} and R^{32} may be taken together with adjacent carbon atoms to form an alkylene bridge.
R^{31} and R^{32} substitute at any substitutable position other than U^1 and U^2.

[0064]
The "alkyl" for R^{31} and R^{32} is preferably methyl and ethyl, more preferably methyl.

[0065]
The "halogen" for R^{31} and R^{32} is preferably a fluorine atom.

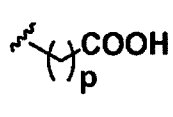
[0066]
"Alkyl "of "alkoxyalkyl" for R^{31} and R^{32} is preferably methyl, ethyl or n-propyl, more preferably methyl or ethyl.

[0067]
The alkoxy of "alkoxyalkyl" for R^{31} and R^{32} is preferably methoxy and ethoxy, more preferably methoxy.

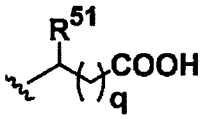
[0068]
The alkylene bridge formed by R^{31} and R^{32} is preferably a linear alkylene bridge having 1 to 3 carbon atoms, more preferably a methylene bridge or an ethylene bridge.

[0069]
In the formula [1], B is preferably B-1, B-2, B-4, more preferably B-1, B-4, and even more preferably B-1.

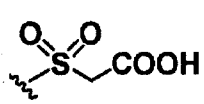
[0070]
Y is selected from a hydrogen atom or Y-1 to Y-4 or Y-11 to Y-16:



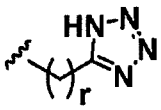
Y-1



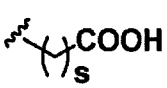
Y-2



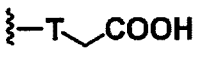
Y-3



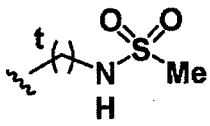
Y-4



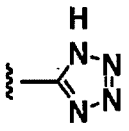
Y-11



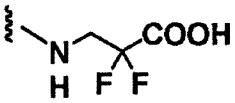
Y-12



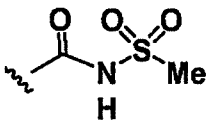
Y-13



Y-14



Y-15



Y-16

[0071]

R^{51} is alkyl; p is 1, 2, or 3; q is 0, 1, or 2; r is 1, 2, or 3; T is O, S, SO_2, or NR^{61} wherein R^{61} is a hydrogen atom or alkyl; s is 0, 1, 2, or 3; and t is 0 or 1.

[0072]

The "alkyl" for R^{51} and R^{61} is preferably methyl, ethyl and n-propyl, more preferably methyl and ethyl.

[0073]

In the formula [1], Y is preferably Y-1, Y-2, Y-3, Y-11, Y-12, or Y-15.

[0074]

The combination of W, B and Y in the formula [1] is preferably

(a) When W is a bond,

if B is B-1 or B-2 and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4, preferably Y-1, Y-2, or Y-3,

if B is B-1 or B-2 and U^2 is CR^{42} wherein R^{42} is as defined above, then U^1 is a nitrogen atom and Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, preferably Y-11, Y-12, or Y-15, and

if B is B-3 or B-4, then Y is a hydrogen atom;

(b) when W is W-1,

if B is B-1, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4, preferably Y-1, Y-2, or Y-3, and

if B is B-1, U^1 is a nitrogen atom, and U^2 is CR^{42} wherein R^{42}

is as defined above, then Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, preferably Y-11, Y-12, or Y-15;

(c) when W is W-2,

if B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4, preferably Y-1, Y-2, or Y-3, if B is B-1 or B-2, U^1 is a nitrogen atom, and u^2 is CR^{42} wherein R^{42} is as defined above, then Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, preferably Y-11, Y-12, or Y-15, and

if Bis B-3 or B-4, then Y is a hydrogen atom; and

(d) when Wis W-3,

if B is B-1, U^1 is CR^{41} wherein R^{41} is as defined above, and u^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4, preferably Y-1, Y-2, or Y-3.

[0074a]

The term "comprise" and variants of the term such as "comprises" or "comprising" are used herein to denote the inclusion of a stated integer or stated integers but not to exclude any other integer or any other integers, unless in the context or usage an exclusive interpretation of the term is required.

[0074b]

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

[0075]

The compound of the invention can be, for example, prepared from a known compound or an easily synthesizable intermediate according to the following method. In the production of the compound of the invention, in the case where a starting material has a substituent which influences the reaction, it is general to perform the reaction after protecting the starting material with a suitable protective group in advance by a known method. The protective group can be

removed after the reaction by a known method.

[0076]

The azabenzimidazole compound of the invention may be used as it is for pharmaceuticals, and can also be used in the form of a pharmaceutically acceptable salt, solvate or salt of the solvate thereof, according to a known method. Examples of pharmaceutically acceptable salts include salts with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, and organic acids such as acetic acid, malic acid, lactic acid, citric acid, tartaric acid, maleic acid, succinic acid, fumaric acid, p-toluenesulfonic acid, benzenesulfonic acid, methanesulfonic acid, salts with alkali metal such as lithium, potassium and sodium, salts with alkaline earth metal such as magnesium and calcium, and salts with organic base such as ammonium salts. These salts can be formed

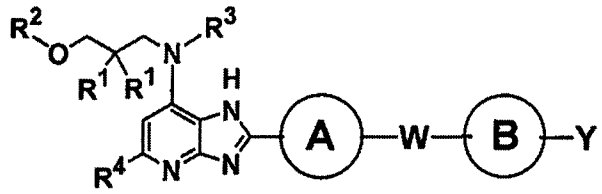
by methods well known in the art.

[0077]
The solvates include hydrates as well as solvates with organic solvents. Examples of pharmaceutically acceptable solvates include alcoholates, such as ethanolate, and hydrates. The hydrate may include, for example, monohydrate and dihydrate. The solvate is formed by coordination with any type and number of solvents. The pharmaceutically acceptable salt may form a solvate.

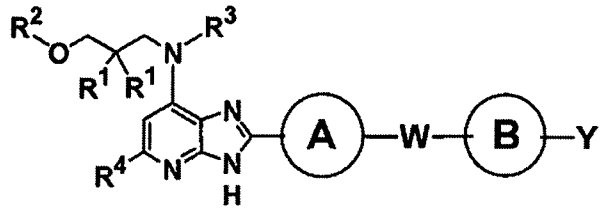
[0078]
For example, a hydrochloride salt of the azabenzimidazole compound of the invention can be prepared by dissolving the azabenzimidazole compound in a solution of hydrogen chloride in alcohol, a solution of hydrogen chloride in ethyl acetate, a solution of hydrogen chloride in 1,4-dioxane, a solution of hydrogen chloride in cyclopentyl methyl ether, or a solution of hydrogen chloride in diethyl ether.

[0079]
Some of the compounds of the invention may have an asymmetric carbon, and the respective stereo isomers and mixtures thereof are all included in the present invention. The stereo isomers can be prepared, for example, by means of optical resolution from the racemate thereof according to a known method using an optically active acid (e.g., tartaric acid, dibenzoyltartaric acid, mandelic acid and 10-camphor sulfonic acid, etc.), utilizing its basicity, or by using an optically active compound prepared in advance as a starting material. In addition, the stereo isomers may be prepared by optical resolution using a chiral column or by asymmetric synthesis.

[0080]
The formula [1] of the invention is not limited to a specific isomer, but includes all possible isomers and racemates. For example, as shown below, tautomers [1Eq] and stereoisomers are also included.



[1]



[1Eq]

wherein the symbols are as defined above.

[0081]

The Compound [1] of the invention and a salt thereof can be prepared from a known compound per se or an intermediate easily preparable from the known compound, according to the following method, the Examples described below or a known method.

[0082]

If the solvents, reagents and starting materials used in each step of the following processes are commercially available, such commercially available products can be used as they are. Also, the compounds obtained and the starting materials used in each step of the following process may form a salt and can be converted by a well-known method into another type of salt or a free form. Alternatively, when the compound obtained or the starting material used in each step in the following process is in a free form, it can be converted into a desired salt by a known method. Examples of such salts include those similar to the salts as described for the compound of the present invention.

[0083]

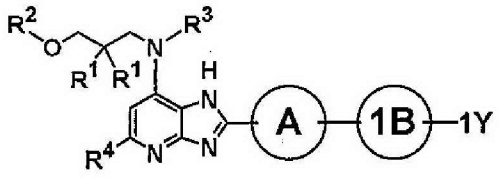
In the production of the compound of the invention, when the starting material has a substituent capable of affecting the reaction, a

protecting group may be introduced in these substituents by a known method in advance, and the target compound can be obtained by removing the protecting group after the reaction if necessary. Such protecting groups can be found, for example, in Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005, and may be selected as appropriate according to the reaction conditions.

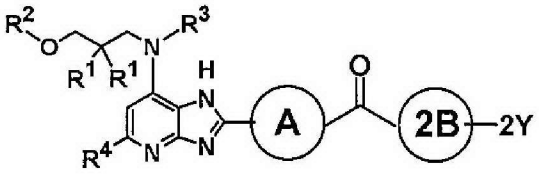
[0084]
The compound obtained in each step of the following processes can be isolated or purified according to a conventional method such as solvent extraction, concentration, distillation, sublimation, recrystallization, reprecipitation, chromatography, and the like. Alternatively, the compound may be used in the next step as a reaction mixture or a crude product.

[0085]
Unless otherwise specified, the reaction in each step of the following processes is conducted according to methods as described in, for example, "Comprehensive Organic Transformations: A Guide to Functional Group Preparations", 2nd Ed. by R. C. Larock, John Wiley & Sons, Inc., 1999; The Chemical Society of Japan, "Experimental Chemistry", 4th edition, Maruzen, 1992; L. Kuerti and B. Czako, "Strategic Applications of Named Reactions in Organic Synthesis", translated by Kiyoshi Tomioka, Kagaku-Dojin Publishing Company, Inc., 2006; G.S. Zweifel and M.H. Nantz, "Modern Organic Synthesis: An Introduction", translated by Tamejiro Hiyama, Kagaku-Dojin Publishing Company, Inc., 2009, or methods in the similar manner as described in the Examples, with modifications or combinations thereof as appropriate.

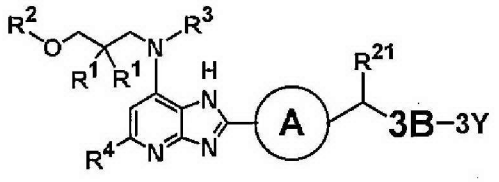
[0086]
The Compound [1] of the invention comprises the following compounds [I], [II], [III] or [IV] depending on the type of W, and can be prepared by the methods described below, but the method for the production of these compounds and the starting materials are not limited to the following examples



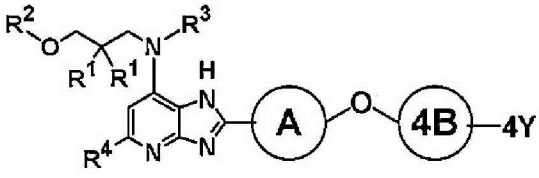
[I]



[II]



[III]



[IV]

wherein R^1, R^2, R^3, R^4, R^{21}, A, B-1, B-2, B-3, B-4, U^1, U^2, CR^{41}, CR^{42}, Y-1, Y-2, Y-3, Y-4, Y-11, Y-12, Y-13, Y-14, Y-15 and Y-16 are as defined above.

In [I],
if 1B is B-1 or B-2, and U^2 is a nitrogen atom, then 1Y is Y-1, Y-2, Y-3, or Y-4,
if 1B is B-1 or B-2, and U^2 is CR^{42}, then U^1 is a nitrogen atom and 1Y is Y-11, Y-12, Y-13, Y-14, Y-15 or Y-16, and
if 1B is B-3 or B-4, then 1Y is a hydrogen atom.

In [II],
if 2B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then 2Y is Y-1, Y-2, Y-3, or Y-4,
if 2B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is CR^{42}, then 2Y is Y-11, Y-12, Y-13, Y-14, Y-15 or Y-16, and
if 2B is B-3 or B-4, then 2Y is a hydrogen atom.

In [III],
if 3B is B-1, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then 3Y is Y-1, Y-2, Y-3 or Y-4,
if 3B is B-1, U^1 is a nitrogen atom, and U^2 is CR^{42}, then 3Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16.

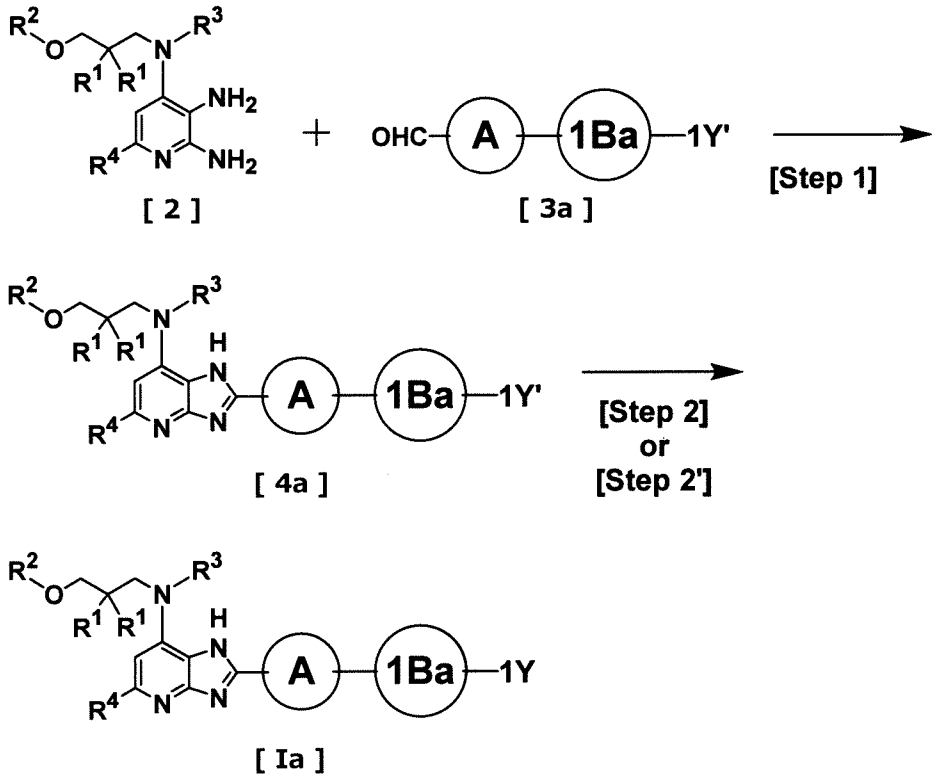
In [IV],
4B is B-1, U^1 is CR^{41}, U^2 is a nitrogen atom, and 4Y is Y-1, Y-2, Y-3, or Y-4.

[0087]

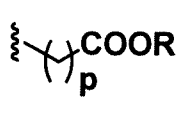
Process 1: Production of Compound [Ia] wherein W is a bond (Part 1)

[0088]

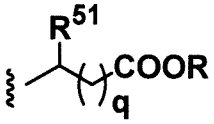
Compound [I] wherein 1B is B-1 or B-2, and 1Y is Y-1, Y-2, Y-3, Y-4, Y-11, Y-12, Y-14 or Y-15; or wherein 1B is B-4, and 1Y is a hydrogen atom, can be prepared according to the following scheme.



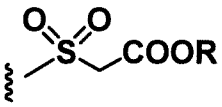
wherein R^1, R^2, R^3, R^4 and A are as defined above. 1Y' is (i) alkyl; (ii) a group of the formula Y'-1, Y'-2, Y'-3, Y'-11, Y'-12 or Y'-15, which is an ester of Y-1, Y-2, Y-3, Y-11, Y-12 or Y-15, respectively; or (iii) a group of the formula Y'-4 or Y'-14, which is a precursor of Y-4 or Y-14, respectively; provided that if 1Ba is B-1 or B- 2, then 1Y' is Y'-1, Y'-2, Y'-3, Y'-11, Y'-12 or Y'-15, and if 1Ba is B-4, then 1Y' is alkyl.



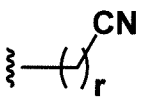
Y'-1



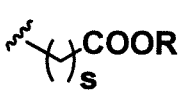
Y'-2



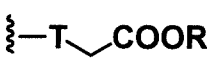
Y'-3



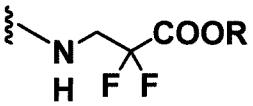
Y'-4



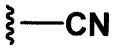
Y'-11



Y'-12



Y'-15



Y'-14

wherein p, q, r, s, T, R^{51} and 1Ba are as defined above. R represents alkyl, for example, methyl or ethyl.

[0089]

Step 1

This step affords Compound [4a] by cyclocondensation of Compound [2] with Compound [3a], which is commercially available or can be prepared according to a known method. The step can be carried out according to a method known per se.

[0090]

The amount of Compound [3a] used in this step is preferably within the range of 0.5 to 2 molar equivalents to Compound [2].

[0091]

This step is carried out in the presence of an oxidizing agent. Examples of the oxidizing agent include sodium dithionite and sodium pyrosulfite.

[0092]

The oxidizing agent is preferably within the range of 1 to 5 molar equivalents to Compound [2].

[0093]

The solvent used in this step is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, tetrahydrofuran (hereinafter referred to as "THF"), ethylene glycol dimethyl ether (hereinafter referred to as "DME"); amides such as dimethylformamide (hereinafter referred to as "DMF"),

dimethylacetamide (hereinafter referred to as "DMA"), N-methylpyrrolidone (hereinafter referred to as "NMP"); alcohols such as ethanol and propanol; dimethyl sulfoxide (hereinafter referred to as "DMSO"); acetonitrile; water; and a mixed solvent thereof.

[0094]
The reaction temperature can vary depending on the starting material and reagents to be used, and usually may be 20°C to 200°C, preferably 50°C to 180°C. Also, a microwave reaction apparatus may be used as necessary.

[0095]
The reaction time can vary depending on the starting material and the reaction temperature and is usually preferably within the range of 0.5 to 24 hours.

[0096]
Step 2
This step is selected when 1Y' is an ester in Compound [4a] obtained in Step 1. Said ester moiety is hydrolyzed in a suitable solvent in the presence of a suitable acid or base to obtain Compound [Ia].

[0097]
Examples of the acid used in this step include inorganic acids such as hydrochloric acid and sulfuric acid; organic acids such as trifluoroacetic acid (hereinafter referred to as "TFA"), methanesulfonic acid, and toluenesulfonic acid. Examples of the base include inorganic bases such as sodium hydroxide, potassium hydroxide and lithium hydroxide.

[0098]
The amount of the acid or the base used in this step is preferably within the range of 1 to 10 molar equivalents to Compound [4a]. If necessary, an excess amount of the acid or the base may be used with respect to Compound [4a].

[0099]
The solvent is not limited so long as it does not participate in the reaction, and examples of such solvent include alcohols such as

methanol, ethanol and 2-propanol; ethers such as THF, diethyl ether, 1,4-dioxane and DME; nitriles such as acetonitrile, propionitrile; ketones such as acetone; water; and a mixed solvent thereof.

[0100]
The reaction temperature can vary depending on the starting material and reagents to be used, and usually may be 20°C to 200°C, preferably 20°C to 100°C. Also, a microwave reaction apparatus may be used as necessary.

[0101]
The reaction time can vary depending on the starting material and the reaction temperature and is usually preferably within the range of 0.5 hours to 4 days.

[0102]
Step 2'
This step is selected when 1Y' is a nitrile in Compound [4a] obtained in Step 1. Said nitrile moiety is reacted with an azide compound and an appropriate amine salt to obtain Compound [Ia] having a tetrazole group.

[0103]
The amount of the azide compound and the amine salt used in this step is preferably within the range of 1 to 10 molar equivalents to Compound [4a].

[0104]
Examples of the azide compound that can be used include sodium azide.

[0105]
Examples of the amine salts that can be used include ammonium chloride and triethylamine hydrochloride.

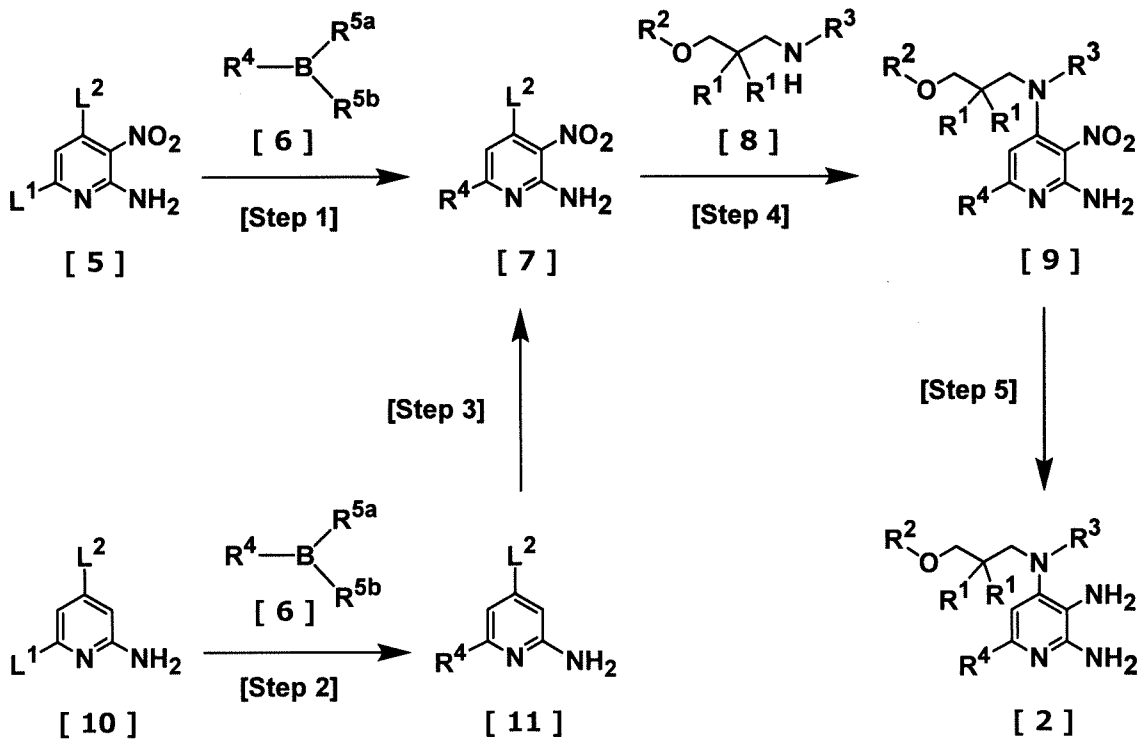
[0106]
The solvent is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; amides such as DMF, DMA, and NMP; DMSO; water, and a mixed solvent thereof.

[0107]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 80°C to 200°C. Also, a microwave reaction apparatus may be used as necessary.

[0108]
The reaction time can vary depending on the starting material and the reaction temperature and is usually preferably within the range of 1 hour to 48 hours.

[0109]
This step 2' can be applied to the synthesis of tetrazole compounds corresponding to compounds [II], [III] and [IV] described below.

[0110]
Production of Compound [2]
A raw material, diamine Compound [2], can be prepared according to the following process.



wherein R^1, R^2, R^3 and R^4 are as defined above. R^{5a} and R^{5b} each represent a hydroxy group, or R^{5a} and R^{5b} are combined together to be

$-O-C(CH_3)_2-C(CH_3)_2-O-$, $-O-(CH_2)_3-O-$, or $-O-CH_2-C(CH_3)_2-CH_2-O-$, L^1 and L^2 are leaving groups, and examples of L^1 and L^2 include a chlorine atom and a bromine atom.

[0111]

Step 1

This step is cross-coupling reaction of Compound [5] with a boron Compound [6], which is commercially available or can be prepared by a known method, in the presence of a palladium catalyst and a base to obtain Compound [7].

[0112]

The amount of Compound [6] is preferably within the range of 1 to 3 molar equivalents to Compound [5].

[0113]

Examples of the palladium catalyst include tris(dibenzylideneacetone)bispalladium chloroform adduct (hereinafter referred to as "$Pd_2(dba)_3 \cdot CHCl_3$"), tris(dibenzylideneacetone)bispalladium (hereinafter referred to as "$Pd_2(dba)_3$"), tetrakistriphenylphosphine palladium (hereinafter referred to as "$Pd(PPh_3)_4$"), [1,1'-bis(diphenylphosphino) ferrocene]-dichloropalladium(II)•dichloromethane adduct (hereinafter referred to as "$Pd(dppf)Cl_2 \cdot CH_2Cl_2$"), bis(triphenylphosphine) palladium(II) dichloride (hereinafter referred to as "$PdCl_2(PPh_3)_2$"), [1,1'-bis(di-tert-butylphosphino)ferrocene] dichloropalladium(II) (hereinafter referred to as "$Pd(dtbpf)Cl_2$"), bis(tricyclohexylphosphine)palladium(II) dichloride (hereinafter referred to as "$PdCl_2(PCy_3)_2$"), and palladium(II) acetate (hereinafter referred to as "$Pd(OAc)_2$").

[0114]

The amount of the palladium catalyst used is preferably within the range of, for example, 0.01 to 0.3 molar equivalents to Compound [5].

[0115]

Examples of the base to be used include inorganic bases such as potassium carbonate, cesium carbonate, sodium carbonate, sodium bicarbonate, sodium acetate, potassium acetate, trisodium phosphate,

and tripotassium phosphate.

[0116]
The amount of the base to be used is preferably within the range of, for example, 1 to 4 molar equivalents to Compound [5].

[0117]
In this step, an appropriate ligand may be used as necessary. Examples of such ligand include 1,1'-bis(diphenylphosphino)ferrocene (hereinafter referred to as "dppf"), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (hereinafter referred to as "Xantphos"), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (hereinafter referred to as "XPhos"), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (hereinafter referred to as "BINAP"), 2-dicyclohexylphosphino-2',6'-diisopropylbiphenyl (hereinafter referred to as "RuPhos"), triphenylphosphine (hereinafter referred to as "PPh_3"), and tricyclohexylphosphine (hereinafter referred to as "PCy_3").

[0118]
The amount of the ligand to be used is preferably within the range of, for example, 1 to 5 molar equivalents to the palladium catalyst.

[0119]
In this step, the solvent is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; amides such as DMF, DMA, NMP; alcohols such as ethanol, 2-propanol and tert-butanol; water, or a mixed solvent thereof.

[0120]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 20°C to 200°C. Also, a microwave reaction apparatus may be used as necessary.

[0121]
The reaction time can vary depending on the starting material and the reaction temperature and is usually preferably within the range of 0.1 to 24 hours.

[0122]
Compound [7] can also be prepared via Step 2 and Step 3 described below.

[0123]
Step 2
This step is cross-coupling reaction of Compound [10] with Compound [6] using a palladium catalyst and can be carried out under the same reaction conditions as described above in Step 1.

[0124]
Step 3
This step is nitration of Compound [11] in the presence of an appropriate nitrating agent to obtain Compound [7]. This step can be carried out according to a method known as nitration reaction.

[0125]
Examples of the nitrating agent to be used include nitric acid, fuming nitric acid, copper nitrate, sodium nitrate, and potassium nitrate.

[0126]
The amount of the nitrating agent to be used is preferably within the range of 1 to 1.1 molar equivalents to Compound [11].

[0127]
In this step, the solvent is selected depending on the type of reagents to be used, and examples include concentrated sulfuric acid and concentrated hydrochloric acid.

[0128]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 40°C, more preferably within the range of 5°C to 15°C.

[0129]
The reaction time can vary depending on the starting material and reagents to be used, and is usually preferably within the range of

0.5 to 12 hours, more preferably within the range of 1 to 3 hours.

[0130]
Step 4
This step affords aromatic amino Compound [9] by the reaction of Compound [7] with Compound [8], which is commercially available or can be prepared according to a known method.

[0131]
Compound [7] may be used in the form of a salt with a suitable acid, such as hydrochloride, trifluoroacetate, and the like.

[0132]
The amount of Compound [8] to be used is preferably within the range of 0.5 to 1.5 molar equivalents to Compound [7].

[0133]
In this step, a base may be used as necessary. Examples of such base that may be used include triethylamine (hereinafter referred to as "TEA"), N,N-diisopropylethylamine (hereinafter referred to as "DIPEA"), 1,8-diazabicyclo[5.4.0]-7-undecene (hereinafter referred to as "DBU"), and inorganic bases such as potassium carbonate, cesium carbonate, and sodium carbonate.

[0134]
The amount of the base is preferably within the range of 1 to 10 molar equivalents to Compound [7].

[0135]
The solvent to be used is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; amides such as DMF and DMA; nitriles such as acetonitrile and propionitrile; alcohols such as 2-propanol and tert-butanol; DMSO, water; and a mixed solvent thereof.

[0136]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range

of 20°C to 200°C. Also, a microwave reaction apparatus may be used as necessary.

[0137]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 0.5 to 24 hours.

[0138]
If Compound [9] is prepared using Compound [5] as a starting material, the order of step 1 and step 4 can be exchanged to obtain Compound [9]. The reaction conditions in this case are the same as those described above in Step 1 and Step 4, respectively.

[0139]
Step 5
This step is reduction of the nitro group in Compound [9] to obtain aromatic diamine Compound [2]. This step can be carried out according to a method known per se. This reduction reaction can be achieved, for example, by performing iron reduction using reduced iron and ammonium chloride in a suitable solvent, or by zinc reduction using zinc powder and ammonium chloride or acetic acid.

[0140]
Examples of the reducing agent that can be used in the reduction reaction include reduced iron, zinc powder, and tin (II) chloride.

[0141]
The amount of reducing agent used in this step is preferably within the range of 1 to 10 molar equivalents to Compound [9].

[0142]
When using the above metal reagent in the reduction reaction, an acid is usually used. Examples of the acid to be used include hydrochloric acid, acetic acid, ammonium chloride, and the like.

[0143]
The amount of acid used in this step is preferably within the range of 1 to 10 molar equivalents to Compound [9].

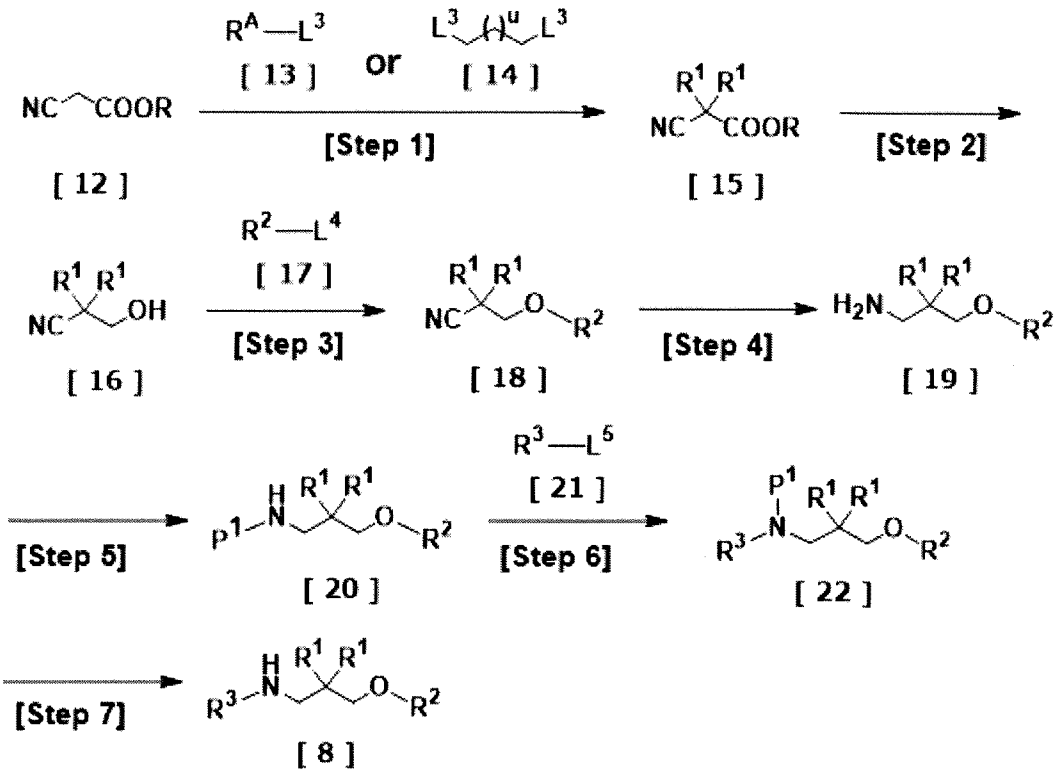
[0144]
The solvent used in this step is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and 1,4-dioxane; ethers such as THF and DME; esters such as ethyl acetate; ketones such as acetone; nitriles such as acetonitrile; amides such as DMF; alcohols such as methanol, ethanol, 2-propanol, and tert-butanol; water; or a mixed solvent thereof.

[0145]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 200°C.

[0146]
The reaction time can vary depending on the starting material, reagents to be used and the reaction temperature, and is usually preferably within the range of 1 to 24 hours.

[0147]
Production of Compound [8]
Compound [8], which is a raw material to obtain the above Compound [2], can be prepared, for example, according to the following process.

[0148]



wherein R^1, R^2, and R^3 are as defined above. R^A is alkyl as defined for R^1. R is alkyl and examples of R include methyl, ethyl, and the like. u is 0, 1, 2, 3, or 4. L^3, L^4, and L^5 represent a leaving group, and examples of L^3, L^4, and L^5 include bromine atom, chlorine atom, iodine atom, and the like. P^1 represents a protecting group, such as tert-butoxycarbonyl (hereinafter referred to as "Boc"), benzyloxycarbonyl (hereinafter referred to as "Cbz"), benzyl (hereinafter referred to as "Bn"), p-methoxybenzyl (hereinafter referred to as "PMB"), 2-nitrobenzenesulfonyl (hereinafter referred to as "Ns"), and 4-toluenesulfonyl (hereinafter referred to as "Ts"), and the like.

[0149]

Step 1

This step affords Compound [15] from cyanoacetic acid ester [12] using alkylating agent [13] or [14] in the presence of a base. This step can be carried out according to a method known per se.

[0150]

Examples of the alkylating agent to be used include methyl iodide, ethyl iodide, 1,3-dibromopropane, 1,4-dibromobutane and 1,5-dibromopentane.

[0151]
The amount of the alkylating agent to be used is preferably within the range of 2 molar equivalents to 2.5 molar equivalents to Compound [12] when using the alkylating agent [13], and within the range of 1 to 1.3 molar equivalents to Compound [12] when using the alkylating agent [14].

[0152]
Examples of the base to be used include sodium hydride, potassium hydride, potassium carbonate, sodium carbonate, cesium carbonate, sodium bicarbonate, sodium methoxide, sodium ethoxide, sodium tert-butoxide, potassium tert-butoxide, DBU, and the like.

[0153]
The amount of base to be used is preferably within the range of 2 to 5 molar equivalents to Compound [12].

[0154]
The reaction solvent is not limited so long as it does not participate in the reaction, and examples of such solvent include amides such as DMF and DMA, ethers such as THF, nitriles such as acetonitrile, DMSO, or a mixed solvent thereof.

[0155]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 20°C to 150°C.

[0156]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 0.5 to 24 hours.

[0157]
Step 2
This step affords Compound [16] by reducing the ester moiety of Compound [15] with a reducing agent.

[0158]
Examples of the reducing agent to be used include lithium borohydride. Lithium borohydride can be prepared by mixing lithium chloride and sodium borohydride in the reaction system.

[0159]
The amount of the reducing agent to be used is preferably within the range of 1 to 5 molar equivalents to Compound [15].

[0160]
When lithium borohydride is prepared in the reaction system as described, the amounts of lithium chloride and sodium borohydride are preferably within the range of 1 to 5 molar equivalents to Compound [15].

[0161]
The solvent used in this step is not limited so long as it does not participate in the reaction, and examples of such solvent include alcohols such as methanol and ethanol; ethers such as THF, 1,4-dioxane and DME; halogenated hydrocarbons such as dichloromethane; water, or a mixed solvent thereof.

[0162]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of -10°C to 80°C.

[0163]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 0.1 to 24 hours.

[0164]
Step 3
This step affords Compound [18] by alkylating the hydroxyl group of Compound [16] with alkylating agent [17] in the presence of a base. This step can be carried out according to a method known as an alkylation reaction.

[0165]
Examples of the alkylating agent to be used include methyl iodide, ethyl iodide, 1-bromobutane, 1-iodobutane, 1-bromo-2-methoxyethane, and the like.

[0166]
The amount of the alkylating agent to be used is preferably within the range of 1 to 1.5 molar equivalents to Compound [16].

[0167]
Examples of the base to be used include sodium hydride, potassium hydride, potassium carbonate, sodium carbonate, cesium carbonate, sodium bicarbonate, sodium methoxide, sodium ethoxide, sodium tert-butoxide, potassium tert-butoxide, DBU, and the like.

[0168]
The amount of base to be used is preferably within the range of 1 to 2 molar equivalents to Compound [16].

[0169]
The solvent used in this step is not limited so long as it does not participate in the reaction, and examples of such solvent include amides such as DMF and DMA; ethers such as THF; nitriles such as acetonitrile; DMSO; or a mixed solvent thereof.

[0170]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 150°C.

[0171]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 1 hour to 48 hours.

[0172]
Step 4
This step affords amine Compound [19] by reducing the nitrile of Compound [18]. This step can be carried out according to a method

known per se as a nitrile reduction reaction (for example, The Chemical Society of Japan, "Experimental Chemistry", 4th edition, Maruzen, 1992, Vol.20, section of Organic Synthesis II Alcohol Amine, p.280-282, and Vol.26, section of Organic Synthesis VIII, p.190-260; The Journal of Organic Chemistry, 1986, Vol.51, Issue 21, p.4000-4005; Tetrahedron, 2003, Vol.59, Issue 29, p.5417-5423, etc.).

[0173]
Reducing of the nitrile may be conducted by hydrogenation using a catalyst such as platinum (IV) oxide, platinum, Raney nickel, platinum-carbon (hereinafter referred to as "Pt–C"), and palladium-carbon (hereinafter referred to as "Pd–C") or by reduction using lithium aluminum hydride, aluminum hydride, lithium borohydride, nickel borohydride, or the like.

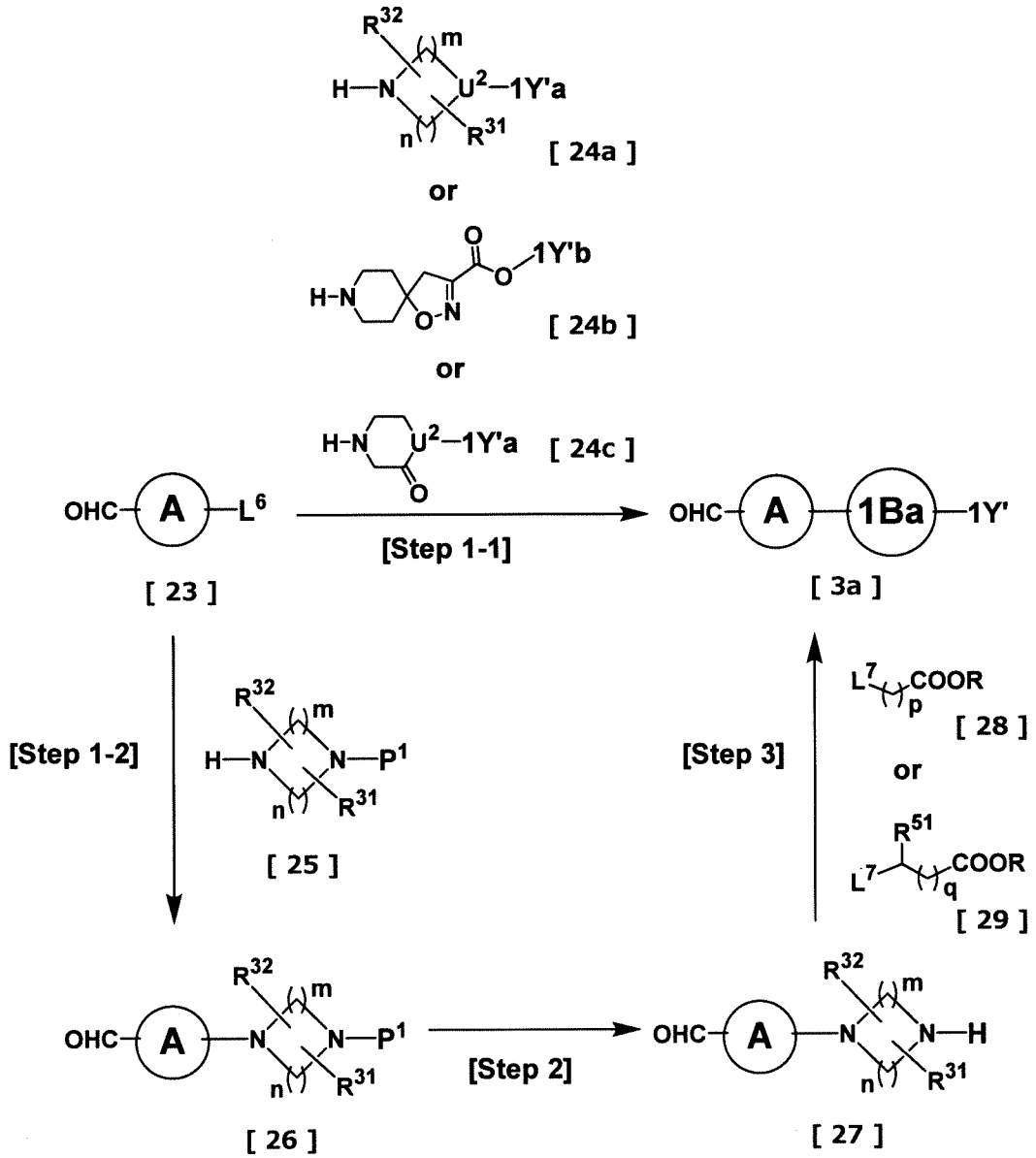
[0174]
Step 5
This step is a reaction for introducing a protecting group into the amino group of Compound [19]. This step can be carried out with reference to Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005.

[0175]
Step 6
This step affords Compound [22] by alkylating the amino group of Compound [20]. This step can be carried out as described above in Step 3.

[0176]
Step 7
This step affords Compound [8] by deprotecting the protecting group from Compound [22]. This step can be carried out with reference to Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005.

[0177]
Production of Compound [3a]

Compound [3a], which is a raw material compound, can be prepared, for example, according to the following process.



wherein A, R^{31}, R^{32}, R^{51}, m, n, p, q, 1Ba, U^2, and P^1 are as defined above. 1Y'a is Y'-1, Y'-2, Y'-3, Y'-4, Y'-11, Y'-12, Y'-14, or Y'-15, and 1Y'b is alkyl. R is alkyl such as methyl and ethyl. L^6 and L^7 are a leaving group. Examples of L^6 include fluorine atom and chlorine atom, and examples of L^7 include chlorine atom, bromine atom, and iodine atom.

[0178]

Step 1-1

This step affords aromatic amino Compound [3a] by reacting Compound

[23] with Compound [24a], [24b] or [24c], which is commercially available or can be prepared according to a known method.

[0179]
Compound [24a], [24b] or [24c] may be used in the form of a salt with an appropriate acid such as hydrochloride, trifluoroacetate, and the like.

[0180]
The amount of Compound [24a], [24b], or [24c] to be used is preferably within the range of 1 to 2 molar equivalents to Compound [23].

[0181]
In this step, a base can be used as necessary. Examples of the base that can be used include organic bases such as TEA, DIPEA, and DBU, and inorganic bases such as sodium bicarbonate, potassium carbonate, cesium carbonate, sodium carbonate, potassium hydroxide, and potassium tert-butoxide.

[0182]
The amount of the base to be used is preferably within the range of 1 to 10 molar equivalents to Compound [23].

[0183]
The solvent used in this step is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; amides such as DMF, DMA; nitriles such as acetonitrile and propionitrile; alcohols such as 2-propanol and tert-butanol; DMSO; water; and a mixed solvent thereof.

[0184]
The reaction temperature can vary depending on the starting material and reagents to be used, and usually can be within a range of 20°C to 200°C. Also, one may use a microwave reaction apparatus as necessary.

[0185]
The reaction time can vary depending on the starting material and

the reaction temperature to be used, and is usually preferably within the range of 0.5 to 24 hours.

[0186]
Step 1-2
This step affords Compound [26] from Compound [23] and Compound [25], which is commercially available or known. This step can be carried out in the similar manner as described in Step 1-1 in the production of Compound [3a].

[0187]
Step 2
This step affords Compound [27] by removing the protecting group P^1 of Compound [26], and the step can be carried out in the similar manner as described in Step 7 in the production of Compound [8].

[0188]
Step 3
This step is alkylation of amine moiety of Compound [27] by the reaction with Compound [28] or Compound [29], which is commercially available or can be prepared according to a method known per se, to obtain Compound [3a].

[0189]
The amount of Compound [28] or Compound [29] to be used is preferably within the range of 1 to 2 molar equivalents to Compound [27].

[0190]
In this step, a base can be used as necessary. Examples of the base to be used include organic bases such as TEA and DIPEA, and inorganic bases such as potassium carbonate, cesium carbonate, and sodium bicarbonate.

[0191]
The amount of the base is preferably within the range of 1 to 5 molar equivalents to Compound [27].

[0192]
The solvent to be used is not limited so long as it does not

participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; amides such as DMF, DMA and NMP; halogenated hydrocarbons such as dichloromethane and chloroform; alcohols such as methanol and ethanol; nitriles such as acetonitrile and propionitrile; and a mixed solvent thereof.

[0193]

The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 150°C.

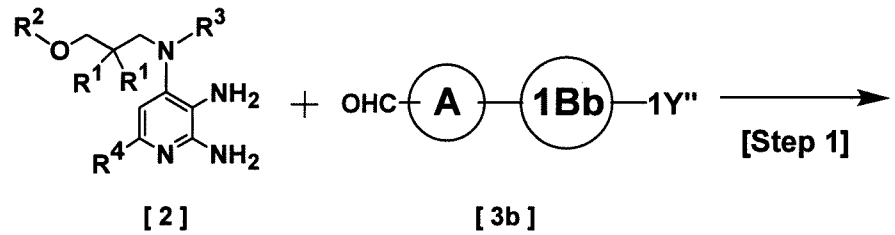
[0194]

The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 1 to 24 hours.

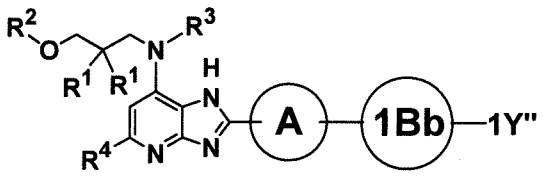
[0195]

Production of Compound [Ib]

Compound [I], wherein 1B is B-1 or B-2 and 1Y is Y-13 or Y-16, or wherein 1B is B-3 and 1Y is hydrogen, can be prepared as follows.



[2] [3b]



[Ib]

wherein A, R^1, R^2, R^3 and R^4 are as defined above. 1Y" is Y-13 or Y-16, and 1Bb is B-1 or B-2.

[0196]

Step 1

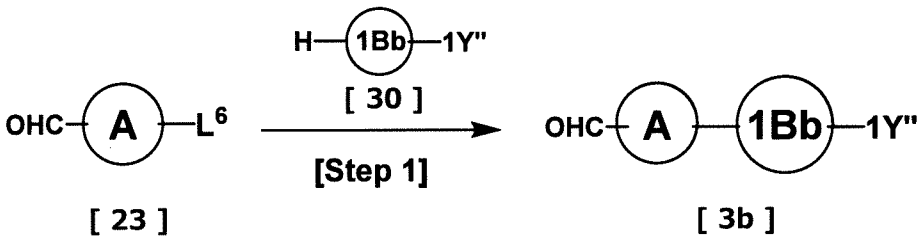
This step affords Compound [Ib] by reacting Compound [3b] with

Compound [2]. This step can be carried out in the similar manner as described in step 1 of Process 1.

[0197]

Production of Compound [3b]

Compound [3b] can be prepared as follows.



wherein A, 1Bb, Y" and L^6 are as defined above.

[0198]

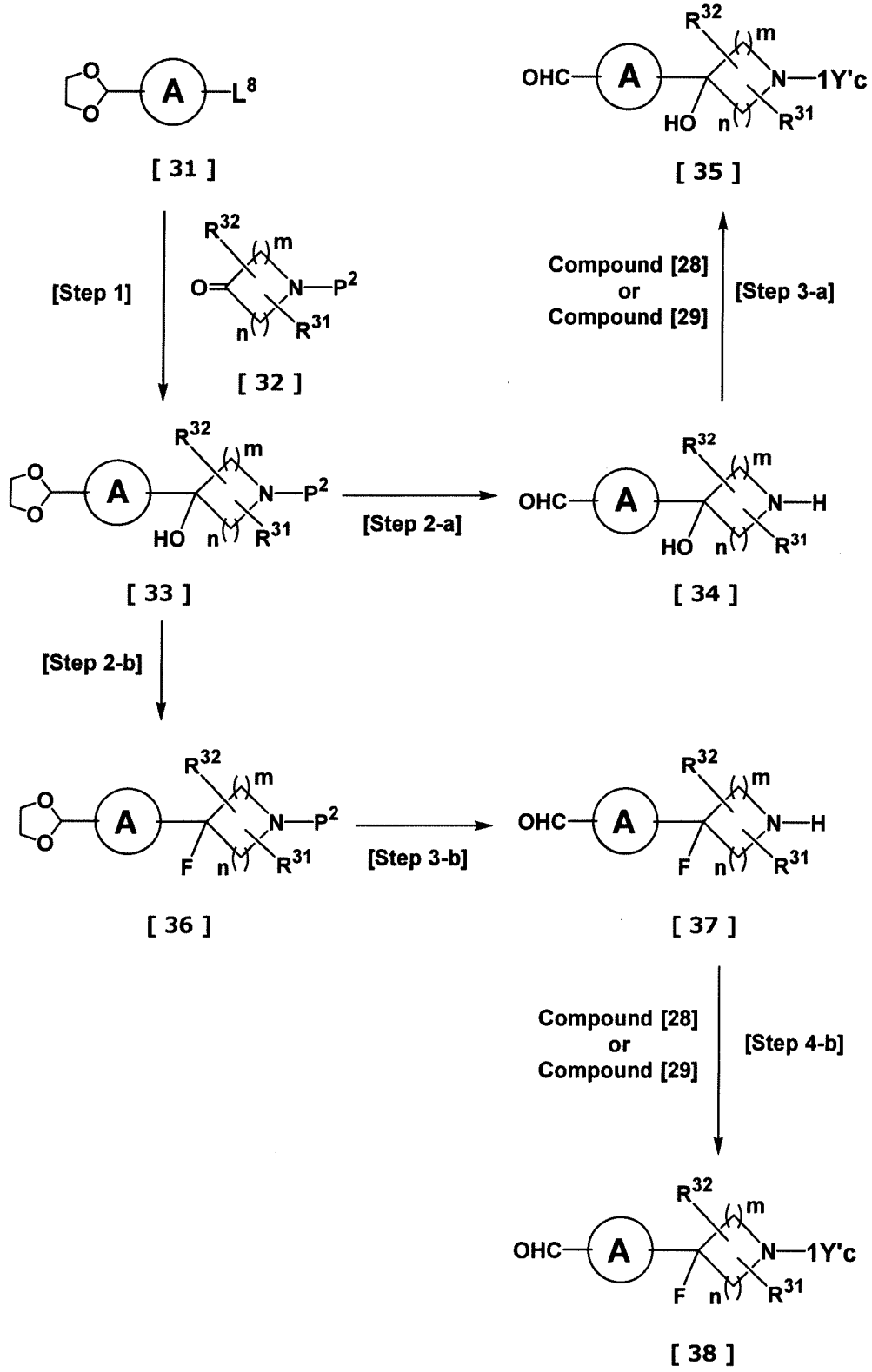
Step 1

This step is an aromatic aminating reaction of Compound [23] with Compound [30], and the step can be carried out in the similar manner as described in Step 1-1 in the production of Compound [3a].

[0199]

Production of Compounds [35] and [38]

Among compounds of formula [3a], Compound [35] having hydroxyl group as R^{41} for CR^{41} as defined above and Compound [38] having fluorine as R^{41} for CR^{41} as defined above can be prepared according to the following process.



wherein A, R^{31}, R^{32}, m and n are as defied above. 1Y'c is Y'-1 or Y'-2. L^8 is a leaving group, and examples of L^8 include bromine atom and iodine atom. P^2 represents a protecting group, and examples of P^2 include Boc group and Cbz group.

[0200]
Step 1
This step affords Compound [33] by reacting Compound [31] with Compound [32] in the presence of a base.

[0201]
The reaction is usually carried out by reacting Compound [31] with a suitable base in a suitable solvent and then reacting with Compound [32].

[0202]
The amount of Compound [32] to be used is preferably within the range of 0.5 to 2 molar equivalents to Compound [31].

[0203]
Examples of the base to be used include organometallic reagents such as isopropylmagnesium chloride, isopropylmagnesium chloride/lithium chloride complex, n-butyllithium, lithium diisopropylamide, and the like.

[0204]
The amount of the organometallic reagent to be used is preferably within the range of 1 to 2 molar equivalents to Compound [31].

[0205]
The solvent to be used is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as n-hexane, toluene and xylene; ethers such as diethyl ether, 1,4-dioxane, THF and DME; and a mixed solvent thereof.

[0206]
In this step, the reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of -80°C to 100°C.

[0207]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 1 to 24 hours.

[0208]

Step 2-a

This step affords Compound [34] by deprotecting the acetal group and P^2 from Compound [33], and the step can be carried out with reference to Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005, as described above.

[0209]

Step 3-a

This step affords Compound [35] by amine alkylation reaction, and the step can be carried out in the similar manner as described in Step 3 in the Production of Compound [3a].

[0210]

Step 2-b

This step affords Compound [36] by fluorinating the hydroxyl group of Compound [33] in the presence of a fluorinating reagent.

[0211]

Examples of the fluorinating reagent to be used include electrophilic fluorinating reagents such as (diethylamino)sulfur trifluoride (hereinafter referred to as "DAST"), bis(2-methoxyethyl)aminosulfur trifluoride, and 4-tert-butyl-2,6-dimethylaminosulfur trifluoride.

[0212]

The amount of the fluorinating reagent to be used is preferably within the range of 1 to 1.5 molar equivalents to Compound [33].

[0213]

The solvent to be used is not limited so long as it does not participate in the reaction, and examples of such solvent include halogenated hydrocarbons such as dichloromethane.

[0214]

In this step, the reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 100°C.

[0215]

The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 1 to 24 hours.

[0216]

Step 3-b

This step affords Compound [37] by deprotecting the acetal group and P^2 from Compound [36], and the step can be carried out in the similar manner as described above in Step 2-a.

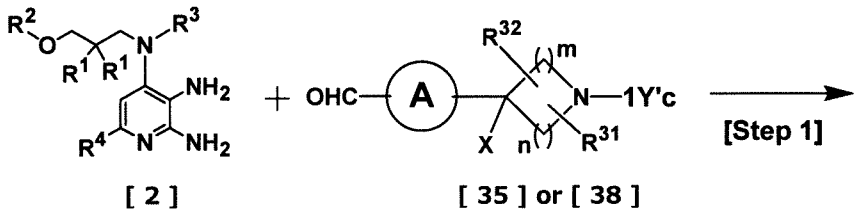
[0217]

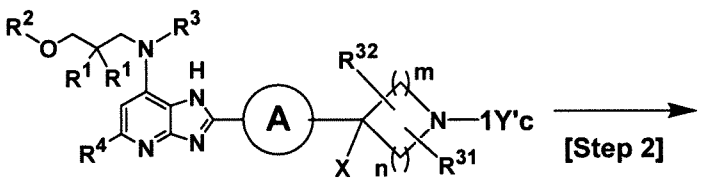
Step 4-b

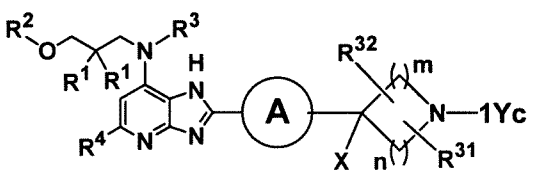
This step affords Compound [38] by alkylation reaction of amine. This step can be carried out in the similar manner as described in Step 3 in the production of Compound [3a].

[0218]

Compounds [35] and [38] can be reacted with Compound [2] according to Step 1 in Process 1 to lead to Compound [Ic], which is a compound corresponding to Compound [Ia].







wherein A, R^1, R^2, R^3, R^4, R^{31}, R^{32}, m, n, 1Y'c, and 1Yc are as defined above. X represents a hydroxyl group or a fluorine atom.

[0219]

Step 1

This step affords Compound [4c] by cyclocondensation of Compound [2] with Compound [35] or Compound [38], and the step can be carried out in the similar manner as described in Step 1 of Process 1.

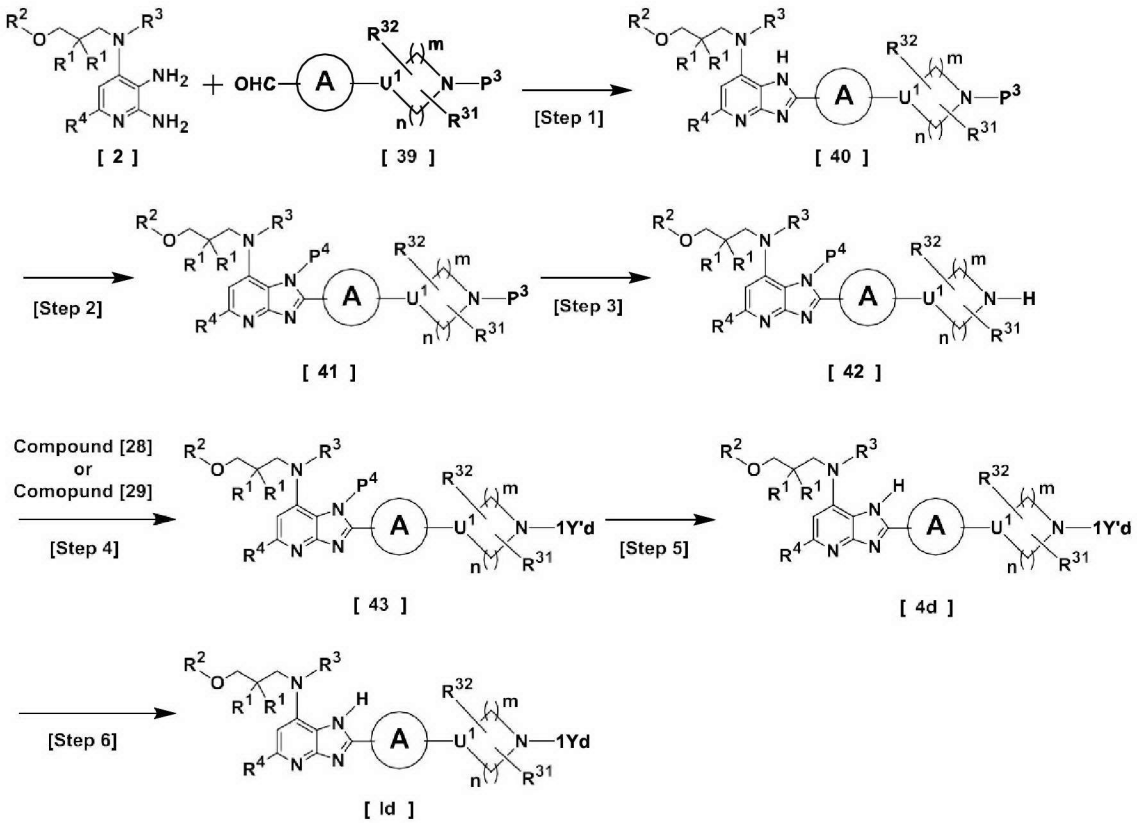
[0220]

Step 2

This step affords Compound [Ic] by hydrolyzing Compound [4c]. This step can be carried out in the similar manner as described in Step 2 of Process 1.

[0221]

Process 2: Production of Compound [Id]



wherein R^1, R^2, R^3, R^4, R^{31}, R^{32}, U^1, m, n, A are as defined above. 1Yd is Y-1, Y-2, Y-3 or Y-4, and 1Y'd is Y'-1, Y'-2, Y'-3, or Y'-4. P^3 and P^4 are a protecting group. P^3 is a protecting group to be

deprotected under basic conditions, such as trifluoroacetyl group, and P^4 is a protecting group not to be deprotected under basic conditions, such as 2-(trimethylsilyl)ethoxymethyl (SEM) group.

[0222]
This process is an alternative to Process 1. That is, as described below, cyclocondensation of Compound [2] and Compound [39] is carried out to form Compound [40] having the basic structure of Compound [1], followed by introducing Y substituent.

[0223]
Step 1
This step affords Compound [40] by cyclocondensation of Compound [2] with Compound [39], and the step can be carried out according to Step 1 of Process 1.

[0224]
Step 2
This step is introducing a protecting group into the imidazole moiety of the azabenzimidazole in Compound [40], and the step can be carried out with reference to Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005.

[0225]
Depending on the conditions, such as protecting reagent and solvent to be used in this step, a compound in which the protecting group is introduced at the 1-position of azabenzoimidazole, a compound in which the protecting group is introduced at the 3-position of azabenzoimidazole, or a mixture thereof may be obtained, which can be used as it is in the next step.

[0226]
The protecting group P^4 to be introduced and/or the reaction conditions in this step should be selected so that the protecting group is not deprotected under the conditions for deprotecting P^3 in the next step (third step). Examples of the combination of such P^3 and P^4 include: P^4 is 2-(trimethylsilyl)ethoxymethyl (SEM), and P^3 may be a trifluoroacetyl group or Bn.

[0227]

Step 3

This step affords Compound [42] by deprotecting P^3 from Compound [41], and can be carried out with reference to Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005.

[0228]

Step 4

This step affords Compound [43] by alkylating the amine of Compound [42], and can be carried out in the similar manner as described in Step 3 of the production of Compound [3a].

[0229]

Step 5

This step affords Compound [4d] by deprotecting P^4 from Compound [43], and can be carried out with reference to Wuts and Greene, "Greene's Protective Groups in Organic Synthesis", 4th edition, John Wiley & Sons Inc., 2006, or P.J. Kocienski, "Protecting Groups", 3rd edition, Thieme, 2005.

[0230]

Step 6

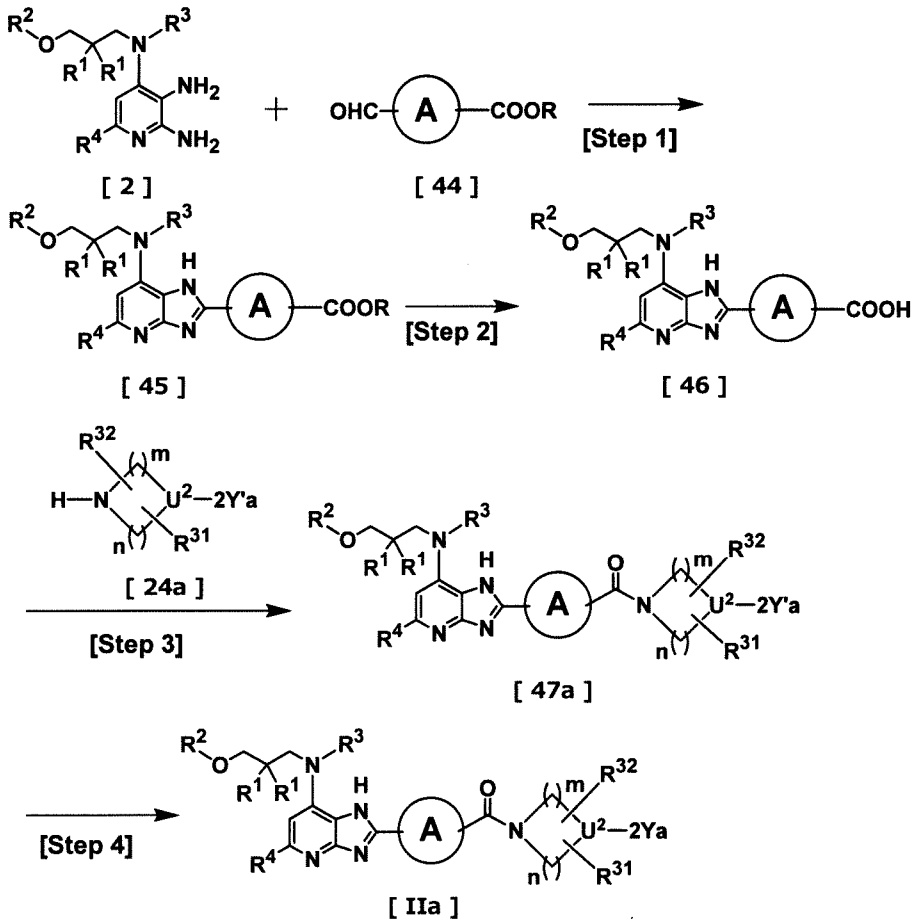
This step affords Compound [Id] by hydrolyzing Compound [4d], and can be prepared in the similar manner as described in Step 2 of Process 1.

[0231]

The Process 2 is also applicable to Compounds [II], [III] and [IV] described below.

[0232]

Process 3: Production of Compound [IIa] (wherein W is W-2)



wherein R^1, R^2, R^3, R^4, R, A, R^{31}, R^{32}, m, n, and U^2 are as defined above. 2Ya is Y-1, Y-2, Y-3, Y-4, Y-11, Y-12, Y-14, or Y-15, and 2Y'a is Y'-1, Y'-2, Y'-3, Y'-4, Y'-11, Y'-12, Y'-14, or Y'-15.

[0233]

This process is directed to the production of a compound of formula [IIa] among those of formula [1].

[0234]

Step 1

This step affords Compound [45] by cyclocondensation of Compound [2] with Compound [44], which is commercially available or can be prepared according to a known method, and the step can be carried out in the similar manner as described in Step 1 of Process 1.

[0235]

Step 2

This step affords Compound [46] by hydrolyzing Compound [45]. This step can be carried out in the similar manner as described in Step 2

of Process 1.

[0236]
Step 3
This step affords Compound [47a] by condensing Compound [46] or a reactive derivative thereof and amine Compound [24a] in the presence of a condensing agent.

[0237]
Examples of the reactive derivative of Compound [46] include those commonly used in amide condensation reactions, such as acid halides (e.g., acid chloride, acid bromide), mixed acid anhydrides, imidazolides, and active amides.

[0238]
The amounts of the condensing agent and amine Compound [24a] to be used in this step are preferably within the range of 1 to 3 molar equivalents to Compound [46].

[0239]
Examples of the condensing agent to be used in this step include 1,1'-carbonyldiimidazole (hereinafter referred to as "CDI"), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (hereinafter referred to as "EDCI"), diisopropylcarbodiimide (hereinafter referred to as "DIC"), diethyl cyanophosphonate, O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (hereinafter referred to as "HBTU"), O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (hereinafter referred to as "HATU"), and the like.

[0240]
In this step, a base can be used as necessary. Examples of the base that can be used include organic bases such as TEA, DIPEA, N,N-dimethylaniline, and DBU.

[0241]
The amount of such base to be used is preferably within the range of 1 to 10 molar equivalents to Compound [46].

[0242]

In this step, an additive, such as 1-hydroxybenzotriazole (hereinafter referred to as "HOBt"), N-hydroxysuccinimide, 1-hydroxy-7-azabenzotriazole (hereinafter referred to as "HOAt"), may be added, as necessary.

[0243]
When the additive is used in this step, the amount of such additive is preferably within the range of 0.1 to 3 molar equivalents to Compound [46].

[0244]
The solvent to be used is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; amides such as DMF and DMA; halogenated hydrocarbons such as dichloromethane and chloroform; nitriles such as acetonitrile and propionitrile; and a mixed solvent thereof.

[0245]
The reaction temperature can vary depending on the starting material and reagents to be used, and is usually preferably within the range of -20°C to 150°C. Also, a microwave reaction apparatus may be used as necessary.

[0246]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 0.1 to 72 hours.

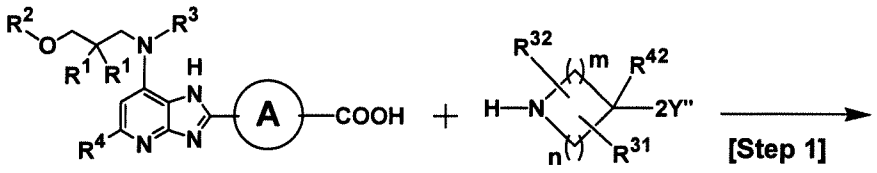
[0247]
Step 4
This step affords Compound [IIa] by hydrolyzing Compound [47a]. This step can be carried out in the similar manner as described in Step 2 of Process 1.

[0248]
When 2Y'a is Y'-4 or Y'-14 (nitrile form) in Compound [47a], Compound [IIa] wherein 2Ya is Y-4 or Y-14 (tetrazole form), respectively, can be obtained in the similar manner as described in Step 2' of Process

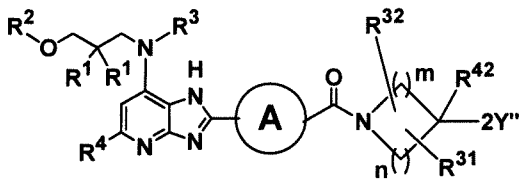
1.

[0249]

Also, Compound [24d] can be reacted with Compound [46] as follows, in the similar manner as described in Step 3 of Process 3, to afford Compound [IIb], which is a compound corresponding to Compound [Ib].



[46] [24 d]

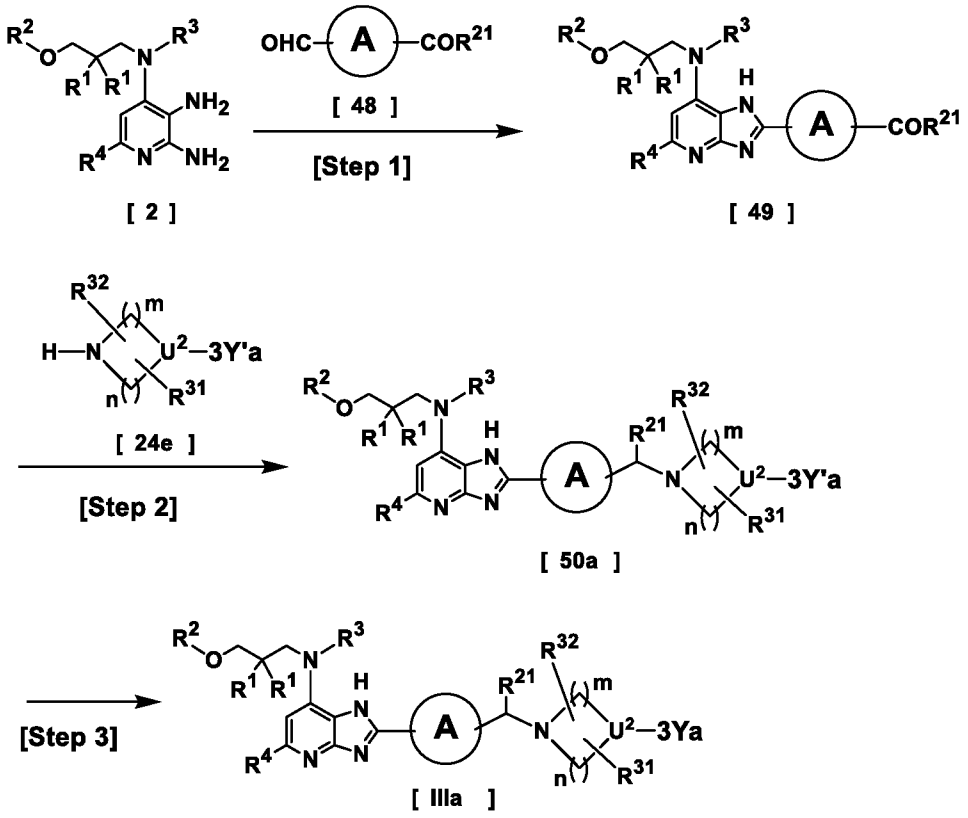


[IIb]

wherein R^1, R^2, R^3, R^4, R, R^{31}, R^{32}, R^{42}, A, m, and n are as defined above. 2Y" is Y-13 or Y-16.

[0250]

Process 4: Production of Compound [IIIa] (wherein W is W-1 and R^{21} is Alkyl)



wherein R^1, R^2, R^3, R^4, R^{31}, R^{32}, R^{21}, A, U^2, m, and n are as defined above. 3Ya is Y-1, Y-2, Y-3, Y-4, Y-11, Y-12, Y-14, or Y-15, and 3Y'a is Y'-1, Y'-2, Y'-3, Y'-4, Y'-11, Y'-12, Y'-14, or Y'-15.

[0251]
This process is directed to a production of a compound of formula [IIIa], which is a compound of formula [1] wherein R^{21} is alkyl.

[0252]
Step 1
This step affords Compound [49] by cyclocondensation of Compound [2] with Compound [48], which is commercially available or can be prepared according to a known method. This step can be carried out in the similar manner as described in Step 1 of Process 1.

[0253]
Step 2
This step affords Compound [50a] by reductive amination reaction of Compound [49] with Compound [24e] and can be carried out according to a method known as reductive amination reaction. In this step, imine formation (first step) and reduction of the imine moiety

(second step) can be carried out sequentially. Also, the first step and the second step may be carried out in one pot.

[0254]
The first step affords an imine form by reacting Compound [49] with Compound [24e].

[0255]
The amount of Compound [24e] to be used in the first step is preferably within the range of 1 to 2.5 molar equivalents to Compound [49].

[0256]
In the first step, an acid or an appropriate Lewis acid may be used as necessary. Examples of the acid that can be used in the reaction include acetic acid, and examples of the Lewis acid that can be used include tetraisopropyl orthotitanate.

[0257]
The amount of the acid, when using in the first step, is preferably within the range of 2 to 3 molar equivalents to Compound [49].

[0258]
The amount of the Lewis acid, when using in the first step, is preferably within the range of 1.5 to 2 molar equivalents to Compound [49].

[0259]
The solvent to be used in the first step is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; halogenated hydrocarbons such as dichloromethane; and a mixed solvent thereof.

[0260]
The reaction temperature in the first step can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 100°C.

[0261]
The reaction time in the first step can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 0.1 to 48 hours.

[0262]
The second step is a reaction with a reducing agent to obtain Compound [50a].

[0263]
Examples of the reducing agent used in the second step include sodium triacetoxyborohydride, sodium cyanoborohydride, and the like.

[0264]
The amount of the reducing agent to be used in the second step is preferably within the range of 1 to 2 molar equivalents to Compound [49].

[0265]
The solvent to be used in the second step is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF and DME; halogenated hydrocarbons such as dichloromethane; and a mixed solvent thereof.

[0266]
The reaction temperature in the second step can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 100°C.

[0267]
The reaction time in the second step can vary depending on the starting material used and the reaction temperature, and is usually preferably within the range of 1 to 24 hours.

[0268]
Step 3
This step affords Compound [IIIa] by hydrolyzing Compound [50a]. This step can be carried out in the similar manner as described in

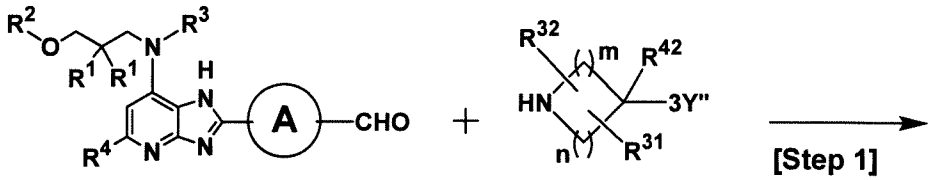
Step 2 of Process 1.

[0269]

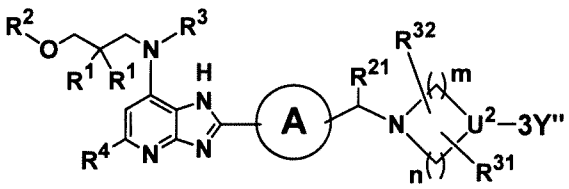
When 3Y'a is Y'-4 or Y'-14 (nitrile form) in Compound [50a], Compound [IIIa] wherein 3Ya is Y-4 or Y-14 (tetrazole form), respectively, can be obtained in the similar manner as described in Step 2' of Process 1.

[0270]

Also, Compound [46] can be reacted with Compound [24f] as follows, in the similar manner as described in Step 2 of Process 4, to afford Compound [IIIb], which is a compound corresponding to Compound [Ib].



[46] [24f]



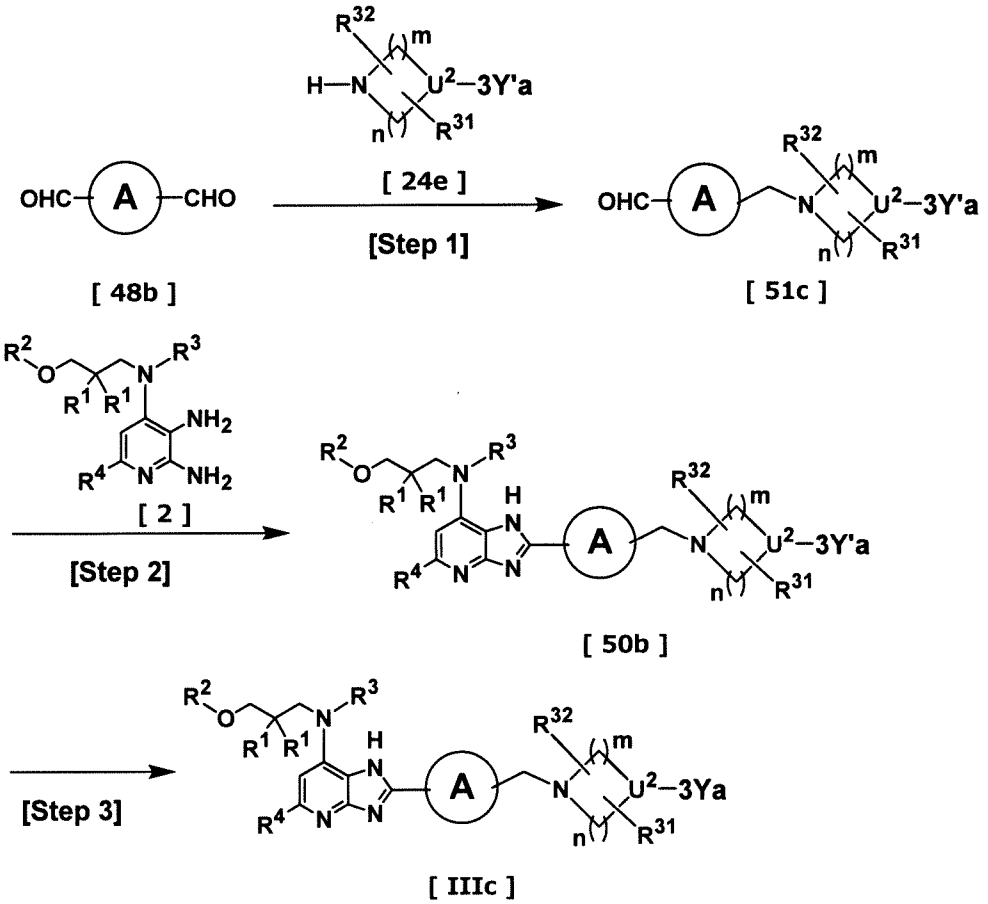
[IIIb]

wherein R^1, R^2, R^3, R^4, R^{31}, R^{32}, R^{42}, A, m, and n are as defined above. 3Y" is Y-13, or Y- 16.

[0271]

Process 5:

Production of Compound [IIIc] (wherein W is W-1 and R^{21} is a hydrogen atom).



wherein R^1, R^2, R^3, R^4, R^{31}, R^{32}, R^{21}, A, U^2, 3Y', 3Y, m, and n are as defined above.

[0272]

This process is directed to the production of a compound of formula [IIIc], which is a compound of formula [1] wherein R^{21} is a hydrogen atom.

[0273]

Step 1

This step affords Compound [51c] by reductive amination reaction of Compound [48b] with Compound [24e]. This step can be carried out in the similar manner as described in Step 2 of process 4.

[0274]

Step 2

This step affords Compound [50b] by reacting Compound [51c] with Compound [2]. This step can be carried out in the similar manner as described in step 1 of process 4.

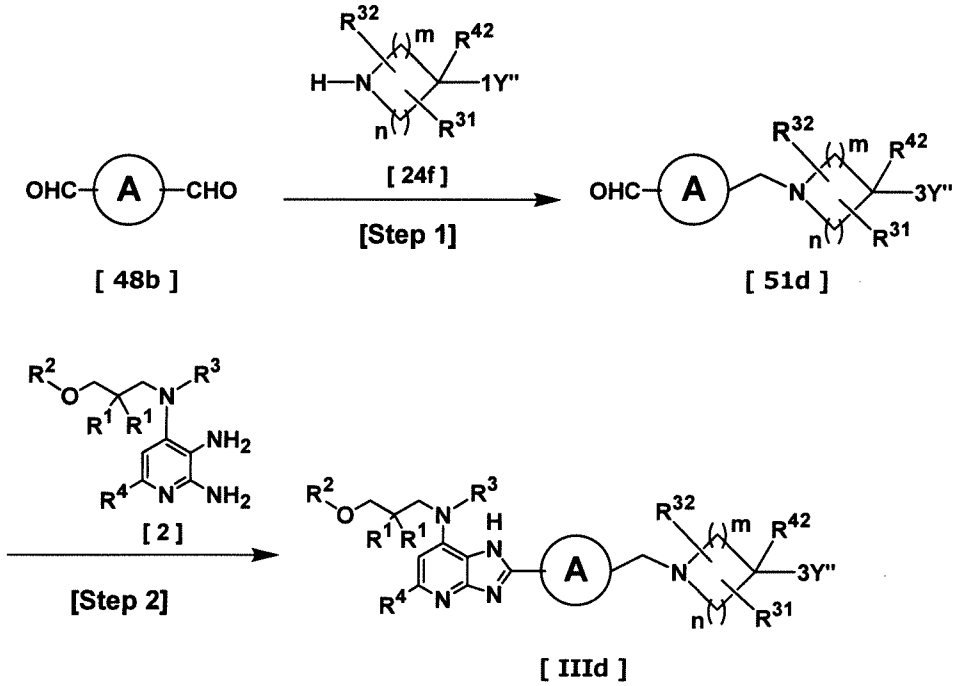
[0275]

Step 3

This step affords Compound [IIIc] by hydrolyzing Compound [50b]. This step can be carried out in the similar manner as described in Step 2 of Process 1.

[0276]

Also, Compound [48b] can be reacted with Compound [24f] as follows, in the similar manner as described in Step 1 of Process 1, to lead to Compound [IIId], which is a compound corresponding to Compound [Ib].

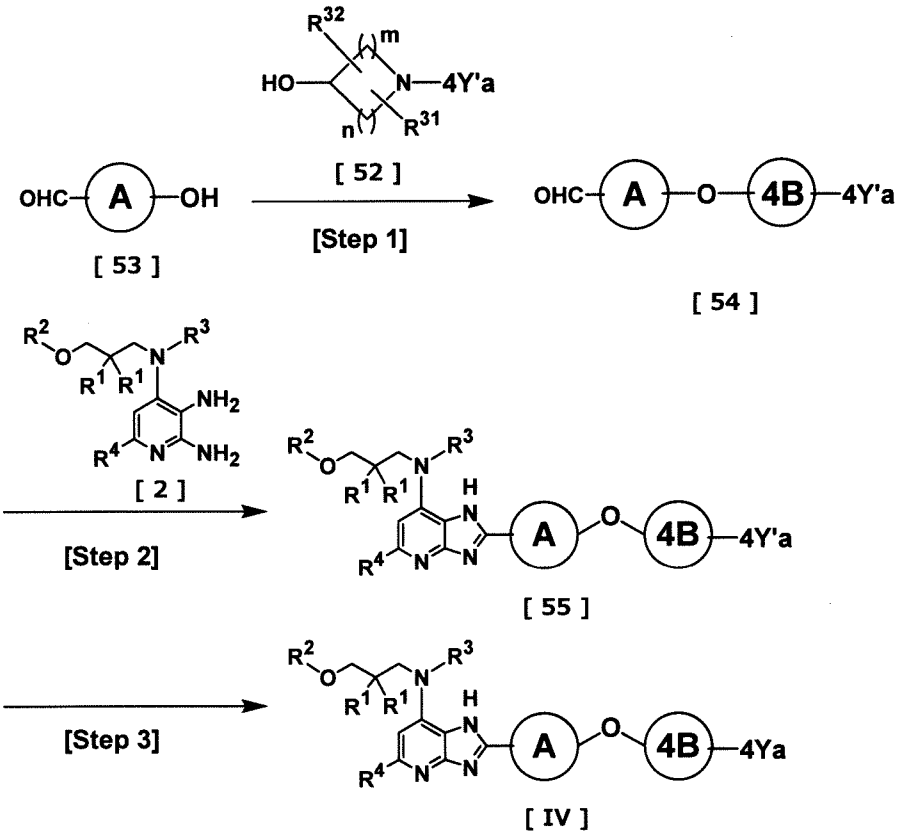


wherein R^1, R^2, R^3, R^4, R^{31}, R^{32}, R^{42}, A, 3Y", m, and n are as defined above.

[0277]

Process 6: Production of Compound [IV] (wherein W is W-3)

[0278]



wherein R^1, R^2, R^3, R^4, R^{31}, R^{32}, A, 4B, m, and n are as defined above. 4Ya is Y-1, Y-2 or Y- 3, and 4Y'a is Y'-1, Y'-2 or Y'-3.

[0279]

Step 1

This step affords ether Compound [54] by Mitsunobu reaction between Compound [52] and Compound [53] and can be carried out according to a known method.

[0280]

This step is usually carried out in an appropriate solvent in the presence of an azodicarboxylic acid ester reagent and a phosphine reagent.

[0281]

The amount of Compound [53] to be used is preferably within the range of 0.5 to 1.5 molar equivalents to Compound [52].

[0282]

Examples of the azodicarboxylate reagent to be used include diethyl azodicarboxylate (hereinafter referred to as "DEAD"), diisopropyl

azodicarboxylate (hereinafter referred to as "DIAD"), and bis(2-methoxyethyl)azodicarboxylate (hereinafter referred to as "DMEAD"). Examples of the phosphine reagent to be used include triphenylphosphine and tributylphosphine.

[0283]
The amount of the azodicarboxylic acid ester reagent to be used is preferably within the range of 1 to 2 molar equivalents to Compound [52].

[0284]
The amount of the phosphine reagent to be used is preferably within the range of 1 to 2 molar equivalents to Compound [52].

[0285]
The solvent to be used is not limited so long as it does not participate in the reaction, and examples of such solvent include hydrocarbons such as toluene and xylene; ethers such as 1,4-dioxane, THF, and DME; or a mixed solvent thereof.

[0286]
The reaction temperature in this step can vary depending on the starting material and reagents to be used, and is usually preferably within the range of 0°C to 100°C.

[0287]
The reaction time can vary depending on the starting material and the reaction temperature to be used, and is usually preferably within the range of 0.5 to 24 hours.

[0288]
In this step, instead of Compound [52], Compound [52'] wherein 4Y'a of Compound [52] is a protecting group P^1 defined above may be used as a starting material. In that case, this step affords Compound [54'] wherein 4Y'a of Compound [54] is substituted with a protecting group P^1. Compound [54'] can be processed in the similar manner as described in Step 2 and Step 3 for the production of Compound [3a] to obtain Compound [54].

[0289]

Step 2

This step affords Compound [55] by cyclocondensation of Compound [54] and Compound [2]. This step can be carried out in the similar manner as described in Step 1 of Process 1.

[0290]

Step 3

This step affords Compound [IV] by hydrolyzing Compound [55], and the step can be carried out in the similar manner as described in Step 2 of Process 1.

[0291]

Urinary storage and voiding are regulated by the action of the bladder and urethra. In urinary storage, urinary restraint is maintained by relaxation of bladder smooth muscle (detrusor) and contraction of urethral sphincter. On the other hand, voiding is caused by contraction of bladder smooth muscle and relaxation of urethral smooth muscle. During voiding, acetylcholine is released from the nerve endings of the pelvic nerve, which is the parasympathetic nerve that governs the bladder. The released acetylcholine binds to M3 receptor of the bladder smooth muscle, whereby the bladder smooth muscle contracts.

[0292]

For example, if urine storage disorder occurs due to overactive bladder or the like, urine cannot be retained for urine storage. Further, if voiding dysfunction occurs due to, for example, underactive bladder, urine cannot be excreted sufficiently during micturition. Furthermore, residual urine after micturition may be found in voiding dysfunction. Increasing residual urine may lead to symptoms such as frequent urination. Thus, urinary storage and voiding dysfunction may develop together (see Current Urology Report, 2016, 17:17).

[0293]

The compound of the invention can be used for the prevention or treatment of diseases involving M3 receptor, in particular, bladder/urethral diseases involving bladder contraction, digestive

system diseases involving gastrointestinal contraction, oral diseases involving salivation, ocular diseases involving tear secretion and pupil contraction. The compound of the invention is particularly useful for the prevention or treatment of voiding and/or storage disorders in bladder/urethral diseases, glaucoma in ocular diseases, and diabetes. As used herein, diabetes refers to diabetes in which the insulin secretion ability involving M3 receptor is reduced (see Cell Metabolism, 2006, Vol.3, p.449-461).

[0294]
Examples of voiding and/or storage disorders for which the prevention or treatment with the compounds of the invention are particularly useful include voiding and/or storage disorders in underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethral relaxation failure, detrusor-external urethral sphincter dyssynergia, overactive bladder, frequent urination, nocturia, urinary incontinence, benign prostatic hyperplasia, interstitial cystitis, chronic prostatitis and urolithiasis.

[0295]
The compound of the invention is particularly useful for the prevention or treatment of voiding and/or storage disorders in underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, benign prostatic hypertrophy and neurogenic bladder. For example, in underactive bladder, voiding dysfunction occurs due to decreased contractile force of the bladder detrusor during micturition, and the compound of the invention can improve the contractile force of the bladder detrusor during micturition to promote bladder emptying.

[0296]
The compound of the present invention is particularly useful for the prevention or treatment of underactive bladder, hypotonic bladder, acontractile bladder and detrusor underactivity due to a specific cause. Specific causes include neurological diseases (multiple system atrophy, Parkinson's disease, multiple sclerosis, spinal cord injury, lumbar disc herniation, etc.), diabetes, pelvic surgery, prostate hypertrophy and aging.

[0297]
Acetylcholine contracts the ciliary muscle via M3 receptor of the ciliary muscle of the eye. By the contraction of the ciliary muscle, Schlemm's canal opens, and aqueous humor outflows through the Schlemm's canal, thereby, intraocular pressure falls. Examples of glaucoma for which prevention or treatment with the compound of the present invention is particularly useful include primary open-angle glaucoma, normal-tension glaucoma, and primary closed-angle glaucoma.

[0298]
When the compound of the present invention is administered as a pharmaceutical, the compound of the present invention is administered to a mammal including human as it is or as a pharmaceutical composition containing the compound in an amount, such as 0.001% to 99.5%, preferably 0.1% to 90%, in a pharmaceutically acceptable non-toxic and inert carrier.

[0299]
The carrier may be one or more of solid, semi-solid or liquid diluents, fillers and other excipients. The pharmaceutical composition according to the present invention is preferably administered in a unit dosage form. The pharmaceutical composition can be administered via intra-tissue, oral, intravenous, topical (transdermal, eye drops, intraperitoneal, intrathoracic, etc.) or rectal route. Of course, the composition is administered in a dosage form suitable for the mode of administration.

[0300]
The dose as a pharmaceutical is preferably adjusted taking into consideration the conditions such as age, weight, type and severity of disease of the patient, administration route, type of the compound of the invention, whether or not it is a salt, and the type of the salt. In general, the effective amount of the compound of the invention or a pharmaceutically acceptable salt thereof for adult, in the case of oral administration, is preferably within a range of 0.01 mg to 5g/day, preferably 1 mg to 500 mg/day. In some cases, a smaller amount may be sufficient or a larger amount may be required. Usually, the dosage can be administered once a day or can be divided

and administered several times a day, or in the case of intravenous administration, the dosage can be administered rapidly or sustainably within 24 hours.

[0301]
One or more hydrogen, carbon and/or the other atoms in the compound of the invention may be replaced with an isotope thereof. Examples of such isotopes include ^{2}H, ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{123}I and ^{36}Cl, i.e., hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, iodine and chlorine. The compound substituted with such isotope may be useful as a pharmaceutical and includes all radiolabeled compounds of the compound of the invention.

[0302]
The present invention is described in more detail with reference to, but is not limited to, the following Comparative Examples, Examples and Test Examples.

[0303]
The following abbreviations are used in the following Examples, Reference Examples and Tables.

REx: Reference Example
PREx: Referenced Reference Example
Ex: Example No.
PEx: Referenced Example
TFA: Trifluoroacetic acid
Pt-C: Platinum-carbon
Pd-C: Palladium-carbon
$Pd_2(dba)_3 \cdot CHCl_3$: Tris(dibenzylideneacetone)bispalladium•chloroform adduct
$Pd_2(dba)_3$: Tris(dibenzylideneacetone)bispalladium
$Pd(dppf)Cl_2 \cdot CH_2Cl_2$: [1,1-Bis(diphenylphosphino)ferrocene]-dichloropalladium(II)•dichloromethane adduct
$Pd(OAc)_2$: Palladium acetate(II)
dppf: 1,1'-Bis(diphenylphosphino)ferrocene
XPhos: 2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl
RuPhos: 2-Dicyclohexylphosphino-2',6'-diisopropylbiphenyl
PPh_3: Triphenylphosphine

Boc: Tert-butoxycarbonyl

Bn: Benzyl

Ts: 4-Toluenesulfonyl

SEM: 2-(Trimethylsilyl)ethoxymethyl

DAST: (Diethylamino)sulfur-trifluoride

HATU: O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate

DEAD: Diethyl azodicarboxylate

DMF: Dimethylformamide

DMSO: Dimethylsulfoxide

DIPEA: N,N-diisopropylethylamine

TEA: Triethylamine

DBU: 1,8-Diazabicyclo[5.4.0]-7-undecene

$CDCl_3$: Deuterochloroform

DMSO-d6: Deuterodimethylsulfoxide

TLC: Thin layer chromatography

MS: Mass spectrometry

LCMS: High performance liquid chromatography-Mass spectrometry

ESI: Electron Spray Ionization

M: Molar concentration (mol/L)

[0304]

MS was performed using LCMS. ESI was used as a method for ionization. Observed values of the mass spectrometry are expressed as m/z.

[0305]

The conditions for LCMS were as follows:

Instrument: ACQUITY UPLC MS/PDA system (Waters)

Mass spectrometry: Waters 3100 MS detector

Photodiode array detector: ACQUITY PDA detector (UV-detected wave length: 210-400nm)

Column: Acquity BEH C18, 1.7μm, 2.1x50mm

Flow rate: 0.5mL/min

Colum temperature: 40°C

Solvent;

A: 0.1% formic acid/H_2O(v/v; the same hereinafter)

B: 0.1% formic acid/acetonitrile

[0306]

^{1}H NMR spectrum was obtained using JNM-ECS400 Nuclear Magnetic Resonance Spectrometer (JEOL RESONANCE Ltd.). The observed peaks were shown as chemical shift values δ (ppm) (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet, dd = double doublet, dt = double triplet).

[0307]
In the experiment using microwave, Initiator 60 (Biotage) was used, which can achieve a temperature of 40-250°C and a pressure up to 20 bar.

[0308]
The compounds described herein were named using naming software, ACD/NAME® (Advanced Chemistry Development Inc.) according to IUPAC nomenclature rules, or ChemBioDraw (version 14.0, Cambridge Soft), or named according to IUPAC nomenclature.

[0309]
In a name of a compound, the descriptors "r" and "s" (lower case) refer to the stereochemistry of pseudoasymmetric carbon atom according IUPAC rules.

[0310]
Reference Example 1: N-{[1-(methoxymethyl)cyclopentyl]methyl}ethanamine hydrochloride

[Step 1] Preparation of tert-butyl {[1-(methoxymethyl)cyclopentyl]methyl}carbamate

1-(Methoxymethyl)cyclopentane-1-carbonitrile (33 g) was dissolved in ethanol (250 mL). After degassing, to the stirred solution was added hydrogen chloride (4M in ethyl acetate, 65 mL) and platinum(IV) oxide (0.27 g) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 2 days under hydrogen atmosphere (0.45MPa). After filtering insolubles off, the solvent was removed under reduced pressure. The residue was dissolved in methanol. To the stirred solution were added nickel(II) chloride hexahydrate (5.65 g) and di-tert-butyl dicarbonate (68 g) at room temperature. Sodium borohydride (63 g) was added portion wise over 30 minutes to the stirred solution under ice-cooling, and then the reaction mixture was stirred at room

temperature for 4 hours. Water was added to the reaction mixture, and insolubles were filtered off. The filtrate was concentrated under reduced pressure. The residue was diluted with water and saturated aq. sodium bicarbonate, and then extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (40 g).

[Step 2] Preparation of tert-butyl ethyl{[1-(methoxymethyl)cyclopentyl]methyl}carbamate

Tert-butyl {[1-(methoxymethyl)cyclopentyl]methyl}carbamate (2.0 g) obtained in Step 1 was dissolved in DMF (20 mL). To the stirred solution was added 60% sodium hydride (0.99 g), and the reaction mixture was stirred at the same temperature for 10 minutes. Ethyl iodide (2.0 mL) was added thereto, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with water, and extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (2.1 g).

[Step 3] Preparation of N-{[1-(methoxymethyl)cyclopentyl]methyl}ethanamine hydrochloride

A solution of tert-butyl ethyl{[1-(methoxymethyl)cyclopentyl]methyl}carbamate (2.09 g) obtained in Step 2 in ethyl acetate (8 mL) was stirred at room temperature, and hydrogen chloride (4M in ethyl acetate, 5.8 mL) was added to the solution, and the reaction mixture was stirred at the same temperature for 4 hours. The reaction mixture was concentrated under reduced pressure. The residue was suspended in hexane (30 mL), and resulting precipitate was collected by filtration. The collected solid was washed with hexane and dried to afford the title compound (1.45 g).

Reference Example 2: 1-{1-[(2-Methoxyethoxy)methyl]cyclopentyl}-N-methylmethanamine hydrochloride

[Step 1] Preparation of 1-[(2-methoxyethoxy)methyl]cyclopentane-1-

carbonitrile

To a stirred solution of 1-(hydroxymethyl)cyclopentane-1-carbonitrile (1.0 g) in DMF (40 mL) was added 60% sodium hydride (697 mg) at room temperature, and the reaction mixture was stirred at the same temperature for 30 minutes. 1-Bromo-2-methoxyethane (2.2 g) was added, and the reaction mixture was stirred at room temperature. After monitoring the consumption of the starting material on TLC, saturated aq. ammonium chloride and ethyl acetate were added to the reaction mixture, and then the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated saline, and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.3 g).

[Step 2] Preparation of 1-{1-[(2-methoxyethoxy)methyl]cyclopentyl}methanamine hydrochloride

A solution of 1-[(2-methoxyethoxy)methyl]cyclopentane-1-carbonitrile obtained in Step 1 (1.3 g) in ethanol (24 mL) was degassed. To the stirred solution were added hydrogen chloride (4M in ethyl acetate, 3.5 mL) and platinum(IV) oxide (32 mg) at room temperature under argon atmosphere, and the reaction mixture was stirred at room temperature for 2 days under hydrogen atmosphere (0.45MPa). After filtering insolubles off, the solvent was removed under reduced pressure. The residue was dried to afford the title compound (1.4 g).

[Step 3] Preparation of tert-butyl ({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)methylcarbamate

To a stirred solution of 1-{1-[(2-methoxyethoxy)methyl]cyclopentyl}methanamine hydrochloride obtained in Step 2 (1.4 g) in dichloromethane (13 mL) were added triethylamine (1.9 mL) and di-tert-butyl dicarbonate (1.6 g) at room temperature, and the reaction mixture was stirred at the same temperature for 2 hours. The reaction mixture was concentrated under reduced pressure. The residue was diluted with water and ethyl acetate, and then extracted with ethyl acetate. The organic layer was washed with water and saturated saline, and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The

residue was dissolved in DMF (13 mL). To the stirred solution was added 60% sodium hydride (0.41 g) at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was cooled on ice, and methyl iodide (0.58 mL) was added dropwise. After the addition, the reaction mixture was warmed to room temperature and stirred overnight. Saturated aq. ammonium chloride was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.87 g).

[Step 4] Preparation of 1-{1-[(2-methoxyethoxy)methyl]cyclopentyl}-N-methylmethanamine hydrochloride

A solution of tert-butyl ({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)methylcarbamate obtained in Step 3 (1.87 g) in ethyl acetate (6.2 mL) was stirred at room temperature. Hydrogen chloride (4M solution in ethyl acetate, 7.8 mL) was added to the solution, and the reaction mixture was stirred at the same temperature for 2 hours. The reaction mixture was concentrated under reduced pressure to afford the title compound (1.45 g).

Reference Example 3: 1-[1-(Butoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride

[Step 1] Preparation of 1-(butoxymethyl)cyclopentane-1-carbonitrile

The title compound was obtained as described in Reference Example 2, Step 1, using 1-iodobutane instead of 1-bromo-2-methoxyethane.

[Step 2] Preparation of tert-butyl {[1-(butoxymethyl)cyclopentyl]methyl}carbamate

To a stirred solution of 1-(butoxymethyl)cyclopentane-1-carbonitrile obtained in Step 1 (0.19 g) in methanol (2.6 mL) were added di-tert-butyl dicarbonate (0.46 g) and nickel(II) chloride hexahydrate (0.25 g) at room temperature. Sodium borohydride (0.28 g) was added portion wise thereto under ice-cooling, and the reaction mixture was stirred at room temperature for 10 hours. The reaction mixture was diluted with saturated aq. sodium bicarbonate and ethyl

acetate, and then the mixture was extracted with ethyl acetate. The organic layer was washed with saturated aq. sodium bicarbonate and saturated saline, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.24 g).

[Step 3] Preparation of tert-butyl {[1-(butoxymethyl)cyclopentyl]methyl}methylcarbamate

Tert-butyl {[1-(butoxymethyl)cyclopentyl]methyl}carbamate obtained in Step 2 (0.24 g) was dissolved in DMF (1.7 mL). 60% sodium hydride (48 mg) was added to the stirred solution under ice-cooling, and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was cooled on ice bath, and methyl iodide (0.078 mL) was added dropwise. After the addition, the reaction mixture was warmed to room temperature and stirred overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate-hexane (1:1). The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (59 mg).

[Step 4] Preparation of 1-[1-(Butoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride

The title compound (47 mg) was obtained as described in Reference Example 1, Step 3, using tert-butyl {[1-(butoxymethyl)cyclopentyl]methyl}methylcarbamate obtained in Step 3 instead of tert-butyl ethyl{[1-(methoxymethyl)cyclopentyl]methyl}carbamate.

Reference Example 4: 1-[1-(Ethoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride

[Step 1] Preparation of 1-(ethoxymethyl)cyclopentane-1-carbonitrile

The title compound was obtained as described in Reference Example 2, Step 1, using ethyl iodide instead of 1-bromo-2-methoxyethane.

[Step 2] Preparation of tert-butyl {[1-

(ethoxymethyl)cyclopentyl]methyl}methylcarbamate

Lithium aluminum hydride (11.4 g) was suspended in THF (800 mL), and a solution of 1-(ethoxymethyl)cyclopentane-1-carbonitrile (46.0 g) obtained in Step 1 in THF (200 mL) was added dropwise to the suspension under ice-cooling. After the addition, the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was cooled on ice bath, and water (11.4 mL), 15% aq. sodium hydroxide (11.4 mL) and water (34.2 mL) were added dropwise sequentially. After the addition, the reaction mixture was stirred at room temperature for 2 hours. Insolubles were filtered off through celite and washed with THF (220 mL) three times. The filtrate was stirred at room temperature, and triethylamine (46.0 mL) and di-tert-butyl dicarbonate (72.1 g) were added. The reaction mixture was stirred at the same temperature for 2 hours, and then concentrated under reduced pressure. The residue was diluted with water and extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was dissolved in DMF (600 mL). To the stirred solution was added 60% sodium hydride (14.4 g) under ice-cooling, and the reaction mixture was stirred for 1 hour at room temperature. The reaction mixture was cooled on ice bath, and methyl iodide (22.5 mL) was added dropwise. After the addition, the reaction mixture was stirred at room temperature for 15 hours. The reaction mixture was cooled on ice bath, diluted with water, and then extracted with ethyl acetate-hexane (1:2). The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (71.2 g).

[Step 3] Preparation of 1-[1-(ethoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride

The title compound (50.3 g) was obtained as described in Reference Example 1, Step 3, using tert-butyl {[1-(ethoxymethyl)cyclopentyl]methyl}methylcarbamate obtained in Step 2 instead of tert-butyl ethyl{[1-(methoxymethyl)cyclopentyl]methyl}carbamate.

[0311]

Reference Example 5: 1-[1-(methoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride

[Step 1] Preparation of tert-butyl {[1-(hydroxymethyl)cyclopentyl]methyl}carbamate

To a stirred solution of [1-(aminomethyl)cyclopentyl]methanol (50.7 g) in THF (304 mL) was added triethylamine (60.2 mL) under ice-cooling. Di-tert-butyl dicarbonate (94.2 g) in THF (101 mL) was added dropwise to this solution. After the addition, the reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with water and ethyl acetate, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was extracted with ethyl acetate-hexane (1:9)(700 mL), and the extract was stirred at room temperature for 3 hours. Insolubles were collected by filtration, washed with hexane, and dried to afford the title compound (49.2 g). For the filtrate, the solvent was removed under the reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (15.9 g).

[Step 2] Preparation of tert-butyl {[1-(methoxymethyl)cyclopentyl]methyl}methylcarbamate

To a stirred solution of tert-butyl {[1-(hydroxymethyl)cyclopentyl]methyl}carbamate (58 g) obtained in Step 1 in DMF (505 mL) was added methyl iodide (47 mL) at room temperature. 60% sodium hydride (30 g) was then added portion wise under ice-cooling. After the reaction mixture was stirred for 30 minutes under ice-cooling, the mixture was warmed to room temperature and stirred overnight. Water (800 mL) was added dropwise to the reaction mixture under ice-cooling, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (68 g).

[Step 3] Preparation of 1-[1-(methoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride

The title compound (52 g) was obtained as described in Reference Example 1, Step 3, using tert-butyl {[1-

(methoxymethyl)cyclopentyl]methyl}methylcarbamate obtained in Step 2 instead of tert-butyl ethyl{[1-(methoxymethyl)cyclopentyl]methyl}carbamate.

Reference Example 6: 4-Chloro-6-[3-fluoro-5-(trifluoromethyl)phenyl]pyridin-2-amine

To a mixture of [3-fluoro-5-(trifluoromethyl)phenyl]boronic acid (0.6 g), 4,6-dichloropyridin-2-amine (0.45 g), and potassium carbonate (1.2 g) were added 1,4-dioxane (9.6 mL) and water (2.4 mL). After degassing, to the stirred solution was added $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (118 mg) at room temperature under argon atmosphere, and the reaction mixture was stirred at 80°C for 3 hours. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and extracted with ethyl acetate. The organic layer was washed with water and saturated saline, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.5 g).

Reference Example 7: 4-Chloro-6-[3-fluoro-5-(trifluoromethyl)phenyl]-3-nitropyridin-2-amine

Under ice-cooling, concentrated sulfuric acid (2.5 mL) was added to 4-chloro-6-[3-fluoro-5-(trifluoromethyl)phenyl]pyridin-2-amine (0.5 g), and then potassium nitrate (165 mg) was added portion wise. The reaction mixture was stirred for 15 minutes under ice-cooling and further stirred at room temperature for 4 hours. The reaction mixture was poured into ice-water. After the addition of 4M aq. sodium hydroxide (25 mL), the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.35 g).

Reference Example 8: 6-Chloro-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-3-nitropyridin-2,4-diamine

A mixture of 4,6-dichloro-3-nitropyridin-2-amine(6.3 g), 3-methoxy-N,2,2-trimethylpropan-1-amine hydrochloride(6.6 g), DIPEA(16 mL), and 2-propanol (100 mL) was stirred at 60°C for 1 hour. The reaction mixture was cooled to room temperature. Water (50 mL) was

added to the mixture, and resulting precipitate was collected by filtration. The collected precipitate was washed with 2-propanol and water sequentially and dried to afford the title compound (8.0 g).

Reference Example 9: 6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridine]-4,6-diamine

A mixture of 6-chloro-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-3-nitropyridine-2,4-diamine (2.5 g), 2-cyclopropyl-5-(4,4,5,5-tetramethyl-1,3,2,-dioxaborolan-2-yl)-3-(trifluoromethyl)pyridine (2.7 g), potassium carbonate (3.0 g), 1,4-dioxane (29 mL) and water (11 mL) was degassed, and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (0.24 g) was added to the mixture with stirring at room temperature under argon atmosphere. The reaction mixture was stirred at 95°C for 2 hours. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated saline, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (3.5 g).

[0312]

Reference Example 10: 2'-Ethoxy-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine

A mixture of 6-chloro-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridine-2,4-diamine(0.70 g), 2-ethoxy-4-(4,4,5,5-tetramethyl-1,3,2,-dioxaborolan-2-yl)-6-(trifluoromethyl)pyridine (0.78 g), potassium carbonate (0.85 g), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$(67 mg), 1,4-dioxane (8.2 mL) and water (3.1 mL) was degassed and stirred at 90°C for 2 hours. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated saline, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford 2'-ethoxy-N^4-{[1-

(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridine]-4,6-diamine. This compound was mixed with 2-propanol (6.8 mL), water (3.4 mL), ammonium chloride (0.33 g) and zinc powder (0.67 mg), and the mixture was stirred at room temperature for 1 hour. Insolubles were filtered off using celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.83 g).

Reference Example 11: 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)-N^4-methylpyridine-2,3,4-triamine

To a stirred mixture of 4-chloro-6-[3-fluoro-5-(trifluoromethyl)phenyl]-3-nitropyridin-2-amine (100 mg), 1-{1-[(2-methoxyethoxy)methyl]cyclopentyl}-N-methylmethanamine hydrochloride (78 mg) and 2-propanol (1 mL) was added DIPEA (0.16 mL) at room temperature, and the mixture was stirred at 90°C for 2 hours. Reduced iron (powder, 50 mg), ammonium chloride (48 mg) and water (0.5 mL) were added to the mixture, and the reaction mixture was stirred at the same temperature for 16 hours. The reaction mixture was cooled to room temperature and diluted with ethyl acetate. Insolubles were filtered off using celite, and the filtrate was extracted with ethyl acetate. The organic layer was washed with water and saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (126 mg).

Reference Example 12: 2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine

To a mixture of 2'-ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridine]-4,6-diamine (684 mg), 2-propanol (7.5 mL) and water (2.5 mL) were added ammonium chloride (234 mg) and reduced iron (powder, 244 mg), and the reaction mixture was stirred at 90°C overnight. The reaction mixture was cooled to room temperature and diluted with ethyl acetate and water. Insolubles were filtered off using celite, and the filtrate was extracted with

ethyl acetate. The organic layer was washed with saturated saline, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (570 mg).

Reference Example 13: 6'-Cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine

To a stirred mixture of 6'-cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridine]-4,6-diamine (5.8 g), ammonium chloride (1.9 g), 2-propanol (39 mL) and water (20 mL) was added zinc powder (3.9 g) at room temperature, and the reaction mixture was stirred at 50°C for 4 hours. The reaction mixture was cooled to room temperature and then diluted with ethyl acetate. Insolubles were filtered off using celite. After concentrating the filtrate under reduced pressure, the residue was purified by silica gel column chromatography to afford the title compound (5.3 g).

Reference Example 14: Ethyl [4-(4-formylphenyl)piperazin-1-yl] acetate

To a stirred solution of ethyl (4-phenylpiperazin-1-yl) acetate (1.1 g) in DMF (10 mL) was added phosphorus oxychloride (1.3 mL) at room temperature, and the reaction mixture was stirred in oil bath at 100°C for 1 hour. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate. Saturated aq. sodium bicarbonate was added thereto, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.1 g).

[0313]

Reference Example 15: Ethyl 3-[(3R)-4-(4-formylphenyl)-3-methylpiperazin-1-yl] propanoate

[Step 1] Preparation of ethyl 3-[(3R)-3-methyl-4-phenylpiperazin-1-yl] propanoate

To a stirred mixture of (2R)-2-methyl-1-phenylpiperazine

dihydrochloride (1.5 g), sodium bicarbonate (1.8 g) and ethanol (30 mL) was added ethyl 3-bromopropanoate (0.92 mL) at room temperature, and the reaction mixture was stirred at 80°C for 4 hours. The reaction mixture was cooled to room temperature and diluted with ethyl acetate. Insolubles were filtered off using celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.52 g).

[Step 2] Preparation of ethyl 3-[(3R)-4-(4-formylphenyl)-3-methylpiperazin-1-yl] propanoate

The title compound (1.35 g) was obtained as described in Reference Example 14, using ethyl 3-[(3R)-3-methyl-4-phenylpiperazin-1-yl]propanoate obtained in Step 1 instead of ethyl (4-phenylpiperazin-1-yl) acetate.

Reference Example 16: Ethyl {4-[(4-formylphenyl)methyl]piperazin-1-yl} acetate

To a stirred mixture of terephthalaldehyde (467 mg), ethyl (piperazin-1-yl) acetate (300 mg) and dichloromethane (10 mL) was added sodium triacetoxyborohydride (517 mg) under ice-cooling, and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with water and ethyl acetate. Saturated aq. sodium bicarbonate was then added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (236 mg).

Reference Example 17: Methyl {1-[(4-formylphenyl)methyl]piperidin-4-yl} acetate

A mixture of terephthalaldehyde(416 mg), methyl (piperidin-4-yl) acetate hydrochloride (300 mg), dichloromethane (10 mL) and DIPEA (0.268 mL) was stirred at room temperature for 1 hour. To the stirred solution was added sodium triacetoxyborohydride (460 mg) under ice-cooing, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with water and ethyl acetate. Saturated aq. sodium bicarbonate was then added, and the mixture was extracted with ethyl acetate. The organic layer was

washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (196 mg).

Reference Example 18: Ethyl 3-[4-(5-formylpyridin-2-yl)-4-hydroxypiperidin-1-yl] propanoate

[Step 1] Preparation of tert-butyl 4-[5-(1,3-dioxoran-2-yl)pyridin-2-yl]-4-hydroxypiperidine-1-carboxylate

To a stirred solution of 2-bromo-5-(1,3-dioxoran-2-yl)pyridine (1.0 g) in THF (15 mL) was added dropwise n-butyllithium (1.6M in hexane, 3.0 mL) at -78°C under argon atmosphere, and the reaction mixture was stirred at the same temperature for 30 minutes. A solution of tert-butyl 4-oxopiperidine-1-carboxylate (1.1 g) in THF (5 mL) was added dropwise, and the reaction mixture was stirred with warming to room temperature for 1 hour. The reaction mixture was diluted with water and saturated aq. ammonium chloride, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline and dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.77 g).

[Step 2] Preparation of ethyl 3-[4-(5-formylpyridin-2-yl)-4-hydroxypiperidin-1-yl]propanoate

Tert-butyl 4-[5-(1,3-dioxoran-2-yl)pyridin-2-yl]-4-hydroxypiperidine-1-carboxylate (200 mg) obtained in Step 1 was mixed with THF (2 mL) and 4M hydrochloric acid (2 mL), and the mixture was stirred at room temperature overnight and further stirred at 60°C for 8 hours. After removing the solvent under reduced pressure, the residue was mixed with acetonitrile (4 mL) at room temperature. To the stirred mixture were added DIPEA (0.494 mL) and ethyl 3-bromopropanoate (0.146 mL), and the reaction mixture was stirred at 60°C for 3 hours. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (107 mg).

Reference Example 19: Tert-butyl 4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]-4-hydroxypiperidine-1-carboxylate

To a stirred solution of 5-bromo-2-(1,3-dioxoran-2-yl)pyridine (1.0 g) in THF (15 mL) was added dropwise isopropylmagnesium chloride-lithium chloride complex (1M in THF, 4.8 mL) at -45°C under argon atmosphere. The reaction mixture was warmed to 0°C and stirred for 30 minutes. The reaction mixture was cooled to -45°C, and tert-butyl 4-oxopiperidine-1-carboxylate (1.1 g) in THF (5 mL) was added thereto. The reaction mixture was stirred with warming to room temperature for 2 hours. The reaction mixture was diluted with water and ethyl acetate, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.3 g).

Reference Example 20: Ethyl [4-(6-formylpyridin-3-yl)-4-hydroxypiperidin-1-yl] acetate

Tert-butyl 4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]-4-hydroxypiperidine-1-carboxylate (100 mg) was mixed with THF (1.5 mL) and 4M hydrochloric acid (1.5 mL), and the mixture was stirred at room temperature for 3 hours. After removing the solvent under reduced pressure, the residue was mixed with dichloromethane (2 mL) at room temperature. To the stirred mixture were added DIPEA(0.30 mL) and bromoethyl acetate (0.038 mL), and the reaction mixture was stirred at room temperature for 6 hours. The reaction mixture was purified by silica gel column chromatography to afford the title compound (45 mg).

[0314]

Reference Example 21: Tert-butyl 4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]-4-fluoropiperidin-1-carboxylate

To a stirred solution of tert-butyl 4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]-4-hydroxypiperidin-1-carboxylate (200 mg) in dichloromethane (3 mL) was added DAST (0.0834 mL) dropwise in ice-water bath, and the reaction mixture was stirred at the same temperature for 1 hour. Saturated aq. sodium bicarbonate was added to the reaction mixture, and the mixture was diluted with water and ethyl acetate and then extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure.

The residue was purified by silica gel column chromatography to afford the title compound (120 mg).

Reference Example 22: Ethyl 3-[4-fluoro-4-(6-formylpyridin-3-yl)piperidin-1-yl]propanoate

The title compound (42 mg) was obtained as described in Reference Example 18, Step 2, using tert-butyl 4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]-4-fluoropiperidin-1-carboxylate instead of tert-butyl 4-[5-(1,3-dioxoran-2-yl)pyridin-2-yl]-4-hydroxypiperidin-1-carboxylate.

Reference Example 23: Ethyl 3-[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[Step 1] Preparation of tert-butyl (3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-carboxylate

A mixture of 5-chloropyrazine-2-carbaldehyde (350 mg), tert-butyl (3R)-3-methylpiperazine-1-carboxylate (541 mg), DIPEA (1.28 mL) and THF (4.9 mL) was stirred at 70°C for 3 hours. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and then extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (755 mg).

[Step 2] Preparation of ethyl 3-[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl] propanoate

Tert-butyl (3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazine-1-carboxylate (816 mg) was dissolved in ethyl acetate (5.3 mL). To the stirred solution was added hydrogen chloride (4M in ethyl acetate, 5.3 mL) at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. After removing the solvent under reduced pressure, the residue was mixed with acetonitrile (5 mL). To the stirred mixture were added DIPEA (2.31 mL) and ethyl 3-bromopropanoate (0.442 mL) at room temperature, and the reaction mixture was stirred at 70°C for 4 hours. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (676 mg).

Reference Example 24: Ethyl [4-(4-formylphenyl)-4-hydroxypiperidin-1-yl] acetate

[Step 1] Preparation of tert-butyl 4-[4-(1,3-dioxoran-2-yl)phenyl]-4-hydroxypiperidine-1-carboxylate

To a stirred solution of 2-(4-bromophenyl)-1,3-dioxorane (1.0 g) in THF (15 mL) was added dropwise n-butyllithium (1.6M in hexane, 3.0 mL) at -78°C, and the reaction mixture was stirred at the same temperature for 30 minutes. Tert-butyl 4-oxopiperidine-1-carboxylate (1.1 g) in THF (5 mL) was added dropwise thereto, and the reaction mixture was stirred with warming to room temperature for 1 hour. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.5 g).

[Step 2] Preparation of ethyl [4-(4-formylphenyl)-4-hydroxypiperidin-1-yl] acetate

Tert-butyl 4-[4-(1,3-dioxoran-2-yl)phenyl]-4-hydroxypiperidine-1-carboxylate (100 mg) obtained in Step 1 was mixed with 1,4-dioxane (2 mL) and hydrogen chloride (4M solution in ethyl acetate, 2 mL), and the mixture was stirred at room temperature overnight. After removing the solvent under reduced pressure, the residue was mixed with dichloromethane (2 mL). To the stirred mixture were added DIPEA (0.297 mL) and bromoethyl acetate (0.038 mL) at room temperature, and the mixture was stirred at the same temperature for 6 hours. The reaction mixture was purified by silica gel column chromatography to afford the title compound (72 mg).

Reference Example 25: Ethyl [4-(4-formylphenoxy)piperidin-1-yl]acetate

To a mixture of ethyl (4-hydroxypiperidin-1-yl)acetate (100 mg), 4-hydroxybenzaldehyde (130 mg) and THF (2.67 mL) were added PPh_3 (210 mg) and DEAD (0.36 mL), and the reaction mixture was stirred at 50°C for 4 hours overnight. The reaction mixture was diluted with ethyl acetate, and washed with saturated aq. sodium bicarbonate and saturated saline sequentially, and then the organic layer was dried over anhydrous magnesium sulfate. The solvent was removed under

reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (246 mg).

[0315]

Reference Example 26: Ethyl 3-[4-(4-formylphenoxy)piperidin-1-yl]propanoate

To a stirred mixture of 4-[(piperidin-4-yl)oxy]benzaldehyde hydrochloride (200 mg) and acetonitrile (2.1 mL) were added DIPEA (0.716 mL) and ethyl 3-bromopropanoate (0.137 mL) at room temperature, and the reaction mixture was stirred at 70°C for 3 hours. The reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (158 mg).

Reference Example 27: Ethyl [4-(3-chloro-4-formylphenoxy)piperidin-1-yl]acetate

[Step 1] Preparation of tert-butyl 4-(3-chloro-4-formylphenoxy)piperidine-1-carboxylate

To a stirred mixture of tert-butyl 4-hydroxypiperidine-1-carboxylate (200 mg), 2-chloro-4-hydroxybenzaldehyde (171 mg) and THF (5 mL) was added PPh_3 (391 mg) at room temperature. DEAD (0.68 mL) was added under ice-cooling, and the reaction mixture was stirred with warming to room temperature for 3 hours. The reaction mixture was diluted with ethyl acetate, and washed with saturated aq. sodium bicarbonate and saturated saline sequentially, and then the organic layer was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (105 mg).

[Step 2] 2-chloro-4-[(piperidin-4-yl)oxy]benzaldehyde hydrochloride

To a stirred solution of tert-butyl 4-(3-chloro-4-formylphenoxy)piperidine-1-carboxylate (105 mg) obtained in Step 1 in ethyl acetate (1.5 mL) was added hydrogen chloride (4M in ethyl acetate, 0.231 mL) at room temperature, and the reaction mixture was stirred at the same temperature for 2 hours. Methanol (0.77 mL) was added thereto, and the mixture was stirred at room temperature for 2 hours and further at 40°C for 2 hours. The reaction mixture was

cooled to room temperature. Hydrogen chloride (4M in ethyl acetate, 0.231 mL) was then added, and the reaction mixture was stirred at the same temperature overnight. The reaction mixture was concentrated under reduced pressure and dried to afford the title compound (85 mg).

[Step 3] Preparation of ethyl [4-(3-chloro-4-formylphenoxy)piperidin-1-yl]acetate

To a stirred mixture of 2-chloro-4-[(piperidin-4-yl)oxy]benzaldehyde hydrochloride (85 mg) obtained in Step 2 and acetonitrile (2 mL) were added DIPEA (0.27 mL) and bromoethyl acetate (0.045 mL), and the reaction mixture was stirred at the same temperature for 6 hours. The reaction mixture was purified by silica gel column chromatography to afford the title compound (77 mg).

Reference Example 28: Ethyl 3-[(1R,3s,5S)-3-(4-formylphenoxy)-8-azabicyclo[3.2.1]octan-8-yl]propanoate

[Step 1] Preparation of tert-butyl (1R,3r,5S)-3-hydroxy-8-azabicyclo[3.2.1]octan-8-carboxylate

To a stirred mixture of (1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-ol (1.0 g), dichloromethane (30 mL) and triethylamine (2.2 mL) was added di-tert-butyl dicarbonate (2.1 g) under ice-cooling, and the reaction mixture was stirred at room temperature for 2.5 hours. The reaction mixture was diluted with chloroform. The organic layer was washed with saturated aq. citric acid and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure. Hexane was added to the residue, and the resulting precipitate was collected by filtration, washed with hexane and dried to afford the title compound (1.6 g).

[Step 2] Preparation of tert-butyl (1R,3s,5S)-3-(4-formylphenoxy)-8-azabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as described in Reference Example 27, Step 1, using tert-butyl (1R,3r,5S)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate obtained in Step 1 instead of tert-butyl 4-hydroxypiperidine-1-carboxylate.

[Step 3] Preparation of ethyl 3-[(1R,3s,5S)-3-(4-formylphenoxy)-8-azabicyclo[3.2.1]octan-8-yl]propanoate

To a stirred mixture of tert-butyl (1R,3s,5S)-3-(4-formylphenoxy)-8-azabicyclo[3.2.1]octane-8-carboxylate (0.774 g) obtained in Step 2 and methanol (5 mL) was added hydrogen chloride (4M in ethyl acetate, 2.92 mL) at room temperature, and the reaction mixture was stirred at the same temperature. After monitoring the completion of the reaction by TLC, the reaction mixture was concentrated under reduced pressure. The residue was diluted with acetonitrile (3 mL). To the stirred solution were added DIPEA (1.05 mL) and ethyl 3-bromopropanoate (0.186 mL) at room temperature, and the reaction mixture was stirred at 70°C overnight. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.353 g)

Reference Example 29: Ethyl {[(1R,3r,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

[Step 1] Preparation of tert-butyl (1R,3r,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octane-8-carboxylate

To a solution of tert-butyl (1R,3r,5S)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate (790 mg) in dichloromethane (8.7 mL) were added rhodium(II) acetate dimer (23 mg) and diazoethyl acetate (1.46 mL), and the reaction mixture was stirred at room temperature for 2 hours. Diazoethyl acetate (0.731 mL) was added thereto, and the reaction mixture was stirred at room temperature for 1 hour. Water was added to the reaction mixture, and the mixture was extracted with dichloromethane. The organic layer was washed with water and saturated saline sequentially, dried over anhydrous magnesium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.08 g).

[Step 2] Preparation of ethyl {[(1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate hydrochloride

Tert-butyl (1R,3r,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octane-8-carboxylate (1.08 g) obtained in Step 1 was mixed with ethanol (5 mL). Hydrogen chloride (4M in ethyl acetate, 2.6 mL) was added to the solution, and the reaction mixture was stirred at 80°C for 1 hour. The reaction mixture was cooled to room temperature, and hexane was added thereto. The resulting solid was

collected by filtration, washed with hexane and then dried to afford the title compound (0.567 g).

[Step 3] Preparation of ethyl {[(1R,3r,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

A mixture of ethyl {[(1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate hydrochloride (0.281 g) obtained in Step 2, 5-chloropyrazine-2-carbaldehyde (0.150 g), DIPEA (0.728 mL) and THF (2.1 mL) was stirred at 70°C for 5 hours. The reaction mixture was cooled to room temperature. Saturated aq. ammonium chloride was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated saline, and dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.258 g).

Reference Example 30: Ethyl {[(1R,3s,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

[Step 1] Preparation of tert-butyl (1R,3s,5S)-3-[(4-nitrobenzoyl)oxy]-8-azabicyclo[3.2.1]octane-8-carboxylate

To a solution of tert-butyl (1R,3r,5S)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate (0.790 g) in THF (10 mL) were added 4-nitrobenzoic acid (0.871 g) and PPh_3 (1.37 g), and DEAD (40% in toluene, 2.05 mL) was further added dropwise under ice-cooling. The reaction mixture was stirred at room temperature overnight. Then the reaction mixture was diluted with ethyl acetate, washed with saturated aq. sodium bicarbonate and saturated saline sequentially, and then the organic layer was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (1.05 g).

[Step 2] Preparation of tert-butyl (1R,3s,5S)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate

To a mixture of tert-butyl (1R,3s,5S)-3-[(4-nitrobenzoyl)oxy]-8-azabicyclo[3.2.1]octane-8-carboxylate (1.05 g) obtained in Step 1, THF (6 mL) and water (2 mL) was added lithium hydroxide monohydrate (0.176 g), and the mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with ethyl acetate, washed with

saturated aq. sodium bicarbonate, and then dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to afford the title compound (0.660 g).

[Step 3] Preparation of tert-butyl (1R,3s,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octan-8-carboxylate

The title compound was obtained as described in Reference Example 29, Step 1, using tert-butyl (1R,3s,5S)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate obtained in Step 2 instead of tert-butyl (1R,3r,5S)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate.

[Step 4] Preparation of ethyl {[(1R,3s,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate hydrochloride

The title compound was obtained as described in Reference Example 29, Step 2, using tert-butyl (1R,3s,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octane-8-carboxylate obtained in Step 3 instead of tert-butyl (1R,3r,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octane-8-carboxylate.

[Step 5] Preparation of ethyl {[(1R,3s,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

The title compound was obtained as described in Reference Example 29, Step 3, using ethyl {[(1R,3s,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate hydrochloride obtained in Step 4 instead of ethyl {[(1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy} acetate hydrochloride.

[0316]

Reference Example 31: Ethyl 3-[4-(5-formylpyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate

[Step 1] Preparation of tert-butyl 4-(3-ethoxy-3-oxopropyl)-3,3-dimethylpiperazin-1-carboxylate

A mixture of tert-butyl 3,3-dimethylpiperazin-1-carboxylate (500 mg), ethanol (1.17 mL) and ethyl acrylate (0.684 mL) was stirred at 90°C overnight. The reaction mixture was cooled to room temperature and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (650 mg).

[Step 2] Preparation of ethyl 3-(2,2-dimethylpiperazin-1-yl)propanoate dihydrochloride

The title compound was obtained as described in Reference Example 29, Step 2, using tert-butyl 4-(3-ethoxy-3-oxopropyl)-3,3-dimethylpiperazine-1-carboxylate obtained in Step 1 instead of tert-butyl (1R,3r,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octan-8-carboxylate.

[Step 3] Preparation of ethyl 3-[4-(5-formylpyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate

The title compound (564 mg) was obtained as described in Reference Example 29, Step 3, using ethyl 3-(2,2-dimethylpiperazin-1-yl)propanoate dihydrochloride obtained in Step 2 instead of ethyl {[(1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate hydrochloride.

Reference Example 32: Ethyl 3-[4-(6-formylpyridin-3-yl)piperazin-1-yl]propanoate

[Step 1] Preparation of ethyl 3-{4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]piperazin-1-yl}propanoate

A mixture of 5-bromo-2-(1,3-dioxoran-2-yl)pyridine (1 g), ethyl 3-(piperazin-1-yl)propanoate (1.62 g), $Pd_2(dba)_3$ (0.199 g), XPhos (0.414 g), cesium carbonate (4.25 g) and 1,4-dioxane (20 mL) was degassed and stirred at 100°C overnight under argon atmosphere. The reaction mixture was cooled to room temperature and diluted with ethyl acetate. Insolubles were filtered off using celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.53 g).

[Step 2] Preparation of ethyl 3-[4-(6-formylpyridin-3-yl)piperazin-1-yl]propanoate

A mixture of ethyl 3-{4-[6-(1,3-dioxoran-2-yl)pyridin-3-yl]piperazin-1-yl}propanoate(1.20 g) obtained in Step 1, p-toluenesulfonic acid (1.36 g), acetone(15 mL) and water (5 mL) was stirred at 60°C for 3 hours. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate. Saturated aq. sodium bicarbonate was added, and the mixture was extracted with

ethyl acetate. The organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.734 g).

Reference Example 33: Ethyl 3-[(3R)-4-(5-formylpyridin-2-yl)-3-methylpiperazin-1-yl]propanoate

[Step 1] Preparation of tert-butyl (3R)-4-[5-(1,3-dioxoran-2-yl)pyridin-2-yl]-3-methylpiperazin-1-carboxylate

A mixture of 2-bromo-5-(1,3-dioxoran-2-yl)pyridine (100 mg), tert-butyl (3R)-3-methylpiperazine-1-carboxylate (95.8 mg), RuPhos (40.6 mg), $Pd(OAc)_2$ (9.76 mg), sodium tert-butoxide (62.7 mg) and 1,4-dioxane (2.2 mL) was degassed and stirred at 120°C for 2 hours under argon atmosphere. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, washed with water and saturated saline, and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (72.6 mg).

[Step 2] Preparation of ethyl 3-[(3R)-4-(5-formylpyridin-2-yl)-3-methylpiperazin-1-yl]propanoate

Tert-butyl (3R)-4-[5-(1,3-dioxoran-2-yl)pyridin-2-yl]-3-methylpiperazin-1-carboxylate (72 mg) obtained in Step 1 was mixed with acetone (1 mL) and 4M hydrochloric acid (1 mL), and the mixture was stirred at 60°C for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was diluted with acetonitrile (1 mL). To the stirred solution were added DIPEA (0.18 mL) and ethyl 3-bromopropanoate (0.053 mL) at room temperature, and the reaction mixture was stirred at 60°C for 3 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (42 mg).

Reference Example 34: Ethyl 1-(5-formylpyrazin-2-yl)piperidin-4-carboxylate

A mixture of 5-chloropyrazine-2-carbaldehyde (0.49 g), ethyl piperidine-4-carboxylate (0.54 g), DMSO (10 mL) and sodium

bicarbonate (1.4 g) was stirred at 70°C for 17 hours. The reaction mixture was cooled to room temperature and then ice-cooled. The mixture was diluted with water, 2M hydrochloric acid (6 mL) and ethyl acetate, and then extracted with ethyl acetate. The organic layer was washed with saturated saline and dried over anhydrous magnesium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (0.79 g).

Reference Example 35: Ethyl 2,2-difluoro-3-{[1-(5-formylpyrazin-2-yl)piperidin-4-yl]amino}propanoate

[Step 1] Preparation of tert-butyl 4-[(3-ethoxy-2,2-difluoro-3-oxopropyl)amino]piperidine-1-carboxylate

A mixture of tert-butyl 4-oxopiperidine-1-carboxylate (210 mg), ethyl 3-amino-2,2-difluoropropanoate hydrochloride (100 mg), dichloromethane (3 mL), and acetic acid (0.091 mL) was stirred at room temperature. Sodium triacetoxyborohydride (224 mg) was added thereto, and the mixture was stirred at the same temperature for three days. The reaction mixture was diluted with water, and saturated aq. sodium bicarbonate was added to the mixture. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The organic layers were combined, washed with saturated saline and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (176 mg).

[Step 2] Preparation of ethyl 2,2-difluoro-3-[(piperidin-4-yl)amino]propanoate dihydrochloride

The title compound was obtained as described in Reference Example 29, Step 2, using tert-butyl 4-[(3-ethoxy-2,2-difluoro-3-oxopropyl)amino]piperidin-1-carboxylate obtained in Step 1 instead of tert-butyl (1R,3r,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octan-8-carboxylate.

[Step 3] Preparation of ethyl 2,2-difluoro-3-{[1-(5-formylpyrazin-2-yl)piperidin-4-yl]amino}propanoate

The title compound (91 mg) was obtained as described in Reference Example 29, Step 3, using ethyl 2,2-difluoro-3-[(piperidin-

4-yl)amino]propanoate dihydrochloride obtained in Step 2 instead of ethyl {[(1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy} acetate hydrochloride.

[0317]

Reference Example 36: Ethyl N-[(3S,4R)-3-fluoro-1-(5-formylpyrazin-2-yl)piperidin-4-yl]glycinate

[Step 1] Preparation of tert-butyl(3S,4R)-4-[(2-ethoxy-2-oxoethyl)amino]-3-fluoropiperidine-1-carboxylate

To a solution of tert-butyl(3S,4R)-4-amino-3-fluoropiperidine-1-carboxylate (500 mg) in acetonitrile (2.86 mL) were added ethyl bromoacetate (0.253 mL) and DIPEA(0.792 mL), and the reaction mixture was stirred at room temperature overnight. After concentrating the reaction mixture under reduced pressure, the residue was purified by silica gel column chromatography to afford the title compound (588 mg).

[Step 2] Preparation of ethyl N-[(3S,4R)-3-fluoropiperidin-4-yl]glycinate dihydrochloride

The title compound was obtained as described in Reference Example 29, Step 2, using tert-butyl(3S,4R)-4-[(2-ethoxy-2-oxoethyl)amino]-3-fluoropiperidine-1-carboxylate obtained in Step 1 instead of tert-butyl (1R,3r,5S)-3-(2-ethoxy-2-oxoethoxy)-8-azabicyclo[3.2.1]octan-8-carboxylate.

[Step 3] Preparation of ethyl N-[(3S,4R)-3-fluoro-1-(5-formylpyrazin-2-yl)piperidin-4-yl]glycinate

The title compound (113 mg) was obtained as described in Reference Example 29, Step 3, using ethyl N-[(3S,4R)-3-fluoropiperidin-4-yl]glycinate dihydrochloride obtained in Step 2 instead of ethyl {[(1R,3r,5S)-8-azabicyclo[3.2.1]octan-3-yl]oxy} acetate hydrochloride.

Reference Example 37: Ethyl N-[(3S,4R)-3-fluoro-1-(5-formylpyrazin-2-yl)piperidin-4-yl]-N-methylglycinate

A mixture of ethyl N-[(3S,4R)-3-fluoro-1-(5-formylpyrazin-2-yl)piperidin-4-yl]glycinate (84 mg), DMF (1.4 mL), potassium carbonate (112 mg) and methyl iodide (0.025 mL) was stirred at room temperature overnight. Additional methyl iodide (0.025 mL) was added

thereto, and the reaction mixture was stirred overnight. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (27 mg).

Reference Example 38: Ethyl 3-[4-(3-fluoro-5-formylpyridin-2-yl)piperazine-1-yl]propanoate

[Step 1] Preparation of tert-butyl 4-(3-fluoro-5-formylpyridin-2-yl)piperazine-1-carboxylate

A solution of tert-butyl 4-(5-bromo-3-fluoropyridin-2-yl)piperazine-1-carboxylate (500 mg) in THF (10 mL) was degassed. Under argon atmosphere, to the stirred solution was added isopropylmagnesium chloride-lithium chloride complex (1M in THF, 1.67 mL) at 0°C, and the reaction mixture was stirred at room temperature for 3 hours. Additional isopropylmagnesium chloride-lithium chloride complex (1M in THF, 0.42 mL) was added, and the reaction mixture was stirred at room temperature for 1 hour. To the stirred solution was added DMF (0.216 mL) dropwise under ice-cooling, and the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was diluted with water and ethyl acetate. The mixture was neutralized by adding dilute hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (269 mg).

[Step 2] Preparation of ethyl 3-[4-(3-fluoro-5-formylpyridin-2-yl)piperazin-1-yl]propanoate

A mixture of tert-butyl 4-(3-fluoro-5-formylpyridin-2-yl)piperazine-1-carboxylate (180 mg) obtained in Step 1, ethyl acetate(2 mL) and hydrogen chloride (4M in ethyl acetate, 2 mL) was stirred at room temperature for 2 hours. After concentrating the reaction mixture under reduced pressure, the residue was diluted with acetonitrile (3 mL). To the stirred solution were added DIPEA (0.50 mL) and ethyl 3-bromopropanoate (0.11 mL) at room temperature, and the reaction mixture was stirred at 70°C for 4 hours. The reaction mixture was cooled to room temperature and concentrated under reduced

pressure. The residue was purified by silica gel column chromatography to afford the title compound (131 mg).

Reference Example 39: Ethyl [4-(3-fluoro-5-formylpyridin-2-yl)piperazin-1-yl] acetate
The title compound (65 mg) was obtained as described in Reference Example 38, Step 2, using ethyl bromoacetate instead of ethyl 3-bromopropanoate.

Reference Example 40: Ethyl 3-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]propanoate
A mixture of ethyl 3-(piperazin-1-yl)propanoate (0.142 mL), 5-chloropyrazine-2-carbaldehyde (100 mg), potassium carbonate (485 mg) and DMSO (3.5 mL) was stirred at 90°C for 2 hours. The reaction mixture was cooled to room temperature, diluted with saturated aq. ammonium chloride, and then extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (138 mg).

[0318]
Reference Example 41: Ethyl {[1-(5-formylpyrazin-2-yl)piperidin-4-yl]oxy} acetate

A mixture of 5-chloropyrazine-2-carbaldehyde (0.55 g), ethyl [(piperidin-4-yl)oxy] acetate hydrochloride(0.92 g), THF (7.7 mL) and DIPEA (2.7 mL) was stirred at 70°C for 4 hours. The reaction mixture was cooled to room temperature, diluted with saturated aq. ammonium chloride, and then extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.0 g).

Reference Example 42: [4-(5-Formylpyrazin-2-yl)piperazin-1-yl]acetonitrile

A mixture of 5-chloropyrazine-2-carbaldehyde (0.10 g), (piperazin-1-yl)acetonitrile dihydrochloride (0.14 g), acetonitrile (1.6 mL) and DIPEA (0.39 mL) was stirred at 150°C for 1 hour in a

microwave reactor. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and extracted with ethyl acetate. The organic layer was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (91 mg).

Reference Example 43: Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate

A mixture of 2'-ethoxy-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (50 mg), ethyl 1-(5-formylpyrazin-2-yl)piperidine-4-carboxylate (32 mg), sodium dithionite (51 mg) and DMF (1 mL) was stirred at 100°C for 8 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (75 mg).

Reference Example 44: Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate

A mixture of 2'-ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (50 mg), ethyl 1-(5-formylpyrazin-2-yl)piperidine-4-carboxylate (31 mg), sodium dithionite (48 mg) and DMF (1 mL) was stirred at 100°C for 8 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (75 mg).

Reference Example 45: Ethyl 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate

A mixture of 6'-cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine(50 mg), ethyl 1-

(5-formylpyrazin-2-yl)piperidine-4-carboxylate (30 mg), sodium dithionite (23 mg) and DMF (0.72 mL) was stirred at 100°C for 8 hours. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (76 mg).

[0319]

Reference Example 46: Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy} acetate

A mixture of 2'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (115 mg), ethyl {[1-(5-formylpyrazin-2-yl)piperidin-4-yl]oxy} acetate (79 mg), sodium dithionite (112 mg) and DMF (2.6 mL) was stirred at 100°C for 5 hours. The reaction mixture was cooled to room temperature, diluted with water and saturated aq. ammonium chloride, and then extracted with ethyl acetate-hexane. The organic layer was washed with brine, and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (142 mg).

Reference Example 47: Ethyl 3-[4-(5-{5-[2-fluoro-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

A mixture of 2'-fluoro-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (30 mg), ethyl 3-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]propanoate (21 mg), sodium dithionite (30 mg) and DMF (1 mL) was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and then extracted with ethyl acetate. Saturated aq. sodium bicarbonate was added to the aqueous layer, and the aqueous layer was extracted with ethyl acetate. The organic layers were combined, dried over anhydrous sodium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title

compound (17 mg).

Reference Example 48: Ethyl 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

A mixture of 6'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (1.12 g), ethyl 3-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]propanoate (0.742 g), sodium dithionite (1.05 g) and DMF (24 mL) was stirred at 110°C for 4 hours. The reaction mixture was cooled to room temperature. Sodium dithionite (1.05 g) was added thereto, and the reaction mixture was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature, diluted with water and saturated aq. sodium bicarbonate, and then extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.24 g).

Reference Example 49: Ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

A mixture of 6'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (1.8 g), ethyl 3-[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (1.3 g), sodium dithionite (1.4 g) and DMF (3.9 mL) was stirred at 100°C for 6 hours. The reaction mixture was cooled to room temperature, diluted with water, and then extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.6 g).

Reference Example 50: Ethyl 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-

(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoate

A mixture of 6'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (38 mg), ethyl 3-[(2S)-4-(5-formylpyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoate (29 mg), sodium dithionite (36 mg) and DMA (0.82 mL) was stirred at 110°C for 11 hours. The reaction mixture was cooled to room temperature, diluted with water, and then extracted with dichloromethane. The organic layer was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (48 mg).

[0320]

Reference Example 51: Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-({[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate

A mixture of 2'-ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (35 mg), ethyl 1-(5-formylpyrazin-2-yl)piperidine-4-carboxylate (23 mg), sodium dithionite (28 mg) and DMF (1 mL) was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (46 mg).

Reference Example 52: Ethyl [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenoxy)piperidin-1-yl] acetate

A mixture of 6'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (35.6 mg), ethyl [4-(3-fluoro-4-formylphenoxy)piperidin-1-yl] acetate (25.7 mg), sodium dithionite (34.5 mg) and DMF (0.79 mL) was stirred at 110°C overnight. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (40.7 mg).

Reference Example 53: Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate

A mixture of 2'-ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (2.30 g), ethyl 1-(5-formylpyrazin-2-yl)piperidine-4-carboxylate (1.45 g), sodium dithionite (2.30 g) and DMF (26 mL) was stirred at 110°C for 4.5 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (3.06 g).

Reference Example 54: Ethyl 3-[4-fluoro-4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperidin-1-yl]propanoate

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (50 mg), ethyl 3-[4-fluoro-4-(6-formylpyridin-3-yl)piperidin-1-yl]propanoate (41 mg), sodium dithionite (42 mg) and DMF (1 mL) was stirred at 100°C for 7 hours. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (38 mg).

Reference Example 55: Ethyl 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

6'-ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine(61 mg), ethyl 3-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]propanoate (45 mg), sodium dithionite (34 mg) and DMF (1.4 mL) was stirred at 110°C for 3 hours. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to afford the title compound (41 mg).

[0321]

Reference Example 56: Ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

A mixture of 6'-cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (1.5 g), ethyl 3-[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (1.1 g), sodium dithionite (1.1 g) and DMF (15 mL) was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and then extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (1.9 g).

Reference Example 57: Ethyl {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

A mixture of 2'-ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (50 mg), ethyl {[(1R,3r,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy} acetate (37 mg), sodium dithionite (48 mg) and DMF (0.5 mL) was stirred at 100°C for 10 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (85 mg).

Reference Example 58: Ethyl 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

A mixture of 2'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridine]-4,5,6-triamine (50 mg), ethyl 3-

[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (36 mg), sodium dithionite (47 mg) and DMF (0.5 mL) was stirred at 100°C for 8 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (76 mg).

Reference Example 59: ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl] acetate

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (30 mg), ethyl [4-(4-formylphenoxy)piperidin-1-yl] acetate (89 mg), sodium dithionite (32 mg) and DMF (2 mL) was stirred at 100°C for 3 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (38 mg).

Reference Example 60: ethyl 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methylpyridine-2,3,4-triamine (95 mg), ethyl 1-(4-formylphenyl)piperidine-4-carboxylate (68 mg), sodium metabisulfite (59 mg) and acetonitrile (2.4 mL) was stirred at 180°C for 1.5 hours, using microwave reactor. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate. The organic layer was washed with brine. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (150 mg).

[0322]

Reference Example 61: 1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carbonitrile

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-

(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (182 mg), 1-(5-formylpyrazin-2-yl)piperidine-4-carbonitrile (95 mg), sodium dithionite (192 mg) and DMF (4.4 mL) was stirred at 90°C for 23 hours. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (247 mg).

Reference Example 181: ethyl 8-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]deca-2-ene-3-carboxylate

A mixture of N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6-[3-(trifluoromethyl)phenyl]pyridine-2,3,4-triamine (70 mg), ethyl 8-(4-formylphenyl)-1-oxa-2,8-diazaspiro[4.5]deca-2-ene-3-carboxylate (59 mg), sodium dithionite (77 mg) and DMF (2.1 mL) was stirred at 90°C overnight. The reaction mixture was cooled to room temperature, diluted with water, and stirred for 15 minutes. The resulting precipitate was collected by filtration and washed with water to afford the crude product. The crude product was purified by silica gel column chromatography to afford the title compound (123 mg).

[0323]

Example 1: 1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

To a solution of ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate (75 mg) in ethanol (1 mL) was added 1M aq. sodium hydroxide (0.56 mL), and the reaction mixture was stirred at 50°C for 2 hours. The reaction mixture was cooled to room temperature, diluted with water, and neutralized with 1M hydrochloric acid. The resulting precipitate was collected by filtration and dried to afford the title compound (62 mg).

Example 2: 1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

To a solution of ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate (75 mg) in ethanol (1 mL) was added 1M aq. sodium hydroxide (0.54 mL), and the reaction mixture was stirred at 50°C for 2 hours. The reaction mixture was cooled to room temperature, diluted with water, and neutralized with 1M hydrochloric acid. The resulting precipitate was collected by filtration and dried to afford the title compound (63 mg).

Example 3 1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

To a mixture of ethyl 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate (76 mg), ethanol (0.54 mL), THF (0.54 mL) and water (0.18 mL) was added lithium hydroxide monohydrate (23 mg), and the reaction mixture was stirred at room temperature for 2 hours. The solvent was removed under reduced pressure, diluted with water, and then neutralized by adding 6M hydrochloric acid. The resulting precipitate was collected by filtration to afford the title compound (40 mg).

Example 4: {[1-(5-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetic acid

To a mixture of ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy} acetate (141 mg), THF (0.78 mL), methanol (0.78 mL), and water (0.78 mL) was added

lithium hydroxide monohydrate (32.8 mg), and the reaction mixture was stirred at room temperature for 30 minutes and further stirred at 50°C overnight. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was diluted with water and neutralized by adding 2M hydrochloric acid with stirring at room temperature. The resulting precipitate was collected by filtration, washed with water, and dried to afford the title compound (133 mg).

Example 5: 3-[4-(5-{5-[2-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid

To a stirring mixture of ethyl 3-[4-(5-{5-[2-fluoro-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate (17.6 mg), ethanol (0.5 mL), water (0.25 mL), and THF (0.25 mL) was added lithium hydroxide monohydrate (5.1 mg) at room temperature. The reaction mixture was stirred at room temperature overnight and further stirred at 70°C for 5 hours. The reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was diluted with water and neutralized by adding 2M hydrochloric acid with stirring at room temperature. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (13.9 mg).

[0324]

Example 6: 3-[4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate (1.24 g), THF (8.4 mL), methanol (8.4 mL), and water (8.4 mL) was added lithium hydroxide monohydrate (0.285 g), and the reaction mixture was stirred at 50°C overnight. The reaction mixture was cooled to room

temperature and concentrated under reduced pressure. The residue was diluted with water, and neutralized by adding 2M hydrochloric acid (3.4 mL) with stirring at room temperature. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (1.14 g).

Example 7: 3-[(3R)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid

A mixture of ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (1.6 g), ethanol (11 mL), and 4M aq. sodium hydroxide (2.7 mL) was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was diluted with water and neutralized by adding 6M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (1.44 g).

Example 8: 3-[(2S)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoate (96.7 mg), THF (0.74 mL), methanol (0.74 mL) and water (0.74 mL) was added lithium hydroxide monohydrate (21.8 mg) at room temperature, and the reaction mixture was stirred at the same temperature for 2 hours. The reaction mixture was concentrated under reduced pressure. The residue was diluted with water and neutralized with 2M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (76.3 mg).

Example 9: 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-({[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

To a stirred mixture of ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-({[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate (45 mg), ethanol (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.082 mL) with stirring at room temperature. The reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature, diluted with water, and then neutralized with 6M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (38 mg).

Example 10: [4-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenoxy)piperidin-1-yl]acetic acid

To a stirred mixture of ethyl [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenoxy)piperidin-1-yl] acetate (39.5 mg) in ethanol (1.1 mL) was added 2M aq. sodium hydroxide (0.134 mL) with stirring at room temperature. The reaction mixture was stirred at the same temperature for 4 hours. The reaction mixture was diluted with water and neutralized with 2M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (35.6 mg).

[0325]

Example 11: 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid dihydrochloride

[Step 1] Preparation of 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

A mixture of ethyl 1-(5-{5-[2-ethoxy-6-

(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate (285 mg), ethanol (8 mL) and 1M aq. sodium hydroxide (2.1 mL) was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature, and the solvent was concentrated under reduced pressure. The residue was diluted with water and neutralized with 1M hydrochloric acid. The resulting precipitate was collected by filtration and dried to afford the title compound (245 mg).

[Step 2] Preparation of 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid dihydrochloride

1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid (245 mg) obtained in Step 1 was diluted with ethyl acetate (8 mL). To the stirred solution was added hydrogen chloride (4M in ethyl acetate, 0.47 mL) at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The solvent was removed under reduced pressure, and the residue was diluted with diethyl ether. The insolubles were collected by filtration, washed with diethyl ether, and then dried to afford the title compound (244 mg).

Example 12: 3-[4-Fluoro-4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperidin-1-yl]propanoic acid trihydrochloride

A mixture of ethyl 3-[4-fluoro-4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperidin-1-yl]propanoate (37 mg) and 2M hydrochloric acid (1 mL) was stirred at 60°C for 3 hours. The solvent was removed under reduced pressure. The residue was diluted with ethyl acetate and stirred at room temperature. The insolubles were collected by filtration and dried to afford the title compound (32

mg).

Example 13: 3-[4-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid dihydrochloride

[Step 1] Preparation of 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate (41 mg), THF (0.38 mL), water (0.38 mL) and ethanol (0.38 mL) was added lithium hydroxide monohydrate (9.7 mg) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 2 hours. The reaction mixture was neutralized by adding 6M hydrochloric acid. The resulting precipitate was collected by filtration and washed with water to afford the title compound (38 mg).

[Step 2] Preparation of 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid dihydrochloride

To a stirred mixture of 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid (36 mg) obtained in Step 1 and ethyl acetate (0.52 mL) was added hydrogen chloride (4M in ethyl acetate, 0.066 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 2 hours. The resulting precipitate was collected by filtration and washed with ethyl acetate to afford the title compound (38 mg).

Example 14: Sodium 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-

(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[Step 1] Preparation of 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (1.82 g), ethanol (9 mL) and water (9 mL) was added 4M aq. sodium hydroxide (3 mL) with stirring at room temperature, and the reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was diluted with water and neutralized with 6M hydrochloric acid. The reaction mixture was stirred at room temperature overnight. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (1.73 g).

[Step 2] Preparation of sodium 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

To a stirred mixture of 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid (1.20 g) obtained in Step 1 and methanol (30 mL) was added sodium methoxide (0.5M in methanol, 3.32 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The solvent was removed under reduced pressure. The residue was diluted with diethyl ether (20 mL) and stirred at room temperature for 3 hours. Hexane (20 mL) was added thereto, and the mixture was stirred at room temperature for 1 hour. The insolubles were collected by filtration, washed with diethyl ether-hexane (1:1), and then dried to afford the title compound (1.16 g).

Example 15: Sodium {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-

(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

[Step 1] Preparation of {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid

To a stirred solution of ethyl {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate (85 mg) in ethanol (1 mL) was added 1M aq. sodium hydroxide (0.53 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was neutralized by adding 2M hydrochloric acid. After the solvent was removed under reduced pressure, the residue was diluted with water. The resulting precipitate was collected by filtration, washed with water and hexane-ethyl acetate (7:3) sequentially, and dried to afford the title compound (59 mg).

[Step 2] Preparation of sodium {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

To a stirred mixture of {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid (58 mg) obtained in Step 1 and methanol (1 mL) was added sodium methoxide (0.5M in methanol, 0.16 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The solvent was removed under reduced pressure. The residue was diluted with diethyl ether-hexane (1:1) and stirred at room temperature for 1 hour. The insolubles were collected by filtration, washed with diethyl ether-hexane (1:1), and then dried to afford the title compound (56 mg).

[0326]

Example 16: Sodium 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[Step 1] Preparation of 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid

To a stirred solution of ethyl 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (76 mg) in ethanol (1 mL) was added 1M aq. sodium hydroxide (0.50 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was neutralized by adding 2M hydrochloric acid and concentrated under reduced pressure. The residue was diluted with water. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (68 mg).

[Step 2] Preparation of sodium 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

To a stirred mixture of 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid (68 mg) obtained in Step 1 and methanol (1 mL) was added sodium methoxide (0.5M in methanol, 0.19 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The solvent was removed under reduced pressure. The residue was diluted with diethyl ether-hexane (1:1) and stirred at room temperature for 1 hour. The insolubles were collected by filtration, washed with diethyl ether-hexane (1:1), and then dried to afford the title compound (63 mg).

Example 17: Sodium [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate

[Step 1] Preparation of [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetic acid

To a stirred mixture of ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl] acetate (38 mg) in ethanol (1 mL) was added 1M aq. sodium hydroxide (0.28 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was neutralized by adding 2M hydrochloric acid and diluted with water. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (32 mg).

[Step 2] Preparation of sodium [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetic acid

To a stirred mixture of 4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetic acid (32 mg) obtained in Step 1 and methanol (2 mL) was added sodium methoxide (0.5M in methanol, 0.098 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The solution was removed under reduced pressure. The residue was diluted with diethyl ether-hexane (1:1) and stirred at room temperature for 1 hour. The insolubles were collected by filtration and washed with diethyl ether-hexane (1:1), and then dried to afford the title compound (23 mg).

Example 18: 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid

[Step 1] Preparation of ethyl 1-(4-{5-[6-ethoxy-5-

(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate

A mixture of 6'-ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (50 mg), ethyl 1-(4-formylphenyl)piperidine-4-carboxylate (33 mg), sodium dithionite (40 mg) and DMF (1 mL) was stirred at 100°C for 7 hour. The reaction mixture was cooled to room temperature, and then purified by silica gel column chromatography to afford the title compound (57 mg).

[Step 2] Preparation of 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid

To a stirred mixture of ethyl 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate (58 mg) obtained in Step 1, THF (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.11 mL) with stirring at room temperature, and the reaction mixture was stirred at 50°C for 2 hours. Ethanol (0.5 mL) was added thereto, and the reaction mixture was stirred at 50°C for 2 hours. The reaction mixture was cooled to room temperature, diluted with water and then neutralized by adding 1M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (52 mg).

Example 19: [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl]acetic acid trihydrochloride

[Step 1] Preparation of ethyl [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl] acetate

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (50 mg), ethyl [4-(6-formylpyridin-3-yl)-4-hydroxypiperidin-1-yl]

acetate (39 mg), sodium dithionite (42 mg) and DMF (1 mL) was stirred at 100°C for 7 hours. The reaction mixture was cooled to room temperature, and then purified by silica gel column chromatography to afford the title compound (52 mg).

[Step 2] Preparation of [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl]acetic acid

To a stirred mixture of ethyl [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl] acetate (52 mg) obtained in Step 1, THF (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.095 mL) with stirring at room temperature, and the reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature, diluted with water, and then neutralized by adding 1M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (39 mg).

[Step 3] Preparation of [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl]acetic acid trihydrochloride

To a stirred mixture of [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl]acetic acid (38 mg) obtained in Step 2 and ethyl acetate (1 mL) was added hydrogen chloride (4M in ethyl acetate, 0.072 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was diluted with ethyl acetate. The insolubles were collected by filtration, washed with ethyl acetate, and then dried to afford the title compound (41 mg).

Example 20: Sodium 3-[(3R)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-

(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[Step 1] Preparation of ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

A mixture of 6'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (50 mg), ethyl 3-[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (38 mg), sodium dithionite (39 mg) and DMF (0.5 mL) was stirred at 110°C for 3 hours. The reaction mixture was cooled to room temperature, and then purified by silica gel column chromatography to afford the title compound (75 mg).

[Step 2] Preparation of 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate (75 mg) obtained in Step 1, THF (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.127 mL) with stirring at room temperature, and the reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature, diluted with water, and then neutralized by adding 1M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (66 mg).

[Step 3] Preparation of sodium 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

To a stirred mixture of 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid

(65 mg) obtained in Step 2 and methanol (2 mL) was added sodium methoxide (0.5M in methanol, 0.184 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 30 minutes. The solvent was removed under reduced pressure. The residue was diluted with diethyl ether-hexane (1:1) and stirred at room temperature for 1 hour. The insolubles were collected by filtration, washed with diethyl ether-hexane (1:1), and then dried to afford the title compound (65 mg).

[0327]

Example 21: 1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid

To a stirred mixture of ethyl 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate (131 mg), THF (2.4 mL) and water (0.82 mL) was added 4M aq. sodium hydroxide (0.255 mL) with stirring at room temperature, and the reaction mixture was stirred at 70°C for 1 hour. The reaction mixture was cooled to room temperature, diluted with water, and then neutralized by adding 6M hydrochloric acid. The resulting precipitate was collected by filtration to afford the title compound (122 mg).

Example 22: Sodium [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]acetate

[Step 1] Preparation of ethyl [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl] acetate

A mixture of 6'-cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (50 mg), ethyl [4-(3-fluoro-5-formylpyridin-2-yl)piperazin-1-yl] acetate (33 mg), sodium dithionite (39 mg) and DMF (0.5 mL) was stirred 110°C for 3 hours. The reaction mixture was cooled to room temperature, and then purified by silica gel column chromatography to afford the title

compound (68 mg).

[Step 2] Preparation of [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]acetic acid

To a stirred mixture of ethyl [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl] acetate (67 mg) obtained in Step 1, THF (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.116 mL) with stirring at room temperature, and the reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature, diluted with water, and then neutralized by adding 1M hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (59 mg).

[Step 3] Preparation of sodium [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]acetate

To a stirred mixture of [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]acetic acid (59 mg) obtained in Step 2 and methanol (2 mL) was added sodium methoxide (0.5M in methanol, 0.169 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 30 minutes. The solvent was removed under reduced pressure. The residue was diluted with diethyl ether-hexane (1:1) and stirred at room temperature for 1 hour. The insolubles were collected by filtration, diluted with diethyl ether-hexane (1:1), and then dried to afford the title compound (56 mg).

Example 23: 5-[3-Fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-{5-[4-(1H-tetrazol-5-yl)piperidin-1-yl]pyrazin-2-yl}-1H-imidazo[4,5-b]pyridine-7-amine

To a stirred solution of 1-(5-{5-[3-fluoro-5-

(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carbonitrile (50 mg) in DMF (1 mL) were added ammonium chloride (13.2 mg) and sodium azide (16 mg) sequentially with stirring under ice-cooling, and the reaction mixture was stirred at 100°C for 3 days. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and then extracted with ethyl acetate. The organic layer was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (7.4 mg).

Example 24: 8-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-2,8-diazaspiro[4.5]decan-3-one

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (25 mg), 4-(3-oxo-2,8-diazaspiro[4.5]decan-8-yl)benzaldehyde (17 mg), sodium metabisulfite (16 mg) and acetonitrile (0.6 mL) was stirred at 180°C for 1 hour, using a microwave reactor. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and extracted with ethyl acetate. The organic layer was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to afford the title compound (16 mg).

Example 25: 1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-N-(methansulfonyl)piperidine-4-carboxamide

A mixture of 6'-cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridine]-4,5,6-triamine (42 mg), 1-(5-formylpyrazin-2-yl)-N-(methansulfonyl)piperidine-4-carboxamide (30 mg), sodium dithionite (39 mg) and DMF (0.9 mL) was stirred at 110°C for 5 hours. The reaction mixture was cooled to room temperature and diluted with water. The resulting solids were collected by filtration and washed with water. The solids were diluted with diethyl ether-hexane (1:1, 2 mL) and stirred at room temperature overnight. The insolubles were collected by filtration, washed with

diethyl ether-hexane (1:1), and then dried to afford the title compound (57 mg).

[0328]

Example 26: [4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]acetic acid

[Step 1] Preparation of 2,2,2-trifluoro-1-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]ethan-1-one

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (300 mg), 4-[1-(trifluoroacetyl)piperidin-4-yl]benzaldehyde (228 mg), sodium dithionite (253 mg) and DMF (3.5 mL) was stirred at 100°C for 7 hours. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and then extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (442 mg).

[Step 2] Preparation of 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperidin-1-yl}ethan-1-one and its isomer 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperidin-1-yl}ethan-1-one

To a stirred solution of 2,2,2-trifluoro-1-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]ethan-1-one (430 mg) obtained in Step 1 in dichloromethane (5 mL) were added DIPEA (0.16 mL) and 2-(chloromethoxy)ethyltrimethylsilane (0.13 mL) with stirring under ice-cooling, and the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced

pressure, and the residue was purified by silica gel column chromatography to afford the title compound (484 mg).

[Step 3] Preparation of 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperidin-4-yl)phenyl]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridine-7-amine and its isomer 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperidin-4-yl)phenyl]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridine-7-amine

To a mixture of 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperidin-1-yl}ethan-1-one and its isomer 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperidin-1-yl}ethan-1-one (480 mg) obtained in Step 2, and potassium carbonate (410 mg) were added methanol (4.5 mL) and water (0.5 mL), and the reaction mixture was stirred at 70°C for 2 hours. The reaction mixture was cooled to room temperature, diluted with water and ethyl acetate, and then extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (391 mg).

[Step 4] Preparation of ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl] acetate

To a stirred mixture of 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperidin-4-yl)phenyl]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridine-7-amine and its isomer 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperidin-4-yl)phenyl]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-

b]pyridine-7-amine (70 mg) obtained in Step 3 and ethanol (1 mL) were added sodium bicarbonate (11 mg) and ethyl bromoacetate (0.012 mL) with stirring at room temperature, and the reaction mixture was stirred at 80°C for 2 hours. The reaction mixture was cooled to room temperature. Concentrated sulfuric acid (0.026 mL) was added thereto, and the reaction mixture was stirred at 80°C for 1 hour. The reaction mixture was cooled to room temperature and then purified by silica gel column chromatography to afford the title compound (58 mg).

[Step 5] Preparation of [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]acetic acid

To a mixture of ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl] acetate (55 mg) obtained in Step 4, ethanol (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.1 mL), and the reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature and diluted with water, and 1M hydrochloric acid was added. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (45 mg).

Example 27: 2-[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride

[Step 1] Preparation of 2,2,2-trifluoro-1-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]ethan-1-one

The title compound was obtained as described in Example 26, Step 1, using 4-[4-(trifluoroacetyl)piperazin-1-yl]benzaldehyde instead of 4-[1-(trifluoroacetyl)piperidin-4-yl]benzaldehyde.

[Step 2] Preparation of 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-

yl)phenyl]piperazin-1-yl}ethan-1-one and its isomer 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}ethan-1-one

The title compound was obtained as described in Example 26, Step 2, using 2,2,2-trifluoro-1-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]ethan-1-one obtained in Step 1 instead of 2,2,2-trifluoro-1-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]ethan-1-one.

[Step 3] Preparation of 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperazin-1-yl)phenyl]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridine-7-amine and its isomer 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperazin-1-yl)phenyl]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridine-7-amine

The title compound was obtained in Example 26, Step 3, using 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}ethan-1-one and its isomer, 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}ethan-1-one obtained in Step 2 instead of 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperidin-1-yl}ethan-1-one and its isomer 2,2,2-trifluoro-1-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperidin-1-yl}ethan-1-one.

[Step 4] Preparation of ethyl 2-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}propanoate and its isomer ethyl 2-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}propanoate

To a stirred mixture of 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperazin-1-yl)phenyl]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridine-7-amine and its isomer 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-[4-(piperazin-1-yl)phenyl]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridine-7-amine (95 mg) obtained in Step 3 and NMP (1 mL) were added potassium carbonate (48 mg) and ethyl 2-bromopropionate (0.035 mL) with stirring at room temperature, and the reaction mixture was stirred at 100°C for 4 hours. The reaction mixture was cooled to room temperature, and then purified by silica gel column chromatography to afford the title compound (67 mg).

[Step 5] Preparation of ethyl 2-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate

To a stirred solution of ethyl 2-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}propanoate and its isomer ethyl 2-{4-[4-(5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-imidazo[4,5-b]pyridin-2-yl)phenyl]piperazin-1-yl}propanoate (65 mg) obtained in Step 4 in dichloromethane (0.5 mL) was added TFA (0.5 mL) with stirring at room temperature, and the reaction mixture was stirred for 2 hours. The

reaction mixture was purified by silica gel column chromatography to afford the title compound (47 mg).

[Step 6] Preparation of 2-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride

To a mixture of ethyl 2-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate (40 mg) obtained in Step 5, ethanol (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.15 mL), and the reaction mixture was stirred with heating at 70°C for 1 hour. The reaction mixture was cooled to room temperature and diluted with water, and 1M hydrochloric acid was added. The resulting precipitate was collected by filtration to afford the solids. To the stirred mixture of the solids and ethyl acetate (1 mL) was added hydrogen chloride (4M in ethyl acetate, 0.052 mL) with stirring at room temperature, and the reaction mixture was stirred for 1 hour. The resulting precipitates were collected by filtration, washed with ethyl acetate, and then dried to afford the title compound (25 mg).

Example 28: 1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperidine-4-carboxylic acid

[Step 1] Preparation of methyl 4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoate

A mixture of 6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridine-2,3,4-triamine (200 mg), 4-formylbenzoate (84 mg), sodium dithionite (211 mg) and DMF (2 mL) was stirred at 100°C for 2 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the title compound (193 mg).

[Step 2] Preparation of 4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-

[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoic acid

To a mixture of methyl 4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoate (193 mg) obtained in Step 1 and ethanol (2.5 mL) was added 1M aq. sodium hydroxide (1.7 mL), and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with water, and 1M hydrochloric acid (1.7 mL) was added. The resulting precipitate was collected by filtration, washed with water, and then dried to afford the title compound (182 mg).

[Step 3] Preparation of ethyl 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperidine-4-carboxylate

To a mixture of 4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoic acid (40 mg) obtained in Step 2 and DMF (1 mL) were added DIPEA (0.038 mL), HATU (34 mg) and ethyl piperidine-4-carboxylate (0.014 mL), and the reaction mixture was stirred overnight at room temperature. The reaction mixture was purified by silica gel column chromatography to afford the title compound (25 mg).

[Step 4] Preparation of 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperidine-4-carboxylic acid

The title compound (19 mg) was obtained as described in Example 26, Step 5, using ethyl 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperidine-4-carboxylate obtained in Step 3 instead of ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl] acetate.

Example 29: {4-[1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethyl]piperazin-1-yl}acetic acid trihydrochloride

[Step 1] Preparation of 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethan-1-one

The title compound was obtained as described in Example 26, Step 1, using 1-formyl-4-acetybenzene instead of 4-[1-(trifluoroacetyl)piperidin-4-yl]benzaldehyde.

[Step 2] Preparation of ethyl {4-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethyl]piperazin-1-yl} acetate

1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethan-1-one (50 mg) obtained in Step 1, 1-piperazine ethyl acetate (32 mg), tetraisopropyl orthotitanate (0.055 mL), acetic acid (0.016 mL) and dichloromethane (1 mL) were mixed, and the mixture was stirred at room temperature overnight. Sodium triacetoxyborohydride (39 mg) was added thereto, and the reaction mixture was stirred at the same temperature overnight. The reaction mixture was purified by silica gel column chromatography to afford the title compound (38 mg).

[Step 3] Preparation of {4-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethyl]piperazin-1-yl}acetic acid trihydrochloride

To a mixture of ethyl {4-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethyl]piperazin-1-yl} acetate (36 mg) obtained in Step 2, THF (0.5 mL) and water (0.5 mL) was added 4M aq. sodium hydroxide (0.065 mL), and the reaction mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to room temperature and

diluted with water, and then 1M hydrochloric acid was added. The resulting precipitate was collected by filtration to afford the solids. To a stirred mixture of the solids and ethyl acetate (1 mL) was added hydrogen chloride (4M in ethyl acetate, 0.056 mL) with stirring at room temperature, and the reaction mixture was stirred for 1 hour. The resulting precipitate was collected by filtration, washed with ethyl acetate, and then dried to afford the title compound (28 mg).

[0329]

Example 89: 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid dihydrochloride

[Step 1] Preparation of 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate (49 mg), THF (0.45 mL), water (0.45 mL) and ethanol (0.45 mL) was added lithium hydroxide monohydrate (11 mg) with stirring at room temperature, and the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was neutralized by adding 6M hydrochloric acid and diluted with water. The resulting solids were collected by filtration, washed with hexane-ethyl acetate (1:1) to afford the title compound (21 mg).

[Step 2] Preparation of 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid dihydrochloride

To a stirred mixture of 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid (21 mg)

obtained in Step 1 and ethyl acetate (0.3 mL) was added hydrogen chloride (4M in ethyl acetate, 0.038 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 2 hours. The reaction mixture was concentrated under reduced pressure to afford the title compound (23 mg).

Example 109: Sodium 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate

[Step 1] Preparation of 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoic acid

To a stirred mixture of ethyl 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{(1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate (59 mg), THF (0.85 mL), methanol (0.85 mL) and water (0.85 mL) was added lithium hydroxide monohydrate (14 mg) with stirring at room temperature, and the reaction mixture was stirred at the same temperature overnight. The reaction mixture was concentrated under reduced pressure. The residue was diluted with water and neutralized with 2M hydrochloric acid. The resulting precipitate was collected by filtration, diluted with water, and then dried to afford the title compound (54 mg).

[Step 2] Preparation of sodium 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate

To a stirred mixture of 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoic acid (51 mg) obtained in Step 1 and methanol (1.5 mL) was added sodium methoxide (0.5M in methanol, 0.15 mL) with stirring at room temperature, and the reaction mixture was stirred at the same temperature for 10 minutes. The reaction mixture was concentrated

under reduced pressure. To the residue was added diethyl ether-hexane (1:1), and the mixture was stirred at room temperature for 2 hours. The solvent was removed. The insolubles were washed with diethyl ether-hexane (1:1), and then dried to afford the title compound (52 mg).

Compounds of Reference Examples and Examples are further provided below in Tables 1 to 109. In the tables, PREx means the Reference Example No. where the compound was prepared according to the method as described in said Reference Example using a corresponding starting material. For example, the compound of the following Reference Example with the indication of PREx No. as 1 was prepared using the method as described in Reference Example 1. Also, in the tables, PEx means the Example No. where the compound was prepared according to the method as described in said Example using a corresponding starting material. For example, the compound of the following Example with the indication of PEx No. as 1 was prepared using the method as described in Example 1. Further, in the tables, Chemical Name refers to the name of the Reference Example (REx) or the Example (Ex). In addition, Data means the instrumental analytical data, such as mass spectrometric data (m/z values), ^{1}H NMR data (δ (ppm) of peaks), and elemental analytical data (composition (%) of C, H and N).

[0330]

[Table 1]

REx	PREx	Chemical Name	Data
1	1	N-{[1-(methoxymethyl)cyclopentyl]methyl}ethanamine hydrochloride	^{1}H-NMR (400 MHz, DMSO-d_6) δ: 8.14 (brs,2H), 3.27 (s ,3H), 3.23 (s, 2H), 2.96-2.90 (m ,2H), 2.88-2.84 (m, 2H), 1.60-1.53 (m, 4H), 1.48-1.43 (m, 4H), 1.20 (t, 3H)
2	2	1-{1-[(2-Methoxyethoxy)methyl]cyclopentyl}-N-methylmethanamine hydrochloride	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.65-3.63 (m, 2H),3.55-3.53 (m, 2H), 3.49 (s, 2H), 3.41 (s, 3H), 3.00 (dd,2H), 2.70 (t,3H), 1.77-1.57 (m, 8H)

3	3	1-[1-(Butoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.52-3.49 (m, 2H), 3.44-3.41 (m, 2H), 3.04 (s, 1H), 2.90 (s,1H), 2.75 (brs, 3H), 1.81-1.28 (m, 12H), 0.96-0.88 (m, 3H)
4	4	1-[1-(Ethoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.58 (dd, 2H), 3.44 (s, 2H), 3.02 (t, 2H), 2.74 (t, 3H), 1.76-1.58 (m, 8H), 1.21 (t, 3H)
5	5	1-[1-(methoxymethyl)cyclopentyl]-N-methylmethanamine hydrochloride	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.42 (s, 3H), 3.41 (s, 2H), 3.02-2.99 (m, 2H), 2.75 (t, 3H), 2.17-2.12 (m, 2H), 1.75-1.56 (m, 6H)

[0331]

[Table 2]

REx	PREx	Chemical Name	Data
6	6	4-Chloro-6-[3-fluoro-5-(trifluoromethyl)phenyl]pyridin-2-amine	MS (ESI+) m/z: 291.0 (M+H)+
7	7	4-Chloro-6-[3-fluoro-5-(trifluoromethyl)phenyl]-3-nitropyridin-2-amine	MS (ESI+) m/z: 235.9 (M+H)+
8	8	6-Chloro-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 303.6 (M+H)+
9	9	6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 494.4 (M+H)+
10	10	2'-Ethoxy-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 468.4 (M+H)+

11	11	6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 471.7 (M+H)+

[0332]

[Table 3]

REx	PREx	Chemical Name	Data
12	12	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 440.2 (M+H)+
13	13	6'-Cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 464.3 (M+H)+
14	14	Ethyl [4-(4-formylphenyl)piperazin-1-yl]acetate	MS (ESI+) m/z: 277.1 (M+H)+
15	15	Ethyl 3-[(3R)-4-(4-formylphenyl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 305.1 (M+H)+
16	16	Ethyl {4-[(4-formylphenyl)methyl]piperazin-1-yl}acetate	MS (ESI+) m/z: 291.1 (M+H)+
17	17	Methyl {1-[(4-formylphenyl)methyl]piperidin-4-yl}acetate	MS (ESI+) m/z: 276.1 (M+H)+
18	18	Ethyl 3-[4-(5-formylpyridin-2-yl)-4-hydroxypiperidin-1-yl]propanoate	MS (ESI+) m/z: 307.1 (M+H)+
19	19	Tert-butyl 4-[6-(1,3-dioxolan-2-yl)pyridin-3-yl]-4-hydroxypiperidine-1-carboxylate	MS (ESI+) m/z: 351.6 (M+H)+

[0333]

[Table 4]

REx	PREx	Chemical Name	Data
20	20	Ethyl [4-(6-formylpyridin-3-yl)-4-hydroxypiperidin-1-yl]acetate	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.08 (s, 1H), 8.96 (d, 1H), 8.02 (dd, 1H), 7.96 (d, 1H), 4.22 (q, 2H), 3.75 (s, 1H), 3.31 (s, 1H), 2.93-2.90 (m, 2H), 2.70 (dt, 2H), 2.29 (dt, 2H), 1.80-1.77 (m, 2H), 1.30 (t, 2H)
21	21	Tert-butyl 4-[6-(1,3-dioxolan-2-yl)pyridin-3-yl]-4-fluoropiperidine-1-carboxylate	MS (ESI+) m/z: 353.3 (M+H)+
22	22	Ethyl 3-[4-fluoro-4-(6-formylpyridin-3-yl)piperidin-1-yl]propanoate	MS (ESI+) m/z: 309.1 (M+H)+
23	23	Ethyl 3-[(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 307.1 (M+H)+
24	24	Ethyl [4-(4-formylphenyl)-4-hydroxypiperidin-1-yl]acetate	MS (ESI+) m/z: 292.1 (M+H)+

[0334]

[Table 5]

REx	PREx	Chemical Name	Data
25	25	Ethyl [4-(4-formylphenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 292.3 (M+H)+
26	26	Ethyl 3-[4-(4-formylphenoxy)piperidin-1-yl]propanoate	MS (ESI+) m/z: 306.2 (M+H)+
27	27	Ethyl [4-(3-chloro-4-formylphenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 326.1 (M+H)+

28	28	Ethyl 3-[(1R,3s,5S)-3-(4-formylphenoxy)-8-azabicyclo[3.2.1]octan-8-yl]propanoate	MS (ESI+) m/z: 332.2 (M+H)+
29	29	Ethyl {[(1R,3r,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 320.1 (M+H)+
30	30	Ethyl {[(1R,3s,5S)-8-(5-formylpyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 320.6 (M+H)+
31	31	Ethyl 3-[4-(5-formylpyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 321.6 (M+H)+

[0335]

[Table 6]

REx	PREx	Chemical Name	Data
32	32	Ethyl 3-[4-(6-formylpyridin-3-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 292.5 (M+H)+
33	33	Ethyl 3-[(3R)-4-(5-formylpyridin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 306.3 (M+H)+
34	34	Ethyl 1-(5-formylpyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 264.2 (M+H)+
35	35	Ethyl 2,2-difuloro-3-{[1-(5-formylpyrazin-2-yl)piperidin-4-yl]amino}propanoate	MS (ESI+) m/z: 343.6 (M+H)+
36	36	Ethyl N-[(3S,4R)-3-fluoro-1-(5-formylpyrazin-2-yl)piperidin-4-yl]glycinate	MS (ESI+) m/z: 311.2 (M+H)+

37	37	Ethyl N-[(3S,4R)-3-fluoro-1-(5-formylpyrazin-2-yl)piperidin-4-yl]-N-methylglycinate	MS (ESI+) m/z: 325.6 (M+H)+
38	38	Ethyl 3-[4-(3-fluoro-5-formylpyridin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 310.1 (M+H)+

[0336]

[Table 7]

REx	PREx	Chemical Name	Data
39	38	Ethyl [4-(3-fluoro-5-formylpyridin-2-yl)piperazin-1-yl]acetate	MS (ESI+) m/z: 296.1 (M+H)+
40	40	Ethyl 3-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 293.5 (M+H)+
41	41	Ethyl {[1-(5-formylpyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 294.1 (M+H)+
42	42	[4-(5-Formylpyrazin-2-yl)piperazin-1-yl]acetonitrile	MS (ESI+) m/z: 232.5 (M+H)+
43	43	Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 671.9 (M+H)+
44	44	Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 697.9 (M+H)+

[0337]

[Table 8]

REx	PREx	Chemical Name	Data
45	45	Ethyl 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 708.0 (M+H)+
46	46	Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 724.4 (M+H)+
47	47	Ethyl 3-[4-(5-{5-[2-fluoro-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 700.4 (M+H)+
48	48	Ethyl 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 736.6 (M+H)+

[0338]

[Table 9]

REx	PREx	Chemical Name	Data

49	49	Ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 750.8 (M+H)+
50	50	Ethyl 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 780.5 (M+H)+
51	51	Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-({[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 683.7 (M+H)+
52	52	Ethyl [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 740.2 (M+H)+

[0339]

[Table 10]

REx	PREx	Chemical Name	Data

53	53	Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 683.9 (M+H)+
54	54	Ethyl 3-[4-fluoro-4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperidin-1-yl]propanoate	MS (ESI+) m/z: 701.3 (M+H)+
55	55	Ethyl 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 712.5 (M+H)+
56	56	Ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 751.0 (M+H)+

[0340]

[Table 11]

REx	PREx	Chemical Name	Data
57	57	Ethyl {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-	MS (ESI+) m/z: 754.0 (M+H)+

		imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	
58	58	Ethyl 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 751.0 (M+H)+
59	59	Ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 684.6 (M+H)+
60	60	Ethyl 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 642.8 (M+H)+

[0341]

[Table 12]

REx	PREx	Chemical Name	Data
61	61	1-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carbonitrile	MS (ESI+) m/z: 609.9 (M+H)+

62	5	1-[1-(methoxymethyl)cyclohexyl]-N-methylmethanamine hydrochloride	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.16(brs,2H), 3.49 (s, 2H), 3.41 (s, 3H), 2.94 (s, 2H), 2.74 (s, 3H), 1.62-1.39 (m, 10H)
63	8	6-Chloro-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 315.5 (M+H)+
64	8	6-Chloro-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 329.1 (M+H)+
65	8	6-Chloro-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 343.5 (M+H)+
66	8	6-Chloro-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 343.2 (M+H)+

[0342]

[Table 13]

REx	PREx	Chemical Name	Data
67	8	6-Chloro-N^4-ethyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 343.6 (M+H)+
68	8	6-Chloro-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-ethyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 357.2 (M+H)+
69	8	6-Chloro-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 315.4 (M+H)+

70	9	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-3-nitro-6-[3-(trifluoromethyl)phenyl]pyridin-2,4-diamine	MS (ESI+) m/z: 425.6 (M+H)+
71	9	6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 443.6 (M+H)+
72	9	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 431.7 (M+H)+
73	9	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 443.1 (M+H)+

[0343]

[Table 14]

REx	PREx	Chemical Name	Data
74	9	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 457.7 (M+H)+
75	9	6-[3,5-Bis(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 507.7 (M+H)+

76	9	6-[3-Ethoxy-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 483.8 (M+H)+
77	9	6-[4-Cyclopropyl-3-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 479.3 (M+H)+
78	9	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 426.4 (M+H)+
79	9	2'-Fluoro-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 444.6 (M+H)+

[0344]

[Table 15]

REx	PREx	Chemical Name	Data
80	9	2'-Fluoro-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 458.2 (M+H)+
81	9	6-Amino-4-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-6'-carbonitrile	MS (ESI+) m/z: 465.3 (M+H)+

82	9	6'-Ethoxy-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 458.6 (M+H)+
83	9	6'-Ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 470.2 (M+H)+
84	9	6'-Ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 484.1 (M+H)+
85	9	6'-Ethoxy-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 498.7 (M+H)+
86	9	2'-Ethoxy-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 458.7 (M+H)+

[0345]

[Table 16]

REx	PREx	Chemical Name	Data
87	9	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 470.2 (M+H)+
88	9	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 484.7 (M+H)+

89	9	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 498.7 (M+H)+
90	9	6'-Cyclopropyl-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 454.7 (M+H)+
91	9	6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS(ESI+)m/z: 466.7 (M+H)+
92	9	6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 480.6 (M+H)+

[0346]

[Table 17]

REx	PREx	Chemical Name	Data
93	9	6'-Cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 494.3 (M+H)+
94	9	6'-Cyclopropyl-N^4-ethyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-5-nitro-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 494.4 (M+H)+

95	9	5'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.89 (s, 1H), 7.95 (d, 1H), 6.90 (s, 1H), 6.17 (brs, 2H), 3.58 (s, 2H), 3.40 (s, 2H), 3.21 (s, 3H), 2.93 (s, 3H), 2.31-2.24 (m, 1H), 2.03-1.82 (m, 6H), 1.17-1.12 (m, 2H), 0.90-0.86 (m, 2H)
96	9	5'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 480.2 (M+H)+

[0347]

[Table 18]

REx	PREx	Chemical Name	Data
97	9	5'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 494.2 (M+H)+
98	9	N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-5',6'-bis(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 508.2 (M+H)+
99	9	2'-Cyclopropyl-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 454.7 (M+H)+
100	9	2'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 466.7 (M+H)+

101	9	2'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 480.6 (M+H)+
102	9	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-6-[4-methoxy-3-(trifluoromethyl)phenyl]-N^4-methyl-3-nitropyridin-2,4-diamine	MS (ESI+) m/z: 455.6 (M+H)+
103	9	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5-nitro-6'-propyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 468.7 (M+H)+

[0348]

[Table 19]

REx	PREx	Chemical Name	Data
104	9	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-5-nitro-6'-(trifluoromethyl)[2,4'-bipyridin]-4,6-diamine	MS (ESI+) m/z: 470.6 (M+H)+
105	12	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6-[3-(trifluoromethyl)phenyl]pyridin-2,3,4-triamine	MS (ESI+) m/z: 395.7 (M+H)+
106	11	6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 401.7 (M+H)+
107	13	6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 413.6 (M+H)+

108	11	6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 427.3 (M+H)+
109	11	6-[3-Fluoro-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 441.4 (M+H)+
110	11	N^4-{[1-(Ethoxymethyl)cyclopentyl]methyl}-6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 441.7 (M+H)+

[0349]

[Table 20]

REx	PREx	Chemical Name	Data
111	11	N^4-{[1-(Butoxymethyl)cyclopentyl]methyl}-6-[3-fluoro-5-(trifluoromethyl)phenyl]-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 469.5 (M+H)+
112	12	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 401.2 (M+H)+
113	12	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 413.7 (M+H)+
114	12	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 427.7 (M+H)+

115	12	6-[3,5-Bis(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 477.7 (M+H)+
116	12	6-[3-Ethoxy-5-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 453.3 (M+H)+
117	12	6-[4-Cyclopropyl-3-(trifluoromethyl)phenyl]-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 449.7 (M+H)+

[0350]

[Table 21]

REx	PREx	Chemical Name	Data
118	12	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 396.6 (M+H)+
119	12	2'-Fluoro-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 414.2 (M+H)+
120	12	2'-Fluoro-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 428.2 (M+H)+
121	12	5,6-Diamino-4-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-5'-(trifluoromethyl)[2,3'-bipyridin]-6'-carbonitrile	MS (ESI+) m/z: 435.3 (M+H)+

122	13	6'-Ethoxy-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 428.7 (M+H)+
123	13	6'-Ethoxy-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 440.6 (M+H)+
124	13	6'-Ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 454.7 (M+H)+

[0351]

[Table 22]

REx	PREx	Chemical Name	Data
125	12	6'-Ethoxy-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.74 (d, 1H), 8.38 (d, 1H), 7.05 (s, 1H), 4.51 (q,2H), 4.23 (brs, 2H), 3.72 (brs, 2H), 3.14 (s, 2H), 3.12 (s, 3H), 3.08 (s, 2H), 2.72 (s, 3H), 1.46-1.24 (m, 13H)
126	13	2'-Ethoxy-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 428.4 (M+H)+
127	13	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 454.4 (M+H)+

128	12	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 468.7 (M+H)+

[0352]

[Table 23]

REx	PREx	Chemical Name	Data
129	12	6'-Cyclopropyl-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 424.3 (M+H)+
130	12	6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 436.3 (M+H)+
131	13	6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 450.6 (M+H)+
132	13	6'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 464.5 (M+H)+
133	12	6'-Cyclopropyl-N^4-ethyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 464.7 (M+H)+
134	10	6'-Cyclopropyl-N^4-{[1-(ethoxymethyl)cyclopentyl]methyl}-N^4-ethyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 478.6 (M+H)+

135	12	5'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 436.6 (M+H)+

[0353]

[Table 24]

REx	PREx	Chemical Name	Data
136	12	5'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 450.3 (M+H)+
137	12	5'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 464.3 (M+H)+
138	12	N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-5',6'-bis(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 478.2 (M+H)+
139	12	2'-Cyclopropyl-N^4-(3-methoxy-2,2-dimethylpropyl)-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 424.7 (M+H)+
140	12	2'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 436.7 (M+H)+
141	13	2'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 450.6 (M+H)+

142	10	2'-Cyclopropyl-N^4-{[1-(methoxymethyl)cyclohexyl]methyl}-N^4-methyl-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 464.8 (M+H)+

[0354]

[Table 25]

REx	PREx	Chemical Name	Data
143	13	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-6-[4-methoxy-3-(trifluoromethyl)phenyl]-N^4-methylpyridin-2,3,4-triamine	MS (ESI+) m/z: 425.6 (M+H)+
144	13	N^4-{[1-(methoxymethyl)cyclobutyl]methyl}-N^4-methyl-6'-propyl-5'-(trifluoromethyl)[2,3'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 438.7 (M+H)+
145	13	2'-Ethoxy-N^4-{[1-(methoxymethyl)cyclopentyl]methyl}-6'-(trifluoromethyl)[2,4'-bipyridin]-4,5,6-triamine	MS (ESI+) m/z: 440.6 (M+H)+
146	14	Ethyl 3-[4-(4-formylphenyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 291.1 (M+H)+
147	40	Ethyl 8-(4-formylphenyl)-1-oxa-2,8-diazaspiro[4.5]deca2-ene-3-carboxylate	MS (ESI+) m/z: 317.1 (M+H)+
148	34	4-(3-Oxo-2,8-diazaspiro[4.5]decan-8-yl)benzaldehyde	MS (ESI+) m/z: 259.1 (M+H)+
149	40	Methyl N-[1-(4-formylphenyl)piperidin-4-yl]-N-methylglycinate	MS (ESI+) m/z: 293.2 (M+H)+

[0355]

[Table 26]

REx	PREx	Chemical Name	Data

150	40	Ethyl N-[1-(4-formylphenyl)piperidin-4-yl]glycinate	MS (ESI+) m/z: 291.6 (M+H)+
151	40	Methyl {[1-(4-formylphenyl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 278.2 (M+H)+
152	40	Ethyl 1-(3-fluoro-4-formylphenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 280.6 (M+H)+
153	40	Ethyl 1-(4-formyl-3-methylphenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 276.5 (M+H)+
154	27	Ethyl [4-(3-fluoro-4-formylphenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 310.2 (M+H)+
155	41	Methyl {[1-(5-formylpyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 280.1 (M+H)+
156	41	Ethyl 3-[(2S)-4-(5-formylpyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 337.2 (M+H)+
157	40	Ethyl [4-(5-formylpyrazin-2-yl)piperazin-1-yl]acetate	MS (ESI+) m/z: 279.3 (M+H)+
158	40	Ethyl 4-fluoro-1-(5-formylpyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 282.1 (M+H)+
159	40	Methyl 3-[4-(5-formylpyrazin-2-yl)-2-oxopiperazin-1-yl]propanoate	MS (ESI+) m/z: 293.2 (M+H)+
160	40	Ethyl [4-(5-formylpyrazin-2-yl)-1,4-diazepan-1-yl]acetate	MS (ESI+) m/z: 293.1 (M+H)+

[0356]

[Table 27]

REx	PREx	Chemical Name	Data
161	41	Ethyl 3-[(2S)-4-(5-formylpyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 307.6 (M+H)+

162	42	1-(5-Formylpyrazin-2-yl)piperidine-4-carbonitrile	MS (ESI+) m/z: 217.4 (M+H)+
163	40	Methyl 4-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]butanoate	MS (ESI+) m/z: 293.2 (M+H)+
164	40	Ethyl N-[1-(5-formylpyrazin-2-yl)piperidin-4-yl]glycinate	MS (ESI+) m/z: 293.1 (M+H)+
165	23	Ethyl 3-[(3S)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 307.6 (M+H)+
166	41	N-{2-[4-(5-Formylpyrazin-2-yl)piperazin-1-yl]ethyl}methanesulfonamide	MS (ESI+) m/z: 314.6 (M+H)+
167	41	Ethyl 3-[4-(5-formylpyrazin-2-yl)piperazin-1-yl]butanoate	MS (ESI+) m/z: 307.2 (M+H)+
168	42	3-[4-(5-Formylpyrazin-2-yl)piperazin-1-yl]propanenitrile	MS (ESI+) m/z: 246.5 (M+H)+
169	23	Ethyl [(3R)-4-(5-formylpyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 293.1 (M+H)+
170	31	Ethyl 3-[(2R,6S)-4-(5-formylpyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 321.7 (M+H)+

[0357]

[Table 28]

REx	PREx	Chemical Name	Data
171	41	Ethyl 3-[(2R)-4-(5-formylpyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 307.8 (M+H)+
172	41	Methyl [4-(5-formylpyrazin-2-yl)piperazine-1-sufonyl]acetate	MS (ESI+) m/z: 329.1 (M+H)+

173	41	Ethyl {[1-(5-formylpyrazin-2-yl)-3,3-dimethylpiperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 322.1 (M+H)+
174	41	Ethyl {[1-(5-formylpyrazin-2-yl)-4-methylpiperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 308.6 (M+H)+
175	41	Ethyl {[1-(5-formylpyrazin-2-yl)piperidin-4-yl]sulfanyl}acetate	MS (ESI+) m/z: 310.2 (M+H)+
176	34	1-(5-Formylpyrazin-2-yl)-N-(methansulfonyl)piperidine-4-carboxamide	MS (ESI+) m/z: 313.1 (M+H)+
177	32	Ethyl [4-(6-formylpyridin-3-yl)-1,4-diazepan-1-yl]acetate	MS (ESI+) m/z: 292.6 (M+H)+
178	38	Ethyl 3-[(3R)-4-(3-fluoro-5-formylpyridin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 324.6 (M+H)+
179	41	Methyl 1-(5-formylpyrazin-2-yl)-4-hydroxypiperidine-4-carboxylate	MS (ESI+) m/z: 266.4 (M+H)+

[0358]

[Table 29]

REx	PREx	Chemical Name	Data
180	49	Methyl 4-hydroxy-1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 640.9 (M+H)+

181	181	Ethyl 8-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3-carboxylate	MS (ESI+) m/z: 691.4 (M+H)+
182	45	Ethyl 1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[4-methoxy-3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 668.7 (M+H)+
183	46	Ethyl 8-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3-carboxylate	MS (ESI+) m/z: 692.4 (M+H)+

[0359]

[Table 30]

REx	PREx	Chemical Name	Data
184	181	Methyl 1-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)pyrrolidine-3-carboxylate	MS (ESI+) m/z: 608.3 (M+H)+
185	45	Ethyl {4-[(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)methyl]piperazin-1-yl}acetate	MS (ESI+) m/z: 683.8 (M+H)+

186	181	Ethyl 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 685.3 (M+H)+
187	181	Ethyl [4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]acetate	MS (ESI+) m/z: 671.3 (M+H)+

[0360]

[Table 31]

REx	PREx	Chemical Name	Data
188	181	Ethyl 4-fluoro-1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 674.8 (M+H)+
189	45	Ethyl [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperazin-1-yl]acetate	MS (ESI+) m/z: 670.3 (M+H)+

190	181	Methyl N-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-4-yl]-N-methylglycinate	MS (ESI+) m/z: 683.9 (M+H)+
191	181	Ethyl [4-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]acetate	MS (ESI+) m/z: 652.8 (M+H)+

[0361]

[Table 32]

REx	PREx	Chemical Name	Data
192	46	Ethyl 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 883.9 (M+H)+
193	45	Ethyl [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-4-hydroxypiperidin-1-yl]acetate	MS (ESI+) m/z: 684.3 (M+H)+

194	181	Methyl 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-oxopiperazin-1-yl]propanoate	MS (ESI+) m/z: 685.8 (M+H)+
195	181	Ethyl 3-[4-(5-{5-[2-fluoro-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 686.3 (M+H)+

[0362]

[Table 33]

REx	PREx	Chemical Name	Data
196	181	Ethyl [4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetate	MS (ESI+) m/z: 685.9 (M+H)+
197	181	Ethyl 3-[(2S)-4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 700.0 (M+H)+

198	181	Methyl 4-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoate	MS (ESI+) m/z: 685.6 (M+H)+
199	181	Ethyl N-[1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]glycinate	MS (ESI+) m/z: 685.9 (M+H)+
200	181	Methyl {[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 670.9 (M+H)+

[0363]

[Table 34]

REx	PREx	Chemical Name	Data
201	181	Methyl {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 699.9 (M+H)+
202	181	Ethyl N-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-4-yl]glycinate	MS (ESI+) m/z: 683.9 (M+H)+

203	181	Ethyl [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-1,4-diazepan-1-yl]acetate	MS (ESI+) m/z: 684.5 (M+H)+
204	181	Ethyl [4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetate	MS (ESI+) m/z: 673.9 (M+H)+
205	181	Ethyl [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetate	MS (ESI+) m/z: 723.0 (M+H)+

[0364]

[Table 35]

REx	PREx	Chemical Name	Data
206	181	Ethyl 3-[(2S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 727.0 (M+H)+

207	45	Ethyl 3-[4-(5-{7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[3-fluoro-5-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 713.5 (M+H)+
208	45	Ethyl 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 743.5 (M+H)+
209	181	Methyl {[1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 709.4 (M+H)+

[0365]

[Table 36]

REx	PREx	Chemical Name	Data
210	181	Ethyl 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 736.9 (M+H)+

211	49	Ethyl 1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 693.9 (M+H)+
212	181	Ethyl 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 665.9 (M+H)+
213	181	Ethyl 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 692.0 (M+H)+

[0366]

[Table 37]

REx	PREx	Chemical Name	Data
214	181	Ethyl 1-(4-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 719.9 (M+H)+
215	43	Ethyl 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 696.0 (M+H)+

216	43	Ethyl 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 667.9 (M+H)+
217	43	Ethyl 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 692.0 (M+H)+
218	46	Ethyl 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 714.0 (M+H)+

[0367]

[Table 38]

REx	PREx	Chemical Name	Data
219	43	Ethyl 1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 679.9 (M+H)+

220	43	Ethyl 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 698.0 (M+H)+
221	43	Ethyl 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 671.9 (M+H)+
222	43	Ethyl 1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 667.9 (M+H)+
223	43	Ethyl 1-(5-{5-[3-ethoxy-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 696.9 (M+H)+

[0368]

[Table 39]

REx	PREx	Chemical Name	Data
224	46	Ethyl 1-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 713.9 (M+H)+

225	43	Ethyl 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 711.9 (M+H)+
226	43	Ethyl 1-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 709.8 (M+H)+
227	43	Ethyl 1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 679.8 (M+H)+

[0369]

[Table 40]

REx	PREx	Chemical Name	Data
228	43	Ethyl 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 693.8 (M+H)+

229	43	Ethyl 1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 707.9 (M+H)+
230	43	Ethyl 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 711.9 (M+H)+
231	43	Ethyl 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 705.9 (M+H)+

[0370]

[Table 41]

REx	PREx	Chemical Name	Data
232	45	Ethyl 1-(4-{7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 709.6 (M+H)+
233	45	Ethyl 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(ethyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 721.8 (M+H)+

234	46	Ethyl 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 699.8 (M+H)+
235	46	Ethyl 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-methylphenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 695.8 (M+H)+

[0371]

[Table 42]

REx	PREx	Chemical Name	Data
236	50	Ethyl 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 780.8 (M+H)+
237	49	Ethyl 1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[6-propyl-5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 681.9 (M+H)+

238	45	Ethyl 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 699.9 (M+H)+
239	45	Ethyl 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 727.0 (M+H)+

[0372]

[Table 43]

REx	PREx	Chemical Name	Data
240	49	Ethyl 3-[4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 699.4 (M+H)+
241	181	Ethyl 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 696.9 (M+H)+

242	181	Ethyl 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 695.0 (M+H)+
243	181	Ethyl 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 711.0 (M+H)+

[0373]

[Table 44]

REx	PREx	Chemical Name	Data
244	181	Methyl {[1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 683.9 (M+H)+
245	45	Methyl {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 713.4 (M+H)+

246	49	Ethyl 3-[4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z; 750.9 (M+H)+
247	49	Ethyl 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z; 723.0 (M+H)+

[0374]

[Table 45]

REx	PREx	Chemical Name	Data
248	46	Ethyl 3-[4-(4-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 697.4 (M+H)+
249	49	Ethyl 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 700.9 (M+H)+
250	46	Ethyl 3-[(2S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 715.0 (M+H)+

251	181	Ethyl 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoate	MS (ESI+) m/z: 699.9 (M+H)+

[0375]

[Table 46]

REx	PREx	Chemical Name	Data
252	181	Ethyl 3-[4-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 721.0 (M+H)+
253	181	Ethyl 3-[4-(4-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 749.0 (M+H)+
254	181	Ethyl 3-[(2S)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 737.0 (M+H)+

255	181	Ethyl 3-[(2S)-4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 764.9 (M+H)+

[0376]

[Table 47]

REx	PREx	Chemical Name	Data
256	181	Methyl [1-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 737.9 (M+H)+
257	46	Ethyl 3-[4-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 699.0 (M+H)+
258	46	Ethyl 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 688.0 (M+H)+
259	46	Ethyl 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{(1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 699.9 (M+H)+

[0377]

[Table 48]

REx	PREx	Chemical Name	Data
260	46	Methyl {[1-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 686.9 (M+H)+
261	181	Ethyl 3-[(3R)-4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 764.9 (M+H)+
262	48	Ethyl 2,2-difuloro-3-{[1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]amino}propanoate	MS (ESI+) m/z: 735.9 (M+H)+
263	181	Ethyl N-[(3S,4R)-1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-fluoropiperidin-4-yl]glycinate	MS (ESI+) m/z: 741.0 (M+H)+

[0378]

[Table 49]

REx	PREx	Chemical Name	Data

264	43	Ethyl 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoate	MS (ESI+) m/z: 723.0 (M+H)+
265	46	Ethyl 3-[(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 726.4 (M+H)+
266	46	Methyl {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 687.9 (M+H)+
267	46	Ethyl 3-[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 713.9 (M+H)+

[0379]

[Table 50]

REx	PREx	Chemical Name	Data

268	43	Ethyl N-[(3S,4R)-1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-fluoropiperidin-4-yl]-N-methylglycinate	MS (ESI+) m/z: 755.0 (M+H)+
269	45	Ethyl 3-[4-(5-{7-[{[1-(butoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[3-fluoro-5-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 742.0 (M+H)+
270	43	Ethyl 3-[(2R,6S)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 729.0 (M+H)+
271	43	Ethyl 3-[(2R,6S)-4-(5-{5-[3,5-bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 778.0 (M+H)+

[0380]

[Table 51]

REx	PREx	Chemical Name	Data

272	43	Methyl {[1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 714.0 (M+H)+
273	43	Ethyl 3-[(2R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 737.0 (M+H)+
274	46	Ethyl 3-[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 687.9 (M+H)+
275	43	Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 710.0 (M+H)+

[0381]

[Table 52]

REx	PREx	Chemical Name	Data

276	45	Ethyl 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 727.0 (M+H)+
277	45	Ethyl 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 715.0 (M+H)+
278	45	Ethyl 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 723.0 (M+H)+
279	45	Ethyl 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 711.0 (M+H)+

[0382]

[Table 53]

REx	PREx	Chemical Name	Data

280	45	Ethyl 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 727.0 (M+H)+
281	45	Ethyl 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 723.0 (M+H)+
282	45	Ethyl 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 715.0 (M+H)+
283	45	Ethyl 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 711.0 (M+H)+

[0383]

[Table 54]

REx	PREx	Chemical Name	Data

284	46	Ethyl [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 700.0 (M+H)+
285	43	Ethyl 3-[(2R,6S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 741.0 (M+H)+
286	43	Ethyl {[(1R,3r,5S)-8-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 739.7 (M+H)+
287	43	Ethyl {[(1R,3r,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 749.4 (M+H)+

[0384]

[Table 55]

REx	PREx	Chemical Name	Data

288	45	Methyl [4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazine-1-sulfonyl]acetate	MS (ESI+) m/z: 758.4 (M+H)+
289	46	Ethyl [(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 701.0 (M+H)+
290	46	Ethyl [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 674.0 (M+H)+
291	46	Ethyl [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 685.9 (M+H)+

[0385]

[Table 56]

REx	PREx	Chemical Name	Data

292	46	Ethyl[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 700.0 (M+H)+
293	45	Ethyl 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 737.0 (M+H)+
294	43	Ethyl 3-[(2R,6S)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 755.1 (M+H)+
295	43	Ethyl{[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3,3-dimethylpiperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 752.0 (M+H)+

[0386]

[Table 57]

REx	PREx	Chemical Name	Data

296	45	Ethyl 1-(4-{5-[6-cyano-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 676.4 (M+H)+
297	46	Ethyl 3-[(2R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 741.0 (M+H)+
298	46	Ethyl [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 727.0 (M+H)+
299	43	Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 738.0 (M+H)+

[0387]

[Table 58]

REx	PREx	Chemical Name	Data

300	43	Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-4-methylpiperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 738.0 (M+H)+
301	43	Ethyl {[(1R,3r,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 764.0 (M+H)+
302	43	Ethyl{[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-4-methylpiperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 728.0 (M+H)+
303	43	Ethyl 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 706.0 (M+H)+

[0388]

[Table 59]

REx	PREx	Chemical Name	Data

304	45	Ethyl 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 741.0 (M+H)+
305	45	Ethyl 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 741.0 (M+H)+
306	43	Ethyl 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate	MS (ESI+) m/z: 737.0 (M+H)+
307	46	Ethyl 1-(5-{5-[4-cyclopropyl-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 692.9 (M+H)+

[0389]

[Table 60]

REx	PREx	Chemical Name	Data

308	46	Ethyl 1-(4-{5-[4-cyclopropyl-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate	MS (ESI+) m/z: 690.9 (M+H)+
309	43	Ethyl {[1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 723.9 (M+H)+
310	43	Ethyl 3-[(3R)-4-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 736.9 (M+H)+
311	43	Ethyl {[(1R,3s,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 763.9 (M+H)+

[0390]

[Table 61]

REx	PREx	Chemical Name	Data

312	43	Ethyl 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 750.9 (M+H)+
313	49	Ethyl 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 735.9 (M+H)+
314	46	Ethyl [(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 736.3 (M+H)+
315	46	Ethyl [(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate	MS (ESI+) m/z: 740.9 (M+H)+

[0391]

[Table 62]

REx	PREx	Chemical Name	Data

316	43	Ethyl 3-[4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 754.9 (M+H)+
317	43	Ethyl 3-[(2R,6S)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 764.9 (M+H)+
318	43	Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3,3-dimethylpiperidin-4-yl]oxy}acetate	MS (ESI+) m/z: 765.9 (M+H)+
319	43	Ethyl 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-(ethyl{[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate	MS (ESI+) m/z: 750.9 (M+H)+

[0392]

[Table 63]

REx	PREx	Chemical Name	Data

320	43	Ethyl {[(1R,3s,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate	MS (ESI+) m/z: 753.5 (M+H)+
321	43	Ethyl 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate	MS (ESI+) m/z: 707.9 (M+H)+
322	43	Ethyl {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]sulfanyl}acetate	MS (ESI+) m/z: 739.8 (M+H)+
323	43	Ethyl {[1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]sulfanyl}acetate	MS (ESI+) m/z: 729.8 (M+H)+

[0393]

[Table 64]

REx	PREx	Chemical Name	Data

324	43	Ethyl [4-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 711.8 (M+H)+
325	43	Ethyl [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 721.8 (M+H)+
326	43	Ethyl 3-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]propanoate	MS (ESI+) m/z: 698.6 (M+H)+
327	43	Ethyl [4-(3-chloro-4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate	MS (ESI+) m/z: 755.5 (M+H)+

[0394]

[Table 65]

REx	PREx	Chemical Name	Data
328	43	Ethyl 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]propanoate	MS (ESI+) m/z: 735.5 (M+H)+

329	43	Ethyl 3-[(1R,3s,5S)-3-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)-8-azabicyclo[3.2.1]octan-8-yl]propanoate	MS (ESI+) m/z: 761.5 (M+H)+
330	61	[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]acetonitrile	MS (ESI+) m/z: 624.9 (M+H)+
331	61	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl}piperazin-1-yl]propanenitrile	MS (ESI+) m/z: 638.9 (M+H)+

[0395]

[Table 66]

Ex	PEx	Chemical Name
1	1	1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
2	2	1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
3	3	1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

4	4	{[1-(5-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetic acid
5	5	3-[4-(5-{5-[2-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid
6	6	3-[4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid
7	7	3-[(3R)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid

[0396]

[Table 67]

Ex	PEx	Chemical Name
8	8	3-[(2S)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoic acid
9	9	1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-({[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
10	10	[4-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenoxy)piperidin-1-yl]acetic acid
11	11	1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid dihydrochloride

12	12	3-[4-Fluoro-4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperidin-1-yl]propanoic acid trihydrochloride
13	13	3-[4-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid dihydrochloride

[0397]

[Table 68]

Ex	PEx	Chemical Name
14	14	Sodium 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
15	15	Sodium {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate
16	16	Sodium 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
17	17	Sodium [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate
18	18	1-(4-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
19	19	[4-(6-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidin-1-yl]acetic acid trihydrochloride

[0398]

[Table 69]

Ex	PEx	Chemical Name
20	20	3-[(3R)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
21	21	1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
22	22	Sodium [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]acetate
23	23	5-[3-Fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-{5-[4-(1H-tetrazol-5-yl)piperidin-1-yl]pyrazin-2-yl}-1H-imidazo[4,5-b]pyridin-7-amine
24	24	8-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-2,8-diazaspiro[4.5]decan-3-one
25	25	1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-N-(methansulfonyl)piperidine-4-carboxamide
26	26	[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]acetic acid

[0399]

[Table 70]

Ex	PEx	Chemical Name

27	27	2-[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride
28	28	1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperidine-4-carboxylic acid
29	29	{4-[1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethyl]piperazin-1-yl}acetic acid trihydrochloride
30	9	4-Hydroxy-1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
31	7	8-(4-{7-[{[1-(Methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3-carboxylic acid
32	4	1-(5-{7-[{[1-(Methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[4-methoxy-3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
33	7	8-(4-{7-[{[1-(Methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3-carboxylic acid

[0400]

[Table 71]

Ex	PEx	Chemical Name
34	1	1-(4-{7-[{[1-(Methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)pyrrolidine-3-carboxylic acid
35	9	{4-[(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)methyl]piperazin-1-yl}acetic acid

36	10	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid
37	10	[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]acetic acid
38	10	4-Fluoro-1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
39	9	[4-(6-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperazin-1-yl]acetic acid
40	10	N-[1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-4-yl]-N-methylglycine

[0401]

[Table 72]

Ex	PEx	Chemical Name
41	8	[4-(4-{7-[{[1-(Methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]acetic acid
42	1	1-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
43	21	[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-4-hydroxypiperidin-1-yl]acetic acid

44	7	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-oxopiperazin-1-yl]propanoic acid
45	7	3-[4-(5-{5-[2-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid
46	10	[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetic acid
47	10	3-[(2S)-4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoic acid

[0402]

[Table 73]

Ex	PEx	Chemical Name
48	10	4-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoic acid
49	10	N-[1-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]glycine
50	10	{[1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-4-yl]oxy}acetic acid
51	10	{[1-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetic acid

52	10	N-[1-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-4-yl]glycine
53	10	[4-(6-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-1,4-diazepan-1-yl]acetic acid
54	10	[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetic acid

[0403]

[Table 74]

Ex	PEx	Chemical Name
55	10	[4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetic acid
56	10	3-[(2S)-4-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoic acid
57	9	3-[4-(5-{7-[{[1-(Ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[3-fluoro-5-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid
58	9	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid
59	10	{[1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetic acid

60	10	3-[(2S)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoic acid
61	1	1-(5-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

[0404]

[Table 75]

Ex	PEx	Chemical Name
62	10	1-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
63	10	1-(4-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
64	10	1-(4-{5-[5,6-Bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
65	1	1-(4-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
66	1	1-(4-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
67	1	1-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid

68	4	1-(4-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylic acid

[0405]

[Table 76]

Ex	PEx	Chemical Name
69	1	1-(5-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
70	1	1-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
71	1	1-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
72	1	1-(5-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
73	1	1-(5-{5-[3-Ethoxy-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
74	4	1-(4-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylic acid
75	1	1-(5-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

[0406]

[Table 77]

Ex	PEx	Chemical Name
76	1	1-(4-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
77	1	1-(5-{5-[5-Cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
78	1	1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
79	1	1-(5-{5-[5-Cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
80	1	1-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
81	10	1-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
82	7	1-(4-{7-[{[1-(Ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid

[0407]

[Table 78]

Ex	PEx	Chemical Name
83	7	1-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(ethyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

84	4	1-(4-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylic acid
85	10	1-(4-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-methylphenyl)piperidine-4-carboxylic acid
86	8	3-[(2S)-4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoic acid
87	1	1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[6-propyl-5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid
88	11	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid trihydrochloride
89	89	3-[4-(5-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid dihydrochloride

[0408]

[Table 79]

Ex	PEx	Chemical Name
90	89	3-[4-(5-{5-[4-Fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid trihydrochloride
91	15	Sodium 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

92	17	Sodium 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate
93	17	Sodium 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
94	17	Sodium {[1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
95	14	Sodium {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
96	14	Sodium 3-[4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

[0409]

[Table 80]

Ex	PEx	Chemical Name
97	14	Sodium 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate
98	89	3-[4-(4-{5-[4-Fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride
99	15	Sodium 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

100	15	Sodium 3-[(2S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
101	17	Sodium 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoate
102	17	Sodium 3-[4-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate
103	17	Sodium 3-[4-(4-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate

[0410]

[Table 81]

Ex	PEx	Chemical Name
104	17	Sodium 3-[(2S)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
105	17	Sodium 3-[(2S)-4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
106	17	Sodium [1-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
107	15	Sodium 3-[4-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoate

108	15	Sodium 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
109	109	Sodium 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate

[0411]

[Table 82]

Ex	PEx	Chemical Name
110	15	Sodium {[1-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
111	15	Sodium 3-[(3R)-4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
112	17	Sodium 2,2-difuloro-3-{[1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]amino}propanoate
113	17	Sodium {[(3S,4R)-1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-fluoropiperidin-4-yl]amino}acetate
114	15	Sodium 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoate

115	15	Sodium 3-[(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[0412]

[Table 83]

Ex	PEx	Chemical Name
116	15	Sodium {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
117	15	Sodium 3-[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
118	17	Sodium {[(3S,4R)-1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-fluoropiperidin-4-yl](methyl)amino}acetate
119	109	Sodium 3-[4-(5-{7-[{[1-(butoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[3-fluoro-5-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate
120	15	Sodium 3-[(2R,6S)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate
121	17	Sodium 3-[(2R,6S)-4-(5-{5-[3,5-bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate

[0413]

[Table 84]

Ex	PEx	Chemical Name
122	17	Sodium {[1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
123	15	Sodium 3-[(2R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
124	15	Sodium 3-[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
125	17	Sodium {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
126	14	Sodium 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
127	14	Sodium 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[0414]

[Table 85]

Ex	PEx	Chemical Name
128	14	Sodium 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

129	14	Sodium 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
130	14	Sodium 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
131	14	Sodium 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
132	14	Sodium 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
133	14	Sodium 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate

[0415]

[Table 86]

Ex	PEx	Chemical Name
134	15	Sodium [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
135	15	Sodium 3-[(2R,6S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate

136	15	Sodium {[(1R,3r,5S)-8-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate
137	15	Sodium {[(1R,3r,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate
138	109	Sodium [4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazine-1-sulfonyl]acetate
139	15	Sodium [(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate

[0416]

[Table 87]

Ex	PEx	Chemical Name
140	15	Sodium [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
141	15	Sodium [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
142	15	Sodium [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
143	14	Sodium 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate

144	15	Sodium 3-[(2R,6S)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate
145	15	Sodium {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3,3-dimethylpiperidin-4-yl]oxy}acetate

[0417]

[Table 88]

Ex	PEx	Chemical Name
146	109	Sodium 1-(4-{5-[6-cyano-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate
147	15	Sodium 3-[(2R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
148	15	Sodium [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
149	15	Sodium {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
150	15	Sodium {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-4-methylpiperidin-4-yl]oxy}acetate

151	15	Sodium {[(1R,3r,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate

[0418]

[Table 89]

Ex	PEx	Chemical Name
152	15	Sodium {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-4-methylpiperidin-4-yl]oxy}acetate
153	15	Sodium 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate
154	14	Sodium 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
155	14	Sodium 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
156	15	Sodium 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate
157	15	Sodium 1-(5-{5-[4-cyclopropyl-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylate

[0419]

[Table 90]

Ex	PEx	Chemical Name

158	15	Sodium 1-(4-{5-[4-cyclopropyl-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate
159	15	Sodium {[1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetate
160	15	Sodium 3-[(3R)-4-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate
161	15	Sodium {[(1R,3s,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate
162	15	Sodium 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate
163	109	Sodium 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-2-yl)-3-methylpiperazin-1-yl]propanoate

[0420]

[Table 91]

Ex	PEx	Chemical Name
164	15	Sodium [(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate

165	15	Sodium [(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
166	15	Sodium 3-[4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propanoate
167	15	Sodium 3-[(2R,6S)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propanoate
168	15	Sodium {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3,3-dimethylpiperidin-4-yl]oxy}acetate
169	17	Sodium 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-(ethyl{[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[0421]

[Table 92]

Ex	PEx	Chemical Name
170	17	Sodium {[(1R,3s,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetate
171	10	Sodium 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid

172	17	Sodium {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]sulfanyl}acetate
173	17	Sodium {[1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]sulfanyl}acetate
174	17	Sodium [4-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate
175	17	Sodium [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate
176	17	Sodium 3-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]propanoate

[0422]

[Table 93]

Ex	PEx	Chemical Name
177	17	Sodium [4-(3-chloro-4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]acetate
178	17	Sodium 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidin-1-yl]propanoate
179	17	Sodium 3-[(1R,3s,5S)-3-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)-8-azabicyclo[3.2.1]octan-8-yl]propanoate

180	18	[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]acetic acid
181	18	1-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
182	18	1-(4-{5-[3,5-Bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
183	18	1-(4-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid

[0423]

[Table 94]

Ex	PEx	Chemical Name
184	18	1-(4-{5-[2-Cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
185	18	1-(4-{5-[2-Ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid
186	19	{1-[(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)methyl]piperidin-4-yl}acetic acid dihydrochloride
187	19	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-2-yl)-4-hydroxypiperidin-1-yl]propanoic acid trihydrochloride

188	19	3-[4-(5-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid trihydrochloride
189	19	3-[4-(6-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperazin-1-yl]propanoic acid trihydrochloride
190	19	3-[4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid trihydrochloride

[0424]

[Table 95]

Ex	PEx	Chemical Name
191	19	3-[4-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride
192	19	3-[4-(4-{5-[6-Ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride
193	19	3-[4-(4-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propanoic acid dihydrochloride
194	20	Sodium 3-[4-(5-{5-[3,5-bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate
195	20	Sodium 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoate

196	20	Sodium 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propanoate
197	20	Sodium 3-[(3S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoate

[0425]

[Table 96]

Ex	PEx	Chemical Name
198	20	Sodium [(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
199	20	Sodium [(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
200	20	Sodium [(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate
201	20	Sodium 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]propanoate
202	20	Sodium [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate

203	20	Sodium [(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetate

[0426]

[Table 97]

Ex	PEx	Chemical Name
204	20	Sodium 1-(4-{5-[4-ethoxy-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate
205	20	Sodium 1-(4-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylate
206	20	Sodium 3-[(3R)-4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-3-methylpiperazin-1-yl]propanoate
207	20	Sodium 3-[(3R)-4-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-3-methylpiperazin-1-yl]propanoate
208	20	Sodium 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)-3-methylpiperazin-1-yl]propanoate
209	23	5-[3-Fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-(5-{4-[(1H-tetrazol-5-yl)methyl]piperazin-1-yl}pyrazin-2-yl)-1H-imidazo[4,5-b]pyridin-7-amine

[0427]

[Table 98]

Ex	PEx	Chemical Name
210	23	5-[3-Fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-(5-{4-[2-(1H-tetrazol-5-yl)ethyl]piperazin-1-yl}pyrazin-2-yl)-1H-imidazo[4,5-b]pyridin-7-amine
211	24	N-{2-[4-(5-{5-[6-Cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]ethyl}methansulfonamide
212	26	3-[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidin-1-yl]propanoic acid
213	28	[4-(4-{5-[3-Fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperazin-1-yl]acetic acid

[0428]

[Table 99]

Ex	Data
1	MS (ESI+) m/z: 643.9 (M+H)+
2	MS (ESI+) m/z: 669.9 (M+H)+
3	MS (ESI+) m/z: 679.4 (M+H)+
4	MS (ESI+) m/z: 695.9 (M+H)+
5	MS (ESI+) m/z: 698.5 (M+H)+
6	MS (ESI+) m/z: 708.9 (M+H)+
7	MS (ESI+) m/z: 722.8 (M+H)+
8	MS (ESI+) m/z: 752.8 (M+H)+
9	MS (ESI+) m/z: 655.7 (M+H)+
10	MS (ESI+) m/z: 712.1 (M+H)+
11	MS (ESI+) m/z: 655.9 (M+H)+ Elemental analysis value as $C_{32}H_{39}C_{12}F_3N_8O_4$ + $0.8H_2O$ Calculated (%) C: 51.80 H: 5.52 N: 15.10 Found (%) C: 51.83 H: 5.50 N:14.90
12	MS (ESI+) m/z: 673.3 (M+H)+

13	MS (ESI+) m/z: 684.4 (M+H)+ Elemental analysis value as $C_{33}H_{42}Cl_2F_3N_9O_4$ + 2.1H_2O Calculated (%) C: 49.90 H: 5.86 N: 15.87 Found (%) C: 49.79 H: 6.06 N: 15.49
14	MS (ESI+) m/z: 722.9 (M+H)+ Elemental analysis value as $C_{37}H_{45}F_3N_9NaO_3$ + 3H_2O Calculated (%) C: 55.70 H: 6.44 N: 15.80 Found (%) C: 55.92 H: 6.82 N: 15.53
15	MS (ESI+) m/z: 726.0 (M+H)+ Elemental analysis value as $C_{36}H_{42}F_3N_8NaO_5$ + 4H_2O Calculated (%) C: 52.81 H: 6.16 N:13.69 Found (%) C: 52.93 H: 5.76 N: 13.70
16	MS (ESI+) m/z: 723.0 (M+H)+ Elemental analysis value as $C_{37}H_{45}F_3N_9NaO_3$ + 3H_2O Calculated (%) C: 55.70 H: 6.44 N: 15.80 Found (%) C: 55.33 H: 6.29 N: 15.65

[0429]

[Table 100]

Ex	Data
17	MS (ESI+) m/z: 656.7 (M+H)+
18	MS (ESI+) m/z: 653.9 (M+H)+
19	MS (ESI+) m/z: 657.3 (M+H)+ Elemental analysis value as $C_{33}H_{36}F_4N_6O_4$•3HCl + 1.2H_2O Calculated (%) C: 50.32 H: 5.30 N: 10.67 Found (%) C: 50.37 H: 5.49 N: 10.56
20	MS (ESI+) m/z: 709.0 (M+H)+ Elemental analysis value as $C_{36}H_{43}F_3N_9NaO_3$ + 3.9H_2O Calculated (%) C: 54.05 H: 6.40 N: 15.76 Found (%) C: 53.95 H: 6.15 N: 15.54
21	MS (ESI+) m/z: 614.8 (M+H)+
22	MS (ESI+) m/z: 698.0 (M+H)+ Elemental analysis value as $C_{35}H_{39}F_4N_8NaO_3$ + 3.8H_2O Calculated (%) C: 53.40 H: 5.97 N: 14.24 Found (%) C: 53.14 H: 5.66 N: 14.09
23	MS (ESI+) m/z: 652.7 (M+H)+
24	MS (ESI+) m/z: 651.3 (M+H)+
25	MS (ESI+) m/z: 756.7 (M+H)+
26	MS (ESI+) m/z: 640.3 (M+H)+
27	MS (ESI+) m/z: 655.3 (M+H)+
28	MS (ESI+) m/z: 654.7 (M+H)+
29	MS (ESI+) m/z: 669.4 (M+H)+
30	MS (ESI+) m/z: 626.3 (M+H)+

31	MS (ESI+) m/z: 663.3 (M+H)+
32	MS (ESI+) m/z: 640.8 (M+H)+
33	MS (ESI+) m/z: 664.8 (M+H)+
34	MS (ESI+) m/z: 594.5 (M+H)+
35	MS (ESI+) m/z: 655.3 (M+H)+
36	MS (ESI+) m/z: 657.3 (M+H)+
37	MS (ESI+) m/z: 643.8 (M+H)+
38	MS (ESI+) m/z: 646.7 (M+H)+

[0430]

[Table 101]

Ex	Data
39	MS (ESI+) m/z: 642.8 (M+H)+
40	MS (ESI+) m/z: 669.9 (M+H)+
41	MS (ESI+) m/z: 624.8 (M+H)+
42	MS (ESI+) m/z: 655.8 (M+H)+
43	MS (ESI+) m/z: 656.3 (M+H)+
44	MS (ESI+) m/z: 671.3 (M+H)+
45	MS (ESI+) m/z: 684.8 (M+H)+
46	MS (ESI+) m/z: 657.9 (M+H)+
47	MS (ESI+) m/z: 671.6 (M+H)+
48	MS (ESI+) m/z: 671.9 (M+H)+
49	MS (ESI+) m/z: 657.8 (M+H)+
50	MS (ESI+) m/z: 656.4 (M+H)+
51	MS (ESI+) m/z: 685.3 (M+H)+
52	MS (ESI+) m/z: 655.4 (M+H)+
53	MS (ESI+) m/z: 656.9 (M+H)+
54	MS (ESI+) m/z: 645.9 (M+H)+
55	MS (ESI+) m/z: 694.9 (M+H)+
56	MS (ESI+) m/z: 698.9 (M+H)+
57	MS (ESI+) m/z: 685.4 (M+H)+
58	MS (ESI+) m/z: 715.5 (M+H)+
59	MS (ESI+) m/z: 695.4 (M+H)+
60	MS (ESI+) m/z: 708.9 (M+H)+
61	MS (ESI+) m/z: 685.9 (M+H)+
62	MS (ESI+) m/z: 637.9 (M+H)+
63	MS (ESI+) m/z: 663.9 (M+H)+
64	MS (ESI+) m/z: 691.9 (M+H)+
65	MS (ESI+) m/z: 667.9 (M+H)+
66	MS (ESI+) m/z: 649.9 (M+H)+

67	MS (ESI+) m/z: 663.9 (M+H)+
68	MS (ESI+) m/z: 685.9 (M+H)+

[0431]

[Table 102]

Ex	Data
69	MS (ESI+) m/z: 651.9 (M+H)+
70	MS (ESI+) m/z: 669.9 (M+H)+
71	MS (ESI+) m/z: 643.9 (M+H)+
72	MS (ESI+) m/z: 639.9 (M+H)+
73	MS (ESI+) m/z: 668.8 (M+H)+
74	MS (ESI+) m/z: 685.8 (M+H)+
75	MS (ESI+) m/z: 683.8 (M+H)+
76	MS (ESI+) m/z: 681.8 (M+H)+
77	MS (ESI+) m/z: 651.8 (M+H)+
78	MS (ESI+) m/z: 665.8 (M+H)+
79	MS (ESI+) m/z: 679.8 (M+H)+
80	MS (ESI+) m/z: 683.8 (M+H)+
81	MS (ESI+) m/z: 677.9 (M+H)+
82	MS (ESI+) m/z: 681.6 (M+H)+
83	MS (ESI+) m/z: 693.8 (M+H)+
84	MS (ESI+) m/z: 671.8 (M+H)+
85	MS (ESI+) m/z: 667.8 (M+H)+
86	MS (ESI+) m/z: 753.2 (M+H)+
87	MS (ESI+) m/z: 653.9 (M+H)+
88	MS (ESI+) m/z: 671.6 (M+H)+
89	MS (ESI+) m/z: 698.9 (M+H)+ Elemental analysis value as $C_{34}H_{44}Cl_2F_3N_9O_4$ + $3.5H_2O$ Calculated (%) C: 48.98 H: 6.17 N: 15.12 Found (%) C: 48.74 H: 5.86 N: 14.94
90	MS(ESI+)m/z 671.3 (M+H)+ Elemental analysis value as $C_{33}H_{41}Cl_3F_4N_8O_3$ + $0.5H_2O$ Calculated (%) C: 50.23 H: 5.37 N: 14.20 Found (%) C: 49.98 H: 5.72 N: 13.94

[432]

[Table 103]

Ex	Data
91	MS (ESI+) m/z: 668.9 (M+H)+ Elemental analysis value as $C_{33}H_{39}F_3N_9NaO_3$ + $3.5H_2O$ Calculated (%) C: 52.65 H: 6.16 N:16.75 Found (%) C: 52.60 H: 6.18 N:16.54

92	MS (ESI+) m/z: 667.0 (M+H)+
93	MS (ESI+) m/z: 683.0 (M+H)+
94	MS (ESI+) m/z: 669.9 (M+H)+
95	MS (ESI+) m/z: 699.9 (M+H)+
96	MS (ESI+) m/z: 722.9 (M+H)+
97	MS (ESI+) m/z: 694.9 (M+H)+
98	MS (ESI+) m/z: 669.9 (M+H)+ Elemental analysis value as $C_{35}H_{42}Cl_2F_4N_6O_3$ + $0.5H_2O$ Calculated (%) C: 56.00 H: 5.77 N:11.20 Found (%) C: 55.92 H: 5.57 N:11.15
99	MS (ESI+) m/z: 672.9 (M+H)+
100	MS (ESI+) m/z: 682.9 (M+H)+
101	MS (ESI+) m/z: 671.9 (M+H)+
102	MS (ESI+) m/z: 693.0 (M+H)+
103	MS (ESI+) m/z: 720.9 (M+H)+
104	MS (ESI+) m/z: 709.0 (M+H)+
105	MS (ESI+) m/z: 736.9 (M+H)+
106	MS (ESI+) m/z: 723.9 (M+H)+
107	MS (ESI+) m/z: 670.3 (M+H)+
108	MS (ESI+) m/z: 659.9 (M+H)+
109	MS (ESI+) m/z: 671.9 (M+H)+
110	MS (ESI+) m/z: 672.9 (M+H)+
111	MS (ESI+) m/z: 736.9 (M+H)+
112	MS (ESI+) m/z: 707.9 (M+H)+
113	MS (ESI+) m/z: 713.0 (M+H)+
114	MS (ESI+) m/z: 695.0 (M+H)+

[433]

[Table 104]

Ex	Data
115	MS (ESI+) m/z: 698.9 (M+H)+ Elemental analysis value as $C_{34}H_{41}F_3N_9NaO_4$ + $2.5H_2O$ Calculated (%) C: 53.40 H: 6.06 N:16.48 Found (%) C: 53.34 H: 6.30 N:16.33
116	MS (ESI+) m/z: 673.9 (M+H)+ Elemental analysis value as $C_{32}H_{38}F_3N_8NaO_5$ + $3.5H_2O$ Calculated (%) C: 50.72 H: 5.99 N: 14.79 Found (%) C: 50.72 H: 5.85 N: 14.65
117	MS (ESI+) m/z: 685.9 (M+H)+
118	MS (ESI+) m/z: 727.0 (M+H)+

119	MS (ESI+) m/z: 714.0 (M+H)+ Elemental analysis value as $C_{36}H_{43}F_4N_8NaO_3$ + 4.5H_2O Calculated (%) C: 53.00 H: 6.42 N: 13.74 Found (%) C: 52.66 H: 6.27 N: 13.64
120	MS (ESI+) m/z: 701.0 (M+H)+
121	MS (ESI+) m/z: 749.9 (M+H)+
122	MS (ESI+) m/z: 699.9 (M+H)+
123	MS (ESI+) m/z: 708.9 (M+H)+ Elemental analysis value as $C_{36}H_{43}F_3N_9NaO_3$ + 2.8H_2O Calculated (%) C: 55.42 H: 6.28 N:16.16 Found (%) C: 55.41 H: 6.59 N:16.17
124	MS (ESI+) m/z: 659.9 (M+H)+ Elemental analysis value as $C_{32}H_{37}F_4N_8NaO_3$+5H_2O Calculated (%) C: 49.87 H: 6.15 N: 14.54 Found (%) C: 49.52 H: 5.76 N: 14.43
125	MS (ESI+) m/z: 682.0 (M+H)+
126	MS (ESI+) m/z: 699.0 (M+H)+
127	MS (ESI+) m/z: 687.0 (M+H)+
128	MS (ESI+) m/z: 695.0 (M+H)+
129	MS (ESI+) m/z: 683.0 (M+H)+
130	MS (ESI+) m/z: 699.0 (M+H)+

[434]

[Table 105]

Ex	Data
131	MS (ESI+) m/z: 695.0 (M+H)+
132	MS (ESI+) m/z: 687.0 (M+H)+
133	MS (ESI+) m/z: 683.0 (M+H)+
134	MS (ESI+) m/z: 672.4 (M+H)+ Elemental analysis value as $C_{32}H_{39}F_3N_9NaO_4$ + 4.5H_2O Calculated (%) C: 49.61 H: 6.25 N:16.27 Found (%) C: 49.52 H: 5.89 N:16.28
135	MS (ESI+) m/z: 713.0 (M+H)+
136	MS (ESI+) m/z: 712.0 (M+H)+
137	MS (ESI+) m/z: 722.0 (M+H)+
138	MS (ESI+) m/z: 744.5 (M+H)+ Elemental analysis value as $C_{34}H_{39}F_3N_9NaO_5S$ + 3H_2O Calculated (%) C: 49.81 H: 5.53 N: 15.38 Found (%) C: 49.66 H: 5.39 N: 15.30
139	MS (ESI+) m/z: 673.0 (M+H)+
140	MS (ESI+) m/z: 645.9 (M+H)+
141	MS (ESI+) m/z: 657.9 (M+H)+
142	MS (ESI+) m/z: 671.9 (M+H)+

143	MS (ESI+) m/z: 709.0 (M+H)+
144	MS (ESI+) m/z: 727.0 (M+H)+
145	MS (ESI+) m/z: 724.0 (M+H)+
146	MS (ESI+) m/z: 648.9 (M+H)+
147	MS (ESI+) m/z: 713.0 (M+H)+
148	MS (ESI+) m/z: 699.0 (M+H)+
149	MS (ESI+) m/z: 709.8 (M+H)+
150	MS (ESI+) m/z: 709.8 (M+H)+
151	MS (ESI+) m/z: 736.0 (M+H)+
152	MS (ESI+) m/z: 700.0 (M+H)+
153	MS (ESI+) m/z: 677.9 (M+H)+
154	MS (ESI+) m/z: 712.9 (M+H)+

[435]

[Table 106]

Ex	Data
155	MS (ESI+) m/z: 712.8 (M+H)+
156	MS (ESI+) m/z: 708.9 (M+H)+
157	MS (ESI+) m/z: 664.8 (M+H)+
158	MS (ESI+) m/z: 662.8 (M+H)+
159	MS (ESI+) m/z: 695.8 (M+H)+
160	MS (ESI+) m/z: 708.9 (M+H)+
161	MS (ESI+) m/z: 735.8 (M+H)+
162	MS (ESI+) m/z: 722.8 (M+H)+
163	MS (ESI+) m/z: 707.9 (M+H)+ Elemental analysis value as $C_{37}H_{44}F_3N_8NaO_3$ + $3.4H_2O$ Calculated (%) C: 56.25 H: 6.48 N: 14.18 Found (%) C: 56.10 H: 6.10 N: 13.96
164	MS (ESI+) m/z: 708.8 (M+H)+
165	MS (ESI+) m/z: 712.9 (M+H)+
166	MS (ESI+) m/z: 726.9 (M+H)+
167	MS (ESI+) m/z: 736.8 (M+H)+
168	MS (ESI+) m/z: 737.8 (M+H)+
169	MS (ESI+) m/z: 722.9 (M+H)+
170	MS (ESI+) m/z: 725.9 (M+H)+
171	MS (ESI+) m/z: 679.8 (M+H)+
172	MS (ESI+) m/z: 711.8 (M+H)+
173	MS (ESI+) m/z: 701.7 (M+H)+
174	MS (ESI+) m/z: 683.6 (M+H)+
175	MS (ESI+) m/z: 693.9 (M+H)+
176	MS (ESI+) m/z: 670.5 (M+H)+
177	MS (ESI+) m/z: 727.5 (M+H)+

178	MS (ESI+) m/z: 707.5 (M+H)+
179	MS (ESI+) m/z: 733.5 (M+H)+
180	MS (ESI+) m/z: 641.3 (M+H)+
181	MS (ESI+) m/z: 649.9 (M+H)+

[436]

[Table 107]

Ex	Data
182	MS (ESI+) m/z: 690.9 (M+H)+
183	MS (ESI+) m/z: 668.9 (M+H)+
184	MS (ESI+) m/z: 637.9 (M+H)+
185	MS (ESI+) m/z: 641.9 (M+H)+
186	MS (ESI+) m/z: 654.3 (M+H)+
187	MS (ESI+) m/z: 671.3 (M+H)+
188	MS (ESI+) m/z: 645.5 (M+H)+
189	MS (ESI+) m/z: 684.9 (M+H)+
190	MS (ESI+) m/z: 694.9 (M+H)+
191	MS (ESI+) m/z: 693.0 (M+H)+ Elemental analysis value as $C_{37}H_{44}F_3N_7O_3 \cdot 2HCl + 2.6H_2O$ Calculated (%) C: 54.67 H: 6.36 N:12.08 Found (%) C: 54.77 H: 6.47 N:11.96
192	MS (ESI+) m/z: 711.0 (M+H)+ Elemental analysis value as $C_{37}H_{46}F_3N_7O_4 \cdot 2HCl + 2.7H_2O$ Calculated (%) C: 53.45 H: 6.47 N:11.79 Found (%) C: 53.48 H: 6.40 N:11.74
193	MS (ESI+) m/z: 707.0 (M+H)+ Elemental analysis value as $C_{38}H_{46}F_3N_7O_3 \cdot 2HCl + 2.5H_2O$ Calculated (%) C: 55.40 H: 6.49 N:11.90 Found (%) C: 55.34 H: 6.34 N:11.79
194	MS (ESI+) m/z: 722.0 (M+H)+
195	MS (ESI+) m/z: 680.9 (M+H)+ Elemental analysis value as $C_{34}H_{39}F_3N_9NaO_3 + 2.3H_2O$ Calculated (%) C: 54.95 H: 5.91 N:16.96 Found (%) C: 55.29 H: 6.27 N:16.82
196	MS (ESI+) m/z: 695.0 (M+H)+ Elemental analysis value as $C_{35}H_{41}F_3N_9NaO_3 + 2.6H_2O$ Calculated (%) C: 55.13 H: 6.11 N:16.53 Found (%) C: 55.42 H: 6.41 N:16.32

[437]

[Table 108]

Ex	Data
197	MS (ESI+) m/z: 694.9 (M+H)+

198	MS (ESI+) m/z: 709.0 (M+H)+ Elemental analysis value as $C_{36}H_{43}F_3N_9NaO_3$ + 4.1H_2O Calculated (%) C: 53.80 H: 6.42 N: 15.69 Found (%) C: 53.50 H: 6.03 N: 15.47
199	MS (ESI+) m/z: 680.9 (M+H)+ Elemental analysis value as $C_{34}H_{39}F_3N_9NaO_3$ + 3.6H_2O Calculated (%) C: 53.27 H: 6.08 N:16.45 Found (%) C: 53.08 H: 5.82 N:16.20
200	MS (ESI+) m/z: 680.9 (M+H)+ Elemental analysis value as $C_{34}H_{39}F_3N_9NaO_3$ + 4.1H_2O Calculated (%) C: 52.65 H: 6.13 N:16.25 Found (%) C: 52.31 H: 5.80 N:16.09
201	MS (ESI+) m/z: 712.0 (M+H)+ Elemental analysis value as $C_{36}H_{41}F_4N_8NaO_3$ + 4.2H_2O Calculated (%) C: 53.49 H: 6.16 N: 13.86 Found (%) C: 53.25 H: 5.89 N: 13.70
202	MS (ESI+) m/z: 684.4 (M+H)+ Elemental analysis value as $C_{33}H_{39}F_3N_9NaO_4$+5H_2O Calculated (%) C: 49.81 H: 6.21 N: 15.84 Found (%) C: 49.96 H: 5.82 N: 15.92
203	MS (ESI+) m/z: 709.0 (M+H)+ Elemental analysis value as $C_{36}H_{43}F_3N_9NaO_3$ + 3.6H_2O Calculated (%) C: 54.29 H: 6.12 N: 15.80 Found (%) C: 54.41 H: 6.37 N: 15.86
204	MS (ESI+) m/z: 666.8 (M+H)+
205	MS (ESI+) m/z: 677.9 (M+H)+
206	MS (ESI+) m/z: 720.9 (M+H)+ Elemental analysis value as $C_{39}H_{47}F_3N_7NaO_3$ + 3.7H_2O Calculated (%) C:57.94 H: 6.78 N:12.13 Found (%) C:57.95 H: 6.74 N:12.00

[438]

[Table 109]

Ex	Data
207	MS (ESI+) m/z: 724.9 (M+H)+ Elemental analysis value as $C_{37}H_{45}F_3N_7NaO_3$ + 4H_2O Calculated (%) C: 56.70 H: 6.54 N:12.07 Found (%) C: 56.41 H: 6.78 N:12.45
208	MS (ESI+) m/z: 725.8 (M+H)+ Elemental analysis value as $C_{37}H_{43}F_4N_8NaO_3$ + 3.5H_2O Calculated (%) C: 54.88 H: 6.22 N: 13.84 Found (%) C: 54.80 H: 6.06 N: 13.68
209	MS (ESI+) m/z: 667.9 (M+H)+
210	MS (ESI+) m/z: 681.9 (M+H)+
211	MS (ESI+) m/z: 743.9 (M+H)+

212	MS (ESI+) m/z: 654.4 (M+H)+
213	MS (ESI+) m/z: 669.3 (M+H)+

[0439]

Biological test examples of the compounds of the present invention are described below.

[0440]

Pharmacological activity of each compound was evaluated in the following tests. Each compound may be referred to as "test compound" in the following descriptions.

[0441]

<Test Example 1: Evaluation of M3 PAM activity>

CHO-K1 cells in which human muscarinic M3 receptor gene (GenBank registered number: NM_000740.2) was transducted to express M3 receptor stably (hereinafter also referred as "M3R expressing cells"), were subcultured in a growth medium at 37°C, 5% CO_2. For growth medium, alpha Modified Eagle Minimum Essential Medium (α-MEM, D8042, Sigma) containing final concentration of 10% inactivated fetal bovine serum (Cat. No.172012, Sigma), final concentration of 2 mM GlutaMAX® (Cat. No.35050, GIBCO), final concentration of 20 U/mL of penicillin and final concentration of 20 μg/mL of streptomycin (penicillin-streptomycin mixed solution, Cat. No.26253-84, NACALAI TESQUE, INC.), and final concentration of 0.2 mg/mL G418 (Cat. No.16513-26, NACALAI TESQUE, INC.) was used.

[0442]

On the day before measurement of intracellular Ca^{2+} concentration, the M3R expressing cells were suspended in the growth medium and seeded at 40,000 cells/well on a 96-well black plate with clear bottom (Cat. No.215006, Porvair Sciences). The M3R expressing cells seeded on the 96-well plate were cultured at 37°C, 5% CO_2.

[0443]

Intracellular Ca^{2+} concentration in the M3R expressing cells was measured using a calcium assay kit (Screen Quest® Fluo-8 Medium Removal Calcium Assay Kit, Cat. No.36309, AAT Bioquest) according to the attached instructions. On the day of the measurement, the growth

medium was removed, and 100 μL/well of loading buffer was added to the 96-well plate. After culturing at 37°C, 5% CO_2 for 30 minutes, the plate was left at room temperature for 30 minutes, whereby the M3R expressing cells were loaded with visible light-excited calcium indicator (Fluo-8®, AAT Bioquest). A buffer containing the calcium indicator was used as loading buffer. The buffer used was Hanks' Balanced Salt Solution (HBSS buffer) (pH7.4) containing final concentration of 20 mM HEPES (Cat. No.340-01371, Dojindo Molecular Technologies, Inc.) and final concentration of 2.5 mM probenecid (165-15472, Wako Pure Chemical Corporation). Hanks' Balanced Salt Solution was prepared by 10-fold dilution of 10×HBSS (Cat. No.14065-056, GIBCO) with ultrapure water.

[0444]

Then, the 96-well plate was placed in fluorescence screening system (FLIPR TETRA®, Molecular Devices) and fluorescence intensity, which depends on the intracellular Ca^{2+} concentration induced by a test compound was measured. In the measurement of fluorescence intensity, the excitation wavelength was in the range of 470-495 nm and the fluorescence wavelength was in the range of 515-575 nm.

[0445]

The test compound in a vehicle or a vehicle alone was added to the 96-well plate, and fluorescence intensity was measured for 2 minutes. HBSS buffer was used as a vehicle. The test compound was dissolved in dimethyl sulfoxide and added to the buffer. The final concentration of dimethyl sulfoxide was 2.5%. The final concentration of the test compound was varied within the range of 0-30 μM. Then, EC_{20} (20% Effective Concentration) of acetylcholine which results in about 20% of maximum activity was added, and fluorescence intensity was measured for 1 minute. The EC_{20} was about 10-30 nM.

[0446]

The fluorescence intensity Lb, where HBSS buffer alone instead of the same containing a test compound and final concentration of 100 μM acetylcholine were added, was defined as 100%. The fluorescence intensity La, where HBSS buffer alone instead of the same containing a test compound was added in presence of EC_{20}

acetylcholine, was defined as 0%. In addition, a fluorescence intensity was defined as Lc where a test compound was added. The enhancement ratio Gr (unit: %) of fluorescence intensity induced by a test compound was calculated according to the following equation (1). Based on the enhancement ratio Gr, M3 PAM activities of test compounds were evaluated.

[0447]

$$Gr = 100 \times (Lc-La)/(Lb-La) \quad (1)$$

[0448]

Based on the enhancement ratio Gr for each concentration of the test compound, EC_{50} (50% Effective Concentration) of the enhancement ratio Gr was estimated from the logistic equation, using statistics program (SASsystem, SAS Institute Japan). The results of the tests are shown in Tables 110 to 115. The lower EC_{50} of the enhancement ratio Gr was considered as the higher M3 PAM activity.

[0449]

[Table 110]

Test Compound (Example No.)	EC_{50} (nM)	Test Compound (Example No.)	EC_{50} (nM)
1	2.14	21	3.67
2	2.59	22	1.39
3	3.04	23	5.73
4	0.288	24	7.42
5	2.83	25	3.48
6	1.40	26	0.566
7	0.923	27	1.52
8	4.92	28	9.98
9	3.06	29	3.01
10	4.58	30	2.39
11	2.66	31	1.85
12	2.86	32	6.67

13	0.500	33	5.23
14	2.17	34	9.42
15	0.557	35	1.46
16	2.07	36	1.24
17	4.58	37	0.930
18	5.24	38	0.690
19	4.74	39	1.00
20	2.33	40	1.03

[0450]

[Table 111]

Test Compound (Example No.)	EC_{50}(nM)	Test Compound (Example No.)	EC_{50}(nM)
41	4.99	61	3.35
42	0.949	62	4.22
43	1.70	63	3.45
44	2.64	64	3.63
45	8.13	65	2.86
46	4.40	66	3.17
47	2.25	67	2.81
48	4.86	68	1.96
49	1.44	69	2.10
50	1.54	70	1.68
51	0.538	71	1.89
52	1.42	72	1.27
53	2.97	73	6.36
54	5.36	74	5.58
55	0.425	75	7.23

56	1.02	76	8.63
57	1.11	77	4.86
58	2.54	78	2.43
59	0.498	79	4.33
60	0.414	80	4.18

[0451]

[Table 112]

Test Compound (Example No.)	EC_{50}(nM)	Test Compound (Example No.)	EC_{50}(nM)
81	4.68	101	2.70
82	9.98	102	0.581
83	7.91	103	0.582
84	4.82	104	0.605
85	7.00	105	0.935
86	1.55	106	0.140
87	4.27	107	0.489
88	2.00	108	1.04
89	0.879	109	1.59
90	2.05	110	0.761
91	0.279	111	1.93
92	0.552	112	6.51
93	0.596	113	0.444
94	0.409	114	1.48
95	0.266	115	2.46
96	0.466	116	0.417
97	0.283	117	2.67
98	1.45	118	0.871

99	0.415	119	2.08
100	0.379	120	0.558

[0452]

[Table 113]

Test Compound (Example No.)	EC_{50} (nM)	Test Compound (Example No.)	EC_{50} (nM)
121	1.98	141	2.00
122	0.585	142	3.63
123	0.784	143	0.784
124	2.25	144	1.38
125	0.695	145	3.14
126	1.99	146	4.77
127	4.23	147	0.331
128	1.58	148	0.648
129	2.52	149	0.310
130	1.57	150	1.21
131	1.37	151	6.81
132	1.31	152	1.43
133	1.14	153	4.87
134	0.503	154	2.86
135	0.391	155	0.768
136	1.92	156	0.376
137	1.98	157	2.78
138	0.548	158	9.08
139	0.248	159	1.12
140	1.61	160	4.93

[0453]

[Table 114]

Test Compound (Example No.)	EC_{50} (nM)	Test Compound (Example No.)	EC_{50} (nM)
161	1.48	181	2.43
162	2.77	182	1.57
163	3.55	183	1.61
164	4.22	184	2.35
165	1.73	185	2.26
166	1.11	186	9.64
167	2.64	187	4.96
168	4.72	188	3.62
169	5.25	189	1.49
170	2.10	190	0.168
171	6.39	191	0.269
172	4.52	192	0.912
173	3.78	193	0.826
174	3.41	194	0.703
175	0.617	195	0.422
176	3.09	196	0.563
177	1.68	197	1.06
178	1.75	198	0.820
179	0.761	199	0.966
180	0.381	200	0.694

[0454]

[Table 115]

Test Compound (Example No.)	EC_{50} (nM)	Test Compound (Example No.)	EC_{50} (nM)
201	5.26	208	9.35

202	1.57	209	4.65
203	1.13	210	2.19
204	9.56	211	3.64
205	9.98	212	0.846
206	2.66	213	4.74
207	4.14		

[0455]
As shown in Tables 110 to 115, all of the test compounds were found to have a high M3 PAM activity.

[0456]
In the absence of acetylcholine, an addition of a test compound alone did not increase fluorescence intensity. This showed that the test compounds do not have M3 receptor agonist activity.

[0457]
<Test Example 2: Effect on the increase in intravesical pressure induced by electrical stimulation of the pelvic nerve in anesthetized rats>
For evaluation of in vivo effect on neurogenic bladder contraction, effects of the test compounds on the increase in intravesical pressure induced by electrical stimulation of the pelvic nerve in rats were determined according to the following method.

[0458]
SD female rats (Japan SLC, Inc.) were anesthetized by subcutaneous administration of 1200 mg/kg of urethane (Wako Pure Chemical Corporation), and the lower abdomen of the rats were incised in the midline. After the ureters were ligated and cut at proximally to bladder, a cannula (PE-60, BECTON DICKINSON) for cystometry was inserted into the bladder through the external urethral orifice and fixed with sutures. After injecting saline (about 200 μL) via the cannula inserted into the bladder, the other end of the cannula was connected to a pressure transducer to measure intravesical pressure.

[0459]

The pelvic nerve near the urinary bladder of the rat was gentry separated and dissected under stereomicroscope observation and attached to the electrode for nerve stimulation (K2-14015M-PT, BrainScience idea. Co., Ltd.). The peritoneal cavity of the rat was filled with liquid paraffin (26114-75, NACALAI TESQUE, INC.). After the postoperative rest period, an electrical stimulator (SEN-7203, NIHON KOHDEN CORPORATION) was used to stimulate the pelvic nerve to induce increase in intravesical pressure. The stimulation frequency was 8 Hz, the pulse width was 0.3 ms, and the stimulation time was 10 seconds. The voltage of the electrical stimulator was adjusted so that the increase in intravesical pressure was about 50-70% of that at stimulation with 10 V.

[0460]
The electric stimulation was repeated with an interval of 10 minutes. After the increase of intravesical pressure induced by electric stimulation was stabilized three times or more, a test compound (dosage 0.3 mg/kg), distigmine bromide (dosage 0.03, 0.1 mg/kg) or a vehicle was intravenously administered at 1.0 mL/kg via the catheter placed into femoral vein. The effect of the test compound on increase of intravesical pressure was measured for 1 hour. Saline was used as a vehicle, and the test compound was dissolved in dimethyl sulfoxide before adding to the vehicle. The final concentration of dimethyl sulfoxide was 10%.

[0461]
The response data (intravesical pressure) were recorded to a personal computer via data collection and analysis system (PowerLab®, ADInstruments) and analyzed using analysis software (LabChart®, ADInstruments). For each electric stimulation, AUC of increase of intravesical pressure (area under the curve of transition of intravesical pressure) was calculated, and percentage change Rc (unit: %) compared to the value (AUC) before the administration of the test compound was calculated according to the following equation (2). In the equation (2), Ab is AUC before administering a test compound, and Aa is AUC after administering a test compound. In addition, the maximum effect observed during 1 hour after administering the test compound (maximum percentage change Rc) was defined as the effect of the test compound. The higher percentage

change Rc, the higher effect on enhancement of bladder contradiction force and increase of intravesical pressure. The result of the test is shown in Table 116.

[0462]

$$Rc = 100 \times (Aa-Ab)/Ab \quad (2)$$

[0463]

[Table 116]

Test Compound (Example No.)	Percentage Change (%)
1	325.6
2	330.7
3	311.0
4	122.8
6	570.8
7	608.5
8	374.0
10	82.6
11	270.4
14	400.0
15	275.9
16	182.5
20	249.3
37	91.2
38	98.1
42	119.1
68	133.1

[0464]

All of the test compounds showed the enhancement effect on bladder contradictility. While distigmine bromide showed enhancement of bladder contradictility, a nicotinic side effect (fasciculation) was observed at 0.1 mg/kg.

[0465]

Also, the compounds evaluated in this test did not induce increase of intravesical pressure under the condition without electrical stimulation to rat. This confirmed that a test compound alone did

not induce rise in intravesical pressure.

[0466]
From the above, it was found that the test compounds in Table 116, when used alone, do not induce bladder contraction, but have an effect enhancing bladder contraction induced by electrical stimulation of the pelvic nerve.

[0467]
As described above, the test compounds were found to have in vitro M3 PAM activities. Also, the test compounds were found to enhance increase of intravesical pressure depending on nerve stimulus.

[0468]
Further, while the test compounds alone did not have agonist activities against M3 receptor, they have effect of bladder contraction enhancement depending on nerve stimulus. This enables the test compounds having M3 PAM activity to enhance signal level of M3 receptor under more physiological conditions, and they are expected to be therapeutically promising for diseases in which M3 receptor is involved. In addition, the test compounds may avoid a cholinergic side effect (cholinergic crisis) which has been reported on well-known medicaments (for example, distigmine bromide), and thus, the compounds may be therapeutic agents with excellent safety.

[0469]
<Test Example 3: Effect in rat lumbar spinal canal stenosis model>
8 weeks-aged SD female rats (CLEA Japan, Inc.) are anesthetized with an intraperitoneal injection of a mixed anesthesia of 40 mg/kg ketamine (ketalar®, DAIICHI SANKYO COMPANY, LIMITED) and 5 mg/kg xylazine (selactar®, Bayer Yakuhin, Ltd). Under the anesthesia, the back of the rat is incised to expose the fifth and sixth lumbar arches.

[0470]
The 5th lumbar arch is drilled to make a hole (about 1.5 mm of diameter), and a piece of silicone rubber (KOKUGO Co., Ltd.) is inserted into the epidural space between the 5th and 6th lumbar vertebrae to compress cauda equina nerve of the rat. The rat

subjected to the compression of cauda equina nerve may be referred to as operated rat hereinafter. The piece is formed into a shape having 3.5 mm of length, 5.0 mm of width, and 0.5 mm of thickness. After inserting the piece, the incision is closed by suturing the incision. Subsequently, antibiotics (viccillin for injection, 100 mg per a rat, Meiji Seika Co., Ltd.) are administered systemically to the operated rat.

[0471]
After two weeks from the surgery, a certain amount of injectable water (hereinafter referred to as "water") was administered orally to the operated rats. Subsequently, the operated rats are taken in a metabolism cage (Natsume Seisakusho Co., Ltd), and its urination within 6 hours after the start of water loading is determined. One hour before the water loading, test compound or distigmine bromide in 0.5% aqueous methylcellulose (vehicle) or a vehicle alone is administered orally to the operated rats. The amount of urination is determined using the electronic balance (GX-200, A&D Company, Limited), and the data are recorded to a personal computer via data collection and analysis system (PowerLab®, ADInstruments) and analyzed using the analysis software (LabChart®, ADInstruments). The metabolism cage has 230 mm of width, 220 mm of length, and 150 mm of height.

[0472]
The total amount of urination in 6 hours after water loading is evaluated. Further, the operated rats are taken out from the metabolism cage 6 hours after the start of water loading. The lower abdomen of the operated rats are pushed with finger to make urination to measure residual urine.

[0473]
As described in Test Example 1 and Test Example 2, since a compound of the present invention has M3 PAM activity, and is effective to in vivo models, it can be useful as a preventive or therapeutic agent for underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, and voiding or storage dysfunction in neurogenic bladder.

[0474]

Formulation Example 1

Tablet (Oral)

In 80 mg tablet of Formulation 1:

Compound of Example 1	5.0mg
Corn starch	46.6mg
Crystalline cellulose	24.0mg
Methylcellulose	4.0mg
Magnesium stearate	0.4mg

According to a conventional method, a mixed powder of the components is compressed to form an oral tablet.

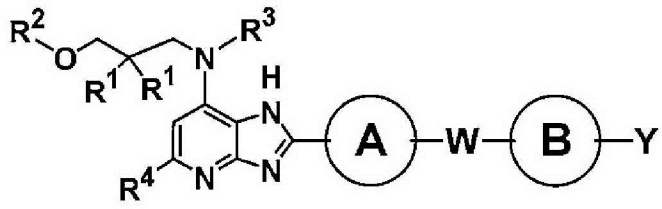
Industrial Applicability

[0475]

Since a compound of the present invention or a pharmaceutically acceptable salt thereof has M3 PAM activity, it can be useful as a preventive or therapeutic agent for voiding and/or storage disorders in bladder/urethral diseases, glaucoma, or diabetes, in which M3 receptor is involved.

Claims

1. An azabenzimidazole compound of the formula [1]:



[1]

wherein:

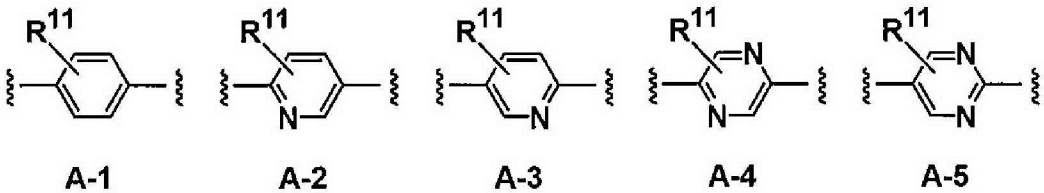
R^1 is a hydrogen atom or alkyl, or two R^1 are taken together with adjacent carbon atom to form a 3- to 7-membered cycloalkyl or an oxygen-containing non-aromatic heterocycle;

R^2 is a hydrogen atom, alkyl, cycloalkyl, alkyl substituted with cycloalkyl, or alkoxyalkyl;

R^3 is a hydrogen atom, alkyl, or alkoxyalkyl;

R^4 is pyridyl optionally substituted with one or two groups selected from the group consisting of alkyl, trihaloalkyl, alkoxy, cyano and cycloalkyl, or phenyl optionally substituted with 1 to 3 groups selected from the group consisting of trihaloalkyl, halogen, alkoxy and cycloalkyl;

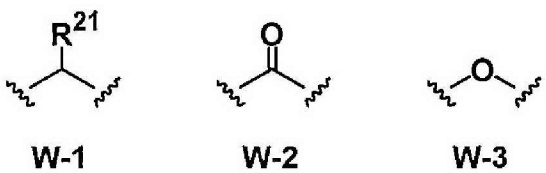
A is a group of the formula A-1, A-2, A-3, A-4, or A-5:



A-1 A-2 A-3 A-4 A-5

wherein the bond on the left side of each group is attached to the 2-position of the azabenzimidazole in the formula [1], and the bond on the right side is attached to W in the formula [1], and R^{11} is a group selected from a hydrogen atom, halogen, alkyl, alkoxy or nitro;

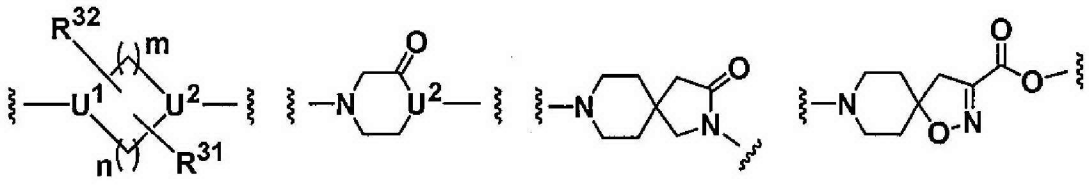
W is a bond, or a group of the formula W-1, W-2, or W-3:



W-1 W-2 W-3

wherein R^{21} is a hydrogen atom or alkyl;

B is a group of the formula B-1, B-2, B-3, or B-4:



B-1 B-2 B-3 B-4

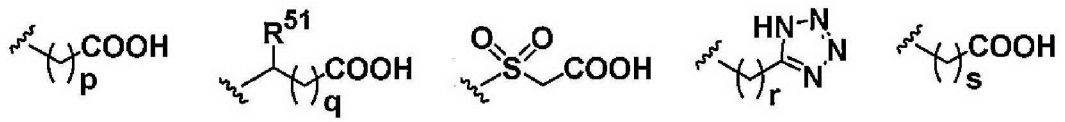
wherein

the bond on the left side of each group is attached to W in the formula [1],

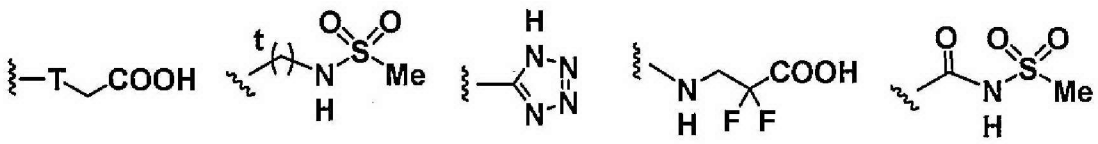
the bond on the right side is attached to Y in the formula [1],

U^1 is a nitrogen atom or CR^{41}, and U^2 is a nitrogen atom or CR^{42}, and R^{41} and R^{42} are independently a hydrogen atom, alkyl, halogen or a hydroxyl group, m and n are independently 1, 2 or 3, and R^{31} and R^{32} are independently a hydrogen atom, alkyl, halogen or alkoxyalkyl, or R^{31} and R^{32} are taken together with adjacent carbon atoms to form an alkylene bridge, provided that R^{31} and R^{32} substitute at any substitutable position other than U^1 and U^2;

Y is a hydrogen atom, or a group of any one of the formula Y-1 to Y-4 and Y-11 to Y-16:



Y-1 Y-2 Y-3 Y-4 Y-11



Y-12 Y-13 Y-14 Y-15 Y-16

wherein

R^{51} is alkyl; p is 1, 2, or 3; q is 0, 1, or 2; r is 1, 2, or 3; T is O, S, SO_2, or NR^{61} wherein R^{61} is a hydrogen atom or alkyl; s is 0, 1, 2, or 3; and t is 0 or 1,

with the proviso that

(a) when W is a bond,

if B is B-1 or B-2 and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4,

if B is B-1 or B-2 and U^2 is CR^{42} wherein R^{42} is as defined above, then U^1 is a nitrogen atom and Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, and

if B is B-3 or B-4, then Y is a hydrogen atom;

(b) when W is W-1,

if B is B-1, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4, and

if B is B-1, U^1 is a nitrogen atom, and U^2 is CR^{42} wherein R^{42} is as defined above, then Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16;

(c) when W is W-2,

if B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4,

if B is B-1 or B-2, U^1 is a nitrogen atom, and U^2 is CR^{42} wherein R^{42} is as defined above, then Y is Y-11, Y-12, Y-13, Y-14, Y-15, or Y-16, and

if B is B-3 or B-4, then Y is a hydrogen atom; and

(d) when W is W-3,

if B is B-1, U^1 is CR^{41} wherein R^{41} is as defined above, and U^2 is a nitrogen atom, then Y is Y-1, Y-2, Y-3, or Y-4,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

2. The azabenzimidazole compound according to claim 1, or a pharmaceutically acceptable salt thereof, or a solvate thereof, wherein W is a bond.

3. The azabenzimidazole compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, or a solvate thereof, wherein

(1) B is B-1 or B-2, U^2 is a nitrogen atom, and Y is Y-1, Y-2 or Y-3;

(2) B is B-1 or B-2, U^2 is CR^{42}, and Y is Y-11, Y-12 or Y-15; or

(3) B is B-4 and Y is a hydrogen atom.

4. The azabenzimidazole compound according to claim 3, or a

pharmaceutically acceptable salt thereof, or a solvate thereof, wherein R^4 is pyridyl substituted with a group selected from the group consisting of alkyl, trihaloalkyl, alkoxy, cyano and cycloalkyl, and with trihaloalkyl.

5. The azabenzimidazole compound according to claim 4, or a pharmaceutically acceptable salt thereof, or a solvate thereof, wherein A is A-4.

6. The azabenzimidazole compound according to any one of claims 1 to 5, wherein the compound is any one of the following (1) to (213), or a pharmaceutically acceptable salt thereof, or a solvate thereof:

(1) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(2) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(3) 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(4) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(5) 3-[4-(5-{5-[2-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(6) 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(7) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(8) 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(

methoxymethyl)piperazin-1-yl]propaonic acid,
(9) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-({[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,
(10) [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenoxy)piperidine-1-yl]acetic acid,
(11) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,
(12) 3-[4-fluoro-4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperidine-1-yl]propaonic acid,
(13) 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,
(14) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(15) {[(1R,3r,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,
(16) 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(17) [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidine-1-yl]acetic acid,
(18) 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,
(19) [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-4-hydroxypiperidine-1-yl]acetic acid,

(20) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(21) 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(22) [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]acetic acid,

(23) 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-{5-[4-(1H-tetrazol-5-yl)piperidine-1-yl]pyrazin-2-yl}-1H-imidazo[4,5-b]pyridin-7-amine,

(24) 8-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-2,8-diazaspiro[4.5]decan-3-one,

(25) 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-N-(methanesulfonyl)piperidine-4-carboxamide,

(26) [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-1-yl]acetic acid,

(27) 2-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,

(28) 1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperidine-4-carboxylic acid,

(29) {4-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)ethyl]piperazin-1-yl}acetic acid,

(30) 4-hydroxy-1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(31) 8-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-

yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3-carboxylic acid,
(32) 1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[4-methoxy-3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,
(33) 8-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-1-oxa-2,8-diazaspiro[4.5]dec-2-ene-3-carboxylic acid,
(34) 1-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[3-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)pyrrolidine-3-carboxylic acid,
(35) {4-[(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)methyl]piperazin-1-yl}acetic acid,
(36) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,
(37) [4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]acetic acid,
(38) 4-fluoro-1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,
(39) [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperazin-1-yl]acetic acid,
(40) N-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-yl]-N-methylglycine,
(41) [4-(4-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]acetic acid,
(42) 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,
(43) [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-4-hydroxypiperidine-1-yl]acetic acid,
(44) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-

b]pyridin-2-yl}pyrazin-2-yl)-2-oxopiperazin-1-yl]propaonic acid,

(45) 3-[4-(5-{5-[2-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(46) [4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetic acid,

(47) 3-[(2S)-4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(48) 4-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoic acid,

(49) N-[1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]glycine,

(50) {[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-yl]oxy}acetic acid,

(51) {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(52) N-[1-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-yl]glycine,

(53) [4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)-1,4-diazepan-1-yl]acetic acid,

(54) [4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetic acid,

(55) [4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-1,4-diazepan-1-yl]acetic acid,

(56) 3-[(2S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(57) 3-[4-(5-{7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[3-fluoro-5-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(58) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[({1-[(2-methoxyethoxy)methyl]cyclopentyl}methyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(59) {[1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(60) 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(61) 1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(62) 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(63) 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(64) 1-(4-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(65) 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(66) 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(67) 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(68) 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-

(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylic acid,

(69) 1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(70) 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(71) 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(72) 1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(73) 1-(5-{5-[3-ethoxy-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(74) 1-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylic acid,

(75) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(76) 1-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(77) 1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(78) 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(79) 1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(80) 1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(81) 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(82) 1-(4-{7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(83) 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(ethyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(84) 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluorophenyl)piperidine-4-carboxylic acid,

(85) 1-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-methylphenyl)piperidine-4-carboxylic acid,

(86) 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propaonic acid,

(87) 1-(5-{7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-5-[6-propyl-5-(trifluoromethyl)pyridin-3-yl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(88) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(89) 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(90) 3-[4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(91) 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(92) 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-

b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,
(93) 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(94) {[1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,
(95) {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,
(96) 3-[4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,
(97) 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,
(98) 3-[4-(4-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,
(99) 3-[4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,
(100) 3-[(2S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(101) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoic acid,
(102) 3-[4-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,
(103) 3-[4-(4-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,
(104) 3-[(2S)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(105) 3-[(2S)-4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(106) [1-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(107) 3-[4-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,

(108) 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(109) 3-[(2S)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(110) {[1-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(111) 3-[(3R)-4-(5-{5-[5,6-bis(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(112) 2,2-difluoro-3-{[1-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]amino}propaonic acid,

(113) {[(3S,4R)-1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-fluoropiperidine-4-yl]amino}acetic acid,

(114) 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]butanoic acid,

(115) 3-[(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(116) {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(117) 3-[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(118) {[(3S,4R)-1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-fluoropiperidine-4-yl](methyl)amino}acetic acid,

(119) 3-[4-(5-{7-[{[1-(butoxymethyl)cyclopentyl]methyl}(methyl)amino]-5-[3-fluoro-5-(trifluoromethyl)phenyl]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(120) 3-[(2R,6S)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propaonic acid,

(121) 3-[(2R,6S)-4-(5-{5-[3,5-bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propaonic acid,

(122) {[1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(123) 3-[(2R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(124) 3-[(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(125) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(126) 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-

yl]propaonic acid,
(127) 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(128) 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(129) 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(130) 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(131) 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(132) 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(133) 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(134) [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(135) 3-[(2R,6S)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propaonic acid,
(136) {[(1R,3r,5S)-8-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,
(137) {[(1R,3r,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-

b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,
(138) [4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-sulfonyl]acetic acid,
(139) [(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(140) [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(141) [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(142) [(3R)-4-(5-{5-[4-fluoro-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(143) 3-[(2R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(144) 3-[(2R,6S)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propaonic acid,
(145) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3,3-dimethylpiperidine-4-yl]oxy}acetic acid,
(146) 1-(4-{5-[6-cyano-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,
(147) 3-[(2R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,
(148) [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-

imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,

(149) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,

(150) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-4-methylpiperidine-4-yl]oxy}acetic acid,

(151) {[(1R,3r,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,

(152) {[1-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-4-methylpiperidine-4-yl]oxy}acetic acid,

(153) 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(154) 3-[(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(155) 3-[(2R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(156) 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(157) 1-(5-{5-[4-cyclopropyl-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(158) 1-(4-{5-[4-cyclopropyl-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-

b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,
(159) {[1-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]oxy}acetic acid,
(160) 3-[(3R)-4-(5-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(161) {[(1R,3s,5S)-8-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,
(162) 3-[4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propaonic acid,
(163) 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,
(164) [(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(165) [(3R)-4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,
(166) 3-[4-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,2-dimethylpiperazin-1-yl]propaonic acid,
(167) 3-[(2R,6S)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2,6-dimethylpiperazin-1-yl]propaonic acid,
(168) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-

[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3,3-dimethylpiperidine-4-yl]oxy}acetic acid,

(169) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-(ethyl{[1-(methoxymethyl)cyclopentyl]methyl}amino)-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(170) {[(1R,3s,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,

(171) 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(172) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]sulfanil}acetic acid,

(173) {[1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-yl]sulfanil}acetic acid,

(174) [4-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidine-1-yl]acetic acid,

(175) [4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidine-1-yl]acetic acid,

(176) 3-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidine-1-yl]propaonic acid,

(177) [4-(3-chloro-4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidine-1-yl]acetic acid,

(178) 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)piperidine-1-yl]propaonic acid,

(179) 3-[(1R,3s,5S)-3-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(

methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenoxy)-8-azabicyclo[3.2.1]octan-8-yl]propaonic acid,

(180) [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]acetic acid,

(181) 1-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(182) 1-(4-{5-[3,5-bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(183) 1-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(184) 1-(4-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(185) 1-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(186) {1-[(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)methyl]piperidine-4-yl}acetic acid,

(187) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-2-yl)-4-hydroxypiperidine-1-yl]propaonic acid,

(188) 3-[4-(5-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(189) 3-[4-(6-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyridin-3-yl)piperazin-1-yl]propaonic acid,

(190) 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(191) 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-

[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,

(192) 3-[4-(4-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,

(193) 3-[4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperazin-1-yl]propaonic acid,

(194) 3-[4-(5-{5-[3,5-bis(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(195) 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid,

(196) 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-methylpiperazin-1-yl]propaonic acid,

(197) 3-[(3S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(198) [(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,

(199) [(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,

(200) [(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,

(201) 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)piperazin-1-yl]propaonic acid,

(202) [(3R)-4-(5-{5-[6-ethoxy-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,

(203) [(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]acetic acid,

(204) 1-(4-{5-[4-ethoxy-3-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(205) 1-(4-{5-[5-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-4-carboxylic acid,

(206) 3-[(3R)-4-(4-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-3-methylpiperazin-1-yl]propaonic acid,

(207) 3-[(3R)-4-(4-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)-3-methylpiperazin-1-yl]propaonic acid,

(208) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}-3-fluoropyridin-2-yl)-3-methylpiperazin-1-yl]propaonic acid,

(209) 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-(5-{4-[(1H-tetrazol-5-yl)methyl]piperazin-1-yl}pyrazin-2-yl)-1H-imidazo[4,5-b]pyridin-7-amine,

(210) 5-[3-fluoro-5-(trifluoromethyl)phenyl]-N-{[1-(methoxymethyl)cyclobutyl]methyl}-N-methyl-2-(5-{4-[2-(1H-tetrazol-5-yl)ethyl]piperazin-1-yl}pyrazin-2-yl)-1H-imidazo[4,5-b]pyridin-7-amine,

(211) N-{2-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]ethyl}sulfonate amide,

(212) 3-[4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-

(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}phenyl)piperidine-1-yl]propanoic acid, and

(213) [4-(4-{5-[3-fluoro-5-(trifluoromethyl)phenyl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}benzoyl)piperazin-1-yl]acetic acid.

7. The azabenzimidazole compound according to any one of claims 1 to 6, wherein the compound is any one of the following (1) to (12), or a pharmaceutically acceptable salt thereof, or a solvate thereof:

(1) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(2) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(3) 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(4) {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetic acid,

(5) 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propanoic acid,

(6) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid,

(7) 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propanoic acid,

(8) 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid,

(9) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-

imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid,

(10) {[(1R,3R,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid,

(11) 3-[(3R)-4-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid, and

(12) 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid.

8. An azabenzimidazole compound which is 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[(3-methoxy-2,2-dimethylpropyl)(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

9. An azabenzimidazole compound which is 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

10. An azabenzimidazole compound which is 1-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

11. An azabenzimidazole compound which is {[1-(5-{5-[2-cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidin-4-yl]oxy}acetic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

12. An azabenzimidazole compound which is 3-[4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperazin-1-yl]propaonic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

13. An azabenzimidazole compound which is 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propaonic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

14. An azabenzimidazole compound which is 3-[(2S)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclohexyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-2-(methoxymethyl)piperazin-1-yl]propaonic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

15. An azabenzimidazole compound which is 1-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclobutyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)piperidine-4-carboxylic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

16. An azabenzimidazole compound which is 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(ethoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

17. An azabenzimidazole compound which is {[(1R,3R,5S)-8-(5-{5-[2-ethoxy-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]oxy}acetic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

18. An azabenzimidazole compound which is 3-[(3R)-4-(5-{5-[2-

cyclopropyl-6-(trifluoromethyl)pyridin-4-yl]-7-[{[1-(methoxymethyl)cyclohexyl]]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

19. An azabenzimidazole compound which is 3-[(3R)-4-(5-{5-[6-cyclopropyl-5-(trifluoromethyl)pyridin-3-yl]-7-[{[1-(methoxymethyl)cyclopentyl]methyl}(methyl)amino]-1H-imidazo[4,5-b]pyridin-2-yl}pyrazin-2-yl)-3-methylpiperazin-1-yl]propanoic acid, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

20. A pharmaceutical composition comprising the azabenzimidazole compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient, and a pharmaceutically acceptable carrier.

21. A method for treating voiding and/or storage disorders in bladder/urethral disease, glaucoma or diabetes in which the M3 receptor is involved, in a subject in need thereof comprising administering to the subject an effective amount of an azabenzimidazole compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, or a solvate thereof.

22. The method according to claim 21, wherein the voiding and/or storage disorders in bladder/urethral disease in which the M3 receptor is involved is due to underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethral relaxation failure, or detrusor-external urethral sphincter dyssynergia.

23. Use of an azabenzimidazole compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, or a solvate thereof in preparation of a medicament for treating voiding and/or storage disorders in bladder/urethral disease, glaucoma or

diabetes in which the M3 receptor is involved.

24. The use according to claim 23, wherein the voiding and/or storage

disorders in bladder/urethral disease in which the M3 receptor is involved is due to underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethral relaxation failure, or detrusor-external urethral sphincter dyssynergia.