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CA 2987019 C 2023/09/26

(11)(21) 2 987 019

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(86) Date de dépôt PCT/PCT Filing Date: 2016/05/27
(87) Date publication PCT/PCT Publication Date: 2016/12/08
(45) Date de délivrance/Issue Date: 2023/09/26
(85) Entrée phase nationale/National Entry: 2017/11/23
(86) N° demande PCT/PCT Application No.: JP 2016/065770
(87) N° publication PCT/PCT Publication No.: 2016/194831
(30) Priorité/Priority: 2015/05/29 (JP2015-110684)

(51) Cl.Int./Int.Cl. *C07D 471/04* (2006.01),
A61K 31/519 (2006.01), *A61K 31/5377* (2006.01),
A61K 31/5386 (2006.01), *A61K 31/541* (2006.01),
A61K 31/55 (2006.01), *A61K 31/551* (2006.01),
A61K 31/553 (2006.01), *A61P 11/00* (2006.01),
A61P 19/02 (2006.01), *A61P 25/28* (2006.01),
A61P 29/00 (2006.01), ...

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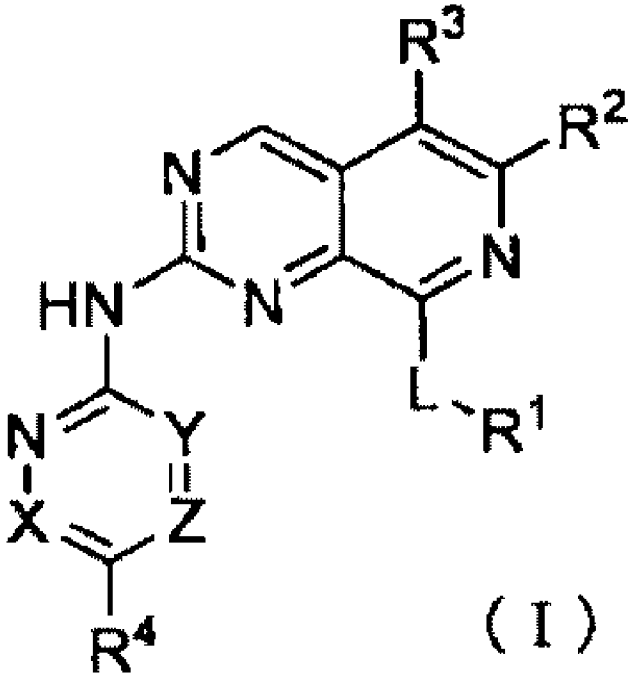
(54) Titre : DERIVE DE PYRIDO[3,4-D]PYRIMIDINE ET SEL PHARMACEUTIQUEMENT ACCEPTABLE DE CELUI-CI
(54) Title: PYRIDO[3,4-D]PYRIMIDINE DERIVATIVE AND PHARMACEUTICALLY ACCEPTABLE SALT THEREOF



(I)

(57) Abrégé/Abstract:
The purpose of the present invention is to provide a compound having an excellent CDK4/6 inhibiting activity. The present invention is a compound represented by general formula (I) or a pharmaceutically acceptable salt thereof.

CA 2987019 C 2023/09/26

(11)(21) 2 987 019

(13) C

(51) Cl.Int./Int.Cl. (suite/continued) *A61P 35/00* (2006.01), *A61P 43/00* (2006.01), *A61P 9/10* (2006.01), *C07D 519/00* (2006.01)

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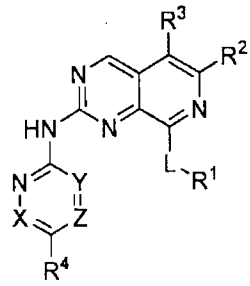
ABSTRACT

The purpose of the present invention is to provide a compound having an excellent CDK4/6 inhibiting activity. The present invention is a compound represented by general formula (I) or a pharmaceutically acceptable salt thereof.



(I)

DEMANDE OU BREVET VOLUMINEUX

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THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

DESCRIPTION

PYRIDO[3,4-d]PYRIMIDINE DERIVATIVE AND PHARMACEUTICALLY ACCEPTABLE SALT THEREOF

Technical Field

[0001]

The present invention relates to a pyrido[3,4-d]pyrimidine derivative and a pharmaceutically acceptable salt thereof. In particular, the present invention relates to a compound that exhibits an inhibitory activity against cyclin-dependent kinase 4 and/or cyclin-dependent kinase 6 (hereinafter referred to as "CDK4/6") and that is useful for the prevention or treatment of rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, or cancer.

Background Art

[0002]

Cell growth, which is a process involving proliferation and division of cells, occurs in response to various stimuli.

Pathological conditions caused by hyperproliferation of cells, such as cancer, are characterized by uncontrollable cell cycle progression and thus excessive progression of the cell cycle, for example, resulting from abnormality in genes or proteins that directly or indirectly regulate the cell cycle progression. Substances that regulate hyperproliferation of cells through control of the cell cycle can be used for the treatment of various pathological conditions characterized by uncontrollable or unwanted cell growth.

Cell cycle progression is a complicated process involving highly regulated transition of phases and multiple checkpoints.

[0003]

Cyclin-dependent kinases and associated serine/threonine protein kinases are important

intracellular enzymes that play essential roles in the regulation of division and proliferation of cells. Catalytic subunits of cyclin-dependent kinases are activated by regulatory subunits known as cyclins, and multiple cyclins have been identified in mammals (NPL 1).

[0004]

The retinoblastoma (Rb) protein is a checkpoint protein for transition from the G1 phase to the S phase in the cell cycle. The Rb protein associates with the E2F transcription factor family and inhibits the activity thereof in the absence of appropriate growth stimulation (NPLs 2 and 3). A cell stimulated by a mitogen enters the S phase through synthesis of cyclin D, which is a CDK4/6 activator. The cyclin D-bound CDK 4/6 inactivates the Rb protein through phosphorylation. The phosphorylation of the Rb protein releases E2F in order to indirective the transcription of a gene necessary for the S phase. The complete inactivation of the Rb protein requires phosphorylation of both cyclin D-CDK4/6 and cyclin E-CDK2. The phosphorylation of the Rb protein by CDK4/6 at a specific site is essential in the phosphorylation of cyclin E-CDK2 (NPL 4). Thus, cyclin D-CDK4/6 is an important enzyme complex which controls the transition from the G1 phase to the S phase.

[0005]

CDK2 forms a complex with cyclin E and also forms a complex with cyclin A. CDK2 also acts on steps subsequent to the S phase and is responsible for DNA replication. The inhibition of CDK2 probably leads to the expression of genotoxicity (NPL 5).

Cyclin D has a molecular mechanism that positively regulates the activity of CDK4/6. In contrast, p16 encoded by the INK4a gene negatively regulates the activity of CDK4/6 (NPL 6).

[0006]

CDK inhibitors can be used for the treatment of various diseases caused by abnormal cell growth, such as

cancer, cardiovascular disorder, renal disease, specific infections, and autoimmune diseases. CDK inhibitors is also expected to be effective for the treatment of diseases including but not limited to rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, and cancer. The inhibition of cell cycle progression and cell growth through CDK inhibition is expected to be effective for such a disease on the basis of the technical findings described below.

[0007]

Rheumatoid arthritis involves the formation of pannus through hyperproliferation of synovial cells. This hyperproliferation can be reduced by the introduction of p16 into an affected area of a model animal or the administration of a CDK4/6 inhibitor to the animal (NPLs 7 to 9). A CDK4-cyclin D complex regulates the production of MMP3 in synovial cells derived from a patient with rheumatoid arthritis. The negative regulation of the activity of CDK4/6 inhibits not only the proliferation but also production of MMP3 (NPL 10).

Thus, CDK4/6 inhibitors are expected to exhibit both an inhibitory effect on proliferation of synovial cells and a cartilage protective effect in rheumatoid arthritis.

[0008]

A pathway for the regulation of cell growth including genes responsible for the checkpoints in the G1 and S phases of the cell cycle is associated with plaque progression, stenosis, and restenosis after angiogenesis. The overexpression of the CDK inhibitory protein p21 inhibits angiogenesis and subsequent growth of vascular smooth muscle and intimal hyperplasia (NPLs 11 and 12).

Abnormal regulation of the cell cycle is also associated with polycystic kidney disease, which is characterized by growth of cysts filled with fluid in the renal tubule. A small-molecule CDK inhibitor is effective for the treatment of the disease (NPL 13).

[0009]

The induction of expression of the cell cycle inhibitory protein p21 with an adenoviral vector is effective in a murine pulmonary fibrosis model (NPL 14).

The level of cyclin D1/CDK4 is known to increase in a rat cerebral infarction model in association with neuronal death caused by local ischemia. The neuronal death is reduced by administering flavopiridol, which is a nonselective CDK inhibitor (NPL 15).

[0010]

The cyclin D-CDK4/6-INK4a-Rb pathway is frequently detected in human cancer caused by abnormality of any factors contributing to growth of cancer cells, such as loss of functional p16INK4a, overexpression of cyclin D1, overexpression of CDK4, or loss of functional Rb (NPLs 16 to 18). Such abnormality promotes the cell cycle progression from the G1 phase to the S phase, and this pathway certainly plays an important role in oncogenic transformation or abnormal growth of cancer cells.

[0011]

CDK4/6 inhibitors may be effective, particularly for tumors involving abnormality in genes that activate the CDK4/6 kinase activity, such as cancers involving the translocation of cyclin D, cancers involving the amplification of cyclin D, cancers involving the amplification or overexpression of CDK4 or CDK6, and cancers involving the inactivation of p16. CDK4/6 inhibitors may be effective for the treatment of cancers involving genetic abnormality in the upstream regulator of cyclin D, the amount of which increases due to defects in the upstream regulator.

In fact, many compounds that inhibit the CDK4/6 activity have been synthesized and disclosed in the art, and such compounds have been clinically tested for the treatment of cancers, such as breast cancer (NPL 19).

[0012]

Most acute and severe radiotherapeutic and

chemotherapeutic toxicities are caused by the effects on stem cells and progenitor cells. A CDK4/6 inhibitor causes temporary cell cycle arrest to hematopoietic stem and progenitor cells, and protects them from radiotherapeutic or chemotherapeutic cytotoxicity. After the treatment with the inhibitor, hematopoietic stem and progenitor cells (HSPCs) return from the temporary dormancy and then function normally. Thus, the chemotherapeutic resistance with use of a CDK4/6 inhibitor is expected to provide a significant protection of bone marrow (NPL 20).

Hence, CDK4/6 inhibitors are expected to be effective for the treatment of rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, or cancer, and the protection of bone marrow, in particular, for the treatment of rheumatoid arthritis or cancer and the protection of bone marrow.

[0013]

PTL 1 and NPL 21 disclose CDK4 inhibitors, PTLs 2 and 3 and NPLs 22 to 24 disclose CDK4/6-containing CDK inhibitors, and NPL 25 discloses CDK4/FLT3 inhibitors.

Pyrido[3,4-d]pyrimidine derivatives exhibit an inhibitory effect on Mps1 (also known as TTK) (PTL 4). This inhibitory effect is completely different from the CDK4/6 inhibitory effect disclosed in the present invention.

NPL 26 and NPL 27 disclose that a plurality of pyrido[3,4-d]pyrimidine derivatives exhibit a CDK2 inhibitory activity, which is completely different from the superior CDK4/6 inhibitory effect exhibited by the present invention.

List of Citations

Patent Literature

[0014]

[PTL 1] WO2003/062236

[PTL 2] WO2010/020675

[PTL 3] WO2010/075074

[PTL 4] WO2014/037750

Non-patent Literature

[0015]

[NPL 1] Johnson D. G. and Walker C.L., Annual Review of Pharmacology and Toxicology 1999; 39: p.295-312

[NPL 2] Ortega et al., Biochimica et Biophysica Acta-Reviews on Cancer 2002; 1602 (1): p.73-87

[NPL 3] Shapiro, Journal of Clinical Oncology 2006; 24 (11): p.1770-1783

[NPL 4] Lundberg et al., Molecular and Cellular Biology 1998; 18 (2): p.753-761

[NPL 5] Andrew J. Olaharski, PLoS Computational Biology 2009; 5 (7): e1000446

[NPL 6] Kamb et al., Science 1994; 264 (5157): p.436-440

[NPL 7] Taniguchi, K et al., Nature Medicine, Vol.5, p.760-767 (1999)

[NPL 8] Sekine, C et al., Journal of immunology 2008, 180: p.1954-1961

[NPL 9] Hosoya, T et al., Annnl Rheumatic Diseases 2014, Aug 27 Epub ahead of print

[NPL 10] Nonomura Y et al., Arthritis & Rheumatology 2006, Jul; 54 (7): p.2074-83

[NPL 11] Chang M.W. et al., Journal of Clinical Investigation, 1995, 96: p.2260

[NPL 12] Yang Z-Y. et al., Proceedings of the National Academy of Sciences (USA) 1996, 93: p.9905

[NPL 13] Bukanov N.O. et al., Nature, 2006, 4444: p.949-952

[NPL 14] American Journal Physiology: Lung Cellular and Molecular Physiology, 2004, Vol. 286, p.L727-L733

[NPL 15] Proceedings of the National Academy of Sciences of the United States of America, 2000, Vol.97, p.10254-10259

[NPL 16] Science, Vol. 254, p.1138-1146 (1991)

[NPL 17] Cancer Research, 1993, Vol. 53, p.5535-5541

[NPL 18] Current Opinion in Cell Biology, 1996, Vol.8,

p.805-814

[NPL 19] Guha M, Nature Biotechnology 2013, Mar; 31 (3): p.187

[NPL 20] Journal of Clinical Investigation 2010; 120 (7): p.2528-2536 Soren M. Johnson

[NPL 21] Journal of Medicinal Chemistry, 2005, 48, p.2371-2387

[NPL 22] Journal of Medicinal Chemistry, 2000, 43, p.4606-4616

[NPL 23] Journal of Medicinal Chemistry, 2005, 48, p.2388-2406

[NPL 24] Journal of Medicinal Chemistry, 2010, 53, p.7938-7957

[NPL 25] Journal of Medicinal Chemistry, 2014, 57, p.3430-3449

[NPL 26] Organic & Biomolecular Chemistry, 2015, 13, p.893-904

[NPL 27] Rapid Discovery of Pyrido[3,4-d]pyrimidine Inhibitors of Monopolar Spindle Kinase 1 (MPS1) Using a Structure-Based Hybridization Approach, Paolo Innocenti et al, J. Med. Chem., Article ASAP,Publication Date (Web): April 7, 2016, DOI: 10.1021/acs.jmedchem.5b01811.

Summary of Invention

Problem to be Solved by the Invention

[0016]

An object of the present invention is to provide a compound exhibiting a superior CDK4/6 inhibitory activity.

Means to Solve the Problem

[0017]

The present inventors have conducted extensive studies for solving the problems described above and have found that a novel pyrido[3,4-d]pyrimidine derivative represented by Formula (I) exhibits a CDK4/6 inhibitory activity. The present invention has been accomplished on the basis of this finding.

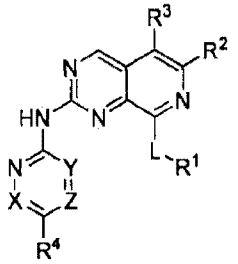
The present invention includes the following

aspects:

[0018]

Aspect (1): A compound represented by Formula (I), or a pharmaceutically acceptable salt thereof:

[Formula 1]



(I)

[0019]

[wherein

L represents $-NR^5-$, $-O-$, or $-S-$;

R^5 represents a hydrogen atom or a C_{1-6} alkyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms;

R^1 represents a C_{1-8} alkyl, C_{3-12} cycloalkyl, (C_{3-12} cycloalkyl)-C_{1-6} alkyl, 4- to 12-membered heterocyclyl, (4- to 12-membered heterocyclyl)-C_{1-6} alkyl, C_{6-10} aryl, (C_{6-10} aryl)-C_{1-6} alkyl, 5- to 10-membered heteroaryl, (5- to 10-membered heteroaryl)-C_{1-6} alkyl, C_{1-8} alkylsulfonyl, or C_{1-8} acyl group;

each of the heteroatom-containing groups represented by R^1 contains one to four heteroatoms selected from oxygen, sulfur, and nitrogen atoms;

R^1 is optionally substituted with one to six substituents selected from the group consisting of a halogen atom, =O, -OH, -CN, -COOH, $-COOR^6$, $-R^7$, a C_{3-6} cycloalkyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms, a 3- to 10-membered heterocyclyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms, a C_{1-8} acyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms, and a C_{1-8} alkoxy group

substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms;
R^6 and R^7 each independently represent a C_{1-6} alkyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms;
R^2 represents a C_{1-8} alkyl, C_{3-8} cycloalkyl, 4- to 6-membered heterocyclyl, or C_{1-8} acyl group, $-COOR^8$, or $-CONR^9R^{10}$;
each of the C_{1-8} alkyl and C_{3-8} cycloalkyl groups represented by R^2 is substituted with zero or one -OH group, zero to two C_{1-8} alkoxy groups substituted with zero or one -OH group, zero or one C_{1-4} alkoxy group, and zero to three fluorine atoms, and zero to five fluorine atoms;
R^2 is neither an unsubstituted C_{1-8} alkyl, nor unsubstituted C_{3-8} cycloalkyl, nor trifluoromethyl group;
R^8, R^9, and R^{10} each independently represent a hydrogen atom or a C_{1-8} alkyl group;
the 4- to 6-membered heterocyclyl group represented by R^2 is optionally substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and C_{1-4} alkyl and C_{1-4} alkoxy groups;
each of the C_{1-8} acyl group, $-COOR^8$, and $-CONR^9R^{10}$ represented by R^2 is optionally substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and a C_{1-4} alkoxy group;
R^9 and R^{10} of $-CONR^9R^{10}$ represented by R^2 are optionally bonded via a single bond or -O- to form a ring including the nitrogen atom bonded to R^9 and R^{10};
the heterocyclyl group represented by R^2 having a 4- or 5-membered ring contains one oxygen heteroatom, and the heterocyclyl group having a 6-membered ring contains one or two oxygen heteroatoms;
R^3 represents a hydrogen atom, a C_{1-8} alkyl group, or a halogen atom;
X represents CR^{11} or a nitrogen atom;
Y represents CR^{12} or a nitrogen atom;

Z represents CR^{13} or a nitrogen atom;
R^{11} to R^{13} each independently represent a hydrogen, fluorine, chlorine atom, a C_{1-6} alkyl, or C_{1-6} alkoxy group;
R^4 represents $-A^1-A^2-A^3$;
A^1 represents a single bond, a C_{1-8} alkylene, C_{2-8} alkenylene, or C_{2-8} alkynylene group;
one or two sp^3 carbon atoms at any positions of A^1 are optionally replaced with one or two structures selected from the group consisting of $-O-$, $-NR^{14}-$, $-C(=O)-$, $-C(=O)-O-$, $-O-C(=O)-$, $-O-C(=O)-O-$, $-C(=O)-NR^{15}-$, $-O-C(=O)-NR^{16}-$, $-NR^{17}-C(=O)-$, $-NR^{18}-C(=O)-O-$, $-NR^{19}-C(=O)-NR^{20}-$, $-S(=O)_p-$, $-S(=O)_2-NR^{21}-$, $-NR^{22}-S(=O)_2-$, and $-NR^{23}-S(=O)_2-NR^{24}-$, and a structure of $-O-O-$, $-O-NR^{14}-$, $-NR^{14}-O-$, $-O-CH_2-O-$, $-O-CH_2-NR^{14}-$, or $-NR^{14}-CH_2-O-$ is not formed in the case of replacement of two sp^3 carbon atoms;
A^2 represents a single bond, a C_{1-7} alkylene, C_{3-12} cycloalkylene, C_{3-12} cycloalkylidene, 4- to 12-membered heterocyclylene, 4- to 12-membered heterocyclylidene, C_{6-10} arylene, or 5- to 10-membered heteroarylene group;
A^3 represents a halogen atom, $-CN$, $-NO_2$, $-R^{25}$, $-OR^{26}$, $-NR^{27}R^{28}$, $-C(=O)R^{29}$, $-C(=O)-OR^{30}$, $-O-C(=O)R^{31}$, $-O-C(=O)-NR^{32}R^{33}$, $-C(=O)-NR^{34}R^{35}$, $-NR^{36}-C(=O)R^{37}$, $-NR^{38}-C(=O)-OR^{39}$, $-S(=O)_2-R^{40}$, $-S(=O)_2-NR^{41}R^{42}$, or $-NR^{43}-S(=O)_2R^{44}$;
A^3 represents $-R^{25}$, if the A^1 end on the A^2 side has a structure selected from the group consisting of $-O-$, $-NR^{14}-$, $-C(=O)-$, $-C(=O)-O-$, $-O-C(=O)-$, $-O-C(=O)-O-$, $-C(=O)-NR^{15}-$, $-O-C(=O)-NR^{16}-$, $-NR^{17}-C(=O)-$, $-NR^{18}-C(=O)-O-$, $-NR^{19}-C(=O)-NR^{20}-$, $-S(=O)_p-$, $-S(=O)_2-NR^{21}-$, $-NR^{22}-S(=O)_2-$, and $-NR^{23}-S(=O)_2-NR^{24}-$ and A^2 is a single bond;
R^{14}, R^{32}, R^{34}, R^{36}, R^{38}, R^{41}, and R^{43} each independently represent a hydrogen atom, a C_{1-8} alkyl, C_{1-8} acyl, C_{1-8} alkylsulfonyl, 4- to 12-membered heterocyclyl, C_{3-12} cycloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, (4- to 12-membered heterocyclyl)-C_{1-3} alkyl, (C_{3-12} cycloalkyl)-C_{1-3} alkyl, (C_{6-10} aryl)-C_{1-3} alkyl, or (5- to 10-membered heteroaryl)-C_{1-3} alkyl group;

R^{15} to R^{31}, R^{33}, R^{35}, R^{37}, R^{39}, R^{40}, R^{42}, and R^{44} each independently represent a hydrogen atom or a C_{1-8} alkyl, 4- to 12-membered heterocyclyl, C_{3-12} cycloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, (4- to 12-membered heterocyclyl)-C_{1-3} alkyl, (C_{3-12} cycloalkyl)-C_{1-3} alkyl, (C_{6-10} aryl)-C_{1-3} alkyl, or (5- to 10-membered heteroaryl)-C_{1-3} alkyl group;

A^1, A^2, A^3, and R^{14} to R^{44} in A^1, A^2, and A^3 are each optionally substituted with one to four substituents selected from the group consisting of -OH, =O, -COOH, -SO_3H, -PO_3H, -CN, -NO_2, a halogen atom, a C_{1-8} alkyl group substituted with zero to two -OH groups, zero to two -OR^{45} groups, and zero to six fluorine atoms, a C_{3-12} cycloalkyl group substituted with zero to two -OH groups, zero to two -OR^{46} groups, and zero to six fluorine atoms, a C_{1-8} alkoxy group substituted with zero to two -OH groups, zero to two -OR^{47} groups, and zero to six fluorine atoms, and a 4- to 12-membered heterocyclyl group substituted with zero to two -OH groups, zero to two -OR^{49} groups, and zero to six fluorine atoms;

R^{14} to R^{44} are optionally bonded in A^1, A^2, or A^3 or between A^1 and A^2, between A^1 and A^3, or between A^2 and A^3 via a single bond, -O-, -NR^{50}-, or -$S(=O)_p$- to form a ring;

R^{11} or R^{13} is optionally bonded to A^1, A^2, or A^3 via a single bond, -O-, -NR^{51}-, or -$S(=O)_p$- to form a ring;

R^{45} to R^{51} each represent a hydrogen atom or a C_{1-4} alkyl group substituted with zero or one -OH group and zero to six fluorine atoms;

p represents an integer of 0 to 2; and

each of the heteroatom-containing groups represented by A^1, A^2, and A^3 contains one to four heteroatoms selected from oxygen, sulfur, and nitrogen atoms].

[0020]

Aspect (2): The compound or pharmaceutically acceptable salt thereof according to Aspect (1), wherein L represents -NH-.

Aspect (3): The compound or pharmaceutically acceptable

salt thereof according to Aspect (1) or (2), wherein R^1 represents a C_{1-8} alkyl, C_{3-12} cycloalkyl, (C_{3-12} cycloalkyl)-C_{1-6} alkyl, 4- to 12-membered heterocyclyl, or (4- to 12-membered heterocyclyl)-C_{1-6} alkyl group.

Aspect (4): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (3), wherein R^2 is a C_{1-8} alkyl group substituted with one to four fluorine atoms.

Aspect (5): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (3), wherein R^2 is a C_{1-8} alkyl group substituted with zero or one -OH group and zero to two C_{1-8} alkoxy groups substituted with zero or one -OH group, zero or one C_{1-4} alkoxy group, and zero to three fluorine atoms.

Aspect (6): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (3), wherein R^2 is a 4- to 6-membered heterocyclyl group optionally substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and C_{1-4} alkyl and C_{1-4} alkoxy groups.

Aspect (7): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (3), wherein R^2 is $-COOR^8$, $-CONR^9R^{10}$, or a C_{1-8} acyl group, optionally each group being substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and a C_{1-8} alkoxy group.

Aspect (8): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (7), wherein X represents CR^{11}, Y represents CR^{12}, and Z represents CR^{13}.

Aspect (9): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (7), wherein X represents a nitrogen atom, Y represents CR^{12}, and Z represents CR^{13}.

Aspect (10): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (7), wherein X represents CR^{11}, Y represents a nitrogen atom,

and Z represents CR^{13}.

Aspect (11): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (7), wherein X represents CR^{11}, Y represents CR^{12}, and Z represents a nitrogen atom.

Aspect (12): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (11), wherein A^1 is a single bond.

Aspect (13): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (11), wherein A^1 represents a C_{1-8} alkylene group, and no sp^3 carbon atom in A^1 is replaced with another structure.

Aspect (14): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (11), wherein A^1 represents a C_{1-8} alkylene group, and one sp^3 carbon atom at any position of A^1 is replaced with -O-.

Aspect (15): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (11), wherein A^1 represents a C_{1-8} alkylene group, and one sp^3 carbon atom at any position of A^1 is replaced with $-NR^{14}-$.

Aspect (16): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (11), wherein A^1 represents a C_{1-8} alkylene group, one sp^3 carbon atom at any position of A^1 is replaced with $-NR^{14}-$, and one sp^3 carbon atom at any other position of A^1 is optionally replaced with -O-.

Aspect (17): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (16), wherein A^2 represents a 4- to 12-membered heterocyclylene group; and A^2 is optionally substituted with one to four substituents selected from the group consisting of -OH, -COOH, $-SO_3H$, $-PO_3H$, -CN, $-NO_2$, a halogen atom, a C_{1-8} alkyl group optionally substituted with zero to two -OH groups, zero to two $-OR^{45}$ groups, and zero to six fluorine atoms, a C_{3-12} cycloalkyl group optionally substituted with zero to two -OH groups, zero to two $-OR^{46}$ groups, and zero to six fluorine atoms, a C_{1-8} alkoxy group optionally

substituted with zero to two -OH groups, zero to two $-OR^{47}$ groups, and zero to six fluorine atoms, and a 4- to 12-membered heterocyclyl group substituted with zero to two -OH groups, zero to two $-OR^{49}$ groups, and zero to six fluorine atoms.

Aspect (18): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (16), wherein A^2 represents a 4- to 12-membered heterocyclylene group substituted with =O; and A^2 is optionally substituted with one to four substituents selected from the group consisting of -OH, =O, -COOH, $-SO_3H$, $-PO_3H$, -CN, $-NO_2$, a halogen atom, a C_{1-8} alkyl group substituted with zero to two -OH groups, zero to two $-OR^{45}$ groups, and zero to six fluorine atoms, a C_{3-12} cycloalkyl group substituted with zero to two -OH groups, zero to two $-OR^{46}$ groups, and zero to six fluorine atoms, a C_{1-8} alkoxy group substituted with zero to two -OH groups, zero to two $-OR^{47}$ groups, and zero to six fluorine atoms, and a 4- to 12-membered heterocyclyl group substituted with zero to two -OH groups, zero to two $-OR^{49}$ groups, and zero to six fluorine atoms.

Aspect (19): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (18), wherein X represents CR^{11}, Y represents CR^{12}, Z represents CR^{13}, and R^{11} or R^{13} is bonded to A^1, A^2, or A^3 via a single bond, -O-, $-NR^{51}-$, or $-S(=O)_p-$ to form a ring.

Aspect (20): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (19), wherein A^3 is a hydrogen atom.

Aspect (21): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (19), wherein A^3 is a halogen atom, -CN, $-R^{25}$, $-OR^{26}$, $-NR^{27}R^{28}$, $-C(=O)R^{29}$, or $-C(=O)-OR^{30}$, and R^{25} to R^{30} each independently represent a hydrogen atom, an optionally substituted C_{1-8} alkyl group, an optionally substituted 4- to 12-membered heterocyclyl group, an optionally substituted C_{3-12} cycloalkyl group, an optionally substituted (4- to 12-

membered heterocyclyl)-C_{1-3} alkyl group, or an optionally substituted (C_{3-12} cycloalkyl)-C_{1-3} alkyl group.

Aspect (22): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (21), wherein R^3 is a hydrogen atom.

Aspect (23): The compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (21), wherein R^3 represents a C_{1-4} alkyl group, a fluorine atom, or a chlorine atom.

Aspect (24):

The compound, or pharmaceutically acceptable salt thereof, selected from;

6-(difluoromethyl)-N8-isopropyl-N2-(5-piperazin-1-yl-2-pyridyl)pyrido[3,4-d]pyrimidine-2,8-diamine

(1R)-1-[8-(isopropylamino)-2-[(5-piperazin-1-yl-2-pyridyl)amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol

1-[2-[(5-piperazin-1-yl-2-pyridyl)amino]-8-(tetrahydrofuran-3-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol

1-[2-[(5-piperazin-1-yl-2-pyridyl)amino]-8-(tetrahydropyran-3-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol

N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-(6-piperazin-1-ylpyridazin-3-yl)pyrido[3,4-d]pyrimidine-2,8-diamine

N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]pyrido[3,4-d]pyrimidine-2,8-diamine

1-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one

1-[6-[[5-chloro-6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one

(1R)-1-[2-[(6-piperazin-1-ylpyridazin-3-yl)amino]-8-(tetrahydropyran-4-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol

(1R)-1-[2-[(6-piperazin-1-ylpyridazin-3-yl)amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-

6-yl]ethanol
(1R)-1-[2-[(6-piperazin-1-ylpyridazin-3-yl)amino]-8-[[(3R)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[5-(piperazin-1-ylmethyl)-2-pyridyl]amino]-8-(tetrahydropyran-4-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[5-(piperazin-1-ylmethyl)-2-pyridyl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[5-(piperazin-1-ylmethyl)-2-pyridyl]amino]-8-[[(3R)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
1-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]pyridazin-3-yl]piperidin-4-ol
(1R)-1-[8-(isopropylamino)-2-[(6-piperazin-1-ylpyridazin-3-yl)amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-2-one
6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine
6-[(1R)-1-methoxyethyl]-N2-(6-piperazin-1-ylpyridazin-3-yl)-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine
6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-(tetrahydropyran-4-ylmethyl)pyrido[3,4-d]pyrimidine-2,8-diamine
N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-(5-piperazin-1-ylpyrazin-2-yl)pyrido[3,4-d]pyrimidine-2,8-diamine
N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-[6-[(2S)-2-methylpiperazin-1-yl]pyridazin-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine
N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-[6-[(2R)-2-methylpiperazin-1-yl]pyridazin-3-yl]pyrido[3,4-

d]pyrimidine-2,8-diamine
(1R)-1-[2-[[6-(4,7-diazaspiro[2.5]octan-7-yl)pyridazin-3-yl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[5-(4,7-diazaspiro[2.5]octan-7-ylmethyl)-2-pyridyl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
2-[1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]-4-piperidyl]propan-2-ol
(1R)-1-[2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[5-[2-(dimethylamino)ethoxy]-2-pyridyl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[6-(4-methylpiperazin-1-yl)pyridazin-3-yl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
2-hydroxy-1-[4-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]pyridazin-3-yl]piperazin-1-yl]ethanone
1-[6-[[8-(isopropylamino)-6-[(2S)-tetrahydrofuran-2-yl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one
(1R)-1-[8-(isopropylamino)-2-(5,6,7,8-tetrahydro-1,6-naphthyridin-2-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
2-[4-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]-2-methyl-propan-1-ol
4-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]-1-[(2S)-2-hydroxypropyl]-1,4-diazepan-5-one
4-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]-1-[(2R)-2-hydroxypropyl]-1,4-diazepan-5-one

N8-isopropyl-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-6-[(2S)-tetrahydrofuran-2-yl]pyrido[3,4-d]pyrimidine-2,8-diamine

1-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-2-methyl-3-pyridyl]piperazin-2-one

1-[6-[[8-(isopropylamino)-6-[(3S)-tetrahydrofuran-3-yl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one

(1R)-1-[2-(5,6,7,8-tetrahydro-1,6-naphthyridin-2-ylamino)-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol

1-[6-[[8-(isopropylamino)-6-(3-methyloxetan-3-yl)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one

(1R)-1-[2-[[5-[4-(dimethylamino)cyclohexoxy]-2-pyridyl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol

6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine

6-[(1R)-1-methoxyethyl]-N2-(6-piperazin-1-ylpyridazin-3-yl)-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine

1-[[6-[[6-(difluoromethyl)-8-[(4-methylcyclohexyl)amino]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidine-4-carboxylic acid

(1R)-1-[8-(ethylamino)-2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol

(1R)-1-[2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]-8-(propylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol

N8-isopropyl-6-(3-methyloxetan-3-yl)-N2-(6-piperazin-1-ylpyridazin-3-yl)pyrido[3,4-d]pyrimidine-2,8-diamine

N8-isopropyl-6-(3-methyloxetan-3-yl)-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]pyrido[3,4-d]pyrimidine-2,8-diamine

6-(3-methyloxetan-3-yl)-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-

d]pyrimidine-2,8-diamine
4-[6-[[6-[(1R)-1-hydroxyethyl]-8-[isopropyl(methyl)amino]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]-1,4-diazepan-5-one
(1R)-1-[8-(isopropylamino)-2-[(6-methyl-5-piperazin-1-yl-2-pyridyl)amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[2-[[6-(2-hydroxyethyl)-7,8-dihydro-5H-1,6-naphthyridin-2-yl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[8-(isopropylamino)-2-[[6-[2-(methylamino)ethyl]-7,8-dihydro-5H-1,6-naphthyridin-2-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
N2-(6-piperazin-1-ylpyridazin-3-yl)-6-[(3S)-tetrahydrofuran-3-yl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine
N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-6-[(3R)-tetrahydrofuran-3-yl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine
(1R)-1-[2-[[6-[2-(dimethylamino)ethyl]-7,8-dihydro-5H-1,6-naphthyridin-2-yl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol
(2S)-1-[4-[[6-[[8-(ethylamino)-6-[(1R)-1-hydroxyethyl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]propan-2-ol
(2R)-1-[4-[[6-[[8-(ethylamino)-6-[(1R)-1-hydroxyethyl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]propan-2-ol
(1R)-1-[8-(isopropylamino)-2-[[5-[(2R)-2-methylpiperazin-1-yl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[8-(isopropylamino)-2-[[5-[(2S)-2-methylpiperazin-1-yl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
N8-isopropyl-N2-(5-piperazin-1-yl-2-pyridyl)-6-[(2S)-tetrahydrofuran-2-yl]pyrido[3,4-d]pyrimidine-2,8-diamine
(1R)-1-[8-(cyclobutylamino)-2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol
(1R)-1-[8-(cyclopropylmethylamino)-2-[[5-[[4-(2-

hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol

6-(3-methyloxetan-3-yl)-N2-(5-piperazin-1-yl-2-pyridyl)-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine

6-(3-methyloxetan-3-yl)-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine

N2-(5-piperazin-1-yl-2-pyridyl)-N8-propyl-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidine-2,8-diamine

N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-propyl-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidine-2,8-diamine

N8-isopropyl-6-(3-methyloxetan-3-yl)-N2-(5-piperazin-1-yl-2-pyridyl)pyrido[3,4-d]pyrimidine-2,8-diamine

N8-isopropyl-N2-(5-piperazin-1-yl-2-pyridyl)-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidine-2,8-diamine

2-[4-[[6-[[8-(isopropylamino)-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]ethanol

2-[4-[[6-[[6-tetrahydrofuran-3-yl-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]ethanol

(1R)-1-[2-[[5-[[4-(hydroxymethyl)-1-piperidyl]methyl]-2-pyridyl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol

1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidin-4-ol

1-[[6-[[8-(tert-butylamino)-6-[(1R)-1-hydroxyethyl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidin-4-ol

(1R)-1-[8-(tert-butylamino)-2-[[5-[[4-(hydroxymethyl)-1-piperidyl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol

1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isobutylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidin-4-ol

(1R)-1-[2-[[5-[[4-(hydroxymethyl)-1-piperidyl]methyl]-2-pyridyl]amino]-8-(isobutylamino)pyrido[3,4-d]pyrimidin-6-

yl]ethanol
1-[6-[[6-[(1R)-1-hydroxypropyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one
(1R)-1-[2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-6-methyl-2-pyridyl]amino]-8-(propylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol

Aspect (25): A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (24) and a pharmaceutically acceptable carrier.

Aspect (26): A pharmaceutical composition exhibiting a CDK4/6 inhibitory activity, comprising the compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (24) as an active ingredient.

Aspect (27): A drug for prevention or treatment of rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, or cancer, the drug comprising the compound or pharmaceutically acceptable salt thereof according to any one of Aspects (1) to (24) as an active ingredient.

Advantageous Effects of Invention

[0021]

The compound of the present invention exhibits a superior CDK4/6 inhibitory activity and is useful as a drug for prevention or treatment of rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, or cancer.

Brief Description of Drawings

[0022]

Fig. 1 is graphs showing the results (scores) obtained through administration of the compound of the present invention to mice.

Description of Embodiments

[0023]

Now will be described the structures (groups) of the compound of the present invention represented by Formula

(I). The description of "groups" with parentheses is as follows: For example, the term "(cycloalkyl)-alkyl" refers to a cycloalkyl group bonded to an alkyl group such that the alkyl group is bonded to a structure other than the cycloalkyl group. Similarly, the term "(heterocyclyl)-alkyl" refers to a heterocyclyl group bonded to an alkyl group such that the alkyl group is bonded to a structure other than the heterocyclyl group.

It must be noted that, as used herein and the annexed claims, the singular form "a", "an" or "the" may include plural referents unless the context clearly dictates otherwise.

[0024]

As used herein, "C_{3-6} cycloalkyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms" refers to the case where the C_{3-6} cycloalkyl group is substituted with the following substituents: zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms. Examples of the substituted C_{3-6} cycloalkyl group include a C_{3-6} cycloalkyl group substituted with two -OH groups, one C_{1-8} alkoxy group, and three fluorine atoms; a C_{3-6} cycloalkyl group substituted with two C_{1-8} alkoxy groups and four fluorine atoms; and a C_{3-6} cycloalkyl group substituted with one -OH group, and the like. The C_{3-6} cycloalkyl group is not substituted in the case where the number of all the substituents is zero.

[0025]

As used herein, "C_{1-8}" refers to a group having one to eight carbon atoms, and "C_{1-6}" refers to a group having one to six carbon atoms. Similarly, "5- to 10-membered" refers to a structure having 5 to 10 carbon atoms, and "5- or 6-membered" refers to a structure having five or six carbon atoms.

[0026]

Non-limiting examples of the groups described in this specification are as follows:

The term "alkyl" as used herein refers to a monovalent group obtained by removal of one hydrogen atom from an alkane at any carbon atom.

The term "alkylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from an alkane at any two different carbon atoms.

The term "alkane" as used herein refers to a saturated aliphatic hydrocarbon.

[0027]

The term "C_{1-8} alkyl" as used herein refers to a linear or branched hydrocarbon group having one to eight carbon atoms. Examples of the C_{1-8} alkyl include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, neopentyl, isopentyl, 1,2-dimethylpropyl, n-hexyl, isohexyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, isoheptyl, n-octyl, isooctyl, and the like.

[0028]

The alkane of "C_{1-8} alkylene" as used herein refers to a linear or branched hydrocarbon having one to eight carbon atoms. Examples of the alkane include methane, ethane, propane, n-butane, 2-methylpropane, n-pentane, 2,2-dimethylpropane, n-hexane, 2-methylpentane, 3-methylpentane, 2,2-dimethylbutane, 2,3-dimethylbutane, n-heptane, 2,2-dimethylhexane, 2,3-dimethylhexane, n-octane, 2-methylheptane, and the like.

[0029]

The term "cycloalkyl" as used herein refers to a monovalent group obtained by removal of one hydrogen atom from a cycloalkane at any carbon atom.

The term "cycloalkylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from a cycloalkane at any two different carbon atoms.

The term "cycloalkylidene" refers to a divalent group obtained by removal of two hydrogen atoms from a cycloalkane at any one carbon atom.

The term "cycloalkane" as used herein refers to an

alicyclic hydrocarbon.

[0030]

The cycloalkane of "C_{3-12} cycloalkyl," "C_{3-12} cycloalkylene," or "C_{3-12} cycloalkylidene" as used herein refers to a monocyclic or polycyclic 3- to 12- membered aliphatic hydrocarbon ring. Specific examples of the cycloalkane include cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, spiro[3.3]heptane, bicyclo[1.1.1]pentane, bicyclo[2.2.2]octane, adamantane, and the like.

[0031]

The term "heterocyclyl" as used herein refers to a monovalent group obtained by removal of one hydrogen atom from a heterocycle at any carbon or nitrogen atom.

The term "heterocyclylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from a heterocycle at any two different carbon or nitrogen atoms.

The term "heterocyclylidene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from a heterocycle at any one carbon atom.

The term "heterocycle" as used herein refers to a ring containing a heteroatom selected from sulfur, nitrogen, and oxygen atoms.

[0032]

The heterocycle of "4- to 12-membered heterocyclyl," "4- to 12-membered heterocyclylene," or "4- to 12-membered heterocyclylidene" as used herein refers to "4- to 12-membered heterocycloalkane," "4- to 12-membered heterocycloalkane" having an unsaturated bond, a 4- to 12-membered ring composed of a heterocycloalkane and a heteroarene or arene bonded to a portion of the heterocycloalkane, a 4- to 12-membered ring composed of a cycloalkane and a heteroarene bonded to a portion of the cycloalkane, a 4- to 12-membered ring containing a heteroatom and having a spiro structure, or a 4- to 12-membered ring containing a heteroatom and having a cross-

linked structure. The term "4- to 12-membered heterocycloalkane" refers to a 4- to 12-membered cyclic heteroalkane; i.e., a monocyclic or polycyclic aliphatic hydrocarbon ring containing one to four heteroatoms selected from sulfur, nitrogen, and oxygen atoms. Specific examples of the "4- to 12-membered heterocycloalkane" include aziridine, thiirane, azetidine, oxetane, thietane, tetrahydrofuran, tetrahydropyran, 1,4-dioxane, piperidine, piperazine, pyrrolidine, imidazolidine, pyrazolidine, morpholine, thiomorpholine, tetrahydrothiopyran, tetrahydrothiophene, 1,4-diazepane, oxepane, and the like. A compound having a "spiro structure" is composed of two cyclic structures (cycloalkanes or heterocycloalkanes) that are bonded to one common carbon atom. Examples of the compound include 2-azaspiro[3.3]heptane, 1,6-diazaspiro[3.3]heptane, 2,6-diazaspiro[3.3]heptane, 2,6-diazaspiro[3.4]octane, 2,7-diazaspiro[3.5]nonane, 1,7-diazaspiro[4.5]decane, 2,8-diazaspiro[4.5]decane, 4,7-diazaspiro[2.5]octane, and the like. A compound having a "cross-linked structure" is composed of two cyclic structures (cycloalkanes and heterocycloalkanes) that are bonded to two or more common carbon, nitrogen, or oxygen atoms. Examples of the compound include 2,5-diazabicyclo[2.2.2]octane, 3,8-diazabicyclo[3.2.1]octane, 1,4-diazabicyclo[3.2.2]nonane, octahydropyrrolo[3,4-b]pyrrole, and the like.

[0033]

The term "aryl" as used herein refers to a monovalent group obtained by removal of one hydrogen atom from an arene at any carbon atom.

The term "arylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from an arene at any two different carbon atoms.

The term "arene" as used herein refers to an aromatic hydrocarbon.

The arene of "C_{6-10} aryl" or "C_{6-10} arylene" as used herein refers to an aromatic hydrocarbon ring having six

to ten carbon atoms. Specific examples of the arene include benzene, naphthalene, and the like.

[0034]

The term "heteroaryl" as used herein refers to a monovalent group obtained by removal of one hydrogen atom from a heteroarene at any carbon or nitrogen atom.

The term "heteroarylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from a heteroarene at any two different carbon or nitrogen atoms.

The term "heteroarene" as used herein refers to an aromatic heterocyclic ring containing a heteroatom selected from sulfur, nitrogen, and oxygen atoms.

The heteroarene of "5- to 10-membered heteroaryl" or "5- to 10-membered heteroarylene" as used herein refers to a 5- to 10-membered aromatic heterocyclic ring containing one to four heteroatoms selected from sulfur, nitrogen, and oxygen atoms. Specific examples of the heteroarene include furan, thiophene, pyrrole, imidazole, pyrazole, triazole, tetrazole, thiazole, oxazole, isoxazole, oxadiazole, thiadiazole, isothiazole, pyridine, pyridazine, pyrazine, pyrimidine, quinolone, isoquinolone, benzofuran, benzothiophene, indole, indazole, benzimidazole, and the like.

[0035]

The term "(4- to 12-membered heterocyclyl)-C_{1-6} alkyl" as used herein refers to a 4- to 12-membered heterocyclyl group bonded to a C_{1-6} alkyl group such that the C_{1-6} alkyl group is bonded to a structure other than the 4- to 12-membered heterocyclyl group. Specific examples of the (4- to 12-membered heterocyclyl)-C_{1-6} alkyl include groups prepared by bonding of any of the above-exemplified 4- to 12-membered heterocyclyl groups to any of the above-exemplified C_{1-6} alkyl groups.

The term "(C_{6-10} aryl)-C_{1-6} alkyl" as used herein refers to a C_{6-10} aryl group bonded to a C_{1-6} alkyl group such that the C_{1-6} alkyl group is bonded to a structure

other than the C_{6-10} aryl group. Specific examples of the (C_{6-10} aryl)-C_{1-6} alkyl include groups prepared by bonding of any of the above-exemplified C_{6-10} aryl groups to any of the above-exemplified C_{1-6} alkyl groups.

The term "(5- to 10-membered heteroaryl)-C_{1-6} alkyl" as used herein refers to a 5- to 10-membered heteroaryl group bonded to a C_{1-6} alkyl group such that the C_{1-6} alkyl group is bonded to a structure other than the 5- to 10-membered heteroaryl group. Specific examples of the (5- to 10-membered heteroaryl)-C_{1-6} alkyl include groups prepared by bonding of any of the above-exemplified 5- to 10-membered heteroaryl groups to any of the above-exemplified C_{1-6} alkyl groups.

[0036]

The term "C_{1-8} alkylsulfonyl" as used herein refers to a C_{1-8} alkyl group bonded to a sulfonyl ($-S(=O)_2-$) group such that the sulfonyl group is bonded to a structure other than the C_{1-8} alkyl group.

The term "C_{1-8} acyl" as used herein refers to a C_{1-7} alkyl group bonded to a carbonyl (-CO-) group such that the carbonyl group is bonded to a structure other than the C_{1-7} alkyl group.

The term "halogen" as used herein refers to a fluorine, chlorine, bromine, or iodine atom.

The term "C_{1-8} alkoxy" as used herein refers to a linear, branched, or cyclic alkoxy group having one to eight carbon atoms. Specific examples of the C_{1-8} alkoxy include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentyloxy, neopentyloxy, tert-pentyloxy, 2-methylbutoxy, n-hexyloxy, isohexyloxy, cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy, cyclooctyloxy, spiro[3.3]heptyloxy, bicyclo[2.2.2]octyloxy, and the like.

[0037]

The term "alkenyl" as used herein refers to a monovalent group obtained by removal of one hydrogen atom

from an alkene at any carbon atom.

The term "alkenylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from an alkene at any two different carbon atoms.

The term "alkene" as used herein refers to an unsaturated aliphatic hydrocarbon having one double bond.

The term "C_{2-8} alkenyl" as used herein refers to a chain aliphatic hydrocarbon having one double bond. Examples of the C_{2-8} alkenyl include ethenyl (or vinyl), propenyl (or allyl), butenyl, and the like.

[0038]

The term "alkynyl" as used herein refers to a monovalent group obtained by one hydrogen atom from an alkyne at any carbon atom.

The term "alkynylene" as used herein refers to a divalent group obtained by removal of two hydrogen atoms from an alkyne at any two different carbon atoms.

The term "alkyne" as used herein refers to an unsaturated aliphatic hydrocarbon having one triple bond.

[0039]

The term "C_{2-4} alkynyl" as used herein refers to a chain hydrocarbon group having one triple bond. Examples of the C_{2-4} alkynyl include ethynyl, propynyl, butynyl, and the like.

L is preferably $-NR^5-$.

The "C_{1-6} alkyl" of R^5 is preferably methyl or ethyl.

R^5 is preferably a hydrogen atom or a methyl group.

The "C_{1-8} alkyl" of R^1 is preferably methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, neopentyl, isopentyl, 1,2-dimethylpropyl, n-hexyl, isohexyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, isoheptyl, n-octyl, or isooctyl.

[0040]

The "C_{3-12} cycloalkyl" of R^1 is preferably cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, spiro[3.3]heptyl, bicyclo[1.1.1]pentane,

bicyclo[2.2.2]octyl, or adamantyl.

The "(C_{3-12} cycloalkyl)-C_{1-6} alkyl" of R^1 is preferably cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, or cyclopentylethyl.

The heterocycle of "4- to 12-membered heterocyclyl" in R^1 is preferably azetidine, oxetane, thietane, tetrahydrofuran, 1,4-dioxane, morpholine, thiomorpholine, tetrahydropyran, tetrahydrothiophene, or oxepane.

The "(4- to 12-membered heterocyclyl)-C_{1-6} alkyl" of R^1 is preferably (tetrahydrofuranyl)methyl, (tetrahydropyranyl)methyl, (tetrahydrofuranyl)ethyl, or (tetrahydropyranyl)ethyl.

[0041]

The "C_{6-10} aryl" of R^1 is preferably phenyl.

The "(C_{6-10} aryl)-C_{1-6} alkyl" of R^1 is preferably phenylmethyl or phenylethyl.

The "5- to 10-membered heteroaryl" of R^1 is preferably furanyl, pyrazolyl, or thienyl.

The "halogen" in the substituent of R^1 is preferably a fluorine or chlorine atom.

The "-$COOR^6$" in the substituent of R^1 is preferably -COOH or -$COOCH_3$.

[0042]

The "R^7" in the substituent of R^1 is preferably ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, neopentyl, isopentyl, 1,1-dimethyl-2-methoxyethyl, 1-methyl-2-methoxyethyl, 1-methyl-2-hydroxyethyl, 2,2,2-trifluoroethyl, hydroxymethyl, or 1-methyl-2,2,2-trifluoroethyl.

[0043]

The "C_{3-6} cycloalkyl optionally substituted with a substituent selected from the group consisting of one or two -OH groups, one or two C_{1-8} alkoxy groups, and one to six fluorine atoms" in the substituent of R^1 is preferably cyclopentyl, cyclohexyl, 4-methoxycyclohexyl, or 4-isopropoxycyclohexyl.

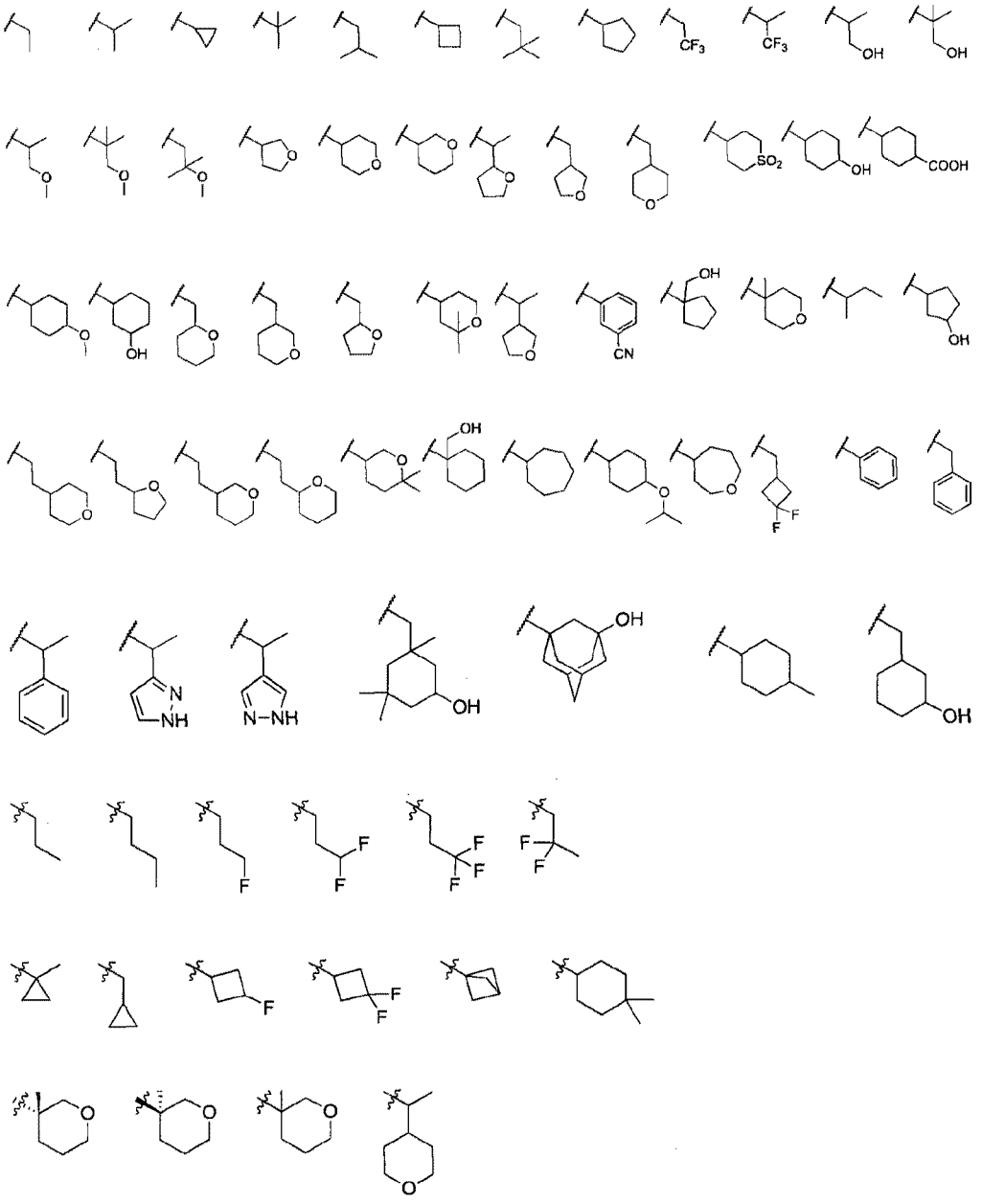
The 3- to 10-membered heterocyclyl optionally

substituted with a substituent selected from the group consisting of one or two -OH groups, one or two C_{1-8} alkoxy groups, and one to six fluorine atoms in the substituent of R^1 is preferably tetrahydrofuranyl, tetrahydropyranyl, or 2,2-dimethyltetrahydropyranyl.

R^1 preferably has any of the following structures:

[0044]

[Formula 2]



[0045]

The "C_{1-6} alkyl" of R^2 is preferably methyl, ethyl, or n-propyl, and the substituent is preferably a hydroxy, methoxy, or ethoxy group or a fluorine atom. The "4- to 6-membered heterocyclyl" of R^2 is preferably oxetane or tetrahydrofuranyl.

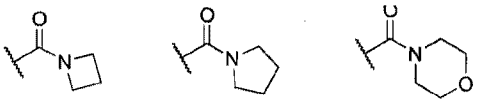
The "C_{1-8} acyl" of R^2 is preferably acetyl.

The "$-COOR^8$" of R^2 is preferably -COOH or $-COOCH_3$.

The "$-CONR^9R^{10}$" of R^2 is preferably $-CON(CH_3)_2$.

R^9 and R^{10} of $-CONR^9R^{10}$ of R^2 may be bonded via a single bond or -O- to form a ring including the nitrogen atom bonded to R^9 and R^{10}. Examples of such a ring include the following structures:

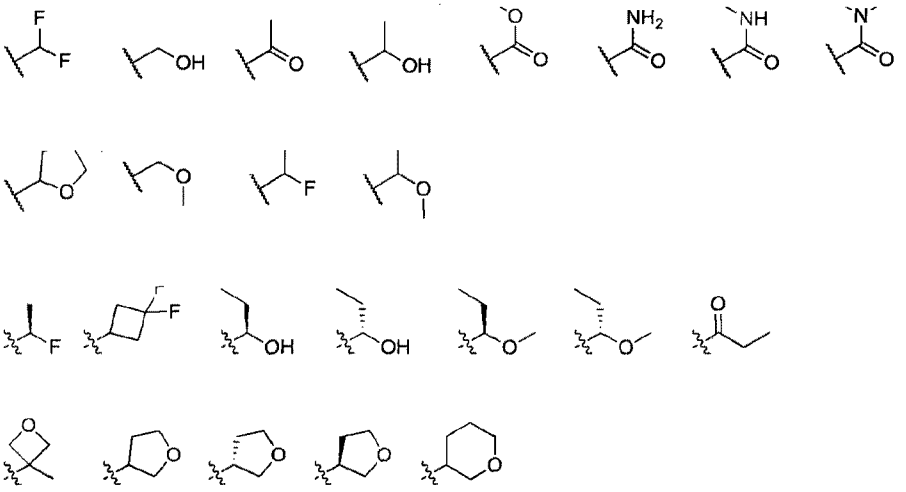
[Formula 3]



R^2 preferably has any of the following structures:

[0046]

[Formula 4]



[0047]

The "C_{1-8} alkyl" of R^3 is preferably methyl.

The "halogen" of R^3 is preferably a fluorine or chlorine atom.

R^3 is preferably a hydrogen, fluorine, or chlorine atom or a methyl group.

X, Y, and Z preferably correspond to any of the following combinations: X, Y, and Z are each CH; X is a nitrogen atom and Y and Z are each CH; Y is a nitrogen atom and X and Z are each CH; and Z is a nitrogen atom and X and Y are each CH.

[0048]

The "C_{1-8} alkylene" of A^1 is preferably methylene, ethylene, or n-propylene.

The structure obtained by replacement of one or two sp^3 carbon atoms at any positions of A^1 is preferably -O-, $-OCH_2-$, $-OCH_2CH_2-$, $-OCH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2OCH_2-$, $-CH_2OCH_2CH_2-$, $-CH_2CO-$, $-COCH_2-$, $-CH_2CH_2CO-$, $-COCH_2CH_2-$, $-CH_2COCH_2-$, $-CH_2COCH_2CH_2-$, $-NR^{14}-$, $-NR^{14}CH_2-$, $-CH_2NR^{14}-$, $-NR^{14}CH_2CH_2-$, $-CH_2NR^{14}CH_2-$, or $-CH_2CH_2NR^{14}-$.

[0049]

The "C_{1-7} alkylene" of A^2 is preferably methylene, ethylene, or n-propylene.

The "C_{3-12} cycloalkylene" of A^2 is preferably cyclopropylene, cyclobutylene, cyclopentylene, or cyclohexylene.

The heterocycle of "4- to 12-membered heterocyclylene" of A^2 is preferably piperidine, piperazine, pyrrolidine, morpholine, tetrahydrofuran, tetrahydropyran, 1,4-diazepane, oxepane, 2-azaspiro[3.3]heptane, 1,6-diazaspiro[3.3]heptane, 2,6-diazaspiro[3.3]heptane, 2,6-diazaspiro[3.4]octane, 2,5-diazabicyclo[2.2.2]octane, 3,8-diazabicyclo[3.2.1]octane, 2,7-diazaspiro[3.5]nonane, 1,7-diazaspiro[4.5]decane, 2,8-diazaspiro[4.5]decane, 4,7-diazaspiro[2.5]octane, 1,4-diazabicyclo[3.2.2]nonane, or octahydropyrrolo[3,4-b]pyrrole.

[0050]

The heterocycle of "4- to 12-membered heterocyclylidene" of A^2 is preferably oxetane, tetrahydrofuran, tetrahydropyran, pyrrolidine, piperidine, piperazine, morpholine, or oxepane.

The "C_{6-10} arylene" of A^2 is preferably phenylene.

The heteroarene of "5- to 10-membered heteroarylene" of A^2 is preferably furan, thiophene, pyrrole, imidazole, pyrazole, triazole, tetrazole, thiazole, oxazole, isoxazole, oxadiazole, thiadiazole, isothiazole, pyridine, pyridazine, pyrazine, pyrimidine, quinolone,

isoquinoline, benzofuran, benzothiophene, indole, indazole, or benzimidazole.

[0051]

The "halogen" of A^3 is preferably a fluorine or chlorine atom.

The "$-R^{25}$" of A^3 is a hydrogen atom or a methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, or tert-butyl group. The $-R^{25}$ substituted with a substituent is preferably a hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 2-hydroxy-2-propyl, 2-hydroxy-1-propyl, 1-hydroxy-2-propyl, 1-hydroxy-2-methyl-2-propyl, 2-hydroxy-2-methyl-1-propyl, trifluoromethyl, 2,2,2-trifluoroethyl, carboxymethyl, 1-carboxyethyl, 2-carboxyethyl, 2-carboxy-2-propyl, or cyanomethyl group.

The "$-OR^{26}$" of A^3 is preferably -OH, methoxy, ethoxy, or isopropoxy.

The "$-NR^{27}R^{28}$" of A^3 is preferably amino, dimethylamino, methylamino, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, or morpholin-1-yl.

The "$-C(=O)R^{29}$" of A^3 is preferably acetyl. The $-C(=O)R^{29}$ substituted with a substituent is preferably hydroxyacetyl.

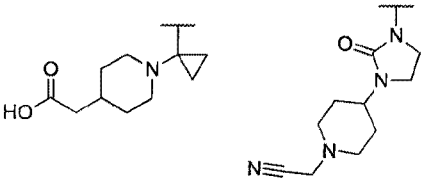
The "$-C(=O)-OR^{30}$" of A^3 is preferably -COOH, methoxycarbonyl, ethoxycarbonyl, or isopropoxycarbonyl.

The "$-C(=O)-NR^{34}R^{35}$" of A^3 is preferably aminocarbonyl (or carbamoyl), (methylamino)carbonyl, (dimethylamino)carbonyl, (pyrrolidin-1-yl)carbonyl, (piperidin-1-yl)carbonyl, (morpholin-1-yl)carbonyl, or (piperazin-1-yl)carbonyl.

The "$-S(=O)_2-R^{40}$" of A^3 is preferably methanesulfonyl or ethylsulfonyl.

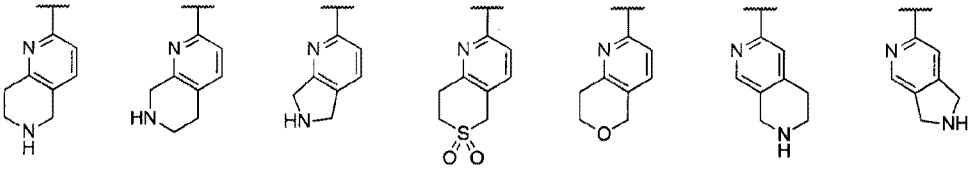
R^{14} to R^{44} in A^1, A^2, and A^3 may be bonded in A^1, A^2, or A^3 or between A^1 and A^2, between A^1 and A^3, or between A^2 and A^3 via a single bond, -O-, $-NR^{50}-$, or $-S(=O)_p-$ to form a ring. Examples of such a ring include the following structures:

[Formula 5]



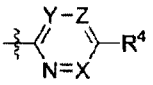
R^{11} or R^{13} may be bonded to A^1, A^2, or A^3 via a single bond, -O-, $-NR^{51}-$, or $-S(=O)_p-$ to form a ring. Examples of such a ring include the following structures:

[Formula 6]



[0052]

[Formula 7]

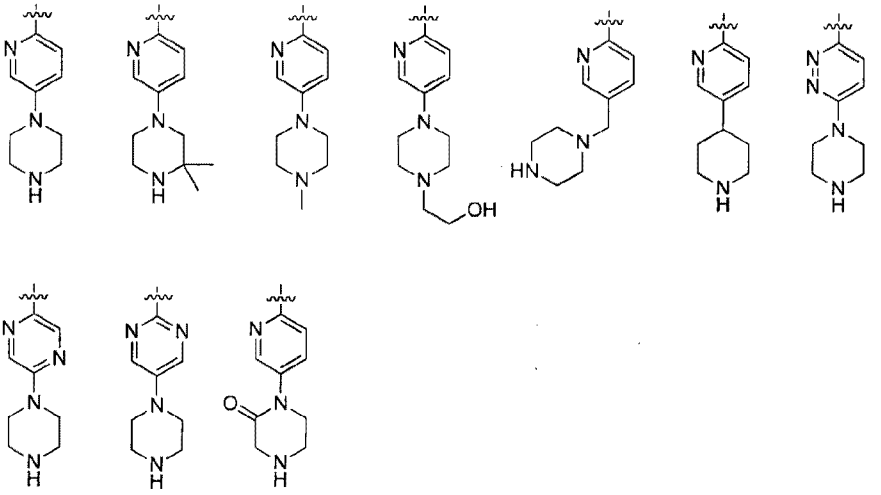


[0053]

Preferred examples of the aforementioned entire structure are as follows:

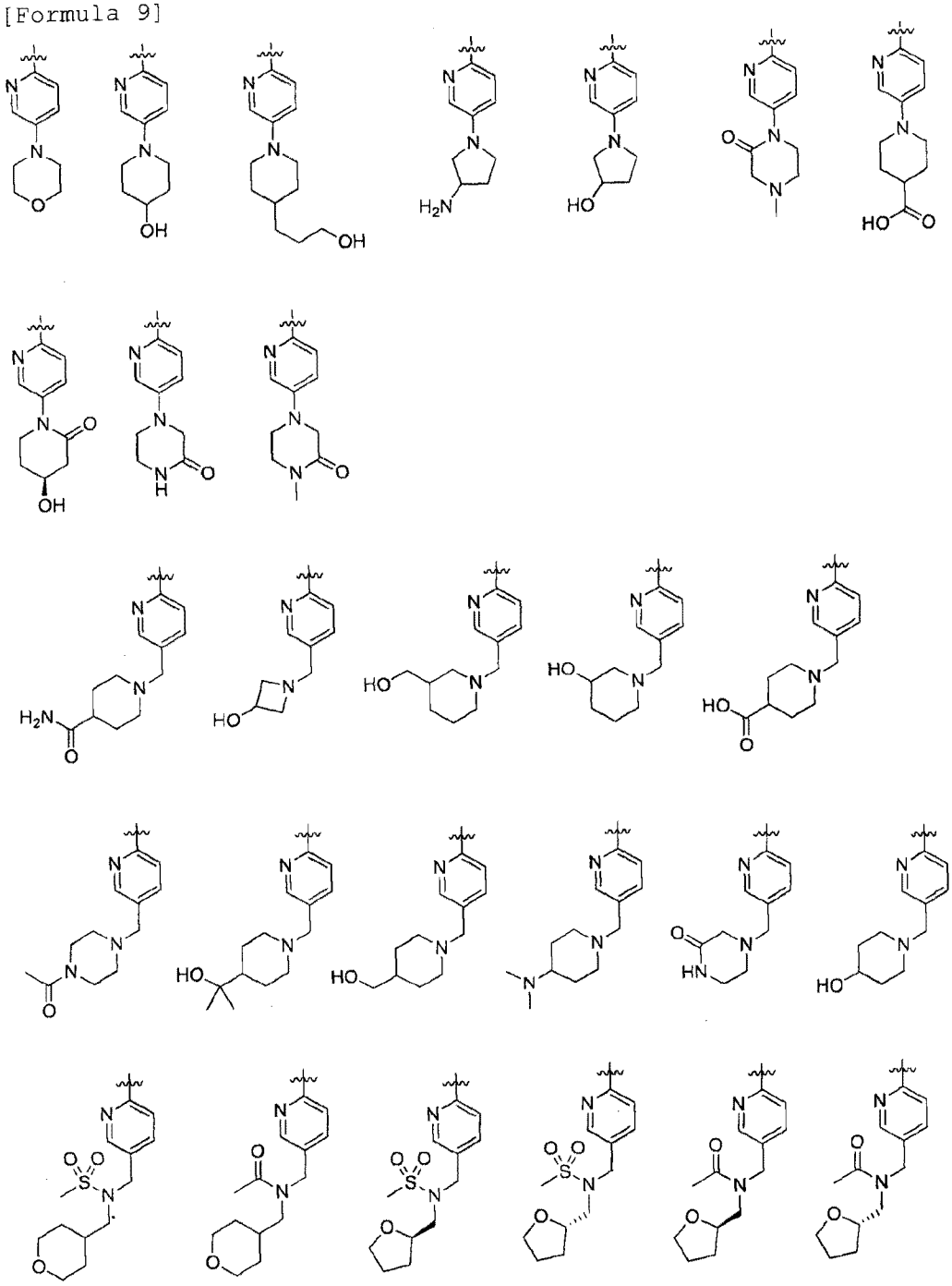
[0054]

[Formula 8]



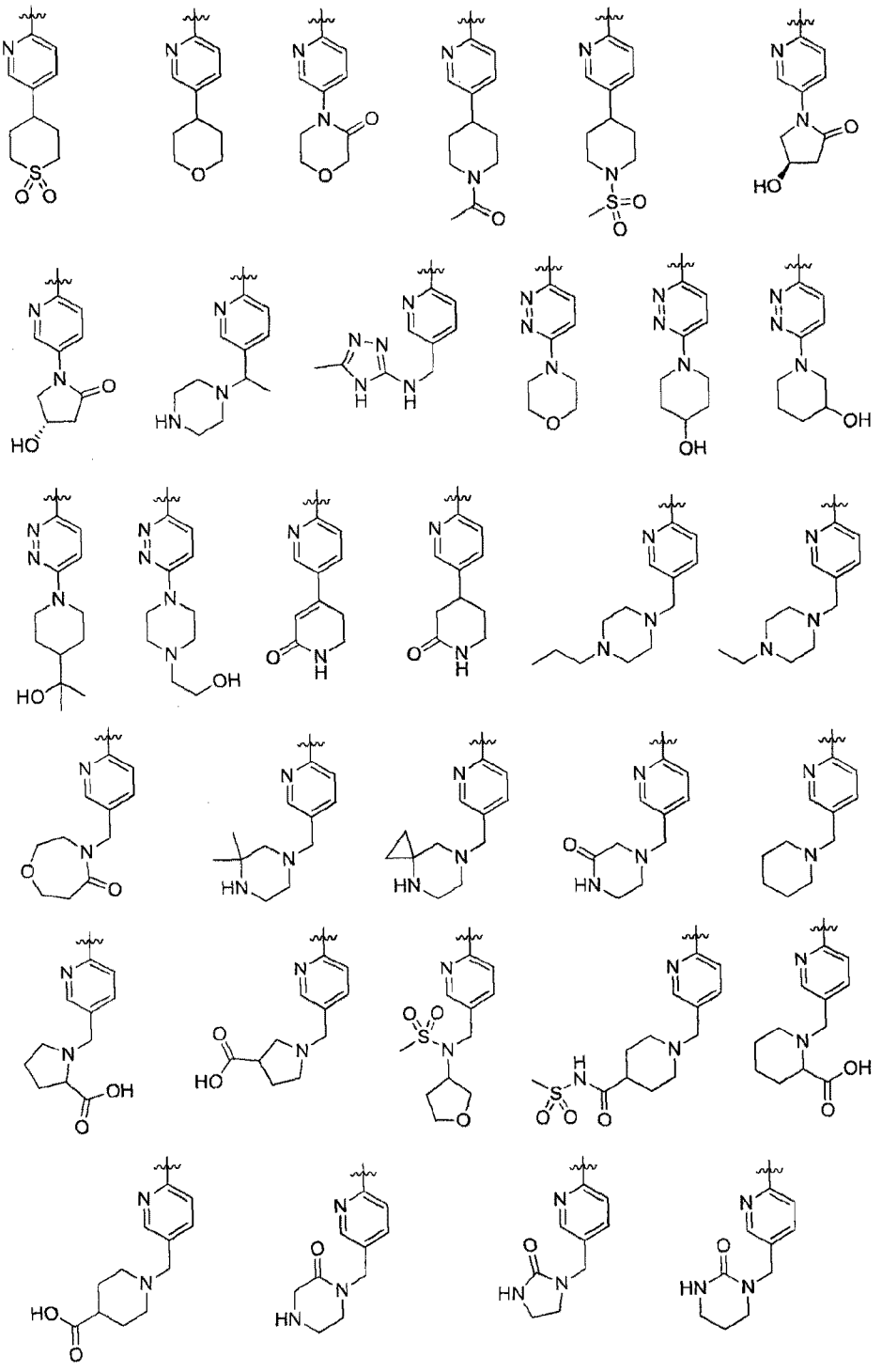
[0055]

[Formula 9]



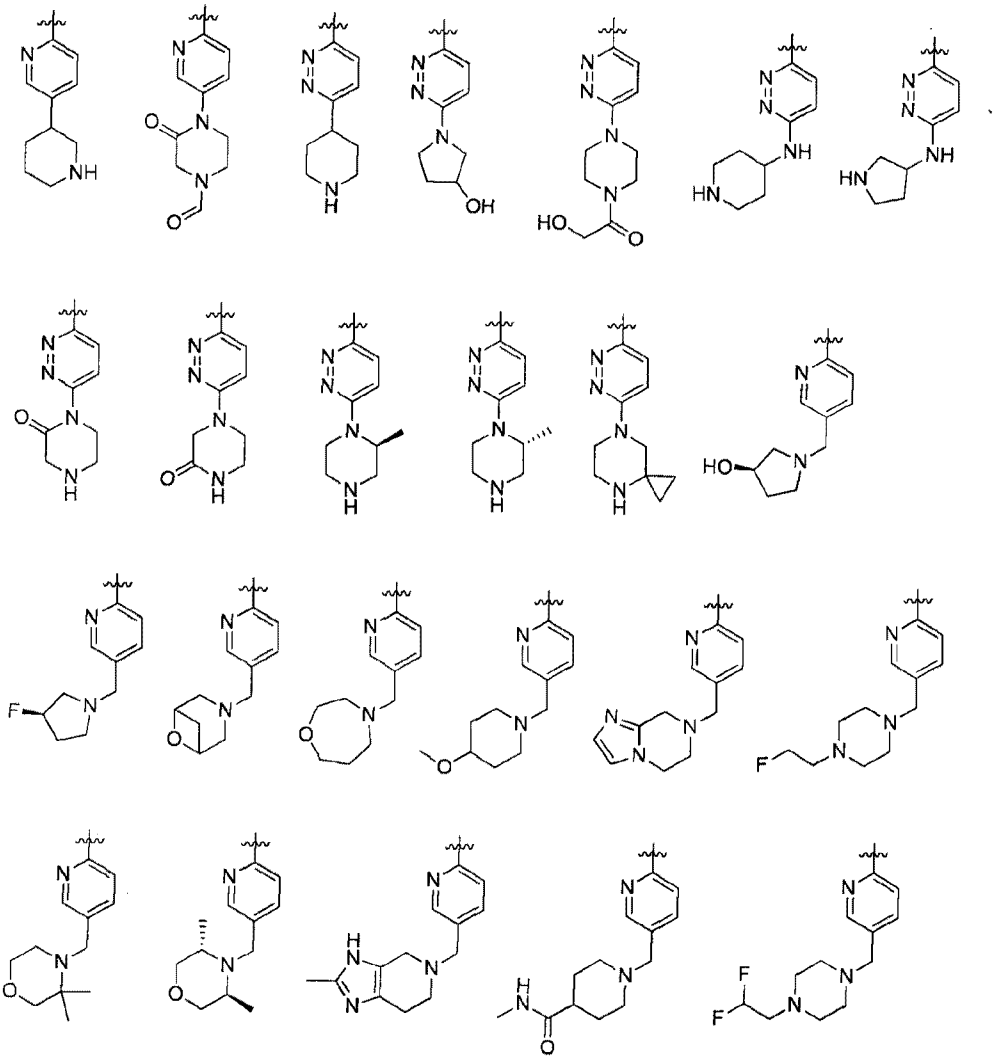
[0056]

[Formula 10]



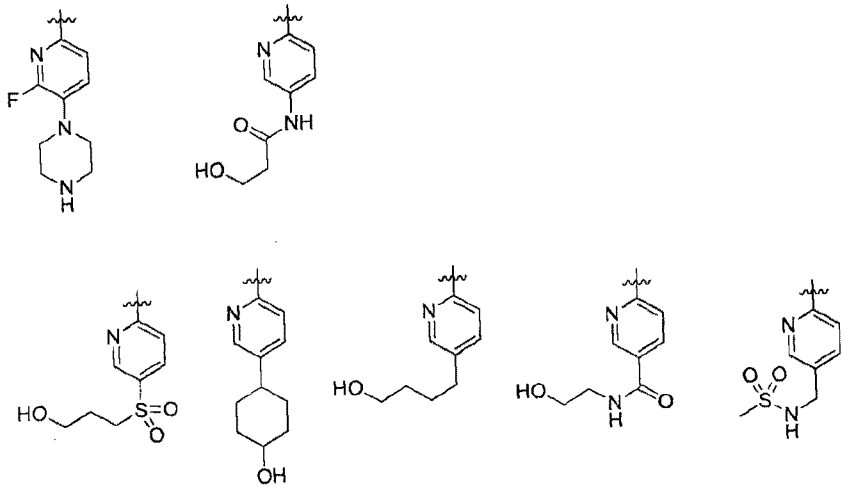
[0057]

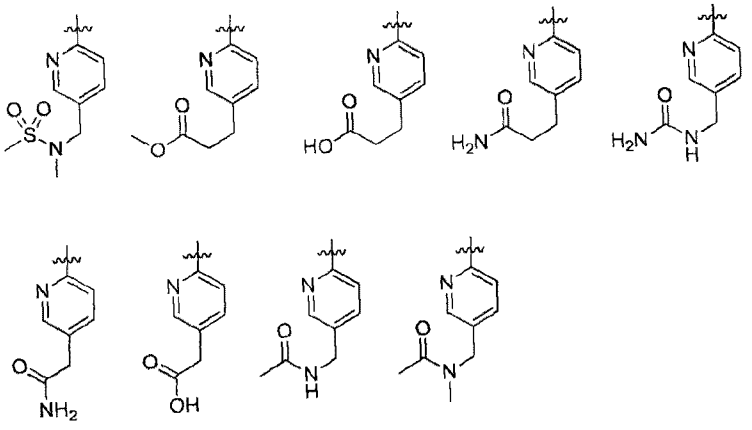
[Formula 11]

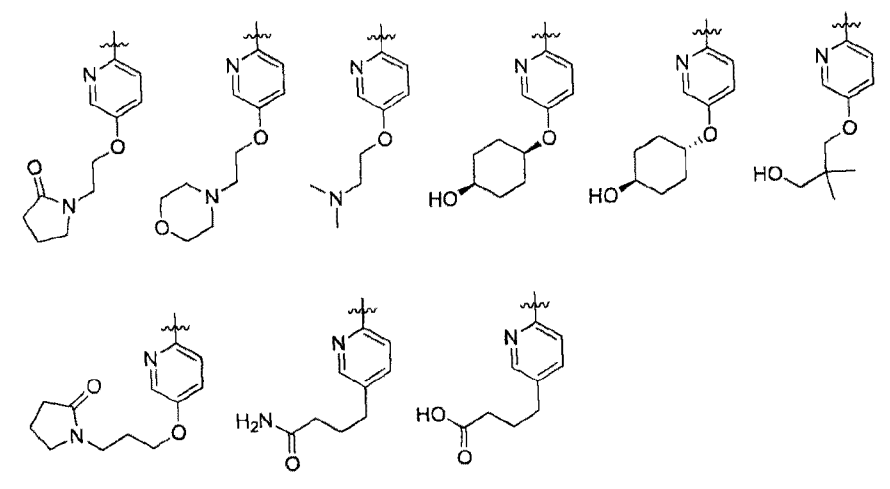


[0058]

[Formula 12]

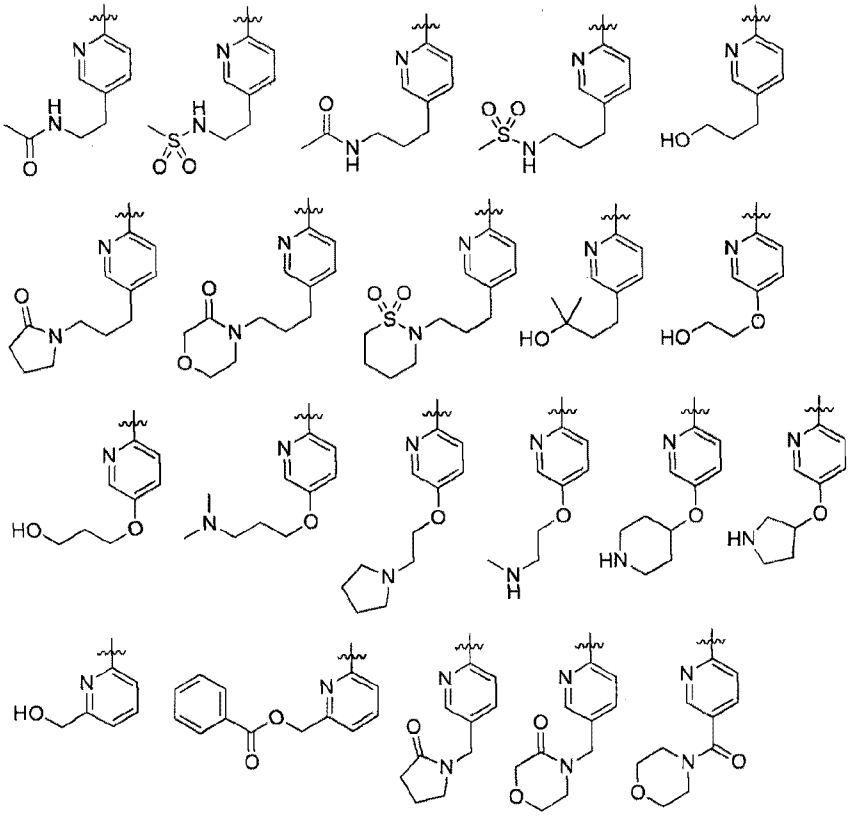


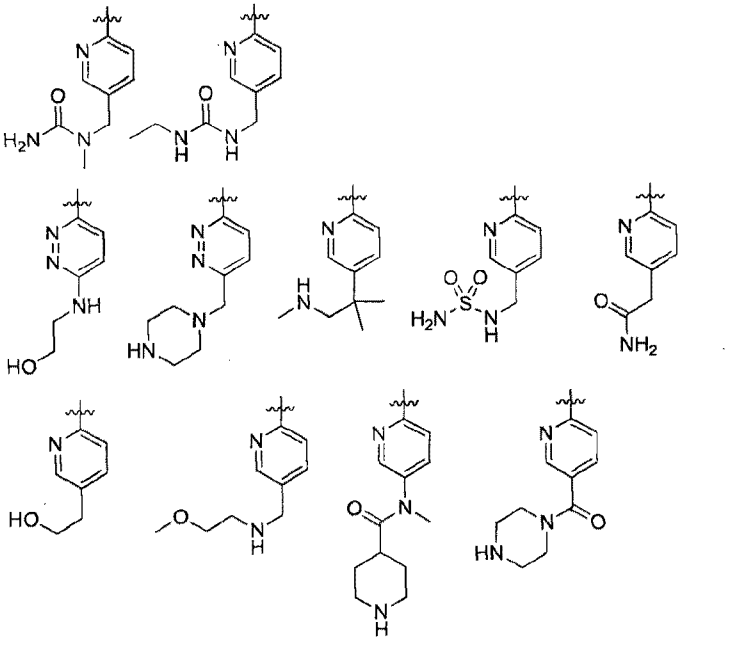




[0059]

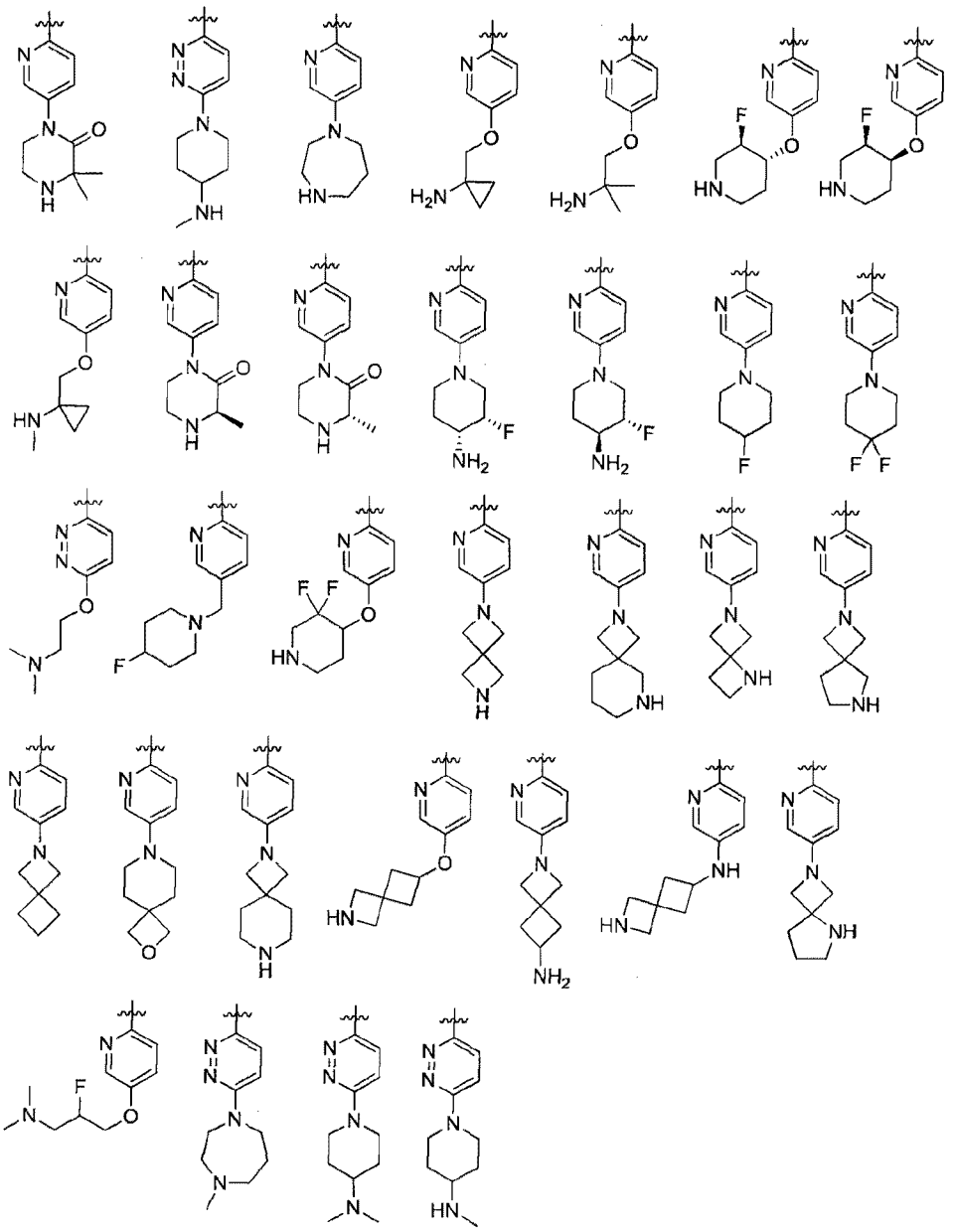
[Formula 13]





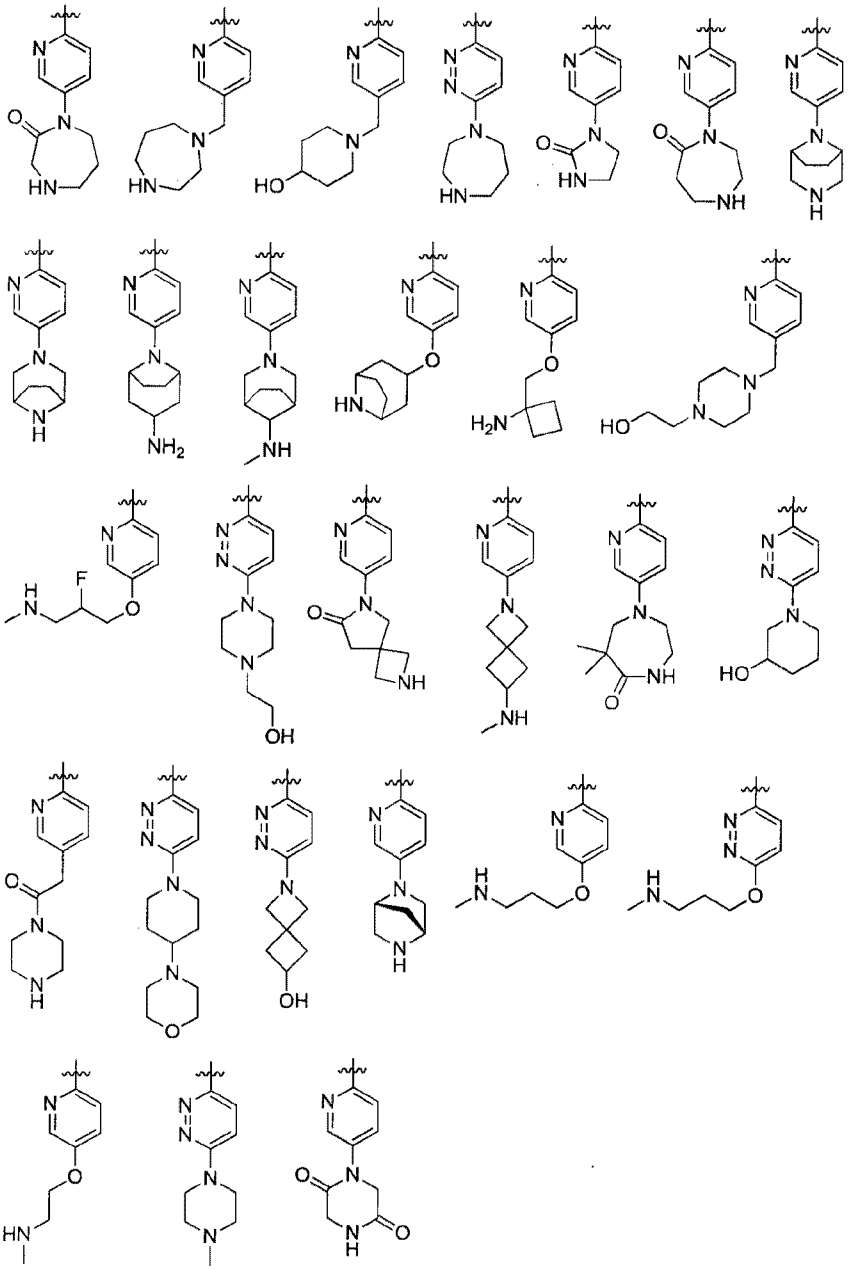
[0060]

[Formula 14]



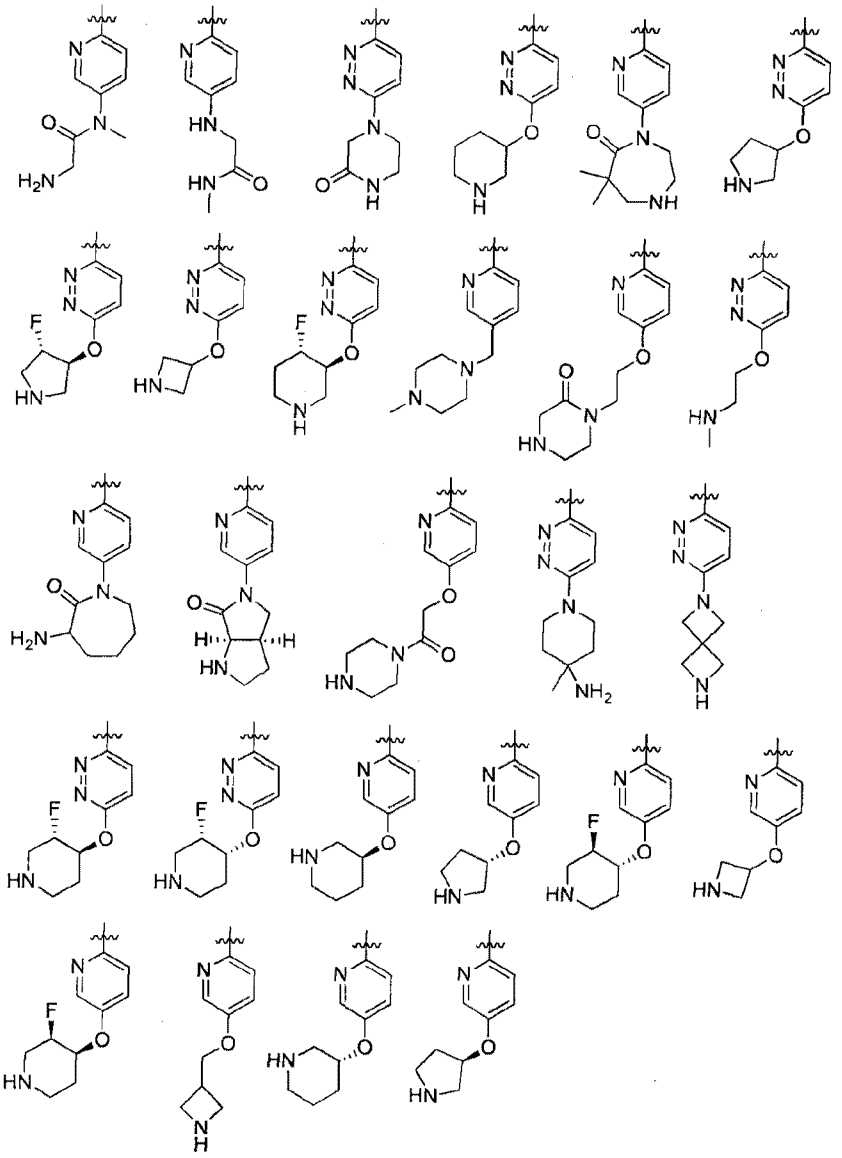
[0061]

[Formula 15]



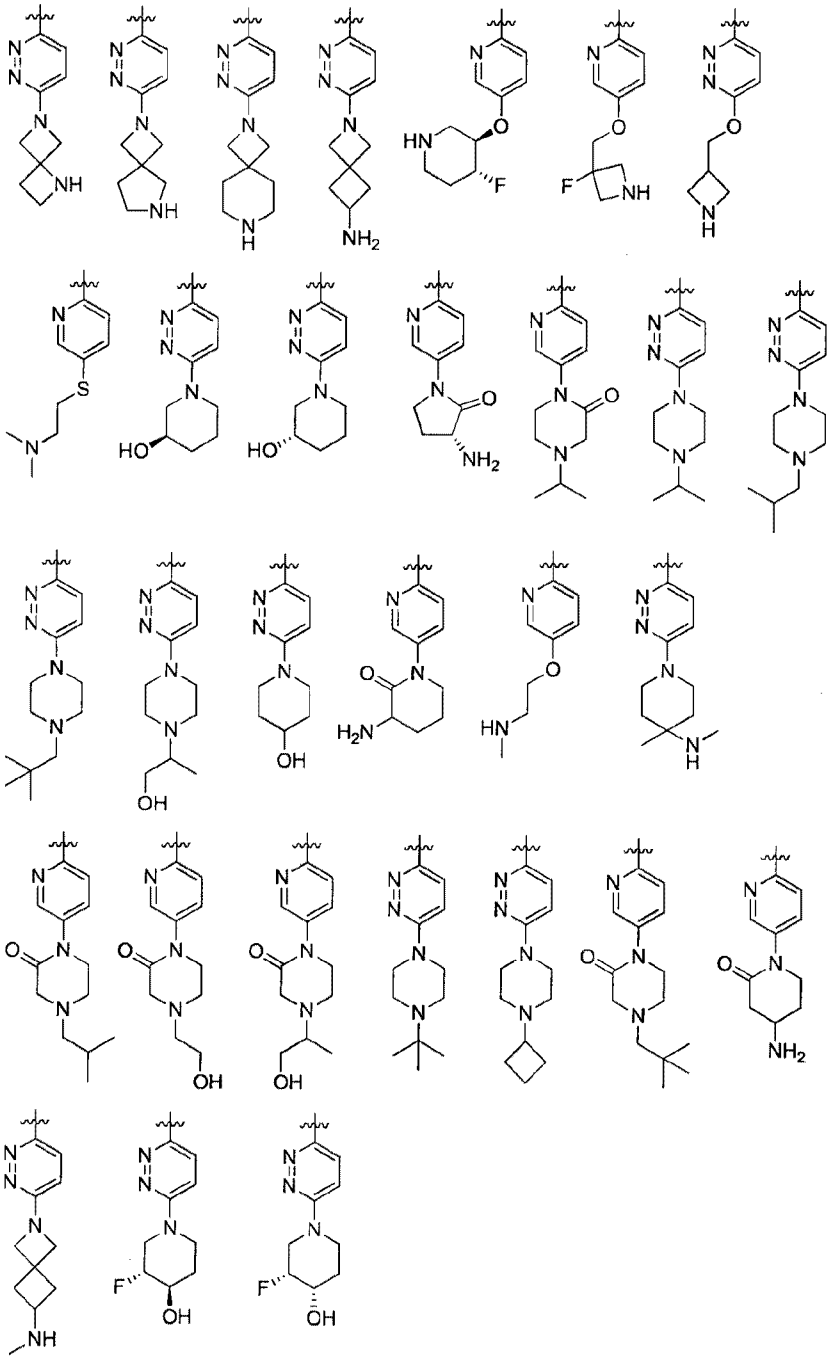
[0062]

[Formula 16]



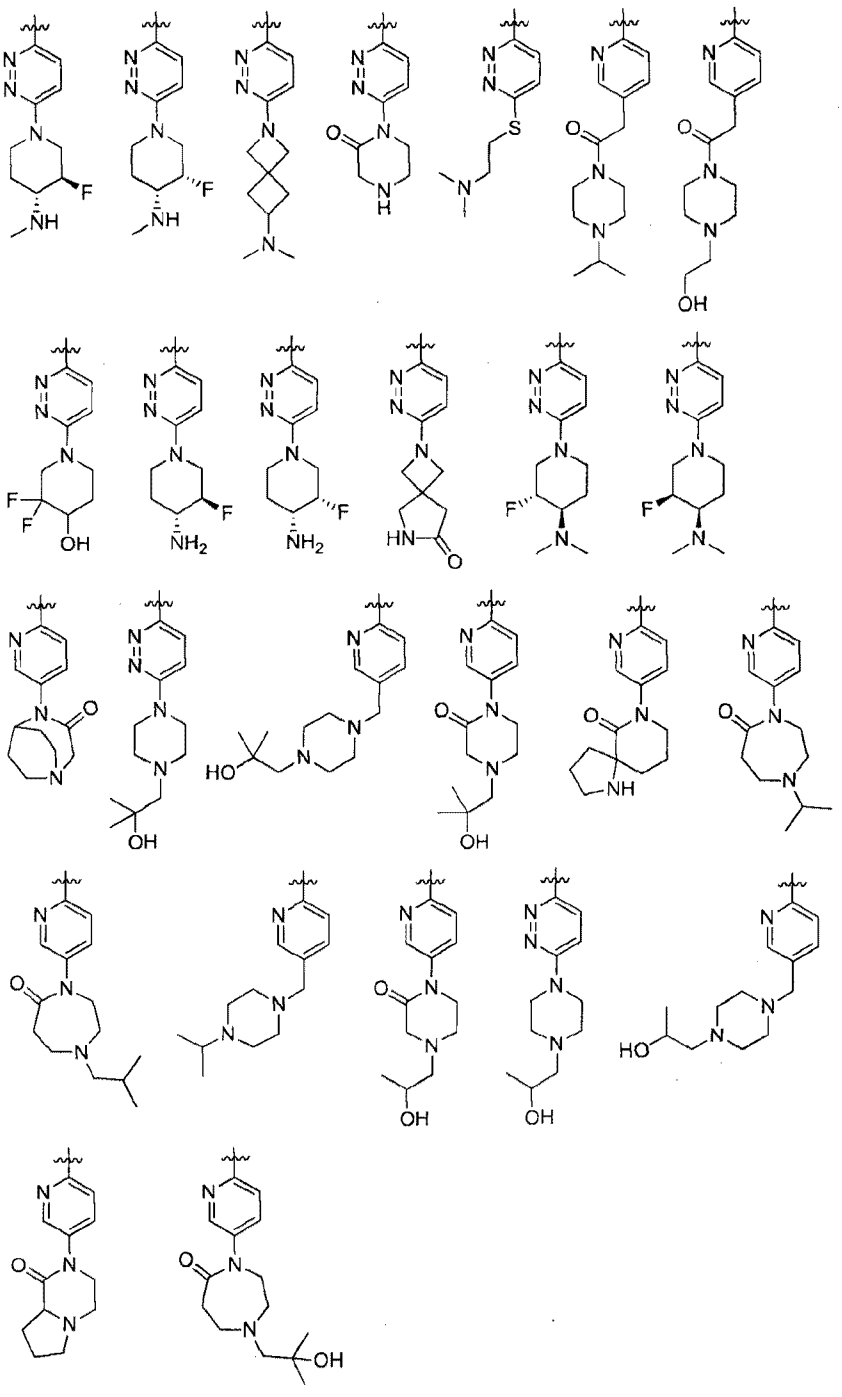
[0063]

[Formula 17]



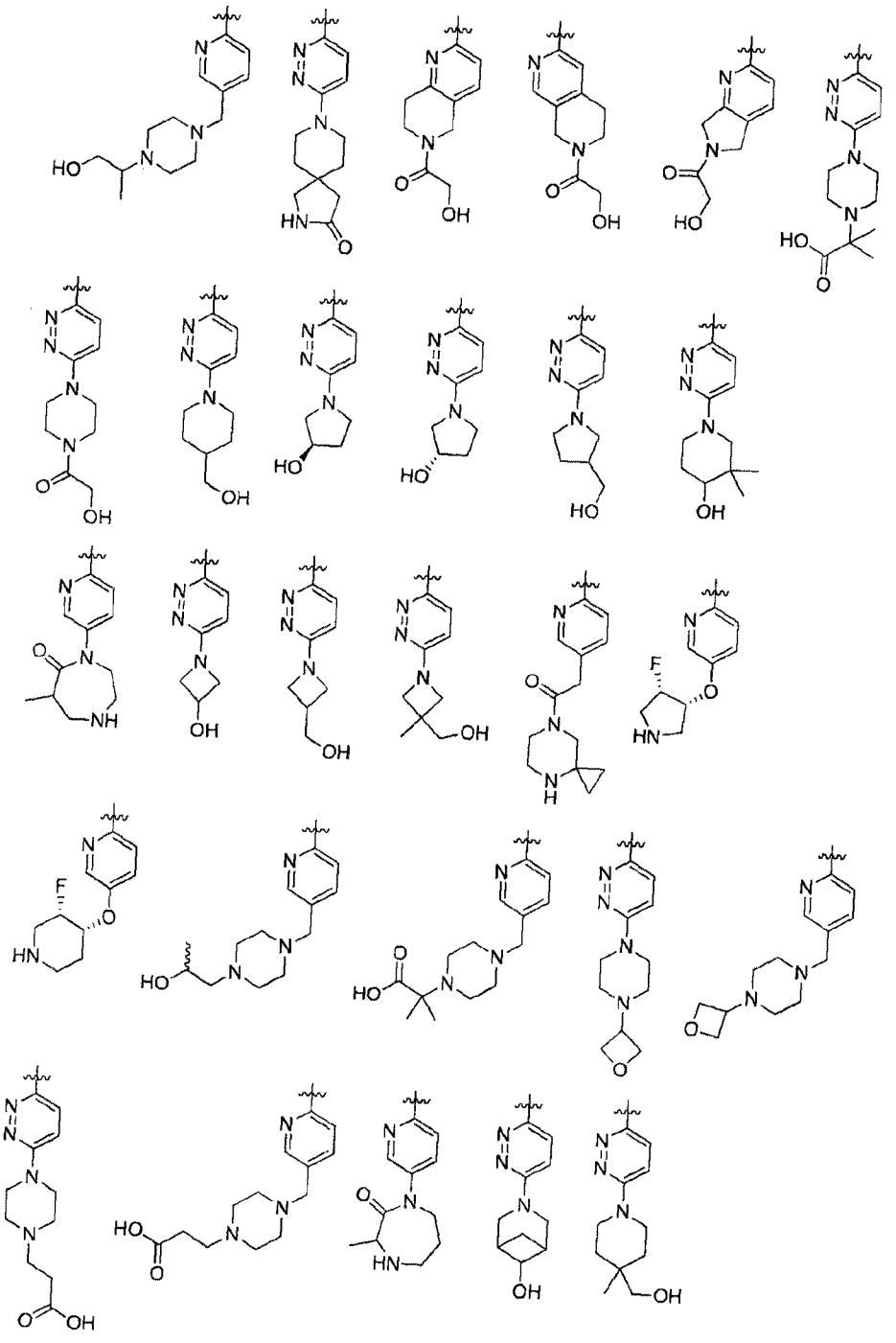
[0064]

[Formula 18]

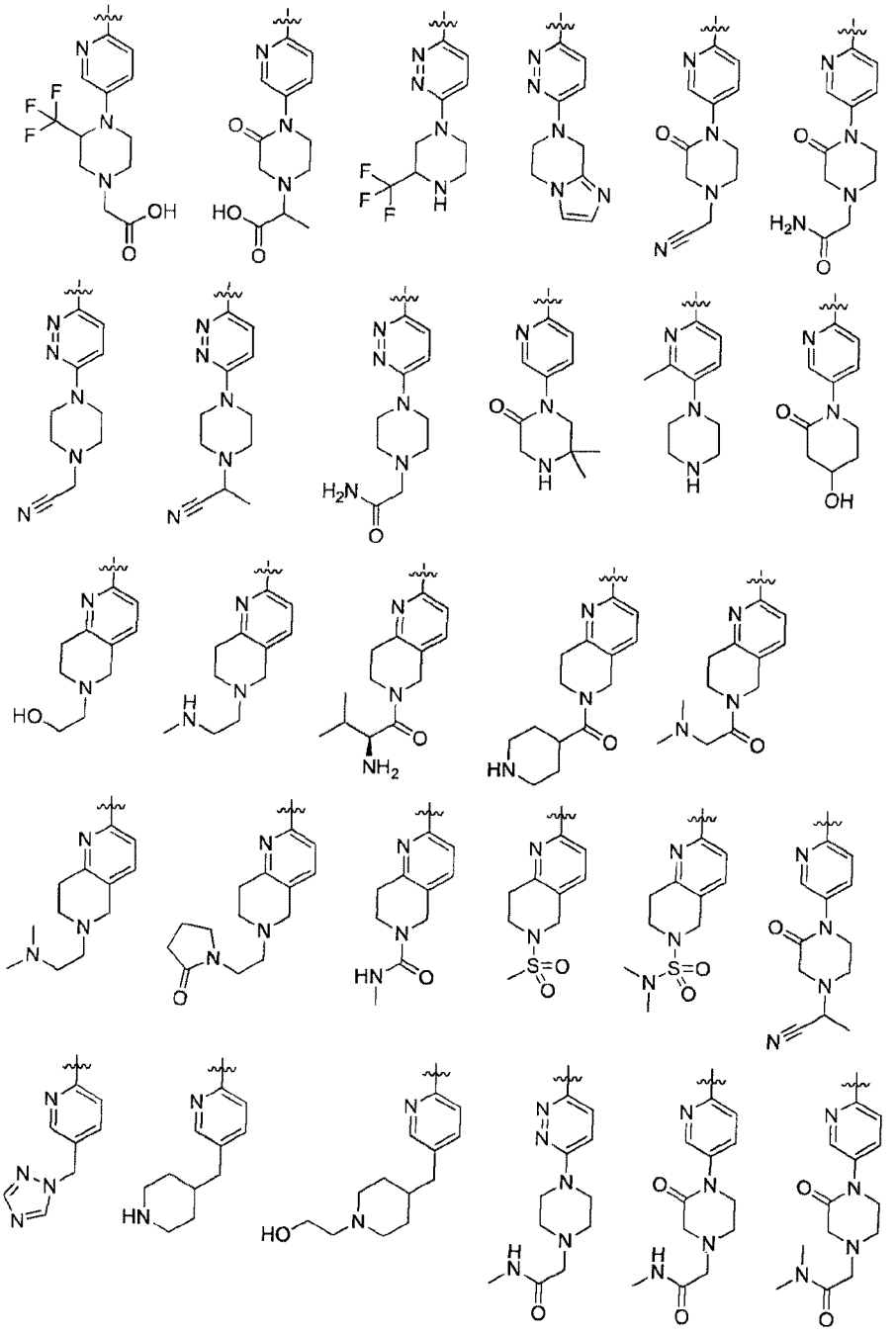


[0065]

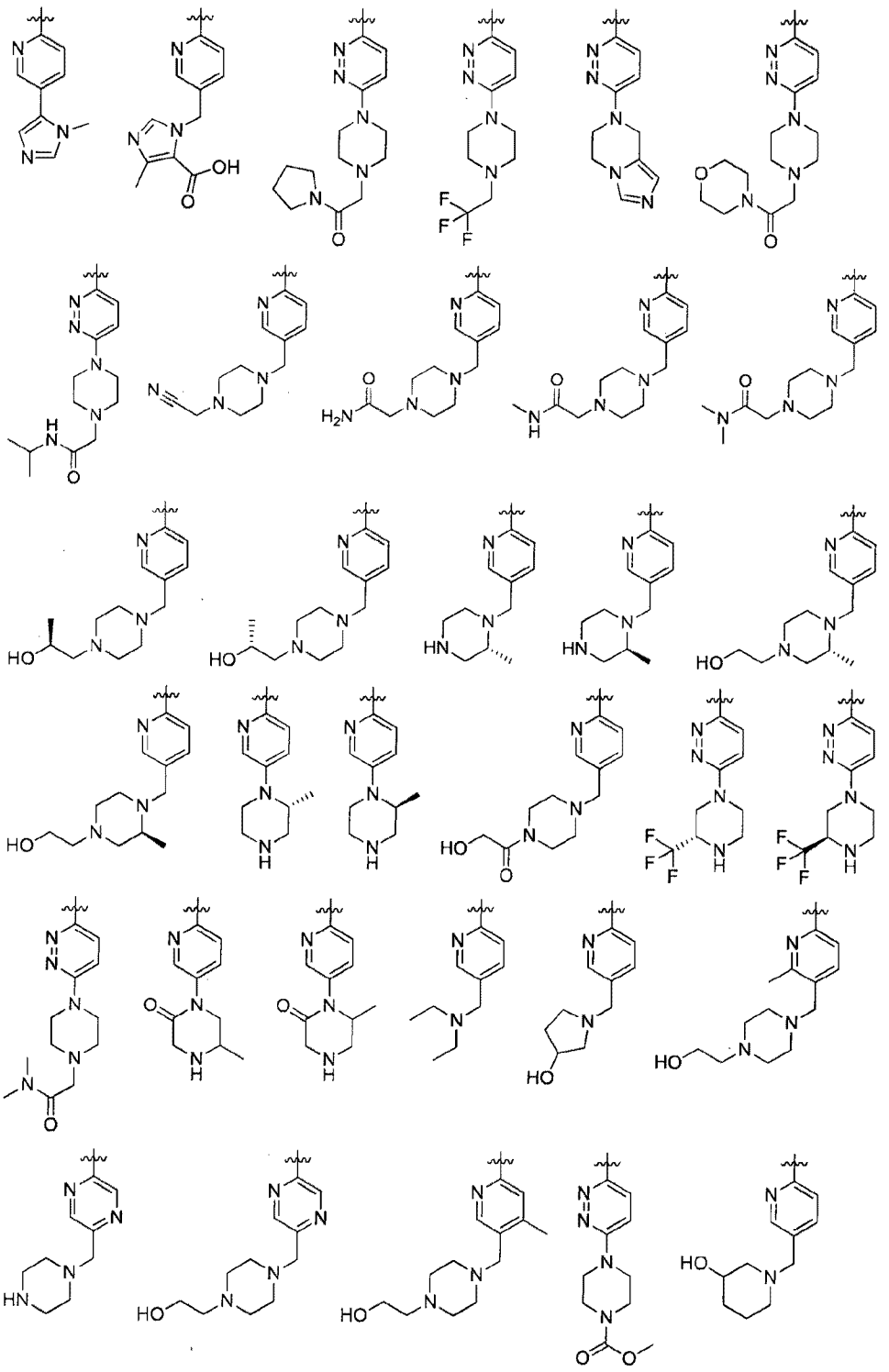
[Formula 19-1]



[Formula 19-2]



[Formula 19-3]



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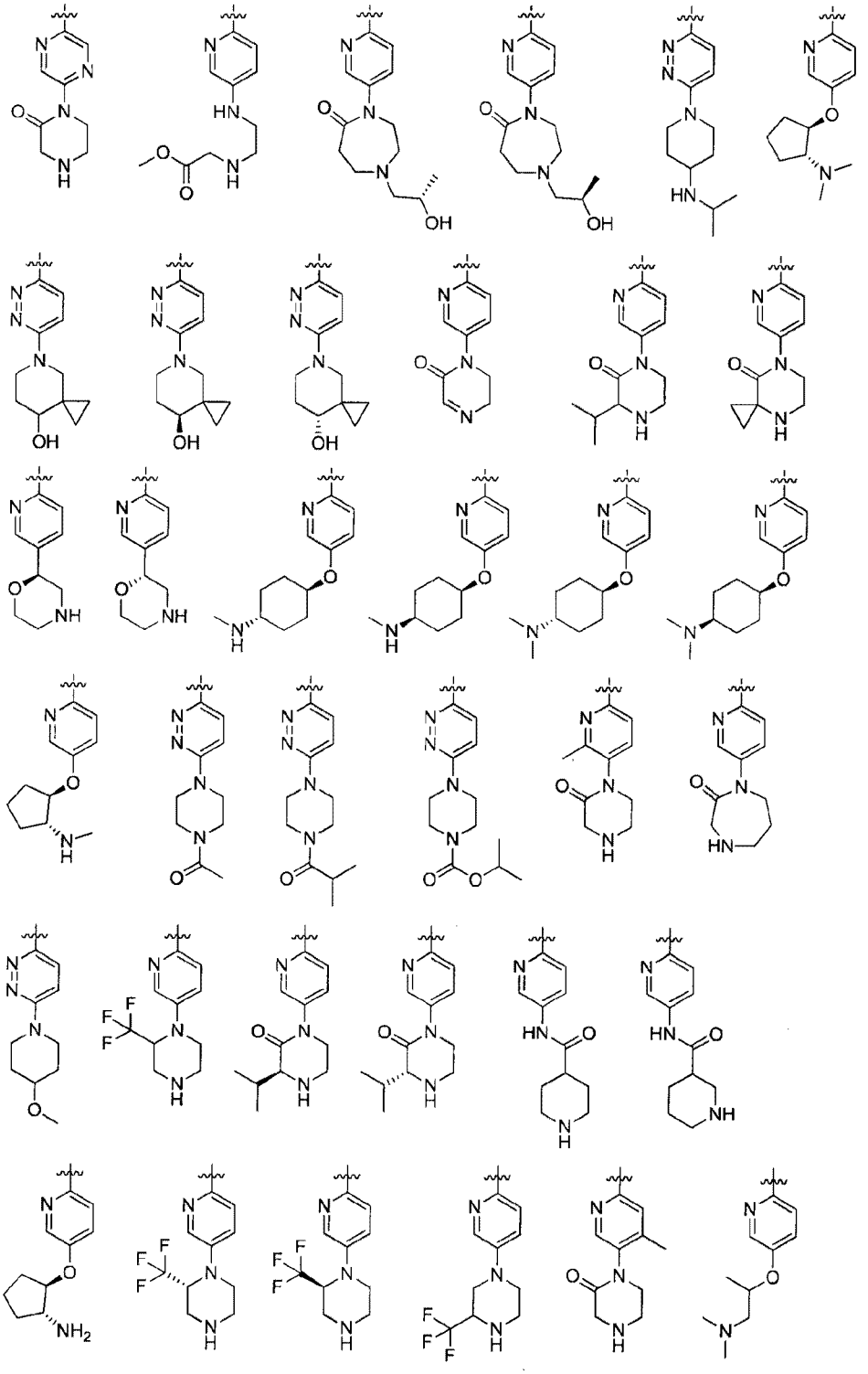
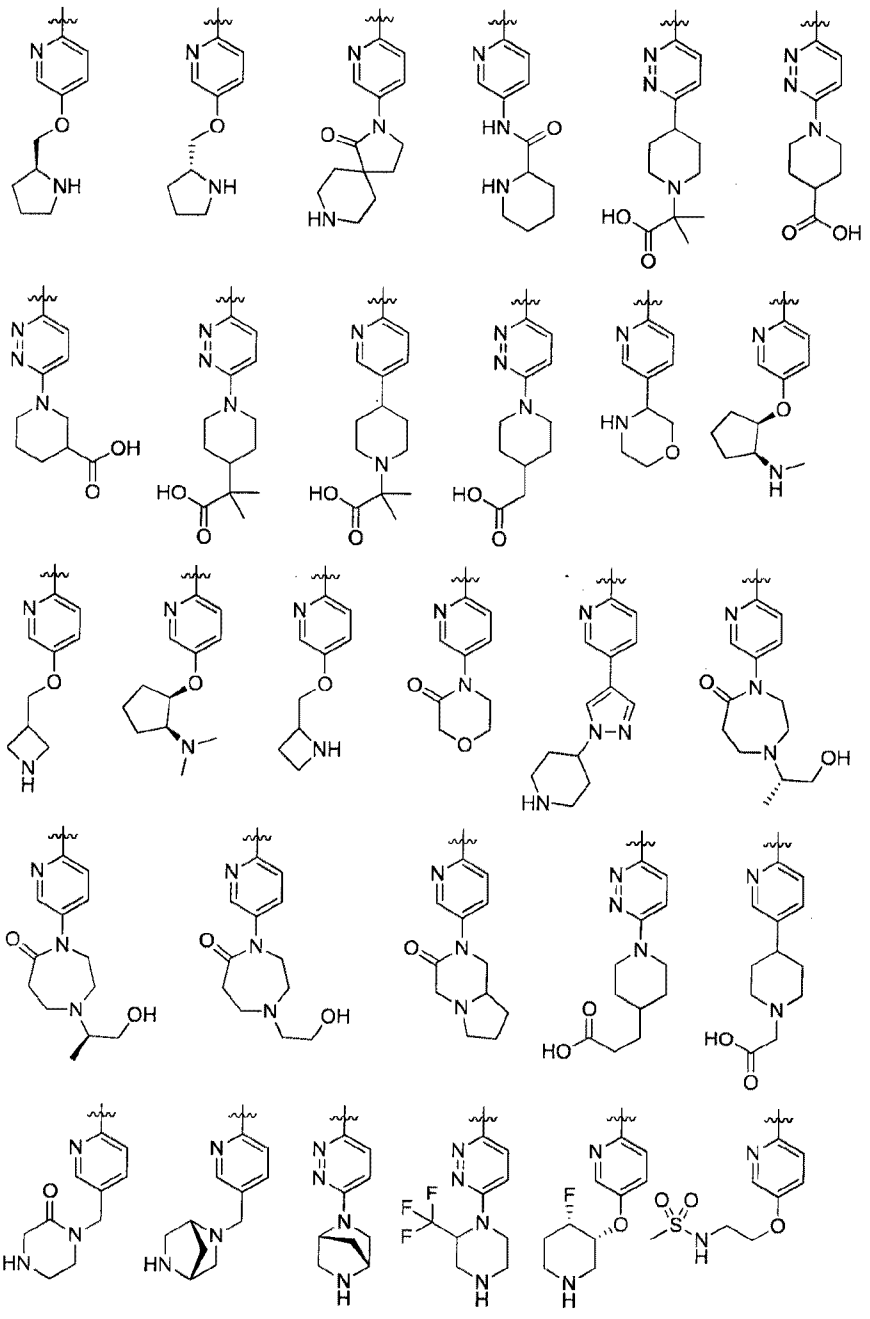
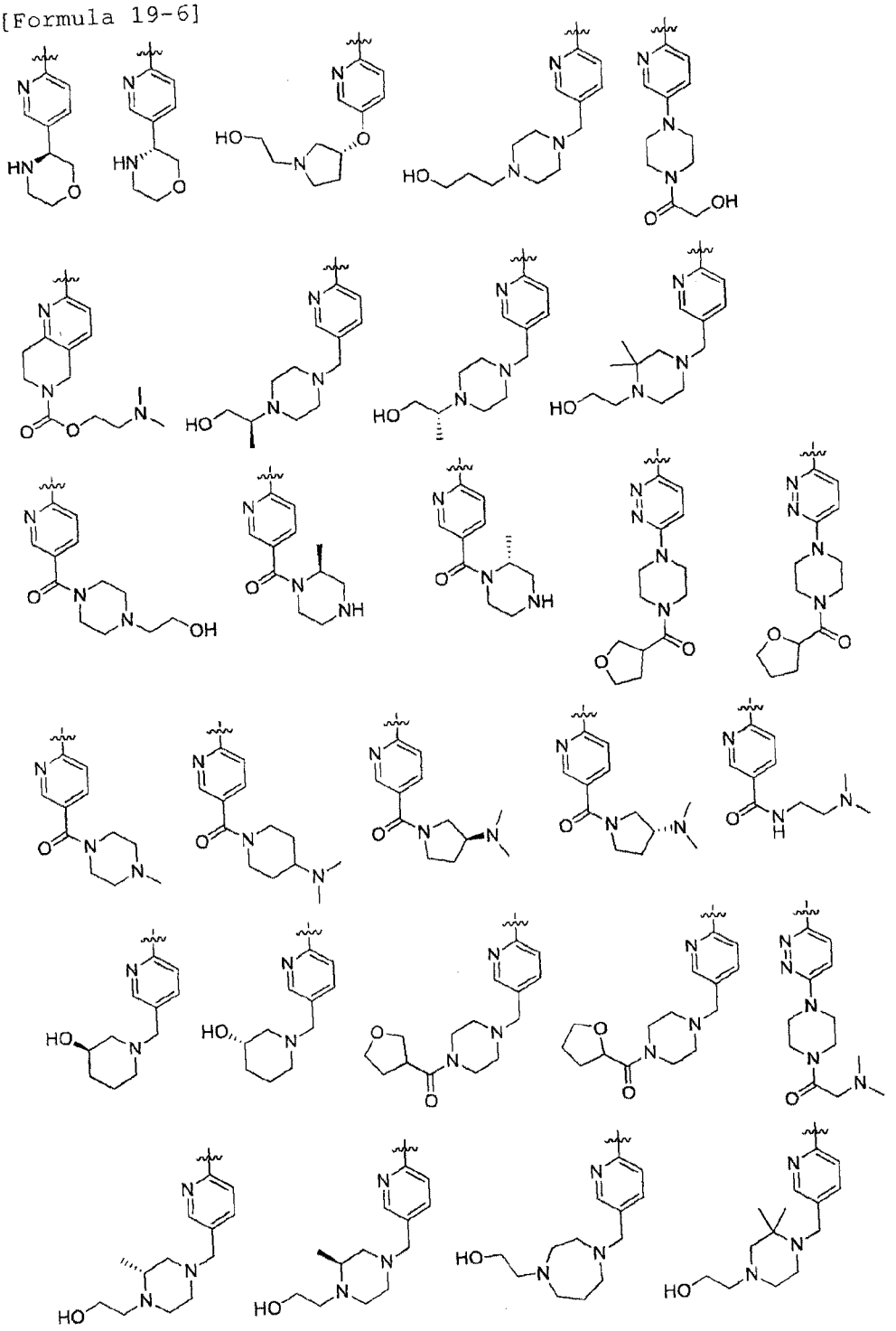


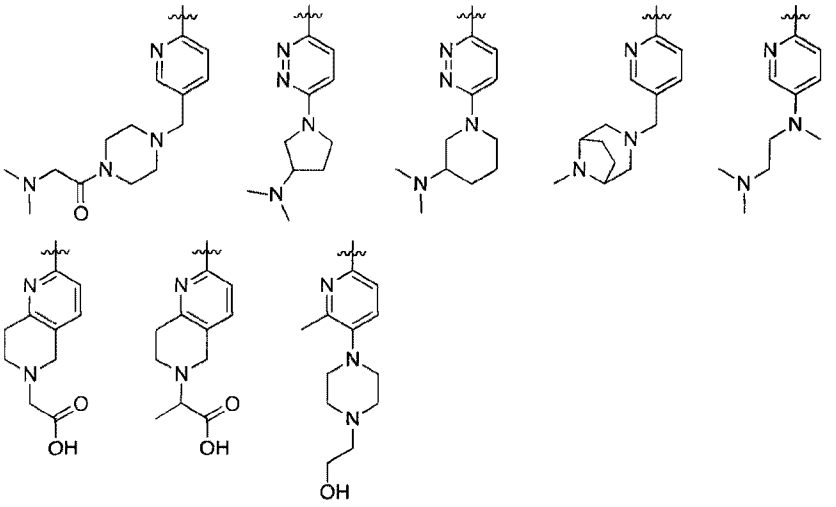
[Formula 19-5]



[Formula 19-6]



[Formula 19-7]



[0066]

A preferred compound represented by Formula (I) is composed of a combination of a group selected from the above-defined ones and a preferred group, or a combination of preferred groups.

[0067]

The compound of the present invention represented by Formula (I) may optionally be formed into a pharmaceutically acceptable salt. Examples of the salt include salts with inorganic acids, such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid, carbonic acid, and the like; salts with organic acids, such as formic acid, acetic acid, propionic acid, trifluoroacetic acid, phthalic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, tartaric acid, citric acid, benzoic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, and the like; salts with amino acids, such as lysine, arginine, ornithine, glutamic acid, aspartic acid, and the like; salts with alkali metals, such as sodium, potassium, lithium, and the like; salts with alkaline earth metals, such as calcium magnesium, and the like; salts with metals, such as

aluminum, zinc, iron, and the like; salts with organic bases, such as methylamine, ethylamine, t-octylamine, diethylamine, trimethylamine, triethylamine, ethylenediamine, piperidine, piperazine, pyridine, picoline, ethanolamine, diethanolamine, triethanolamine, cyclohexylamine, dicyclohexylamine, N-methylglucamine, tris(hydroxymethyl)aminomethane, N,N'-dibenzylethylenediamine, and the like; and ammonium salts and the like.

[0068]

The present invention also encompasses compounds prepared through replacement of one or more atoms of the compound represented by Formula (I) with stable isotopes or radioisotopes.

The present invention also encompasses stereoisomers, racemates, and all acceptable optical isomers of the compound represented by Formula (I).

Tautomers of the compound of the present invention may be generated depending on the combination of substituents. The present invention also encompasses such tautomers.

[0069]

Now will be described a typical process for synthesizing the compound of the present invention represented by Formula (I).

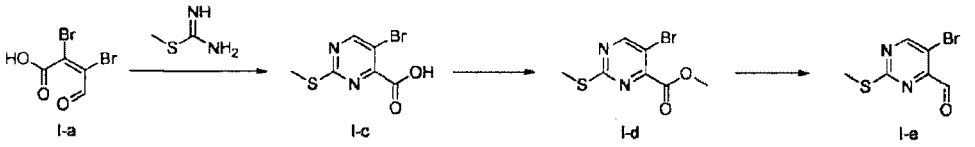
The compound of the present invention can be synthesized by the process described below. R^1, R^3, R^4, and R^7 shown in the following reaction schemes are as defined in Formula (I). The reagents or solvents and the like shown in the reaction schemes are for illustrative purposes only as described below. Each substituent may optionally be protected with an appropriate protective group or deprotected in an appropriate step (reference: PROTECTIVE GROUPS in ORGANIC SYNTHESIS, 4TH EDITION, John Wiley & Sons, Inc.). The abbreviations of substituents, reagents, and solvents described below and in tables are as follows:

Me: methyl
Et: ethyl
Ph: phenyl
Boc: tert-butoxycarbonyl
Cbz: benzyloxycarbonyl
THF: tetrahydrofuran
DMF: N,N-dimethylformamide
NMP: N-methylpyrrolidone
TFA: trifluoroacetic acid
TBS: tert-butyldimethylsilyl
BINAP: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
TBDPS: tert-butyldiphenylsilyl
DIPEA: N,N-Diisopropylethylamine
LAH: Lithium aluminium hydride
DMAP: 4-Dimethylaminopyridine
Ac: acetyl
Ms: mesyl
WSC: water-soluble carbodiimide (1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide)
m-CPBA: m-chloroperoxybenzoic acid
DAST: diethylaminosulfur trifluoride
dba: dibenzylideneacetone
DIBAL-H: diisobutylaluminium hydride

[0070]

1) Synthesis of compound I-e

[Formula 20]



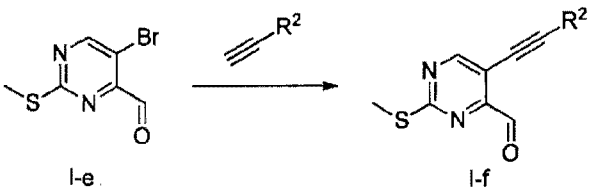
[0071]

Compound I-e, which is a known compound, can be synthesized by any process known to those skilled in the art; for example, the aforementioned process.

[0072]

2) Synthesis of compound I-f from compound I-e

[Formula 21]



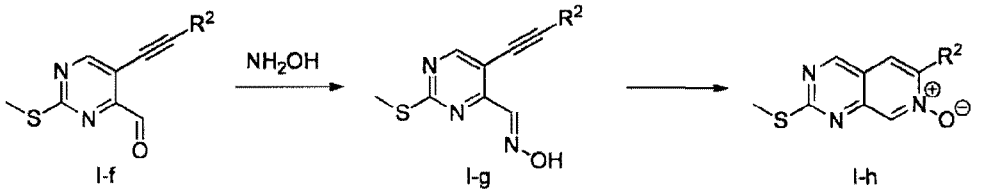
[0073]

Compound I-e is reacted with a terminal alkyne derivative represented by the formula R^2-C≡CH in an appropriate organic solvent (e.g., THF or DMF) in the presence of an appropriate palladium catalyst (e.g., tetrakis(triphenylphosphin)palladium), appropriate copper catalyst (e.g., copper iodide (I)) and appropriate base (e.g., triethylamine) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-f.

[0074]

3) Synthesis of compound I-h from compound I-f

[Formula 22]



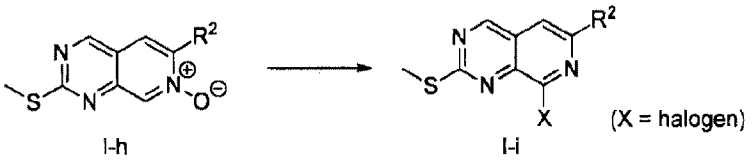
[0075]

Compound I-f is reacted with hydroxylamine or a salt thereof in an appropriate organic solvent (e.g., ethanol) in the presence or absence of an appropriate base (e.g., sodium acetate) at a temperature of 0°C to the reflux temperature of the solvent. The resultant hydroxyimine compound is reacted with an appropriate acid or base (e.g., silver triflate or potassium carbonate) to yield compound I-h.

[0076]

4) Synthesis of compound I-i from compound I-h

[Formula 23]



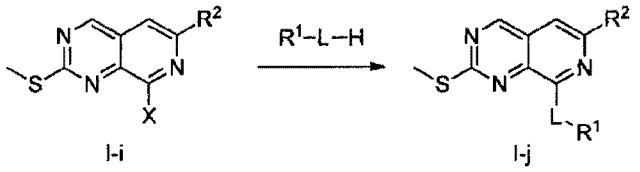
[0077]

Compound I-h is reacted with an appropriate halogenating agent (e.g., thionyl chloride) in an appropriate organic solvent (e.g., dichloromethane) or under solvent-free conditions at a temperature of 0°C to 140°C, to yield compound I-i.

[0078]

5) Synthesis of compound I-j from compound I-i

[Formula 24]



[0079]

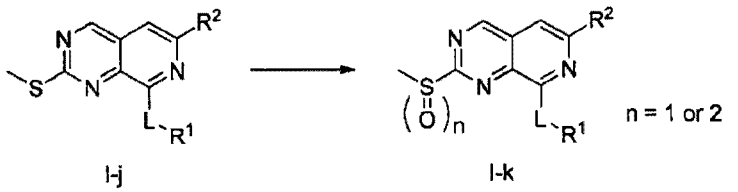
Compound I-i is reacted with an amine, alcohol, or thiol derivative represented by the formula R^1-L-H in an appropriate organic solvent (e.g., THF or 1,4-dioxane) or under solvent-free conditions in the presence or absence of an appropriate base (e.g., triethylamine, potassium carbonate, or sodium hydride) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-j.

In this step, R^2 may be modified by any process known to those skilled in the art in view of the intended structure of the compound.

[0080]

6) Synthesis of compound I-k from compound I-j

[Formula 25]



I-j I-k

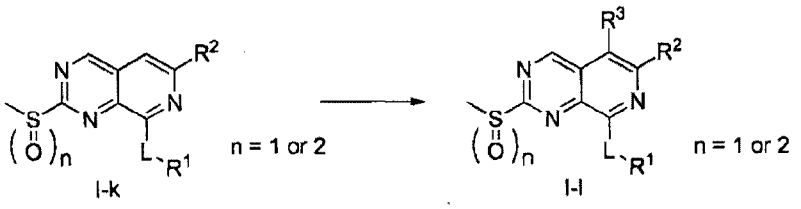
[0081]

Compound I-j is reacted with an appropriate oxidant (e.g., Oxone (R) or m-chloroperbenzoic acid) in an appropriate organic solvent (e.g., dichloromethane or water) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-k.

[0082]

7) Synthesis of compound I-l from compound I-k

[Formula 26]



I-k I-l

[0083]

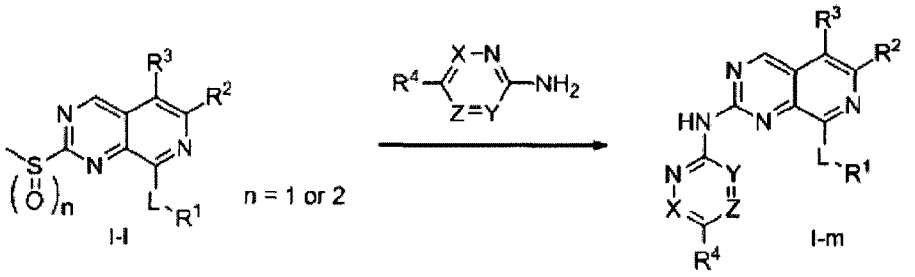
Compound I-k is reacted with an appropriate halogenating agent (e.g., N-chlorosuccinimide) in an appropriate organic solvent (e.g., dichloromethane or 1,2-dichloroethane) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-l.

In this step, R^3 may be modified by any process known to those skilled in the art in view of the intended structure of the compound.

[0084]

8) Synthesis of compound I-m from compound I-l

[Formula 27]



[0085]

Compound I-l is reacted with an amine derivative represented by the formula R^4-NH_2 in an appropriate organic solvent (e.g., NMP, THF, or toluene) or under solvent-free conditions in the presence or absence of an appropriate base (e.g., sodium hydride, triethylamine, or N,N-diisopropyl-N-ethylamine) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-m.

If L, R^1, R^2, or R^4 of compound I-m is protected with an appropriate protective group, deprotection can be performed by any process known to those skilled in the art. For example, deprotection can be performed through reaction of the compound with an appropriate deprotecting reagent (e.g., TFA or hydrogen chloride for a Boc protective group, lithium hydroxide for a benzoyl protective group, or hydrogen in the presence of Pd/C for a Cbz protective group) in an appropriate organic solvent (e.g., dichloromethane, methanol, or THF) or under solvent-free conditions at a temperature of 0°C to the reflux temperature of the solvent (reference: Green's Protective Groups in Organic Synthesis, 4th edition, John Wiley & Sons Inc.).

If compound I-m is protected with two or more protective groups, deprotection may be performed in an appropriate order depending on the structure of compound I-m.

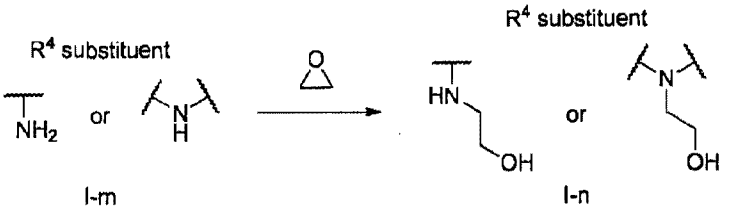
In each of the reactions 9) to 13) described below, L, R^1, R^2, or R^4 of compound I-m is appropriately protected depending on the corresponding reaction

conditions. After completion of the reaction, deprotection can be performed by an appropriate process.

[0086]

9) Synthesis of compound I-n from compound I-m

[Formula 28]



I-m I-n

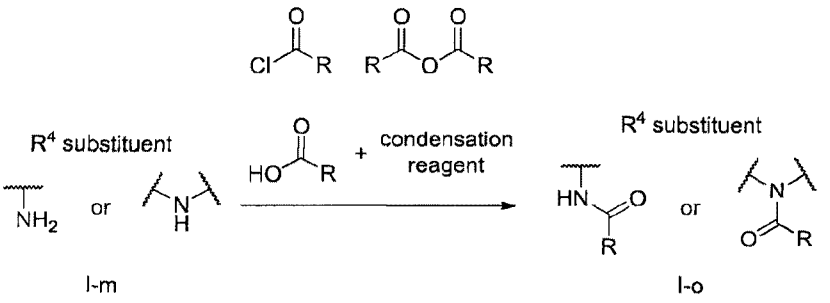
[0087]

Compound I-m in which R^4 has a primary or secondary amine structure is reacted with an optionally substituted epoxide in an appropriate organic solvent (e.g., dichloromethane, NMP, or THF) in the presence or absence of an appropriate acid (e.g., boron trifluoride-diethyl ether complex) or an appropriate base (e.g., potassium carbonate or triethylamine) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-n.

[0088]

10) Synthesis of compound I-o from compound I-m

[Formula 29]



I-m I-o

[0089]

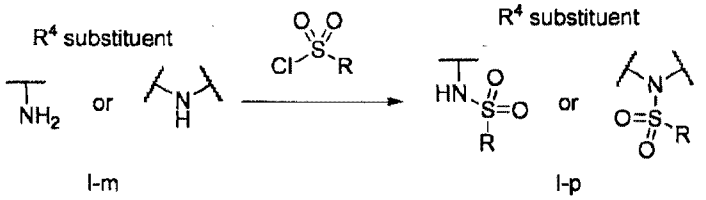
Compound I-m in which R^4 has a primary or secondary amine structure is reacted with a carboxylic acid chloride, a carboxylic anhydride, or a carboxylic acid and a condensation reagent in an appropriate organic solvent (e.g., NMP, THF, or pyridine) in the presence or absence of an appropriate base (e.g., triethylamine or

N,N-diisopropyl-N-ethylamine) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-o.

[0090]

11) Synthesis of compound I-p from compound I-m

[Formula 30]



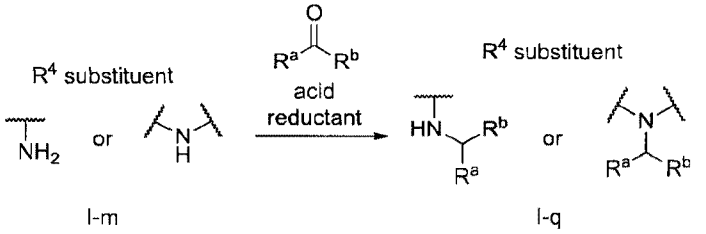
[0091]

Compound I-m in which R^4 has a primary or secondary amine structure is reacted with sulfonic acid chloride in an appropriate organic solvent (e.g., NMP, THF, or pyridine) in the presence or absence of an appropriate base (e.g., triethylamine or N,N-diisopropyl-N-ethylamine) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-p.

[0092]

12) Synthesis of compound I-q from compound I-m

[Formula 31]



[0093]

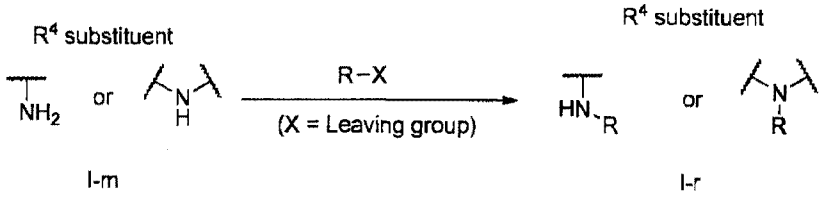
Compound I-m in which R^4 has a primary or secondary amine structure is reacted with an optionally substituted ketone or aldehyde and an appropriate reductant (e.g., sodium triacetoxyborohydride or sodium cyanoborohydride) in an appropriate organic solvent (e.g., NMP or methanol) in the presence of an appropriate acid (e.g., acetic acid) at a temperature of room temperature to the reflux

temperature of the solvent, to yield compound I-q.

[0094]

13) Synthesis of compound I-r from compound I-m

[Formula 32]



I-m I-r

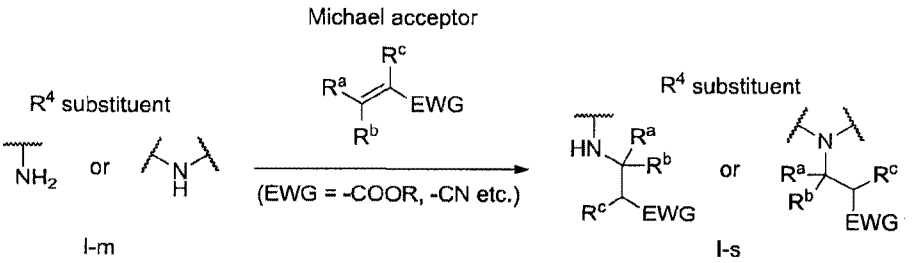
[0095]

Compound I-m in which R^4 has a primary or secondary amine structure is reacted with a compound having a leaving group (e.g., a halogen atom or a sulfonyloxy group) in an appropriate organic solvent (e.g., NMP, THF, or pyridine) in the presence or absence of an appropriate base (e.g., triethylamine or N,N-diisopropyl-N-ethylamine) at a temperature of 0°C to the reflux temperature of the solvent, to yield compound I-r.

[0096]

14) Synthesis of compound I-s from compound I-m

[Formula 33]



I-m I-s

[0097]

Compound I-m in which R^4 has a primary or secondary amine structure is reacted with a compound having a structure of Michael acceptor in an appropriate organic solvent (e.g., methanol, THF) at a temperature of 0°C to the reflux temperature of the solvent to yield compound I-s.

[0098]

The compound of the present invention exhibits a CDK4/6 inhibitory activity and thus is useful for the prevention or treatment of a disease associated with CDK4/6. Specifically, the compound is useful for the treatment of rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, or cancer and the protection of bone marrow. In particular, the compound is effective for the treatment of rheumatoid arthritis or cancer and the protection of bone marrow.

[0099]

The compound of the present invention preferably exhibits selectivity for the CDK4/6 inhibitory activity compared to the inhibitory activity against another cyclin-dependent kinase, such as CDK2 inhibitory activity. Such selectivity of the compound is expected to reduce the expression of genotoxicity because the inhibition of CDK2 is also involved in DNA replication. Preferably, the compound of the present invention selectively inhibits CDK4 rather than CDK2.

The active ingredient of the present invention may be provided in any preparation form, such as a solid, semisolid, or liquid form, and the like. The active ingredient may be provided in any dosage form, such as an oral form or a parenteral form (e.g., an injection, a transdermal agent, an eye drop, a suppository, a nasal agent, or an inhalant, and the like).

[0100]

A drug containing the active ingredient of the present invention is prepared with a common additive used for drug preparation. Examples of the additive for solid drugs include excipients, such as lactose, sucrose, glucose, cornstarch, potato starch, crystalline cellulose, light silicic anhydride, synthetic aluminum silicate, magnesium aluminometasilicate, calcium hydrogen phosphate, and the like; binders, such as crystalline cellulose, carboxymethyl cellulose, hydroxypropyl cellulose, sodium carboxymethyl cellulose,

poly(vinylpyrrolidone), and the like; disintegrants, such as starch, sodium carboxymethyl cellulose, calcium carboxymethyl cellulose, croscarmellose sodium, sodium carboxymethyl starch, and the like; lubricants, such as talc stearic acid, and the like; coating agents, such as hydroxymethyl propyl cellulose, hydroxypropyl methyl cellulose phthalate, ethyl cellulose, and the like; and colorants. Examples of the additive for semisolid drugs include bases, such as white vaseline, and the like. Examples of the additive for liquid drugs include solvents, such as ethanol, and the like; solubilizers, such as ethanol, and the like; preservatives, such as paraoxybenzoic acid esters, and the like; isotonic agents, such as glucose, and the like; buffers, such as citric acid, and the like; antioxidants, such as L-ascorbic acid, and the like; chelators, such as EDTA, and the like; suspending agents and emulsifiers, such as polysorbate 80, and the like; and the like.

The dose of the active ingredient of the present invention is typically about 1 to 1,000 mg/day. The active ingredient is typically administered once to three times a day.

Examples

[0101]

The present invention will now be described in detail by way of Examples, which should not be construed as limiting the invention.

The structure of an isolated novel compound was determined by ^{1}H-NMR and/or mass spectrometry with a single quadrupole instrumentation equipped with an electron spray source, and other appropriate analytical methods. Chemical shifts (δ: ppm) and coupling constants (J: Hz) are shown for the ^{1}H-NMR spectra (400 MHz, DMSO-d_6, CD_3OD or $CDCl_3$). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), brs (broad singlet), and m (multiplet). For the results of mass spectrometry, measurements are represented by $(M+H)^+$;

i.e., a value corresponding to a proton (H^+) attached to the molecular mass (M) of a compound.

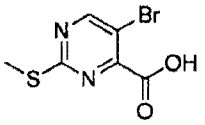
[0102]

Reference Example 1

Synthesis of 5-bromo-2-(methylthio)pyrimidine-4-carboxylic acid

[0103]

[Formula 34]



[0104]

Mucobromic acid (300 g, 1.16 mol) was added to an aqueous solution (2.5 L) of 2-methyl-2-pseudothiourea sulfate (324 g, 1.16 mol) at room temperature. The resultant suspension was cooled to 0°C with stir, and triethylamine (486 mL, 3.49 mol) was added dropwise thereto over four hours. The resultant reaction mixture was stirred overnight, and the completion of the reaction was confirmed by silica gel TLC. The reaction mixture was then acidified with concentrated hydrochloric acid (about 250 mL). The resultant yellow solid was collected by filtration and washed twice with water (500 mL) and then twice with diethyl ether (500 mL). The solid was dried under reduced pressure to yield the title compound (160 g, 55%).

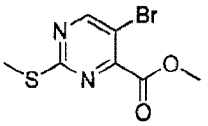
[0105]

Reference Example 2

Synthesis of methyl 5-bromo-2-methylthiopyrimidine-4-carboxylate

[0106]

[Formula 35]



[0107]

A solution of 5-bromo-2-(methylthio)pyrimidine-4-carboxylic acid (110 g, 0.44 mol) in methanol (1.1 L) was cooled to 0°C with stir, and thionyl chloride (50 mL, 0.66 mol) was added dropwise thereto. The resultant reaction mixture was slowly heated, and the reaction was allowed to proceed under reflux for four hours. The completion of the reaction was confirmed by LC/MS and TLC, and the reaction mixture was cooled to room temperature. The volatiles were removed through evaporation under reduced pressure, and the residue was dissolved in ethyl acetate (1 L). The resultant solution was washed three times with 10% aqueous sodium carbonate solution (200 mL) and then twice with saturated brine (200 mL). The resultant organic phase was dried over anhydrous magnesium sulfate, and solid was separated by filtration. The filtrate was then concentrated under reduced pressure, and the resultant crude product was purified by silica gel column chromatography to yield the title compound (88 g, 75%).

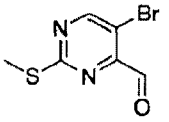
[0108]

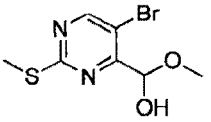
Reference Example 3

Synthesis of mixture of 5-bromo-2-methylthiopyrimidine-4-carbaldehyde and (5-bromo-2-methylthiopyrimidin-4-yl)methoxymethanol

[0109]

[Formula 36]





[0110]

A solution (375 mL) of methyl 5-bromo-2-methylsulfanylpyrimidine-4-carboxylate (25 g, 95 mmol) in THF was cooled to -78°C and stirred under a nitrogen atmosphere. DIBAL-H (84 mL, 143 mmol, 1.7M toluene solution) was added dropwise to the THF solution, and the mixture was stirred at -78°C for four hours. The completion of the reaction was confirmed by TLC, and the

reaction was quenched through dropwise addition of methanol at -78°C. The resultant reaction mixture was allowed to warm slowly to 0°C and diluted with ethyl acetate, and the mixture was filtrated through celite. The filtrate was washed twice with saturated brine (200 mL), and the resultant organic phase was dried over anhydrous magnesium sulfate. The resultant solid was separated by filtration, and the filtrate was concentrated to yield the title compound mixture (25 g, crude product). The crude product was used for the subsequent reaction without further purification.

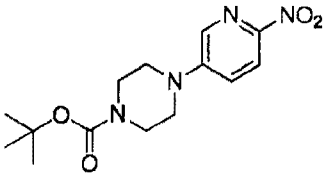
[0111]

Reference Example 4

Synthesis of tert-butyl 4-(6-nitropyridin-3-yl)piperazine-1-carboxylate

[0112]

[Formula 37]



[0113]

A mixture of 5-Bromo-2-nitropyridine (203 g, 1.37 mol), piperazine (153 g, 1.77 mol), tetrabutylammonium iodide (25.2 g, 0.068 mol), and potassium carbonate (207 g, 1.50 mol) in dimethyl sulfoxide (2.6 L) was stirred at 80°C overnight. The resultant reaction mixture was cooled to room temperature, and the mixture was poured into water (7 L). The resultant solid was collected by filtration, and the solid was washed with dichloromethane (1 L × 2) and dried. The filtrate was extracted with chloroform (2 L × 7). The resultant organic phase was washed with water (2 L) and then with saturated brine (2 L), and the organic phase was concentrated under reduced pressure to yield solid. The resultant solid products were combined together and used for the subsequent

reaction without further purification.

[0114]

The solid product (490 g) was dissolved in THF (2 L) and water (500 mL), and sodium hydrogen carbonate (119 g, 1.42 mol) was added to the solution. To the resultant suspension was added di-tert-butyl dicarboxylate (262 g, 1.2 mol), and the mixture was stirred at room temperature for three hours. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with water (1 L) and extracted with dichloromethane (1 L × 3). The resultant organic phases were combined together and then washed with water (1 L). The aqueous phase was extracted with dichloromethane (300 mL). The resultant organic phases were combined together and dried over anhydrous magnesium sulfate. The solid was separated by filtration, and the filtrate was concentrated under reduced pressure. The resultant solid was suspended in ethyl acetate (2 L) and heated to 60°C, and the solid was separated by filtration at 60°C. The solid was dried under reduced pressure to yield the title compound (191 g, 62%)

APCI-MS $(M+H)^+$ 309.1, $C_{14}H_{20}N_4O_4$=308.15

^{1}H-NMR δ(400 MHz, $CDCl_3$): 8.16 (d, J=9 Hz, 1H), 8.11 (d, J=3 Hz, 1H), 7.19 (dd, J=9.3 Hz, 1H), 3.64-3.61 (m, 4H), 3.45-3.42 (m, 4H), 1.47 (s, 9H).

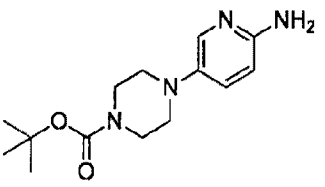
[0115]

Reference Example 5

Synthesis of tert-butyl 4-(6-aminopyridin-3-yl)piperazine-1-carboxylate

[0116]

[Formula 38]



[0117]

The tert-butyl 4-(6-nitropyridin-3-yl)piperazine-1-carboxylate synthesized in Reference Example 4 (83 g, 269 mmol) was dissolved in methanol (1.3 L) in Parr Shaker and Raney nickel (15 g, 50% aqueous suspension) was added thereto. The resultant reaction mixture was stirred under a hydrogen atmosphere (50 psi) for five hours. The reaction mixture was filtered through a Celite pad to separate solid, and the filtrate was concentrated under reduced pressure. The resultant solid was suspended in diethyl ether (120 mL) and stirred for four hours. Heptane was added to the suspension and cooled at 0°C for 45 minutes. The resultant solid was separated by filtration and dried under reduced pressure to yield the title compound (62.5 g, 83%).

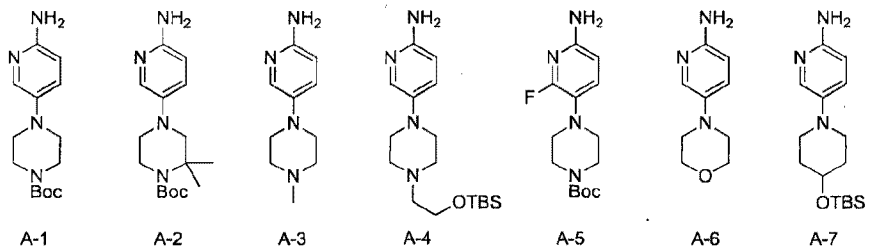
ESI-MS $(M+H)^+$ 279, $C_{14}H_{22}N_4O_2$=278.17

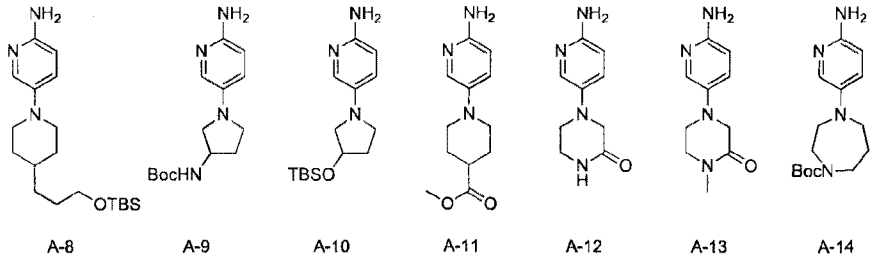
[0118]

Intermediates A-1 to A-44 were each synthesized by the process of Reference Example 4 and/or 5 with the corresponding halopyridine derivatives and amine derivatives. Appropriate protection or deprotection was performed as needed.

[0119]

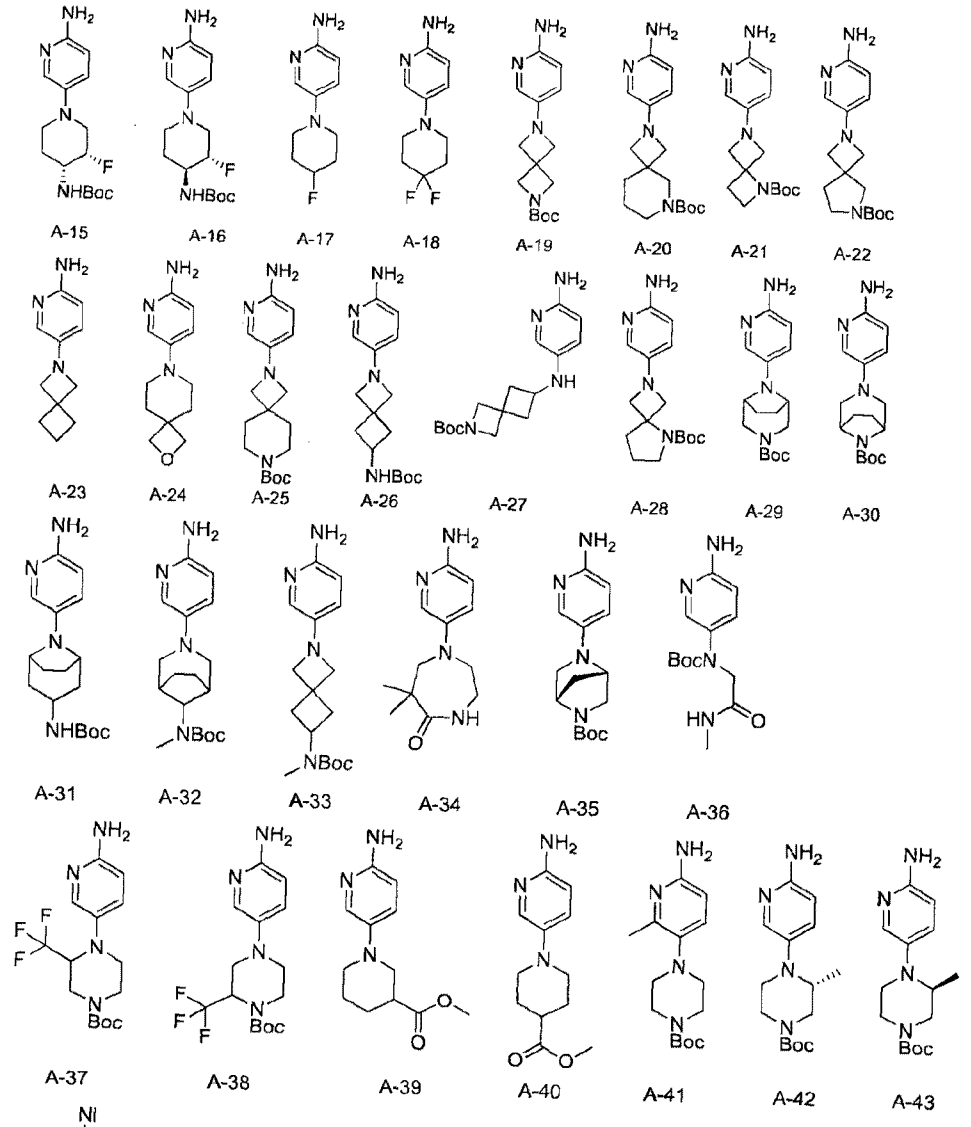
[Formula 39]





[0120]

[Formula 40]



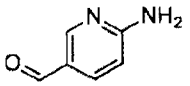
[0121]

Reference Example 6

Synthesis of 6-aminopyridine-3-carbaldehyde

[0122]

[Formula 41]



[0123]

6-Aminopyridine-3-carbonitrile (1.9 g, 16 mmol) was dissolved in THF (160 mL) and cooled to -78°C with stir. Diisobutylaluminium hydride (106.5 mL, 1.5M toluene solution) was slowly added dropwise to the solution at -78°C and the mixture was allowed to warm to 20°C with stir, followed by further stirring for two hours. The reaction was quenched by addition of ice water (100 mL) to the resultant reaction mixture, and the mixture was extracted three times with dichloromethane (50 mL). The resultant organic phases were combined together and then washed once with brine (100 mL) and dried over anhydrous sodium sulfate. The solid was separated by filtration, and the filtrate was concentrated under reduced pressure. The residue was roughly purified by silica gel column chromatography to yield a crude product of the title compound (1.7 g). The crude product was used for the subsequent reaction without further purification.

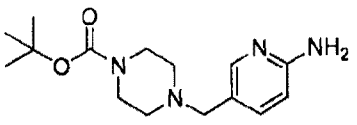
[0124]

Reference Example 7

Synthesis of tert-butyl 4-[(6-aminopyridin-3-yl)methyl]piperazine-1-carboxylate

[0125]

[Formula 42]



[0126]

The crude 6-aminopyridine-3-carbaldehyde synthesized in Reference Example 6 (1.7 g, 13.9 mmol) and tert-butyl

piperazine-1-carboxylate (3.2 g, 17.2 mmol) were dissolved in dichloromethane (50 mL) and stirred at room temperature for eight hours. To the resultant mixture was added sodium triacetoxyborohydride (8.84 g, 40.9 mmol) and stirred at room temperature for two hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction was quenched through addition of saturated aqueous sodium carbonate solution (50 mL), and the reaction mixture was extracted three times with ethyl acetate (50 mL). The resultant organic phases were combined together, and the mixture was washed once with brine (100 mL) and dried over anhydrous sodium sulfate. The resultant solid was separated by filtration, and then the filtrate was concentrated under reduced pressure. The residue was roughly purified by silica gel column chromatography to yield the title compound (3.3 g, 81%).

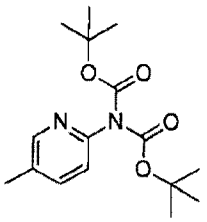
[0127]

Reference Example 8

Synthesis of di-tert-butyl (5-methylpyridin-2-yl)imidodicarbonate

[0128]

[Formula 43]



[0129]

In reference to the process disclosed in WO2010/141406, 5-methylpyridine-2-amine (20 g, 185 mmol) and di-tert-butyl dicarbonate (101 g, 462 mmol) were dissolved in THF (160 mL) and 4-N,N-dimethylaminopyridine (3.6 g, 29.7 mmol) was added to the solution. The resultant reaction mixture was stirred at room temperature for three days. The reaction mixture was concentrated under reduced pressure, and the residue was

dissolved in ethyl acetate and washed with water. The resultant organic phase was washed with saturated brine and dried over anhydrous sodium sulfate. The solid was separated by filtration, and the filtrate was concentrated. The resultant solid was dissolved in ethyl acetate (50 mL) and heptane (50 mL) was added thereto. The solid was collected by filtration and dried under reduced pressure, to yield the title compound (25.1 g, 44%). The filtrate was concentrated, and the residue was purified by silica gel column chromatography to yield the title compound (17.9 g, 31%).

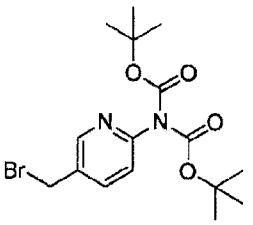
[0130]

Reference Example 9

Synthesis of di-tert-butyl [5-(bromomethyl)pyridin-2-yl]imidodicarbonate

[0131]

[Formula 44]



[0132]

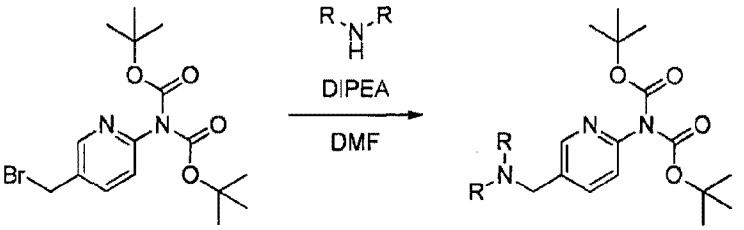
The di-tert-butyl (5-methylpyridin-2-yl)imidodicarbonate synthesized in Reference Example 8 (17.2 g, 55.8 mmol), N-bromosuccinimide (12.17 g, 68.4 mmol), and benzoyl peroxide (1.5 g, 8.1 mmol) were dissolved in carbon tetrachloride (100 mL) and the reaction was stirred at 80°C for six hours. The reaction mixture was cooled to room temperature, and the resultant solid was separated by filtration. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield a mixture of the title compound, di-tert-butyl [5-(dibromomethyl)pyridin-2-yl]imidodicarbonate, and di-tert-butyl (5-methylpyridin-2-yl)imidodicarbonate (14.5

g, 60.3 : 4.4 : 35.3, determined by the ^{1}H-NMR spectrum). The mixture was used for the subsequent reaction without further purification.

[0133]

Reference Example 10

[Formula 45]



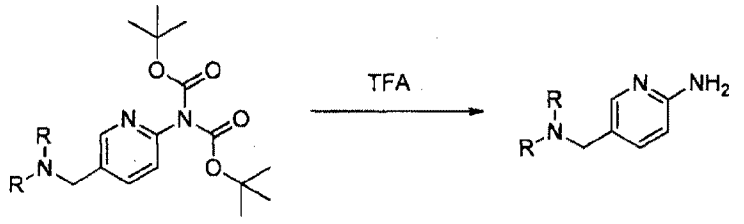
[0134]

Di-tert-butyl [5-(bromomethyl)pyridin-2-yl]imidodicarbonate (1 equivalent) was dissolved in DMF and an appropriate amine derivative (1.5 equivalents) and N,N-diisopropyl-N-ethylamine (3 equivalents) was added to the solution at room temperature. The reaction mixture was stirred at room temperature for several hours, and the mixture was then diluted with ethyl acetate and washed with saturated brine. The resultant organic phase was dried over anhydrous sodium sulfate, and the solid was separated by filtration. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield a target amine derivative.

[0135]

Reference Example 11

[Formula 46]



[0136]

To the compound synthesized in Reference Example 10

was added an excess amount of trifluoroacetic acid and stirred at room temperature for several hours. The reaction mixture was concentrated under reduced pressure, and the resultant TFA salt of the target product was dissolved in methanol and applied onto a strong cation exchange resin (SCX). The SCX column was washed with methanol and the target product was eluted with ammonia (2 mol/L, methanol solution). The eluate was concentrated under reduced pressure to yield a target 2-aminopyridine derivative. The resultant product was used for the subsequent reaction without further purification.

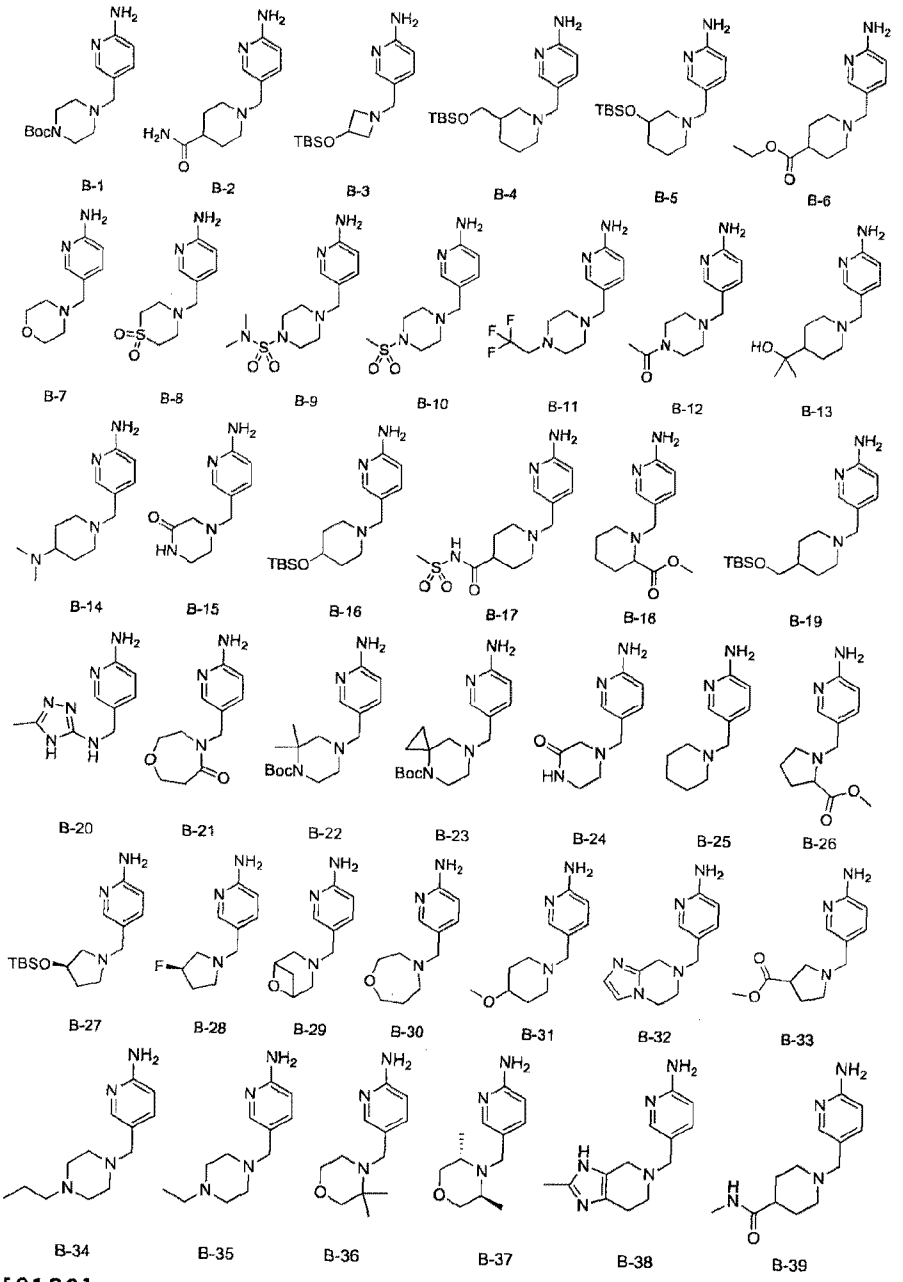
In the case of the presence of a primary or secondary amino group in the compound besides the aminopyridine structure, the crude product was dissolved in THF and reacted with di-tert-butyl dicarbonate at room temperature. After completion of the reaction, the solvent was removed through evaporation, and the residue was roughly purified by silica gel column chromatography to yield a 2-aminopyridine derivative having a primary or secondary amino group protected with a Boc group.

[0137]

Intermediates B-1 to B-68 were each synthesized by any of the processes of Reference Example 6 and/or 7 or Reference Examples 8 to 11 or a combination of the processes with the corresponding aldehyde or alkyl halide derivatives and amine derivatives. Appropriate protection or deprotection was performed as needed.

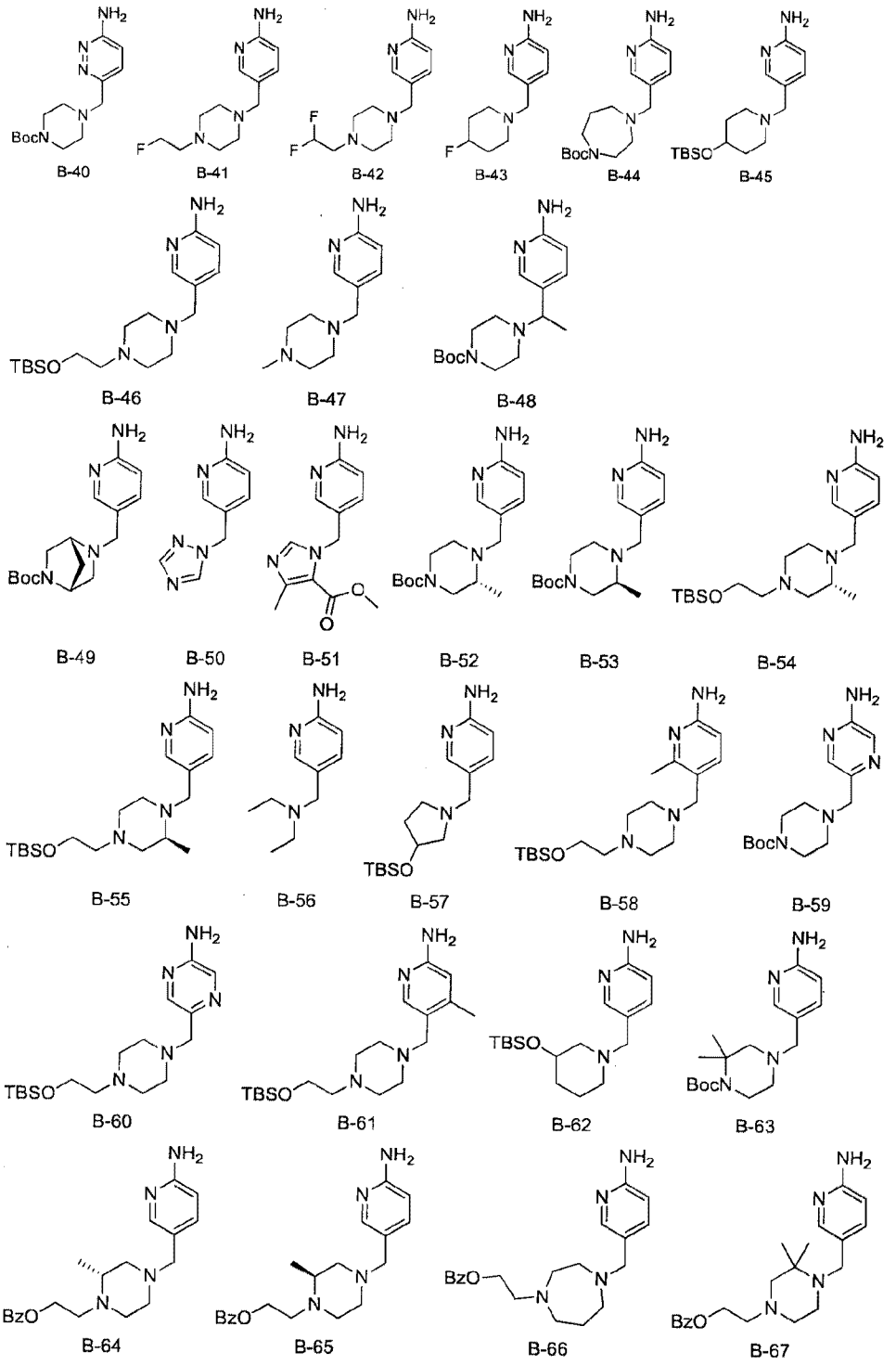
[0138]

[Formula 47]



[0139]

[Formula 48-1]


B-40
B-41
B-42
B-43
B-44
B-45
B-46
B-47
B-48
B-49
B-50
B-51
B-52
B-53
B-54
B-55
B-56
B-57
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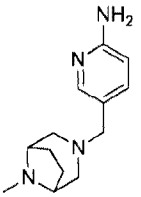
B-65
B-66
B-67

[Formula 48-2]

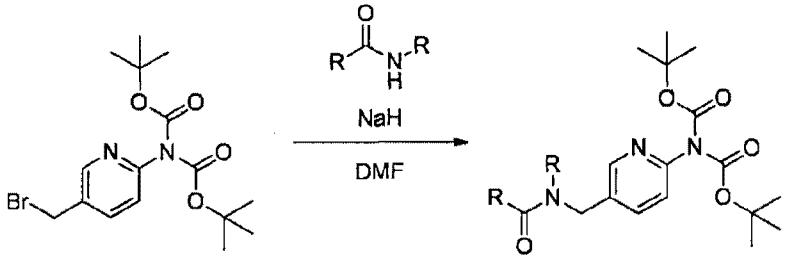


B-68

[0140]

Reference Example 12

[Formula 49]



[0141]

An appropriate amide derivative (1 equivalent) was dissolved in DMF, and sodium hydride (1 equivalent) was gradually added thereto at 0°C and the mixture was stirred at room temperature for several minutes. The resultant reaction mixture was cooled to 0°C and di-tert-butyl [5-(bromomethyl)pyridin-2-yl]imidodicarbonate (1.5 equivalents) was gradually added to the mixture. The reaction mixture was stirred at room temperature for several hours and then water was added to the mixture to stop the reaction. The mixture was extracted with ethyl acetate and washed with saturated brine. The resultant organic phase was dried over anhydrous sodium sulfate, and the solid was separated by filtration. The filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield a target amide derivative.

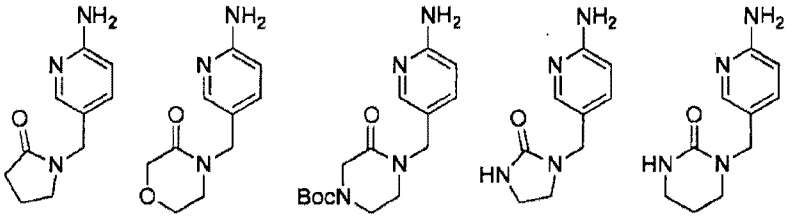
[0142]

The following intermediates C-1 to C-5 were synthesized by the process of Reference Example 12 and 11

with the corresponding alkyl halide derivatives, amide derivatives, or urea derivatives. Appropriate protection or deprotection was performed as needed.

[0143]

[Formula 50]



C-1 C-2 C-3 C-4 C-5

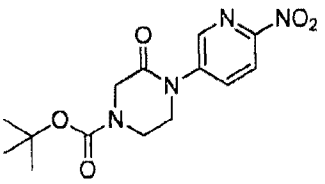
[0144]

Reference Example 13

Synthesis of tert-butyl 4-(6-nitropyridin-3-yl)-3-oxopiperazine-1-carboxylate

[0145]

[Formula 51]



[0146]

In reference to the process disclosed in WO2012/031004, 2-nitro-5-bromopyridine (1.01 g, 5.0 mmol), tert-butyl 2-oxo-4-piperazinecarboxylate (1.00 g, 5.0 mmol, and cesium carbonate (3.26 g, 10.0 mmol) were suspended in 1,4-dioxane, and the suspension was bubbled with nitrogen gas for 30 minutes. To the suspension was added Xantphos (246 mg, 0.43 mmol) and tris(dibenzylideneacetone)dipalladium (229 mg, 0.25 mmol), and the mixture was stirred under reflux for two hours. The resultant reaction mixture was cooled to room temperature, and water and ethyl acetate were then added to the mixture, followed by filtration with Celite. The organic phase was separated from the filtrate, and the aqueous phase was extracted with ethyl acetate. The

resultant organic phases were combined together and dried over anhydrous sodium sulfate, and the resultant solid was separated by filtration. The filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield the title compound (1.08 g, 67%).

^{1}H-NMR ($CDCl_3$)δ: 8.67 (1H, d, J=2.4 Hz), 8.32 (1H, d, J=8.8 Hz), 8.15 (1H, dd, J=8.8, 2.4 Hz), 4.33 (2H, s), 3.93-3.83 (4H, m), 1.51 (9H, s).

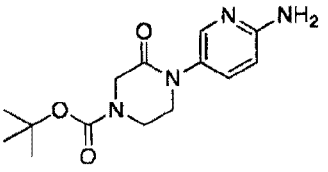
[0147]

Reference Example 14

Synthesis of tert-butyl 4-(6-aminopyridin-3-yl)-3-oxopiperazine-1-carboxylate

[0148]

[Formula 52]



[0149]

The compound synthesized in Reference Example 13 (1.08 g, 3.34 mmol) was dissolved in ethanol (45 mL) and THF (22 mL). Palladium-carbon (108 mg) was added to the solution, and the mixture was stirred under a hydrogen atmosphere for 24 hours. The resultant reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to yield the title compound (0.928 g, 95%).

^{1}H-NMR ($CDCl_3$)δ: 7.99 (1H, d, J=2.4 Hz), 7.38 (1H, dd, J=8.8, 2.4 Hz), 6.53 (1H, d, J=8.8 Hz), 4.50 (2H, brs), 4.24 (2H, s), 3.78 (2H, t, J=5.1 Hz), 3.67 (2H, t, J=5.4 Hz), 1.50 (9H, s).

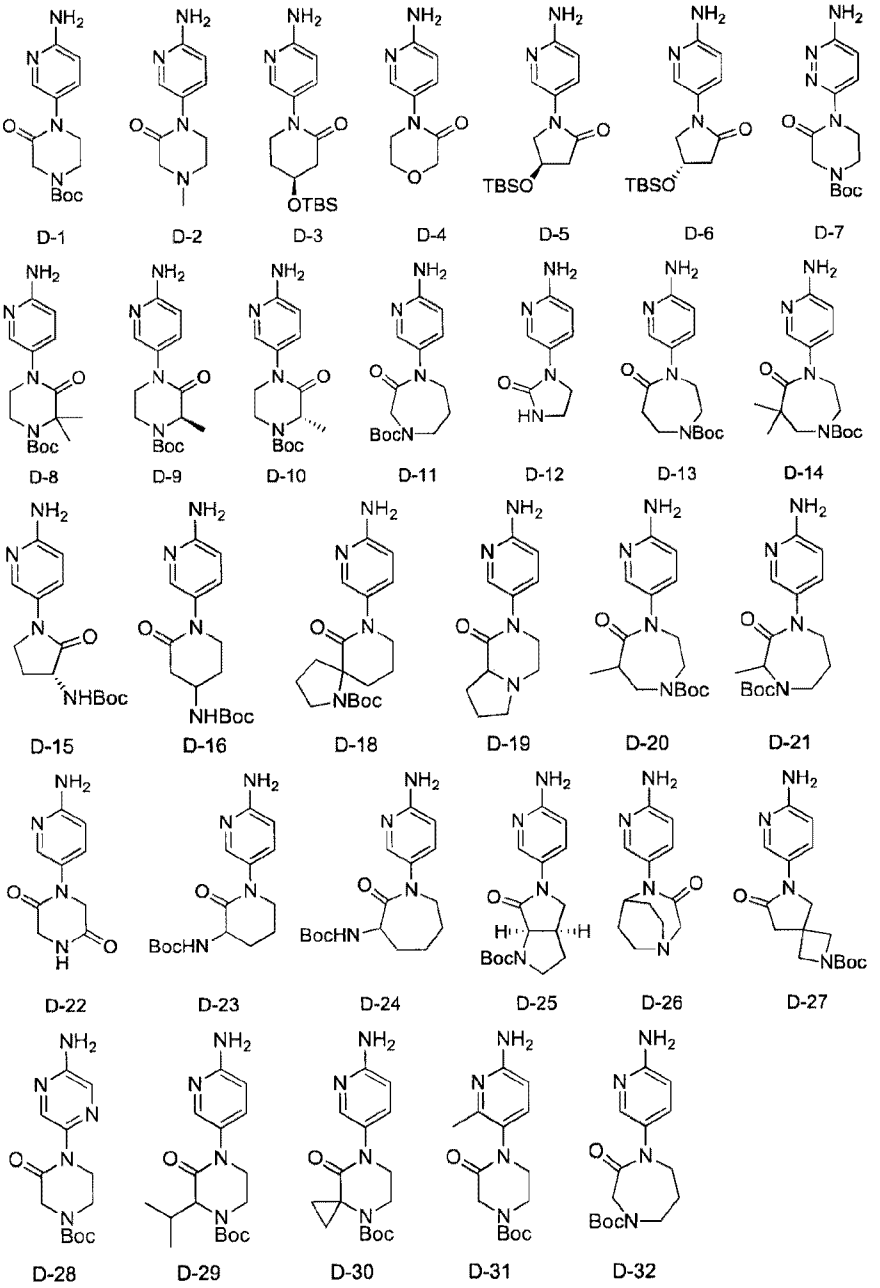
[0150]

Intermediates D-1 to D-41 were each synthesized by the process of Reference Example 13 and/or 14 with the

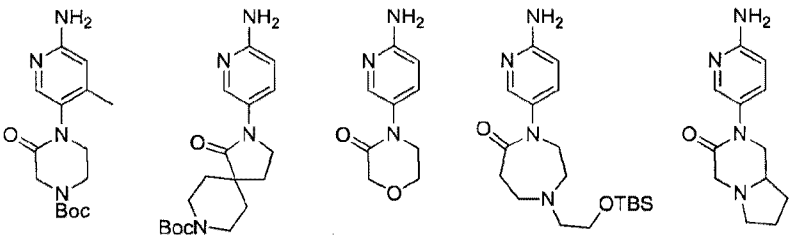
corresponding halopyridine derivatives and amide derivatives. Appropriate protection or deprotection was performed as needed.

[0151]

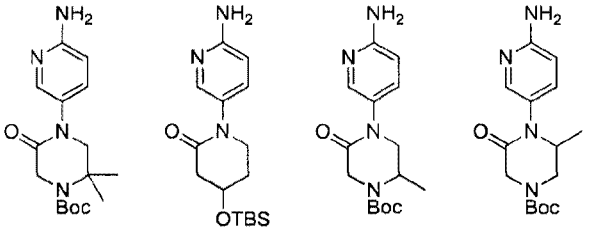
[Formula 53-1]



[Formula 53-2]



D-33 D-34 D-35 D-36 D-37



D-38 D-39 D-40 D-41

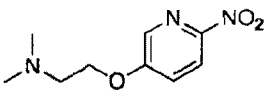
[0152]

Reference Example 15

Synthesis of dimethyl-[2-(6-nitropyridin-3-yloxy)ethyl]amine

[0153]

[Formula 54]



[0154]

2-Dimethylaminoethanol (0.32 mL, 3.17 mmol) was dissolved in DMF (4 mL) and cesium carbonate (1.03 g, 3.17 mmol) was added thereto, and the resultant suspension was stirred at room temperature for 10 minutes. 5-Fluoro-2-nitropyridine (0.30 g, 2.11 mmol) was added to the suspension at room temperature, and the mixture then was stirred at 80°C for 16 hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction was quenched through addition of ice water, and the reaction mixture was extracted with ethyl acetate. The resultant organic phase was dried over anhydrous sodium sulfate, and the solid was separated by filtration. The filtrate was then

concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield the title compound (0.40 g, 90%).

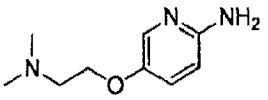
[0155]

Reference Example 16

Synthesis of 5-(2-dimethylaminoethoxy)pyridin-2-ylamine

[0156]

[Formula 55]



[0157]

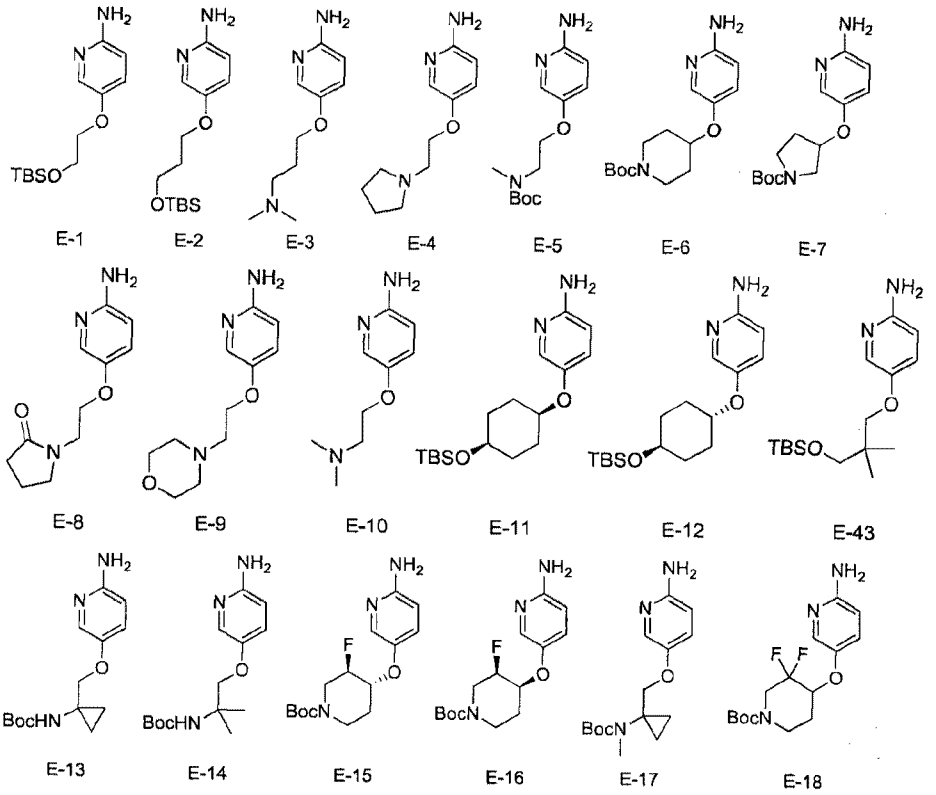
Dimethyl-[2-(6-nitropyridin-3-yloxy)ethyl]amine synthesized in Reference Example 15 (0.40 g, 1.90 mmol) was dissolved in THF (5 mL) and ethanol (5 mL), and palladium-carbon (80 mg) was added to the solution. The mixture was stirred under a hydrogen atmosphere overnight. The resultant reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The resultant crude product was washed with a solvent mixture of ethyl acetate and hexane (1:9) to yield the title compound (0.28 g, 82%).

[0158]

Intermediates E-1 to E-61 were each synthesized by the process of Reference Examples 15 and/or 16 with the corresponding halopyridine derivatives, alcohol derivatives, or thiol derivatives. Appropriate protection or deprotection was performed as needed.

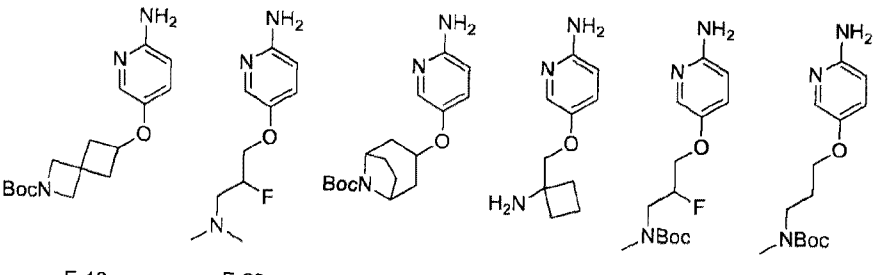
[0159]

[Formula 56]

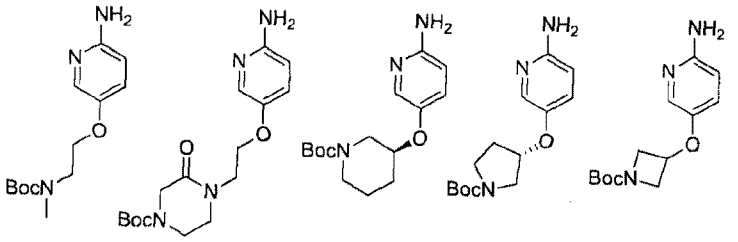


[0160]

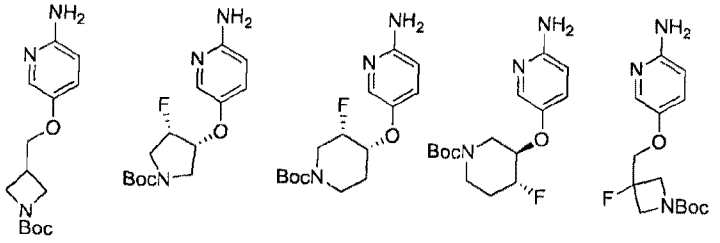
[Formula 57-1]



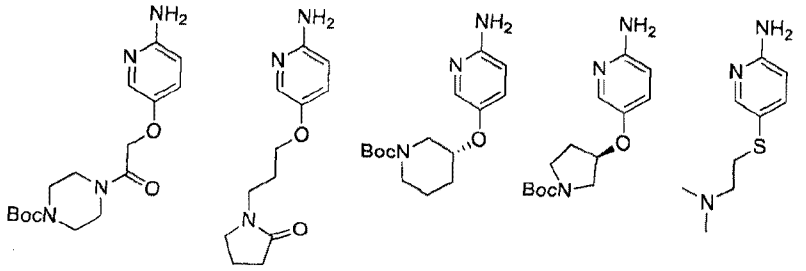
E-19 E-20 E-21 E-22 E-23 E-24



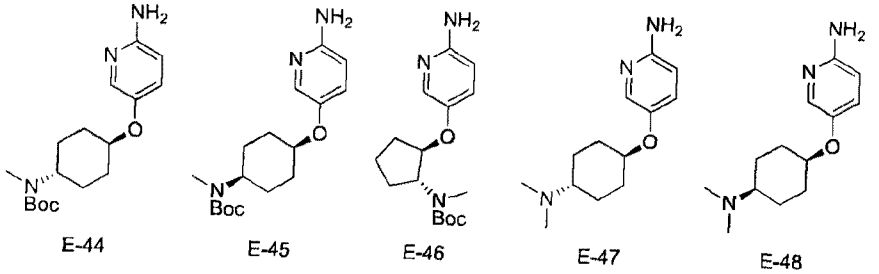
E-25 E-26 E-27 E-28 E-30



E-32 E-33 E-34 E-35 E-36

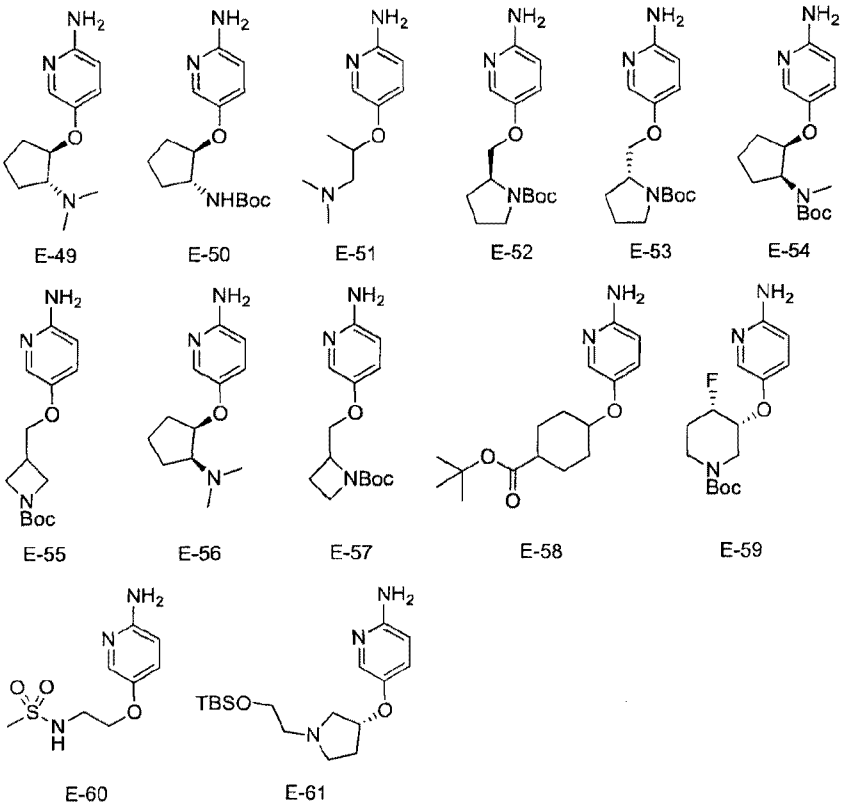


E-38 E-39 E-40 E-41 E-42



E-44 E-45 E-46 E-47 E-48

[Formula 57-2]



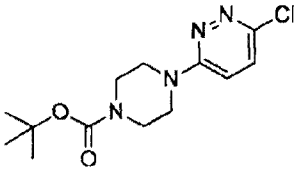
[0161]

Reference Example 17

Synthesis of tert-butyl 4-(6-chloropyridazin-3-yl)piperazine-1-carboxylate

[0162]

[Formula 58]



[0163]

A solution of 3,6-dichloropyridazine (5.01 g, 33.6 mmol) and tert-butyl piperazine-1-carboxylate (6.88g, 37.0 mmol) in DMF (50 mL) was added triethylamine (11.7 mL, 50.4 mmol) and stirred at 80°C overnight. The resultant reaction mixture was cooled to room

temperature, and water was added to the mixture. The mixture was extracted three times with a solvent mixture of dichloromethane and methanol (95:5) (50 mL). The resultant organic phases were combined together and dried over anhydrous magnesium sulfate. The resultant solid was separated by filtration, and the filtrate was then concentrated under reduced pressure. The resultant crude product was washed with diethyl ether to yield the title compound (7.0 g, 70%).

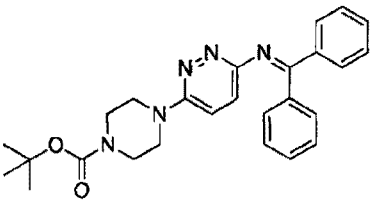
[0164]

Reference Example 18

Synthesis of tert-butyl 4-(6-((diphenylmethylene)amino)pyridazin-3-yl)piperazine-1-carboxylate

[0165]

[Formula 59]



[0166]

Tert-butyl 4-(6-chloropyridazin-3-yl)piperazine-1-carboxylate synthesized in Reference Example 17 (59.8 mg, 0.20 mmol, benzophenone imine (43.5 mg, 0.24 mmol), tris(dibenzylideneacetone)dipalladium (9.2 mg, 0.010 mmol), BINAP (12.5 mg, 0.020 mmol), and cesium carbonate (130.3 mg, 0.40 mmol) were suspended in toluene (1.0 mL), and the suspension was stirred at 100°C overnight. The resultant reaction mixture was cooled to room temperature and then filtered through Celite, and the Celite was washed with ethyl acetate. The filtrate was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solid was separated by filtration. The filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield the title compound (67 mg, 76%).

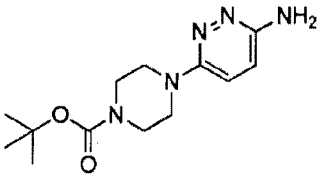
[0167]

Reference Example 19

Synthesis of tert-butyl 4-(6-aminopyridazin-3-yl)piperazine-1-carboxylate

[0168]

[Formula 60]



[0169]

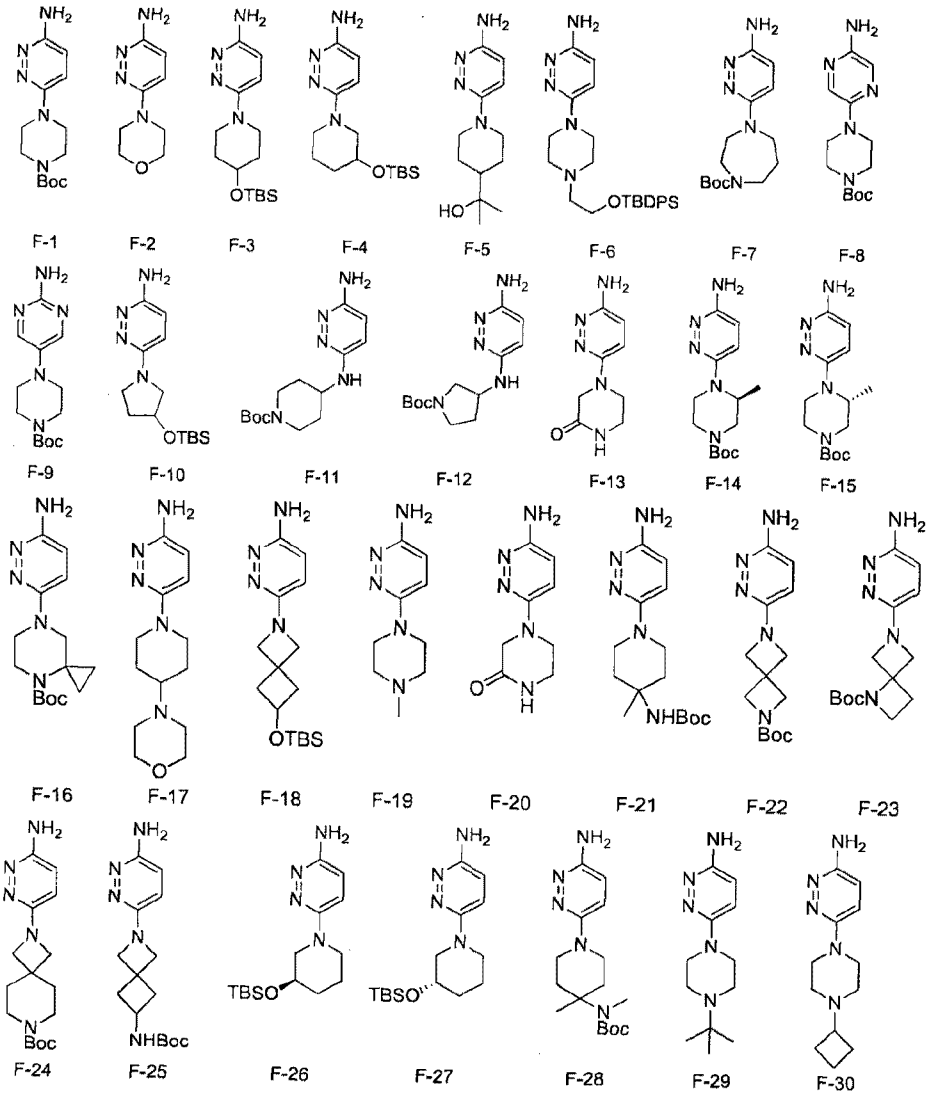
Tert-butyl 4-(6-((diphenylmethylene)amino)pyridazin-3-yl)piperazine-1-carboxylate synthesized in Reference Example 18 (67 mg, 0.151 mmol) was dissolved in THF (0.76 mL). To the solution was added an aqueous citric acid solution (0.378 mL, 0.755 mmol, 2 mol/L) and the mixture was stirred at room temperature overnight. The resultant reaction mixture was neutralized with saturated aqueous sodium hydrogen carbonate solution (5 mL), and the mixture was extracted twice with ethyl acetate (5 mL). The resultant organic phases were combined together and dried over anhydrous magnesium sulfate, and the resultant solid was separated by filtration. The filtrate was concentrated under reduced pressure, and the resultant crude product was washed with tert-butyl methyl ether (5 mL) to yield the title compound (30 mg, 71%).

[0170]

Intermediates F-1 to F-77 were each synthesized by any of the processes of Reference Examples 17 to 19 or a combination of the processes with the corresponding haloheteroaryl derivatives and amine derivatives. Appropriate protection or deprotection was performed as needed.

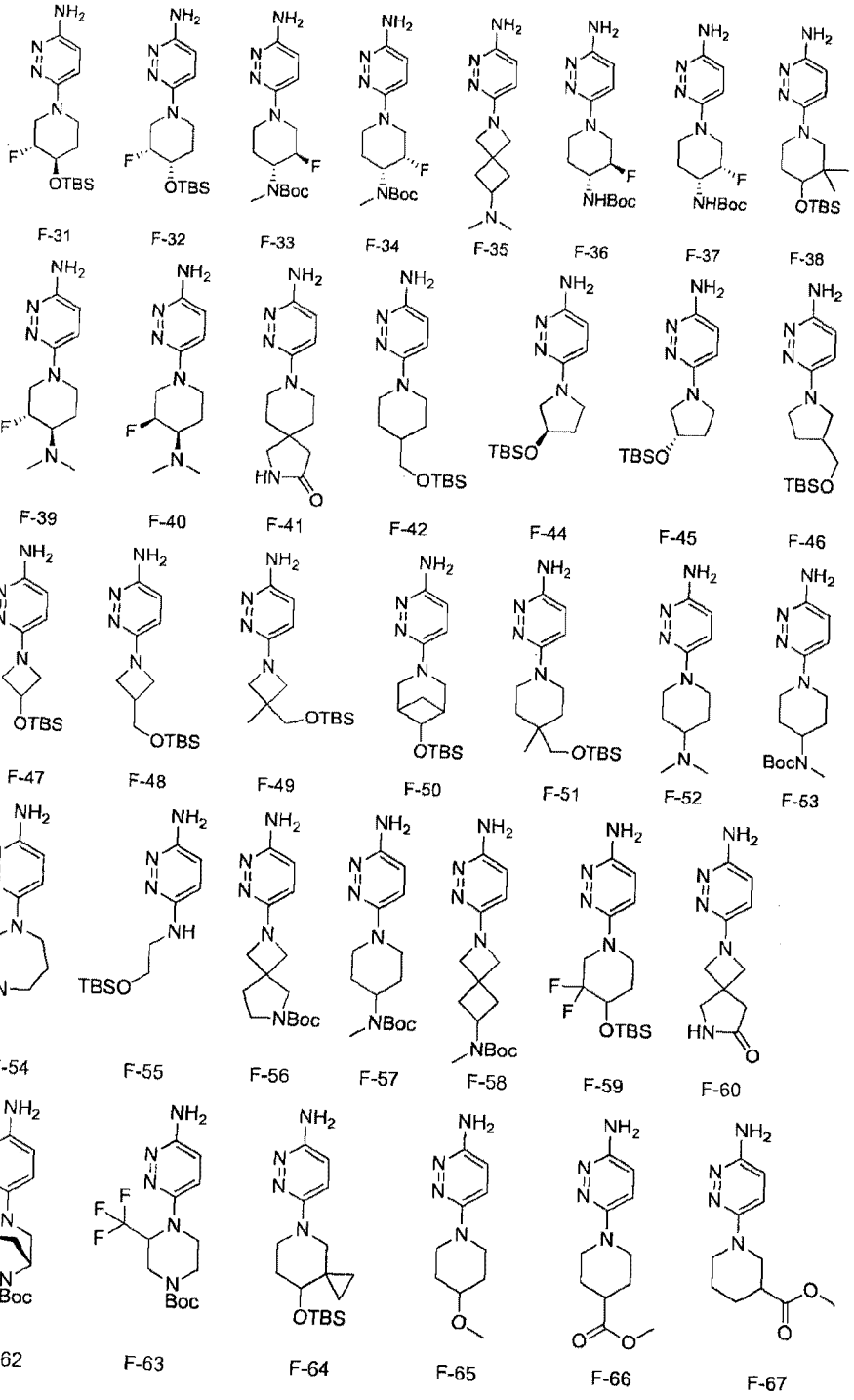
[0171]

[Formula 61]



[0172]

[Formula 62-1]


F-31
F-32
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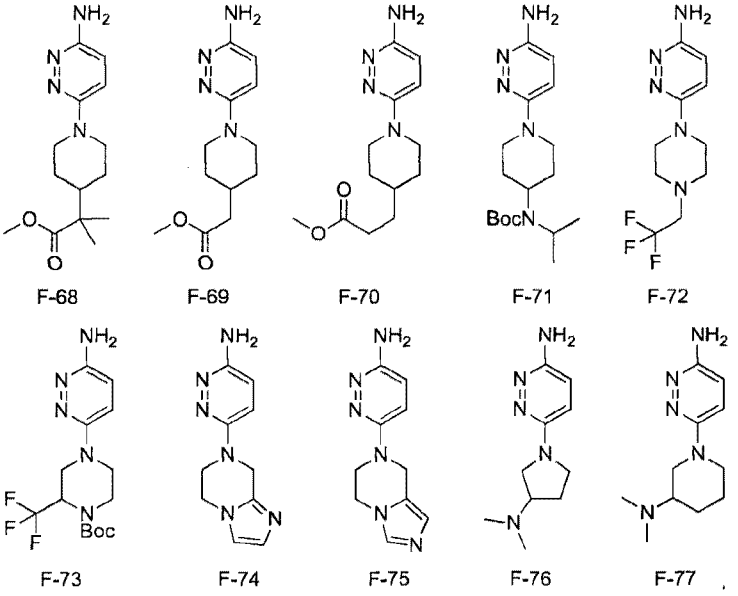
F-64
F-65
F-66
F-67

[Formula 62-2]

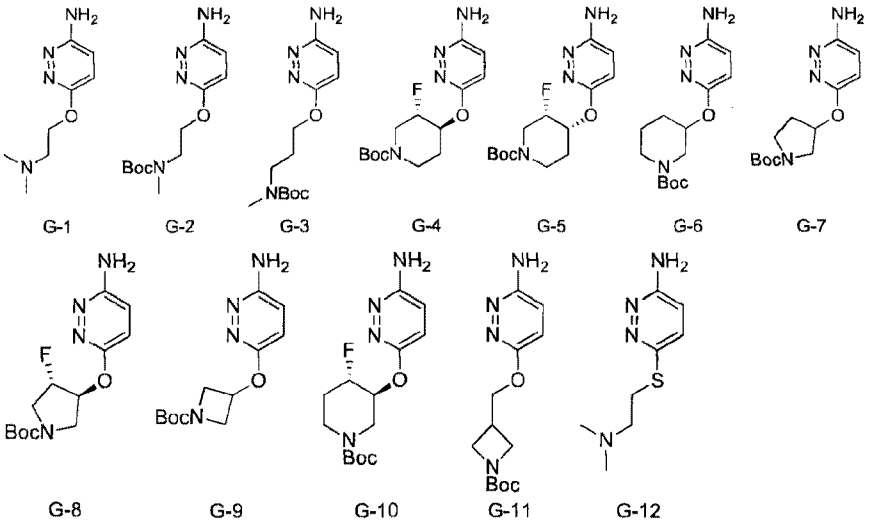


[0173]

Intermediates G-1 to G-12 were each synthesized by any of the processes of Reference Examples 15, 18, and 19 or a combination of the processes with the corresponding halopyridazine, alcohol, or thiol derivative. Appropriate protection or deprotection was performed as needed.

[0174]

[Formula 63]



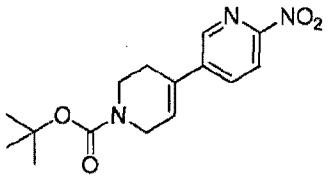
[0175]

Reference Example 20

Synthesis of tert-butyl 4-(6-nitropyridin-3-yl)piperidin-3-ene-1-carboxylate

[0176]

[Formula 64]



[0177]

3-Bromo-6-nitropyridine was reacted with tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate under heating in the presence of a palladium catalyst by using the process described in J. Med. Chem. 2010, 53, p.7938-7957, to yield the title compound.

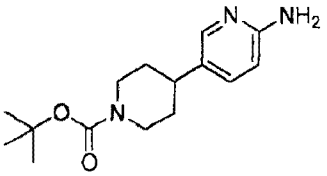
[0178]

Reference Example 21

Synthesis of tert-butyl 4-(6-aminopyridin-3-yl)piperidine-1-carboxylate

[0179]

[Formula 65]



[0180]

Tert-butyl 4-(6-nitropyridin-3-yl)piperidin-3-ene-1-carboxylate synthesized in Reference Example 20 was reduced under a hydrogen atmosphere in the presence of palladium-carbon by using the process described in J. Med. Chem. 2010, 53, p.7938-7957 to yield the title compound.

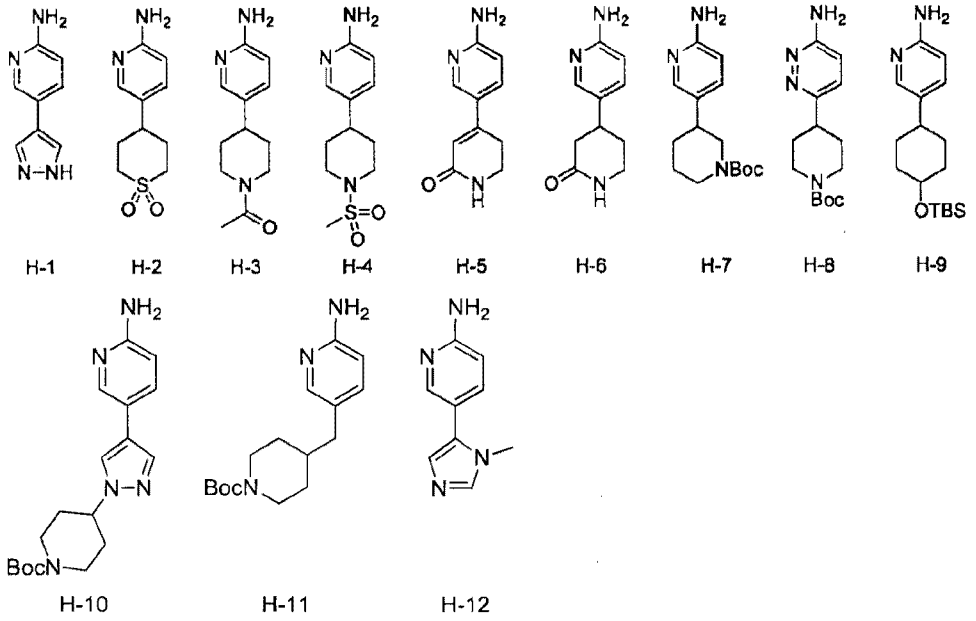
[0181]

Intermediates H-1 to H-12 were each synthesized by

the process of Reference Example 20 and/or 21 with the corresponding haloheteroaryl or boric acid derivative. Appropriate protection or deprotection was performed as needed.

[0182]

[Formula 66]



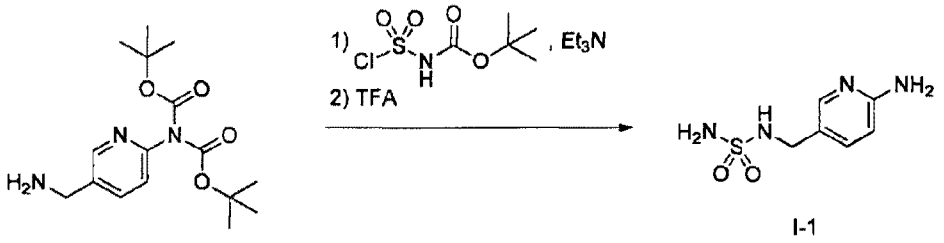
[0183]

Reference Example 22

Intermediate I-1 was synthesized through the reaction of tert-butyl chlorosulfonylcarbamate with tert-butyl N-[5-(aminoethyl)-2-pyridyl]-N-tert-butoxycarbonylcarbamate synthesized by any of the processes of Reference Examples 8 to 10 or a combination of the processes, and then the removal of the Boc groups under acidic conditions.

[0184]

[Formula 67]



I-1

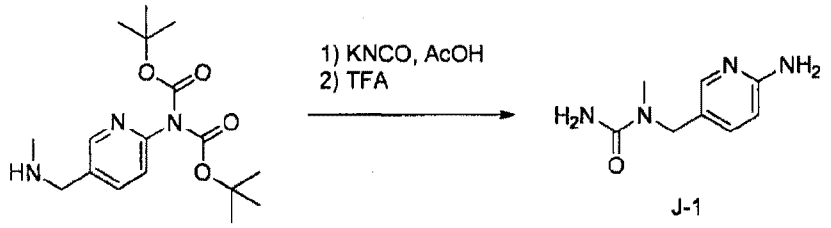
[0185]

Reference Example 23

Intermediate J-1 was synthesized through the reaction of potassium isocyanate with tert-butyl N-tert-butoxycarbonyl-N-[5-(N-methylaminoethyl)-2-pyridyl]carbamate synthesized as in Reference Example 8 to 10, and the removal of the Boc groups under acidic conditions.

[0186]

[Formula 68]



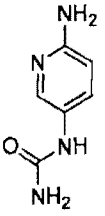
J-1

[0187]

Intermediate J-2 was synthesized through hydrogen reduction of the nitro group of 5-amino-2-nitropyridine in the presence of palladium hydroxide/activated carbon by the process of Reference Example 23.

[0188]

[Formula 69]



J-2

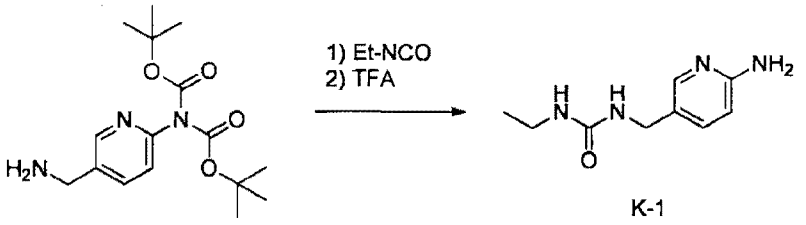
[0189]

Reference Example 24

Intermediate K-1 was synthesized through the reaction of isocyanatoethane with tert-butyl N-[5-(aminoethyl)-2-pyridyl]-N-tert-butoxycarbonylcarbamate synthesized by any of the processes of Reference Examples 8 to 10 or a combination of the processes, and the removal of the Boc groups under acidic conditions.

[0190]

[Formula 70]



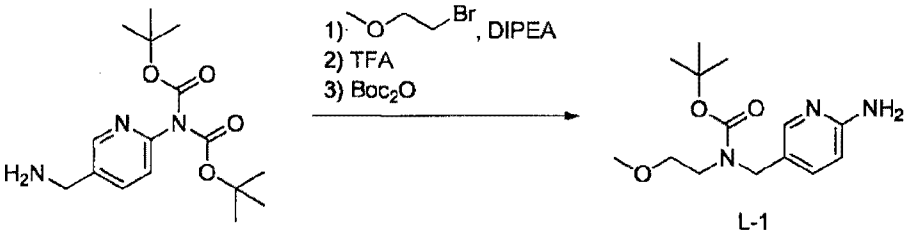
[0191]

Reference Example 25

Intermediate L-1 was synthesized through the reaction of 2-methoxyethyl bromide with tert-butyl N-[5-(aminoethyl)-2-pyridyl]-N-tert-butoxycarbonylcarbamate synthesized by any of the processes of Reference Examples 8 to 10 or a combination of the processes, the removal of the Boc groups under acidic conditions, and the selective protection of the secondary amino moiety with a Boc group as in Reference Example 11.

[0192]

[Formula 71]



[0193]

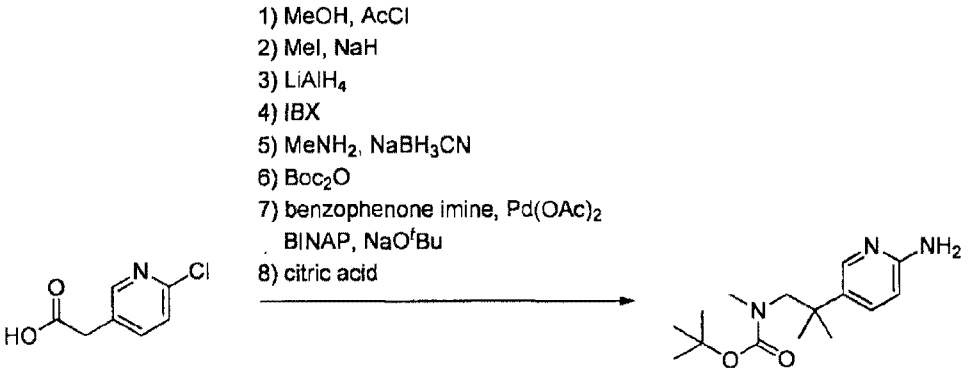
Reference Example 26

Intermediate M-1 was synthesized through the esterification of the carboxylic acid moiety of 2-(6-

chloropyridin-3-yl)acetic acid, dimethylation of the carbonyl group at the α-position, reduction of the ester moiety with LAH, oxidation of the resultant alcohol moiety, reductive amination with methylamine, protection with a Boc group, amination of the 2-chloropyridine moiety in the presence of a Pd catalyst, and deprotection.

[0194]

[Formula 72]



M-1

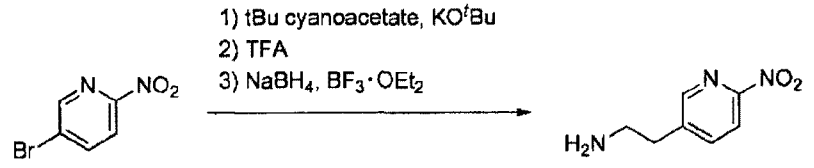
[0195]

Reference Example 27

Intermediate N-1 was synthesized through the reaction of 5-bromo-2-nitropyridine with tert-butyl cyanoacetate under basic conditions, removal of the tert-butyl group and decarboxylation under acidic conditions, and reduction of the cyano group.

[0196]

[Formula 73]



N-1

[0197]

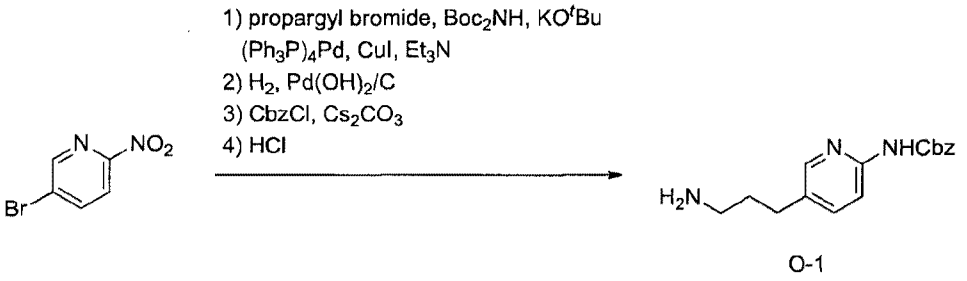
Reference Example 28

Intermediate O-1 was synthesized through the

reaction of an alkyne derivative with imide derivative, subsequent reaction with 5-bromo-2-nitropyridine under Sonogashira coupling reaction conditions, and reduction with hydrogen in the presence of palladium hydroxide/activated carbon, involving protection and deprotection.

[0198]

[Formula 74]



O-1

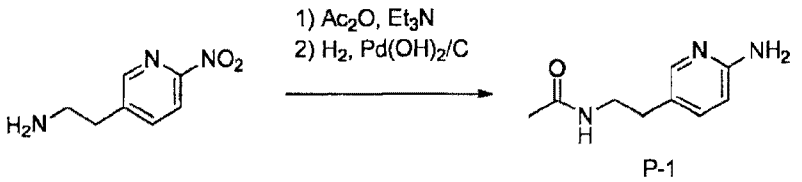
[0199]

Reference Example 29

Intermediate P-1 was synthesized through acylation of 2-(6-nitropyridin-3-yl)ethylamine and reduction with hydrogen in the presence of palladium hydroxide/activated carbon.

[0200]

[Formula 75]



P-1

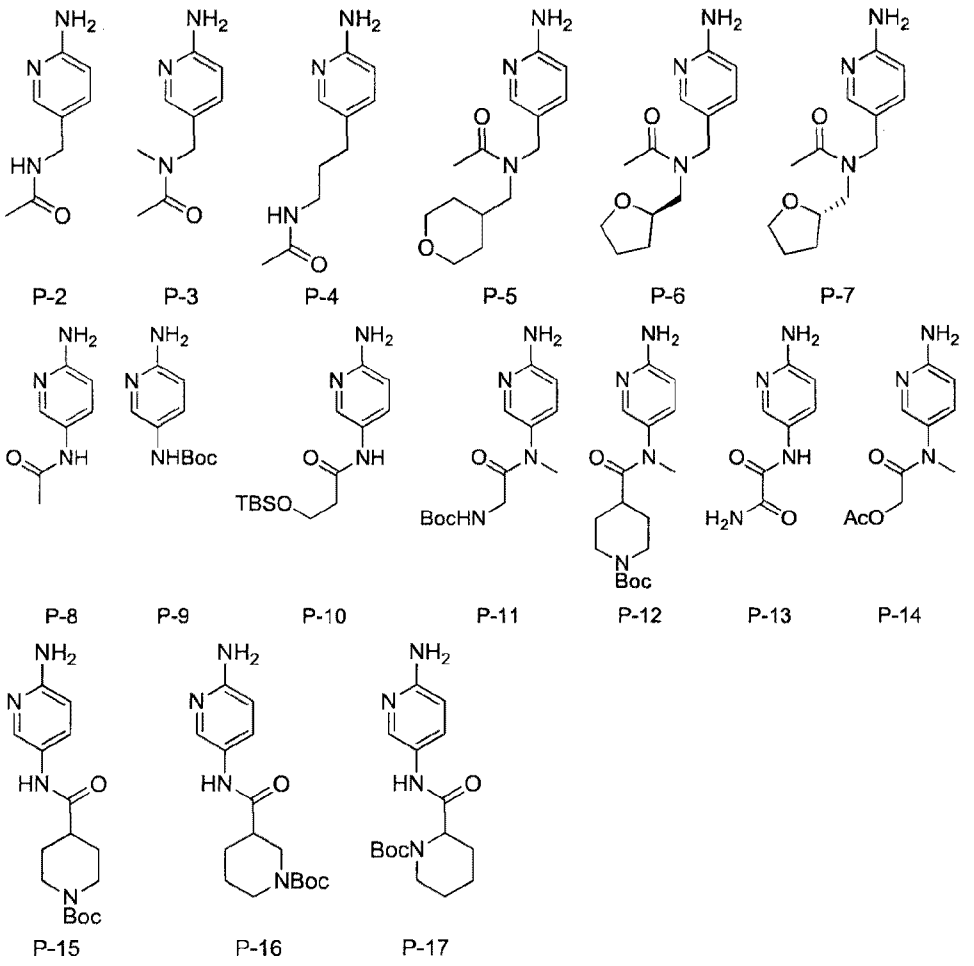
[0201]

Intermediates P-2 to P-17 were each synthesized by the process of Reference Example 29 with the corresponding amine derivative synthesized by, for example, any of the processes of Reference Examples 8 to 10 and the corresponding acylating agent, involving appropriate deprotection as needed. Appropriate acylation conditions were selected depending on the structure to be introduced. For example, an acid

chloride or combination of a carboxylic acid and a condensing agent was used as the acylating agent in place of an acid anhydride.

[0202]

[Formula 76]



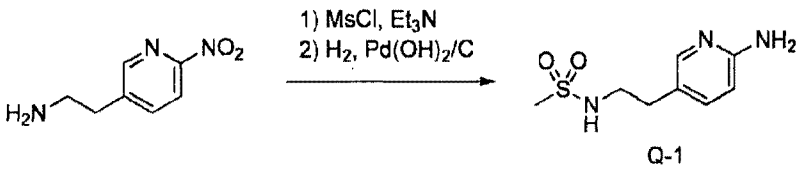
[0203]

Reference Example 30

Intermediate Q-1 was synthesized by mesylation of 2-(6-nitropyridin-3-yl)ethylamine and reduction with hydrogen in the presence of palladium hydroxide/activated carbon.

[0204]

[Formula 77]

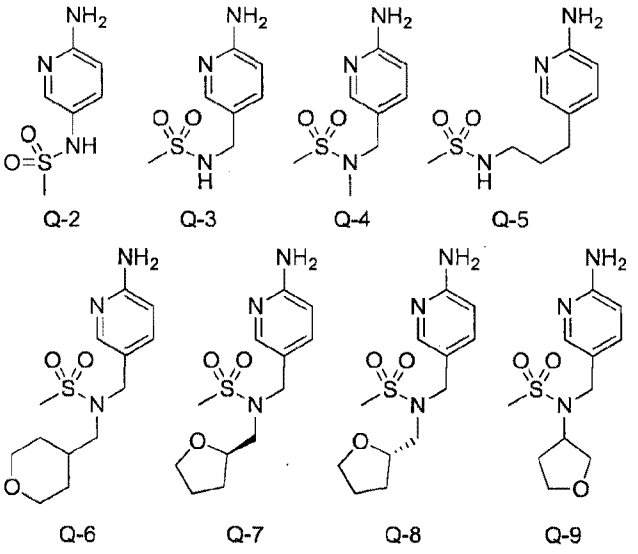


[0205]

Intermediates Q-2 to Q-9 were each synthesized by the process of Reference Example 29 with the corresponding amine derivative synthesized by, for example, any of the processes of Reference Examples 8 to 10, involving appropriate deprotection as needed.

[0206]

[Formula 78]



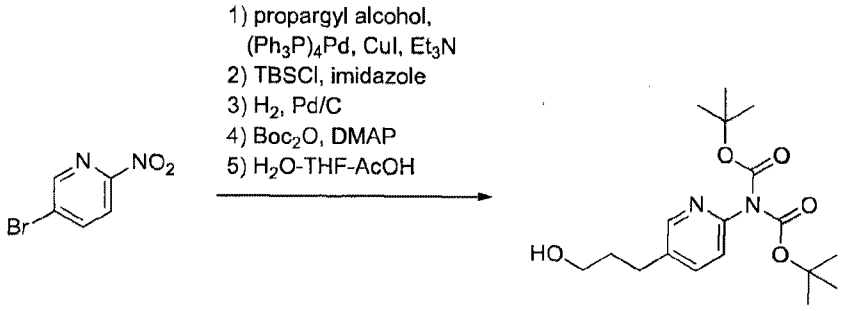
[0207]

Reference Example 31

Intermediate R-1 was synthesized through the reaction of 5-bromo-2-nitropyridine with an alkyne derivative under Sonogashira coupling reaction conditions, protection and reduction with hydrogen in the presence of palladium hydroxide/activated carbon, involving protection and deprotection.

[0208]

[Formula 79]



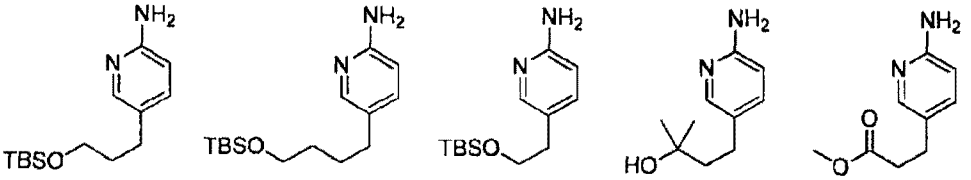
R-1

[0209]

Intermediates R-2 to R-6 were each synthesized by the process of Reference Example 31; i.e., by the reactions 1) to 3) in Reference Example 31 with a halopyridine derivative and the corresponding terminal alkyne derivative.

[0210]

[Formula 80]



R-2 R-3 R-4 R-5 R-6

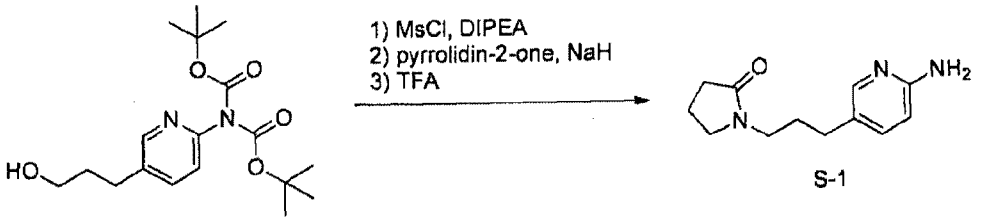
[0211]

Reference Example 32

Intermediate S-1 was synthesized through the mesylation of intermediate R-1 synthesized in Reference Example 31, reaction with an amide derivative under basic conditions and subsequent deprotection.

[0212]

[Formula 81]



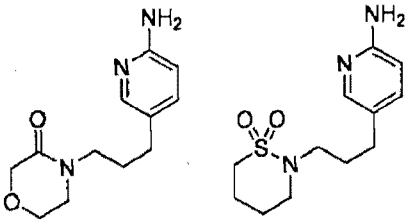
R-1 S-1

[0213]

Intermediates S-2 and S-3 were each synthesized by the process of Reference Example 32 with the corresponding alcohol derivative, amide derivative, or sulfonamide derivative.

[0214]

[Formula 82]



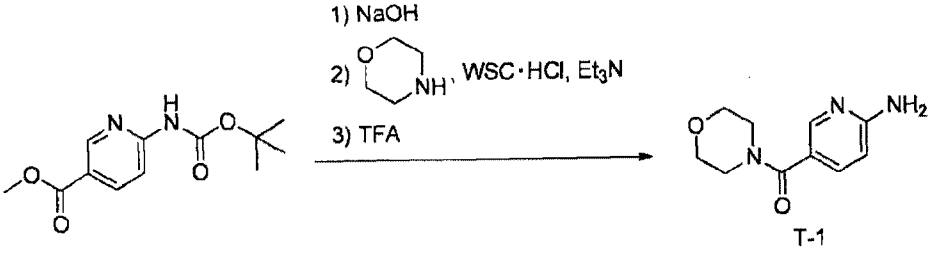
[0215]

Reference Example 33

Intermediate T-1 was synthesized through basic hydrolysis of methyl 6-((tert-butoxycarbonyl)amino)nicotinate, condensation with morpholine, and deprotection.

[0216]

[Formula 83]



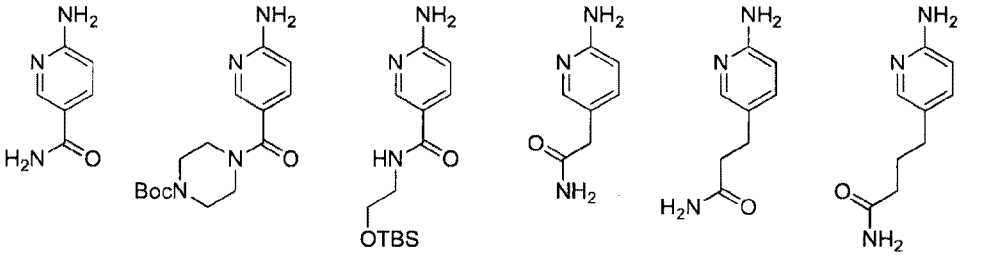
T-1

[0217]

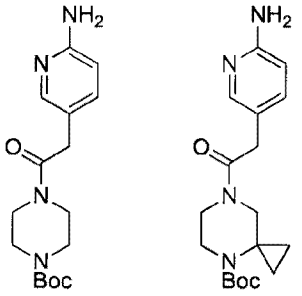
Intermediates T-2 to T-17 were each synthesized by the process of Reference Example 33 with the corresponding ester derivative synthesized by, for example, the process of Reference Example 31, or the corresponding carboxylic acid derivative and amine derivative. Appropriate protection and deprotection were performed as needed.

[0218]

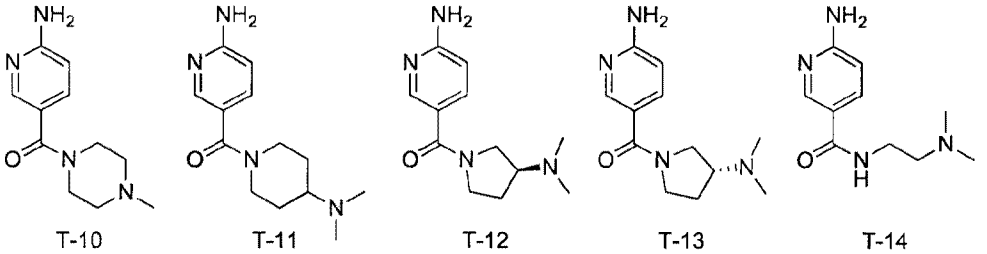
[Formula 84]



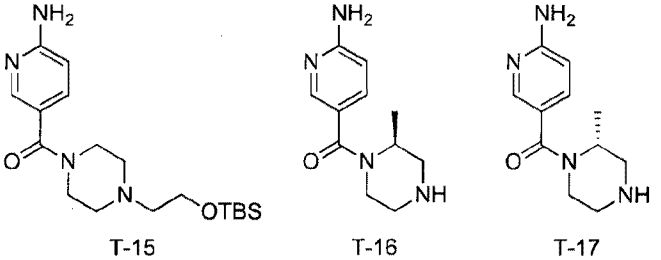
T-2 T-3 T-4 T-5 T-6 T-7



T-8 T-9



T-10 T-11 T-12 T-13 T-14



T-15 T-16 T-17

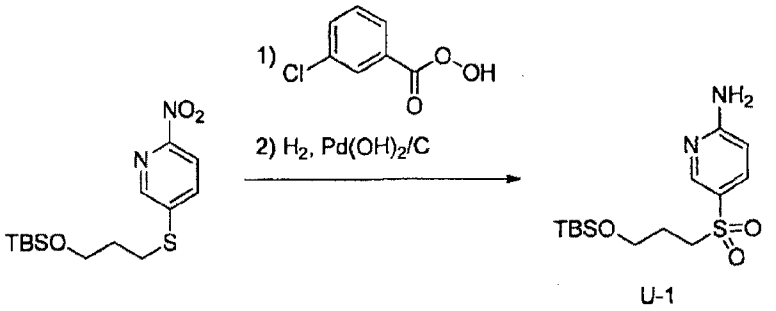
[0219]

Reference Example 34

Intermediate U-1 was synthesized by oxidation of 5-((3-((tert-butyldimethylsilyl)oxy)propyl)thio)-2-nitropyridine synthesized by the process of Reference Example 15 with m-chloroperbenzoic acid and reduction with hydrogen in the presence of palladium hydroxide/activated carbon.

[0220]

[Formula 85]



U-1

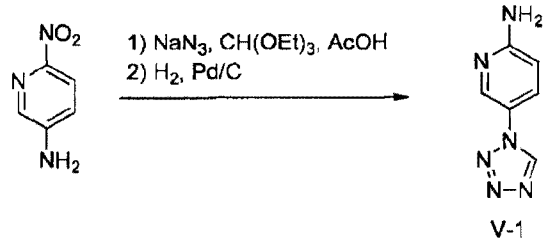
[0221]

Reference Example 35

Intermediate V-1 was synthesized through the reaction of 5-amino-2-nitropyridine with sodium azide and orthoformate and subsequent reduction with hydrogen in the presence of palladium hydroxide/activated carbon.

[0222]

[Formula 86]



V-1

[0223]

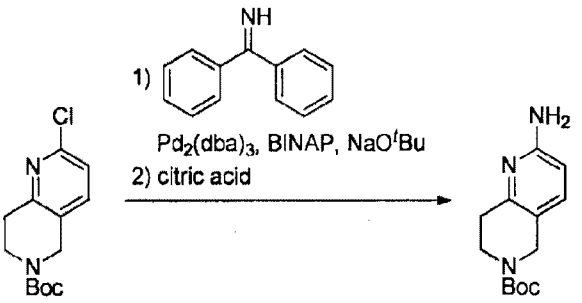
Reference Example 36

Intermediate W-1 was synthesized through the reaction of tert-butyl 2-chloro-7,8-dihydro-1,6-naphthyridine-6(5H)-carboxylate with benzophenone imine

and tert-butoxysodium in the presence of a Pd catalyst and deprotection.

[0224]

[Formula 87]



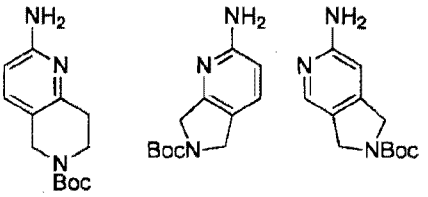
W-1

[0225]

Intermediates W-2 to W-4 were each synthesized by the process of Reference Example 36 with the corresponding halopyridine derivative.

[0226]

[Formula 88]



W-2 W-3 W-4

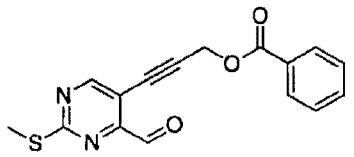
[0227]

Example 1

Synthesis of 3-(4-formyl-2-methylthiopyrimidin-5-yl)-2-propynyl benzoate

[0228]

[Formula 89]



[0229]

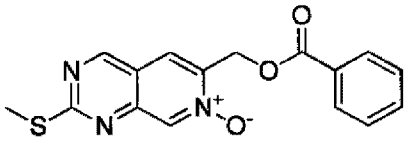
A solution of $Pd(PhCN)_2Cl_2$ (2.4 g, 6.4 mmol), copper

iodide (0.82 g, 4.3 mmol), and $[(t\text{-}Bu)_3P]HBF_4$ (4 g, 13.9 mmol) in 1,4-dioxane (55 mL) was degassed and purged with argon, and diisopropylamine (18.5 mL, 128.8 mmol) was added to the solution at room temperature. The resultant reaction mixture was stirred at room temperature for five minutes. A solution of a mixture (25 g, crude product) of 5-bromo-2-methylsulfanylpyrimidine-4-carbaldehyde and (5-bromo-2-methylsulfanylpyrimidin-4-yl)methoxymethanol described in Reference Example 3 and propargyl benzoate (20 g, 128.8 mmol) in 1,4-dioxane (55 mL) was slowly added dropwise to the reaction mixture, and the reaction mixture was then stirred at room temperature for five hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was diluted with ethyl acetate (1 L). The mixture was subjected to suction filtration through Celite®, and the Celite was washed with ethyl acetate. The filtrate was concentrated under reduced pressure, and the resultant crude product was directly used for the subsequent reaction.

[0230] Example 2

Synthesis of 6-((benzoyloxy)methyl)-2-(methylthio)pyrido[3,4-d]pyrimidine 7-oxide

[0231] [Formula 90]



[0232] The crude product of 3-(4-formyl-2-methylthiopyrimidin-5-yl)-2-propynyl benzoate synthesized in Example 1 was dissolved in ethanol (500 mL), and hydroxylamine hydrochloride (8.3 g, 120 mmol) and sodium acetate (10 g, 120 mmol) were added to the solution at room temperature. The resultant reaction mixture was

stirred at room temperature for six hours, and then diluted with ethanol (1 L). Potassium carbonate (27.8 g, 200 mmol) was added to the mixture, and the mixture was then stirred at 50°C for three hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was subjected to suction filtration through Celite, and the Celite was washed with ethyl acetate. The filtrate was dried over anhydrous sodium sulfate, and solid was separated by filtration. The filtrate was concentrated under reduced pressure, and the resultant crude product was purified by silica gel column chromatography to yield the title compound (5.0 g, 16%).

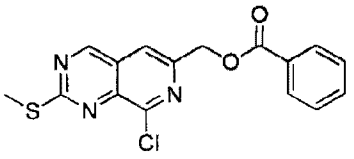
[0233]

Example 3

Synthesis of 8-chloro-2-methylthiopyrido[3,4-d]pyrimidin-6-yl benzoate

[0234]

[Formula 91]



[0235]

The 6-((benzoyloxy)methyl)-2-(methylthio)pyrido[3,4-d]pyrimidine 7-oxide synthesized in Example 2 (5.0 g, 15.3 mmol) was dissolved in dichloromethane (60 mL) and cooled to 0°C. Thionyl chloride (25 mL, 343 mmol) was added dropwise to the solution at 0°C, and the mixture was stirred at room temperature for 16 hours. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was concentrated under reduced pressure, followed by azeotropic distillation twice with toluene (20 mL), to remove thionyl chloride. The residue was roughly purified by neutral alumina column chromatography to yield the title compound (2.75 g, 52%).

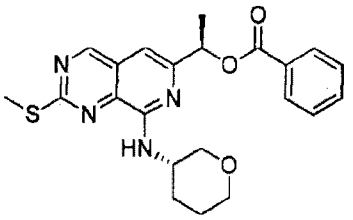
[0236]

Example 4

Synthesis of (R)-1-(2-(methylthio)-8-(((S)-tetrahydro-2H-pyran-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate

[0237]

[Formula 92]



[0238]

A mixture of (R)-1-(8-chloro-2-(methylthio)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate synthesized by the process described in Example 3 (360 mg, 1.0 mmol), (S)-tetrahydro-2H-pyran-3-amine hydrochloride (206 mg, 1.5 mmol), and potassium carbonate (415 mg, 3.0 mmol) in 1,4-dioxane (4.0 mL) was stirred at 100°C overnight. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with water, and the mixture was extracted twice with ethyl acetate (10 mL). The resultant organic phase was washed with brine and dried over anhydrous magnesium sulfate. The solid was separated by filtration, and the filtrate was concentrated under reduced pressure. The resultant crude product was purified by silica gel column chromatography to yield the title compound (232 mg, 55%).

^{1}H-NMR ($CDCl_3$)δ: 8.97 (1H, s), 8.17-8.14 (2H, m), 7.62-7.57 (1H, m), 7.51-7.46 (2H, m), 6.87 (1H, s), 6.65 (1H, d, J=7.8 Hz), 6.10 (1H, q, J=6.7 Hz), 4.39-4.31 (1H, m), 4.08-4.03 (1H, m), 3.82-3.76 (1H, m), 3.70-3.64 (1H, m), 3.56-3.51 (1H, m), 2.65 (3H, s), 2.09-2.02 (1H, m), 1.89-1.78 (2H, m), 1.76-1.65 (4H, m)

LC/MS: $(M+H)^+$=425.2, $C_{22}H_{24}N_4O_3S$=424.16

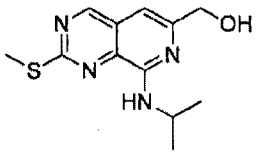
[0239]

Example 5

Synthesis of 2-methylthio-8-(propan-2-yl)aminopyrido[3,4-d]pyrimidin-6-ylmethanol

[0240]

[Formula 93]



[0241]

The 8-isopropylamino-2-methylthiopyrido[3,4-d]pyrimidine-6-yl benzoate synthesized by the process described in Example 4 (3.7 g, 10.0 mmol) was dissolved in methanol (20 mL) and THF (20 mL), and an aqueous solution (10 mL) of lithium hydroxide (0.96 g, 40 mmol) was added dropwise to the solution at room temperature. The resultant reaction mixture was stirred at room temperature for one hour. The reaction was monitored by LC/MS. After completion of the reaction, hydrochloric acid (2 mol/L) was added dropwise to the reaction mixture, to adjust the pH of the mixture to 7. The resultant solid was separated by filtration and dried under reduced pressure to yield the title compound (2.55 g, 96%).

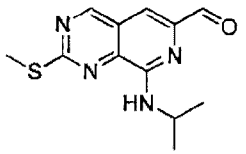
[0242]

Example 6

Synthesis of 2-methylthio-8-(propan-2-yl)aminopyrido[3,4-d]pyrimidine-6-carbaldehyde

[0243]

[Formula 94]



[0244]

The 2-methylthio-8-(propan-2-yl)aminopyrido[3,4-d]pyrimidin-6-ylmethanol synthesized in Example 5 (3.1 g,

11.7 mmol) was dissolved in dichloromethane (30 mL) and the solution was stirred at 0°C. Dess-Martin Periodinane (15 g, 35.2 mmol) was gradually added to the solution at 0°C, and the reaction mixture was stirred at room temperature for three hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction was quenched by addition of an aqueous sodium thiosulfate solution for reduction of excess reagent. The aqueous phase was extracted three times with dichloromethane (50 mL). The resultant organic phases were combined together and dried over anhydrous sodium sulfate. The solid was separated by filtration, and the filtrate was then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to yield the title compound (2.9 g, 94%).

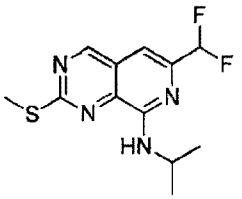
[0245]

Example 7

Synthesis of 6-difluoromethyl-2-methylthio-N-(propan-2-yl)pyrido[3,4-d]pyrimidine-8-amine

[0246]

[Formula 95]



[0247]

The 2-methylthio-8-(propan-2-yl)aminopyrido[3,4-d]pyrimidine-6-carbaldehyde synthesized in Example 6 (2.9 g, 11.1 mmol) was dissolved in dichloromethane (30 mL) and the solution was stirred at 0°C. DAST (7.1 g, 44.2 mmol) was gradually added to the solution at 0°C, and the reaction mixture was stirred at room temperature for three hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction was quenched by addition of saturated aqueous sodium carbonate solution

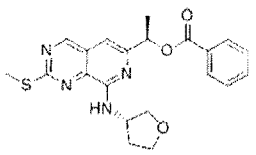
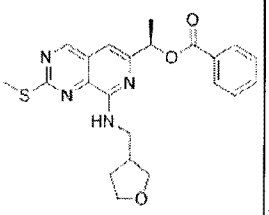
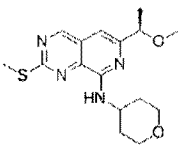
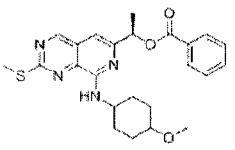
(20 mL). The aqueous phase was extracted three times with dichloromethane (50 mL). The resultant organic phases were combined together and dried over anhydrous sodium sulfate. The solid was separated by filtration, and the filtrate was then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to yield the title compound (2.37 g, 75%).

[0248]

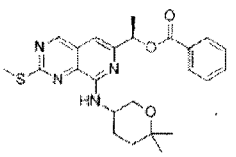
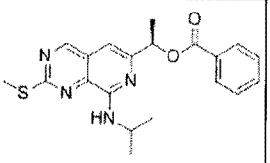
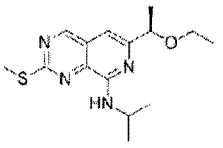
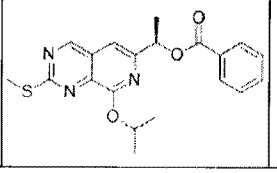
Compounds Int-1 to Int-8 were synthesized by the process described in Example 4 or Examples 5 to 7 in an appropriate order depending on the substituents.

[0249]

[Table 1-1]

Compound No.	Structure	NMR	$(M+H)^+$	Exact Mass
Int-1		1H-NMR (CDCl3) δ: 8.99 (1H, s), 8.17-8.13 (2H, m), 7.63-7.56 (1H, m), 7.52-7.45 (2H, m), 6.90 (1H, s), 6.59 (1H, d, J = 6.3 Hz), 6.11 (1H, q, J = 6.7 Hz), 4.84-4.74 (1H, m), 4.11-4.00 (2H, m), 3.93-3.79 (2H, m), 2.64 (3H, s), 2.47-2.35 (1H, m), 2.06-1.95 (1H, m), 1.73 (3H, d, J = 6.8 Hz).		
Int-2		1H-NMR (CDCl3) δ: 8.98 (1H, s), 8.18-8.12 (2H, m), 7.63-7.56 (1H, m), 7.52-7.44 (2H, m), 6.87 (1H, s), 6.76-6.68 (1H, br m), 6.15-6.06 (1H, m), 3.98-3.55 (6H, m), 2.80-2.62 (4H, m), 2.12-2.01 (1H, m), 1.79-1.69 (4H, m).		
Int-3		1H-NMR (CDCl3) δ: 9.01 (1H, s), 6.87 (1H, s), 6.42 (1H, d, J = 7.3 Hz), 4.39-4.27 (2H, m), 4.07-4.00 (2H, m), 3.66-3.57 (2H, m), 3.40 (3H, s), 2.66 (3H, s), 2.18-2.09 (2H, m), 1.73-1.59 (2H, m), 1.48 (3H, d, J = 6.8 Hz).		
Int-4			453.3	452.19

[Table 1-2]

Compound No.	Structure	NMR	$(M+H)^+$	Exact Mass
Int-5			453.3	452.19
Int-6			383.10	382.15
Int-7			307.15	306.15
Int-8			384.10	383.13

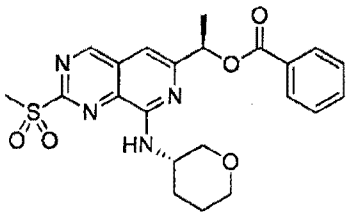
[0250]

Example 8

Synthesis of (R)-1-(2-(methylsulfonyl)-8-(((S)-tetrahydro-2H-pyran-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate

[0251]

[Formula 96]



[0252]

The (R)-1-(2-(methylthio)-8-(((S)-tetrahydro-2H-pyran-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate synthesized in Example 4 (232 mg, 0.55 mmol) and Oxone (R) (672 mg, 1.09 mmol) were added to THF (2.7 mL)

and water (2.7 mL) and the reaction mixture was stirred at room temperature overnight. The reaction was monitored by LC/MS. After completion of the reaction, saturated aqueous sodium hydrogen carbonate solution was slowly added to the reaction mixture, and the aqueous phase was extracted three times with ethyl acetate. The resultant organic phases were combined together and washed with saturated brine, and then dried over anhydrous magnesium sulfate. The solid was separated by filtration, and the filtrate was then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to yield a crude product of the title compound (245 mg, 98%).

^{1}H-NMR ($CDCl_3$)δ: 9.30 (1H, s), 8.16 (2H, d, J=7.3 Hz), 7.65-7.60 (1H, m), 7.53-7.48 (2H, m), 7.02 (1H, s), 6.87 (1H, d, J=7.8 Hz), 6.13 (1H, q, J=6.7 Hz), 4.45-4.36 (1H, m), 4.08-4.04 (1H, m), 3.85-3.80 (1H, m), 3.67-3.60 (1H, m), 3.52-3.47 (1H, m), 3.41 (3H, s), 2.14-2.07 (1H, m), 1.90-1.74 (6H, m).

LC/MS: $(M+H)^+$=457.2, $C_{22}H_{24}N_4O_5S$=456.15

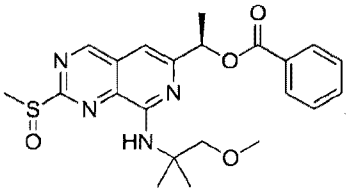
[0253]

Example 9

Synthesis of (R)-1-(8-(1-methoxy-2-methylpropan-2-ylamino)-2-(methylsulfinyl)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate

[0254]

[Formula 97]



[0255]

(R)-1-(8-(1-methoxy-2-methylpropan-2-ylamino)-2-(methylthio)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate synthesized by the process described in Example 7 (1.9 g, 4.46 mmol) was dissolved in dichloromethane (30 mL) and

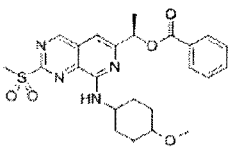
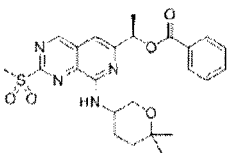
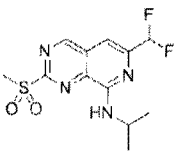
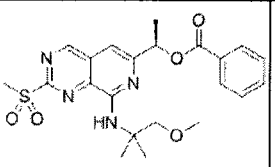
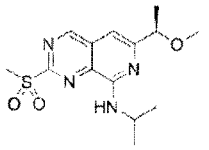
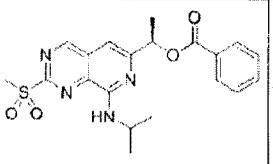
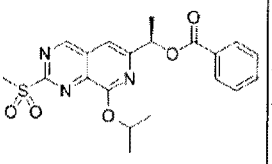
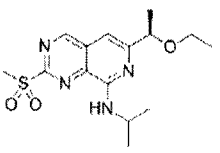
the solution was stirred at 0°C. m-CPBA (0.767 g, 4.46 mmol) was gradually added to the solution at 0°C, and the reaction mixture was stirred at room temperature overnight. The reaction was monitored by LC/MS. After completion of the reaction, the reaction was quenched by addition of an aqueous sodium thiosulfate solution for reduction of excess reagent. The aqueous phase was extracted three times with dichloromethane (30 mL). The resultant organic phases were combined together and washed once with saturated aqueous sodium hydrogen carbonate solution (50 mL) and once with saturated brine (50 mL). The organic phase was dried over anhydrous sodium sulfate, and the solid was separated by filtration. The filtrate was then concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to yield the title compound (1.9 g, 96%).

[0256]

Compounds Int-9 to Int-16 were synthesized by the process described in Example 8 or 9.

[0257]

[Table 2]

Compound No.	Structure	$(M+H)^+$	Exact Mass
Int-9		485.3	484.18
Int-10		485.3	484.18
Int-11		317.10	316.08
Int-12		459.15	458.16
Int-13		325.10	324.13
Int-14		415.10	414.14
Int-15		416.05 374.05	415.12
Int-16		339.15	338.14

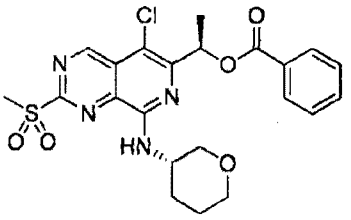
[0258]

Example 10

Synthesis of (R)-1-(5-chloro-2-(methylsulfonyl)-8-(((S)-tetrahydro-2H-pyran-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate

[0259]

[Formula 98]



[0260]

A mixture of (R)-1-(2-(methylsulfonyl)-8-(((S)-tetrahydro-2H-pyran-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate synthesized in Example 8 (268 mg, 0.587 mmol) and N-chlorosuccinimide (96 mg, 0.72 mmol) in 1,2-dichloroethane (2.9 mL) was stirred at 65°C overnight. The reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was cooled to room temperature. The reaction mixture was directly purified by silica gel column chromatography to yield the title compound (255 mg, 89%).

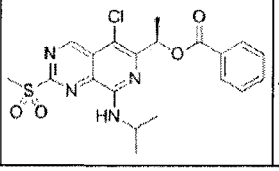
^{1}H-NMR ($CDCl_3$)δ: 9.70 (1H, s), 8.11-8.06 (2H, m), 7.60-7.53 (1H, m), 7.48-7.42 (2H, m), 6.90 (1H, d, J=7.8 Hz), 6.46 (1H, q, J=6.7 Hz), 4.28-4.18 (1H, m), 3.82 (1H, dd, J=11.5, 3.2 Hz), 3.76-3.69 (1H, m), 3.65-3.56 (1H, m), 3.45-3.37 (4H, m), 2.09-2.00 (1H, m), 1.88-1.61 (6H, m).

[0261]

Compound Int-17 was synthesized by the process described in Example 10.

[0262]

[Table 3]

Compound No.	Structure	(M+H)+	Exact Mass
Int-17		449.10	448.10

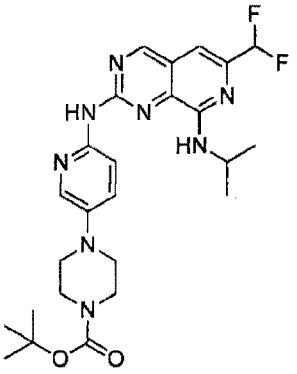
[0263]

Example 11

Synthesis of tert-butyl 4-[6-(6-difluoromethyl-8-isopropylaminopyrido[3,4-d]pyrimidin-2-ylamino)pyridin-3-yl]piperazine-1-carboxylate

[0264]

[Formula 99]



[0265]

The tert-butyl 4-(6-aminopyridin-3-yl)piperazine-1-carboxylate synthesized in Reference Example 5 (88 mg, 0.316 mmol) was dissolved in THF (3.5 mL), and sodium hydride (22.8 mg, 0.57 mmol, 60%) was added to the solution at 0°C and stirred for 10 minutes. To the suspension was added a solution of the (6-difluoromethyl-2-methanesulfonylpyrido[3,4-d]pyrimidine-8-yl)isopropylamine synthesized in Example 8 (Int-11, 100 mg, 0.316 mmol) in THF (3.5 mL) at room temperature and the reaction mixture was stirred at 35°C for one hour. The reaction was monitored by TLC and LC/MS. After completion of the reaction, the reaction was quenched by

addition of ice water (10 mL). The aqueous phase was extracted twice with ethyl acetate (25 mL). The resultant organic phases were combined together and washed with saturated brine, and the mixture was dried over anhydrous sodium sulfate. The solid was separated by filtration, and the filtrate was then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to yield the title compound (56.7 mg, 35%).

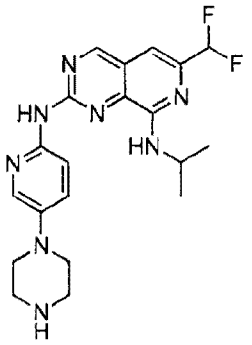
[0266]

Example 12

Synthesis of 6-difluoromethyl-8-isopropyl-2-(5-piperazin-1-ylpyridin-2-yl)pyrido[3,4-d]pyrimidine-2,8-diamine (compound 3)

[0267]

[Formula 100]



(3)

[0268]

The tert-butyl 4-[6-(6-difluoromethyl-8-isopropylaminopyrido[3,4-d]pyrimidin-2-ylamino)pyridin-3-yl]piperazine-1-carboxylate synthesized in Example 11 (195 mg, 0.378 mmol) was dissolved in dichloromethane (5 mL) and stirred at 0°C. Hydrogen chloride (0.4 mL, 4 mol/L, 1,4-dioxane solution) was added dropwise to the solution and stirred at room temperature for 30 minutes. The reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was concentrated under reduced pressure. The resultant crude product was purified by fractionation HPLC (acetonitrile/water/TFA)

to yield a TFA salt of the title compound (114 mg, purity: 99% or more). The TFA salts obtained by multiple reactions were combined and used in the next step.

The TFA salt (200 mg) was dissolved in methanol (0.625 mL) and dichloromethane (1.875 mL) and applied onto a strong cation exchange resin (SCX) column. The SCX column was washed with a solvent mixture of methanol and dichloromethane (1:3). The target compound was subsequently eluted from the SCX column with a solvent mixture of methanol and dichloromethane (1:3) containing 2.5% ammonia (2 mol/L, methanol solution). The eluate was concentrated under reduced pressure to yield the title compound (105 mg, purity: > 99%).

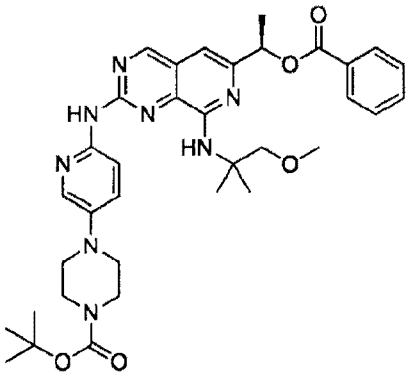
[0269]

Example 13

Synthesis of tert-butyl (R)-4-(6-(6-(benzoyloxy)ethyl-8-(1-methoxy-2-methylpropan-2-ylamino)pyrido[3,4-d]pyrimidin-2-ylamino)pyridin-3-yl)piperazine-1-carboxylate

[0270]

[Formula 101]



[0271]

The (R)-1-(8-(1-methoxy-2-methylpropan-2-ylamino)-2-(methylsulfinyl)pyrido[3,4-d]pyrimidin-6-yl)ethyl benzoate synthesized in Example 9 (1.9 g, 4.3 mmol) and the tert-butyl 4-(6-aminopyridin-3-yl)piperazine-1-carboxylate synthesized in Reference Example 5 (3.59 g,

12.9 mmol) were suspended in toluene (30 mL) and the reaction mixture was stirred at 120°C overnight. The reaction was monitored by LC/MS. The resultant reaction mixture was cooled to room temperature, and the solvent was removed through evaporation under reduced pressure. The residue was purified by silica gel column chromatography to yield the title compound (850 mg, 30%).

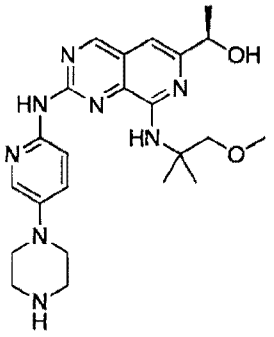
[0272]

Example 14

Synthesis of (R)-1-(8-(1-methoxy-2-methylpropan-2-ylamino)-2-(5-(piperazin-1-yl)pyridin-2-ylamino)pyrido[3,4-d]pyrimidin-6-yl)ethanol (compound 195)

[0273]

[Formula 102]



(195)

[0274]

The tert-butyl (R)-4-(6-(6-(benzoyloxy)ethyl-8-(1-methoxy-2-methylpropan-2-ylamino)pyrido[3,4-d]pyrimidin-2-ylamino)pyridin-3-yl)piperazine-1-carboxylate synthesized in Example 13 (850 mg, 1.3 mmol) was dissolved in THF (15 mL) and methanol (15 mL), and lithium hydroxide (124 mg, 5.2 mmol) was added to the solution. The resultant reaction mixture was stirred at room temperature overnight, and the reaction was monitored by LC/MS. After completion of the reaction, hydrogen chloride (4 mol/L, methanol solution) was added dropwise to the reaction mixture, to adjust the pH of the mixture to 7. The reaction mixture was concentrated

under reduced pressure to yield a crude product. The crude product was used for the subsequent reaction without purification.

The crude product was dissolved in hydrogen chloride (20 mL, 4 mol/L, methanol solution) and stirred at room temperature for four hours. The reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in methanol (30 mL), and concentrated aqueous ammonia (25%) was added dropwise to the solution, to adjust the pH of the solution to 10 or higher. Saturated brine (100 mL) was added to the solution, and the mixture was extracted three times with a solvent mixture of dichloromethane and methanol (9:1) (30 mL). The resultant organic phases were combined together and washed once with saturated brine (50 mL). The organic phase was dried over anhydrous sodium sulfate, and the solid was separated by filtration. The filtrate was concentrated under reduced pressure to yield a crude product of the title compound. The crude product was then washed with methanol to yield the title compound (470 mg, 80%).

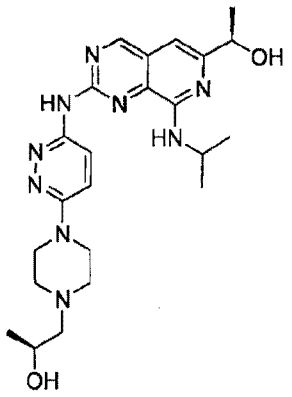
[0275]

Example 15

Synthesis of (S)-1-(4-(6-((6-((R)-1-hydroxyethyl)-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl)amino)pyridazin-3-yl)piperazin-1-yl)propan-2-ol (compound 676)

[0276]

[Formula 103]



(676)

[0277]

(R)-1-(8-(isopropylamino)-2-((6-(piperazin-1-yl)pyridazin-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethanol synthesized by the process described in Example 14 (compound 261, 25 mg, 0.061 mmol) was dissolved in methanol (0.31 mL), and (S)-propylene oxide (3.5 mg, 0.061 mmol) was added to the solution. The resultant reaction mixture was stirred at 55°C overnight, and the reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was concentrated under reduced pressure. The resultant crude product was purified by fractionation HPLC (acetonitrile/water/TFA) and applied onto a strong cation exchange resin (SCX) column. The SCX column was washed with methanol, and the target product was then eluted with ammonia (2 mol/L, methanol solution). The eluate was concentrated under reduced pressure to yield the title compound (19 mg).

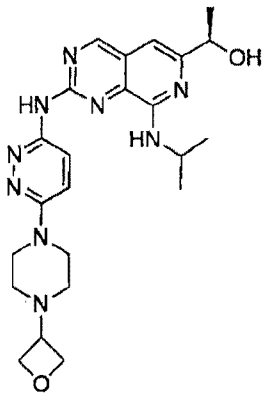
[0278]

Example 16

Synthesis of (R)-1-(8-(isopropylamino)-2-((6-(4-(oxetan-3-yl)piperazin-1-yl)pyridazin-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethanol (compound 682)

[0279]

[Formula 104]



(682)

[0280]

(R)-1-(8-(isopropylamino)-2-((6-(piperazin-1-yl)pyridazin-3-yl)amino)pyrido[3,4-d]pyrimidin-6-yl)ethanol synthesized by the process described in Example 14 (compound 261, 16.4 mg, 0.040 mmol) was dissolved in acetic acid (2.8 μL) and 1,2-dichloroethane (0.4 mL). To the mixture was added 3-oxetanone (2.8 μL, 0.048 mmol) and sodium triacetoxyborohydride (12.7 mg, 0.060 mmol). The resultant reaction mixture was stirred at 55°C for two hours, and the reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was cooled to room temperature, and the reaction was quenched by addition of water. The reaction mixture was extracted with ethyl acetate, and the organic layer was concentrated under reduced pressure. The resultant crude product was then purified by amine-modified column chromatography (ethyl acetate/methanol) to yield the title compound (7.5 mg).

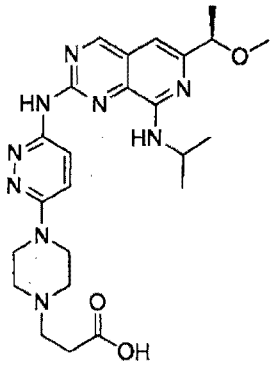
[0281]

Example 17

Synthesis of (R)-3-(4-(6-((8-(isopropylamino)-6-(1-methoxyethyl)pyrido[3,4-d]pyrimidin-2-yl)amino)pyridazin-3-yl)piperazin-1-yl)propanoic acid (compound 684)

[0282]

[Formula 105]



(684)

[0283]

(R)-N8-isopropyl-6-(1-methoxyethyl)-N2-(6-(piperazin-1-yl)pyridazin-3-yl)pyrido[3,4-d]pyrimidine-2,8-diamine synthesized by the process described in Example 14 (compound 217, 29.6 mg, 0.07 mmol) was dissolved in methanol (0.35 mL), and methyl acrylate (6.3 μL, 0.07 mmol) was added to the solution. The resultant reaction mixture was stirred at 55°C for two hours, and the reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resultant crude product was roughly purified by silica gel column chromatography (ethyl acetate/heptane). The crude product was then dissolved in THF (0.56 mL) and methanol (0.56 mL), and 4M aqueous lithium hydroxide solution (0.028 mL, 0.112 mmol) was added to the solution. The resultant reaction mixture was stirred at room temperature overnight, and the reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was acidified with 2M aqueous hydrochloric acid solution and then adsorbed onto a strong cation exchange resin (SCX) column. The SCX column was washed with water and dichloromethane, and the target product was then eluted with ammonia (2 mol/L, methanol solution). The eluate was concentrated under reduced pressure to yield the title compound (27.5 mg).

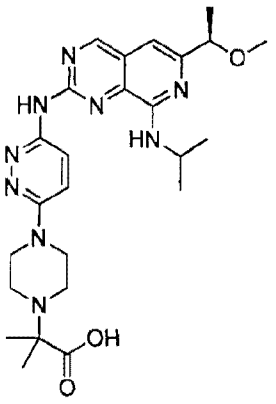
[0284]

Example 18

Synthesis of (R)-2-(4-(6-((8-(isopropylamino)-6-(1-methoxyethyl)pyrido[3,4-d]pyrimidin-2-yl)amino)pyridazin-3-yl)piperazin-1-yl)-2-methylpropanoic acid (compound 678)

[0285]

[Formula 106]



(678)

[0286]

(R)-N8-isopropyl-6-(1-methoxyethyl)-N2-(6-(piperazin-1-yl)pyridazin-3-yl)pyrido[3,4-d]pyrimidine-2,8-diamine synthesized by the process described in Example 14 (compound 217, 42.3 mg, 0.10 mmol) was dissolved in acetonitrile (0.2 mL). To the mixture was added tert-butyl 2-bromo-2-methylpropanoate (22.4 μL, 0.12 mmol) and potassium carbonate (16.6 mg). The resultant reaction mixture was stirred at 85°C overnight, and the reaction was monitored by LC/MS. After completion of the reaction, the reaction mixture was cooled to room temperature, and the reaction was quenched by addition of water. The reaction mixture was extracted with ethyl acetate, and the resultant crude product was briefly purified by silica gel column chromatography (ethyl acetate/heptane). The crude product was then dissolved in dichloromethane (1 mL), and trifluoroacetic acid (1 mL) was added to the solution. The resultant reaction mixture was stirred at room temperature for 24 hours, and the reaction was monitored by LC/MS. After

completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resultant crude product was adsorbed onto a strong cation exchange resin (SCX) column. The SCX column was washed with methanol, and the target product was then eluted with ammonia (2 mol/L, methanol solution). The eluate was concentrated under reduced pressure to yield the title compound (8.5 mg).

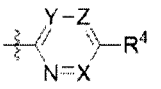
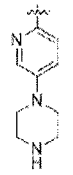
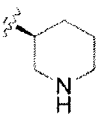
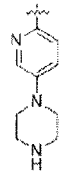
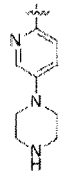
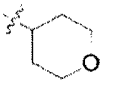
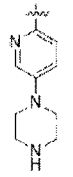
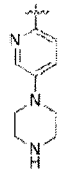
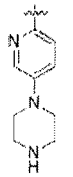
[0287]

Example 19

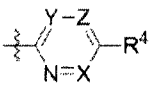
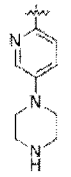
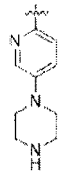
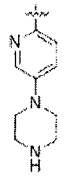
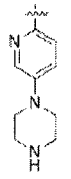
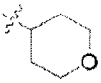
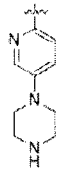
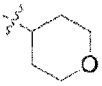
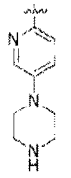
Compounds 1 to 1239 were synthesized by the processes described in Examples 11 to 18.

[0288]

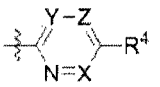
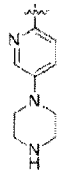
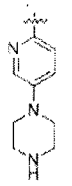
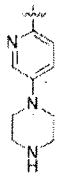
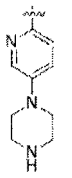
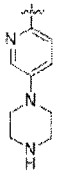
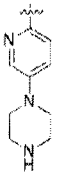
[Table 4-1]

Compound No.	L	R^1	R^2	R^3	
1					
2					
3					
4					
5					
6					

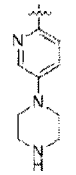
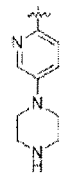
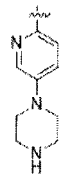
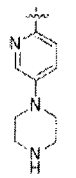
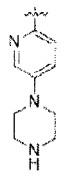
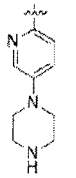
[Table 4-2]

Compound No.	L	R^1	R^2	R^3	
7					
8					
9					
10					
11					
12					

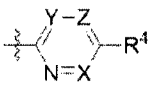
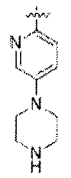
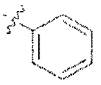
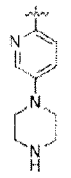
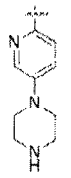
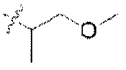
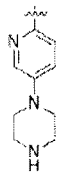
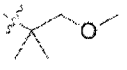
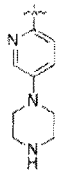
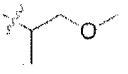
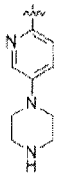
[Table 4-3]

Compound No.	L	R^1	R^2	R^3	
13					
14					
15					
16					
17					
18					

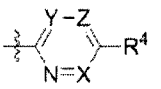
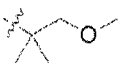
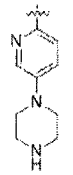
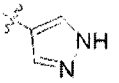
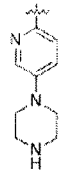
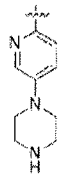
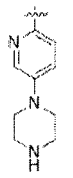
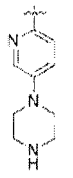
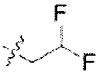
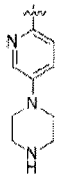
[Table 4-4]

Compound No.	L	R^1	R^2	R^3	
19					
20					
21					
22					
23					
24					

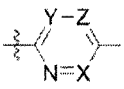
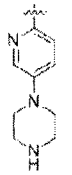
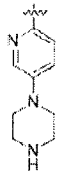
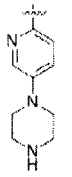
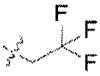
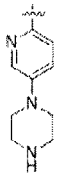
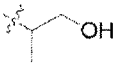
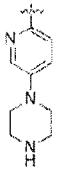
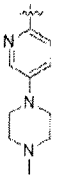
[Table 4-5]

Compound No.	L	R^1	R^2	R^3	
25					
26					
27					
28					
29					
30					

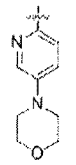
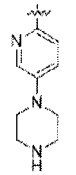
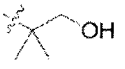
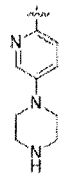
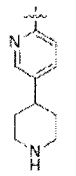
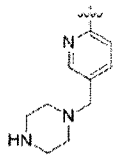
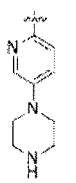
[Table 4-6]

Compound No.	L	R^1	R^2	R^3	
31					
32					
33					
34					
35					
36					

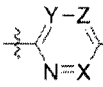
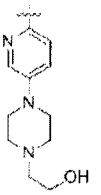
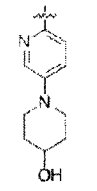
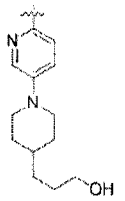
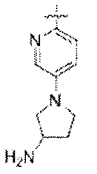
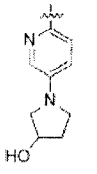
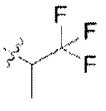
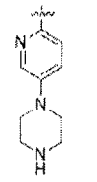
[Table 4-7]

Compound No.	L	R^1	R^2	R^3	
37					
38					
39					
40					
41					
42					

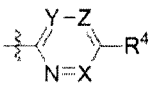
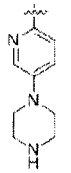
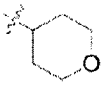
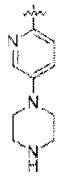
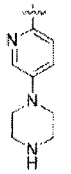
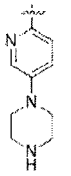
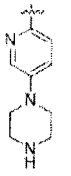
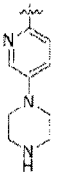
[Table 4-8]

Compound No.	L	R^1	R^2	R^3	
43					
44					
45					
46					
47					
48					

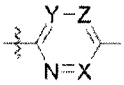
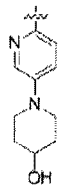
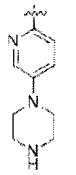
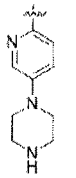
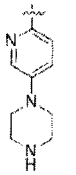
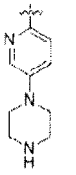
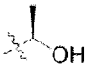
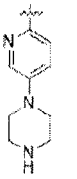
[Table 4-9]

Compound No.	L	R^1	R^2	R^3	
49					
50					
51					
52					
53					
54					

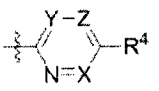
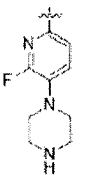
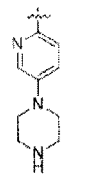
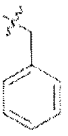
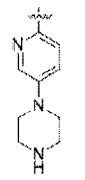
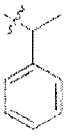
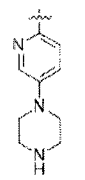
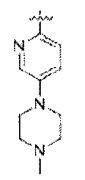
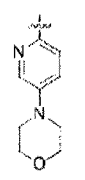
[Table 4-10]

Compound No.	L	R^1	R^2	R^3	
55					
56					
57					
58					
59					
60					

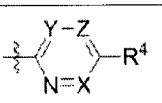
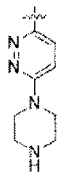
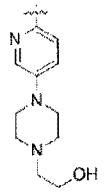
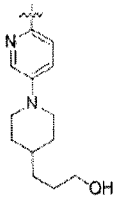
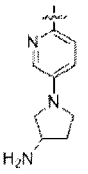
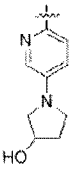
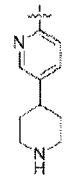
[Table 4-11]

Compound No.	L	R^1	R^2	R^3	
61					
62					
63					
64					
65					
66					

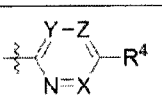
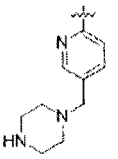
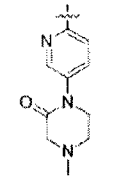
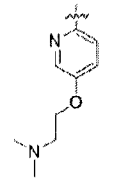
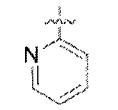
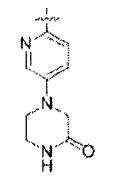
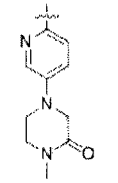
[Table 4-12]

Compound No.	L	R^1	R^2	R^3	
67					
68					
69					
70					
71					
72					

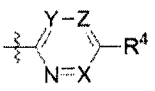
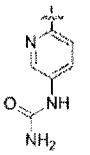
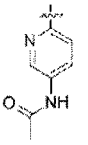
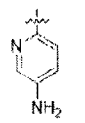
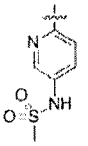
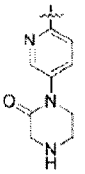
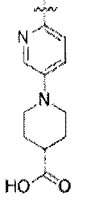
[Table 4-13]

Compound No.	L	R^1	R^2	R^3	
73					
74					
75					
76					
77					
78					

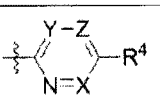
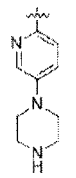
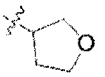
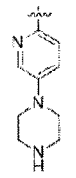
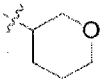
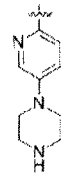
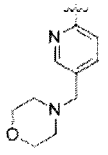
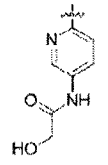
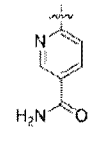
[Table 4-14]

Compound No.	L	R^1	R^2	R^3	
79					
80					
81					
82					
83					
84					

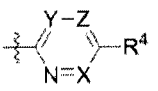
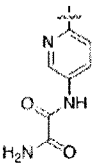
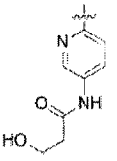
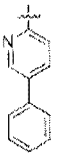
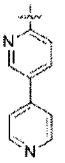
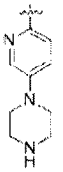
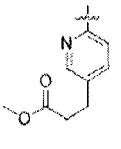
[Table 4-15]

Compound No.	L	R^1	R^2	R^3	
85					
86					
87					
88					
89					
90					

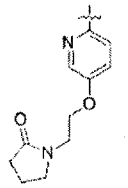
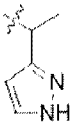
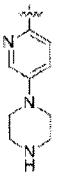
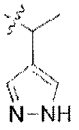
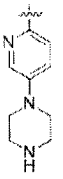
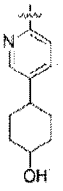
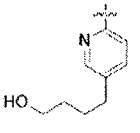
[Table 4-16]

Compound No.	L	R^1	R^2	R^3	
91					
92					
93					
94					
95					
96					

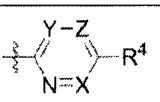
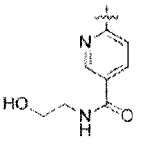
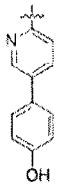
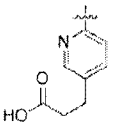
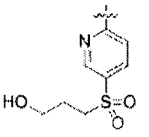
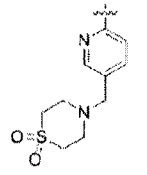
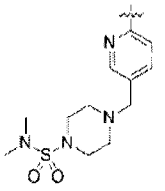
[Table 4-17]

Compound No.	L	R^1	R^2	R^3	
97					
98					
99					
100					
101					
102					

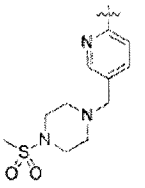
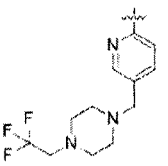
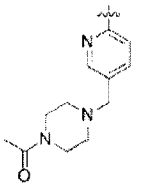
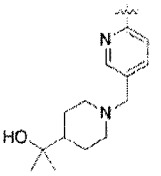
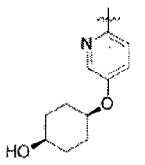
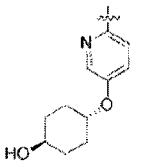
[Table 4-18]

Compound No.	L	R^1	R^2	R^3	
103					
104					
105					
106					
107					
108					

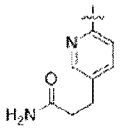
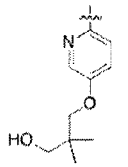
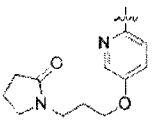
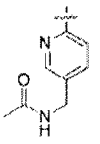
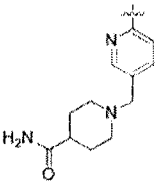
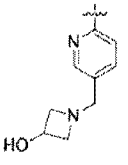
[Table 4-19]

Compound No.	L	R^1	R^2	R^3	
109					
110					
111					
112					
113					
114					

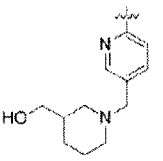
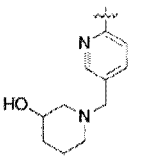
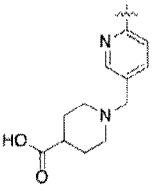
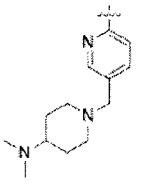
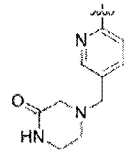
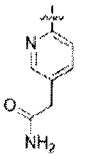
[Table 4-20]

Compound No.	L	R^1	R^2	R^3	
115					
116					
117					
118					
119					
120					

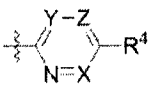
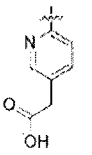
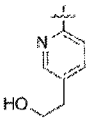
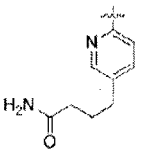
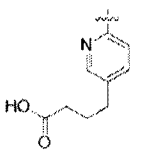
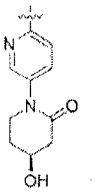
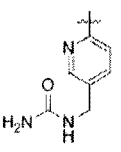
[Table 4-21]

Compound No.	L	R^1	R^2	R^3	
121					
122					
123					
124					
125					
126					

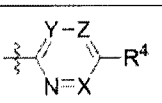
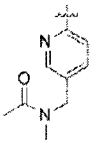
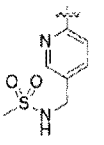
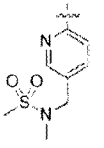
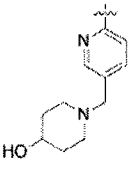
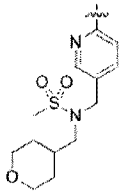
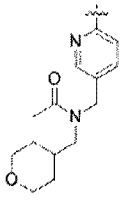
[Table 4-22]

Compound No.	L	R^1	R^2	R^3	
127					
128					
129					
130					
131					
132					

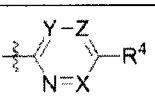
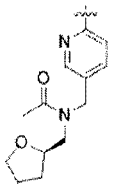
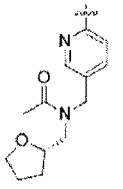
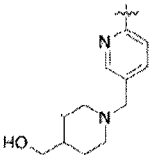
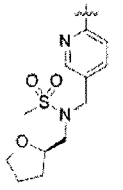
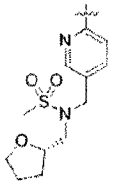
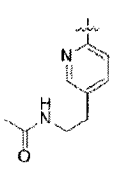
[Table 4-23]

Compound No.	L	R^1	R^2	R^3	
133					
134					
135					
136					
137					
138					

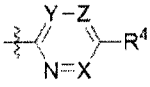
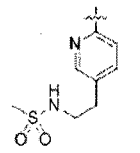
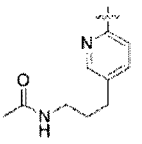
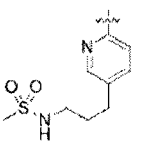
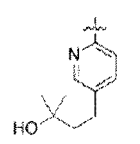
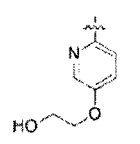
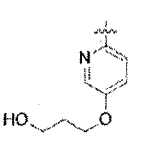
[Table 4-24]

Compound No.	L	R^1	R^2	R^3	
139					
140					
141					
142					
143					
144					

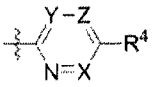
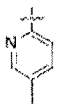
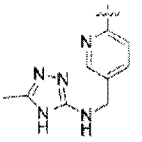
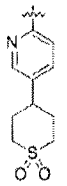
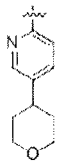
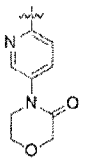
[Table 4-25]

Compound No.	L	R^1	R^2	R^3	
145					
146					
147					
148					
149					
150					

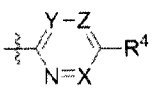
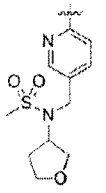
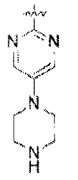
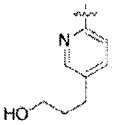
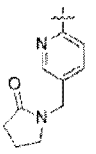
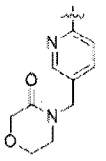
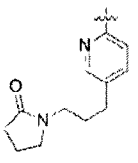
[Table 4-26]

Compound No.	L	R^1	R^2	R^3	
151					
152					
153					
154					
155					
156					

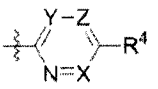
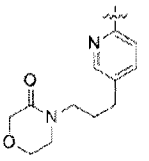
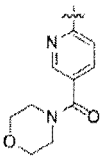
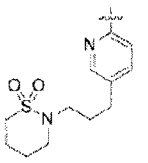
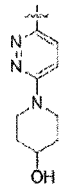
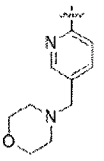
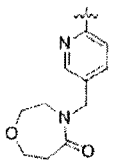
[Table 4-27]

Compound No.	L	R^1	R^2	R^3	
157					
158					
159					
160					
161					

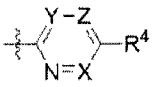
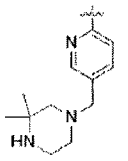
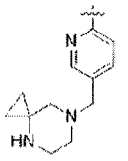
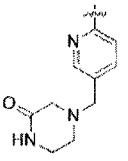
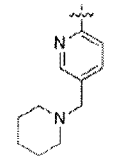
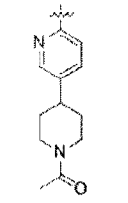
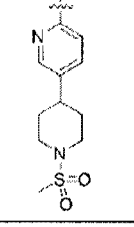
[Table 4-28]

Compound No.	L	R^1	R^2	R^3	
162					
163					
164					
165					
166					
167					

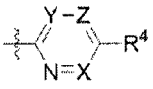
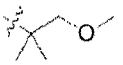
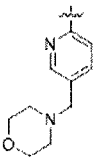
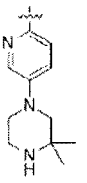
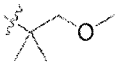
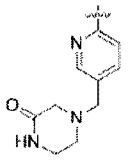
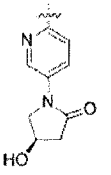
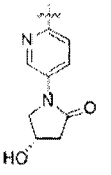
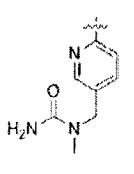
[Table 4-29]

Compound No.	L	R^1	R^2	R^3	
168					
169					
170					
171					
172					
173					

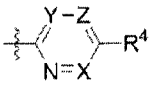
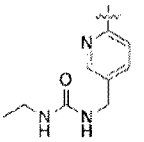
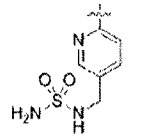
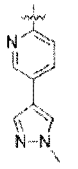
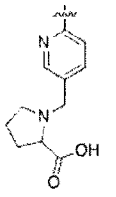
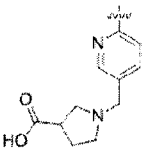
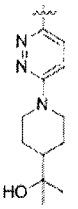
[Table 4-30]

Compound No.	L	R^1	R^2	R^3	
174					
175					
176					
177					
178					
179					

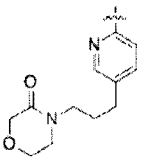
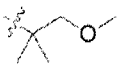
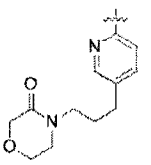
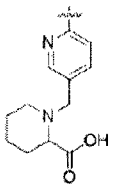
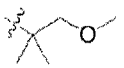
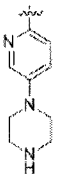
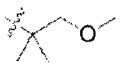
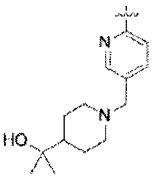
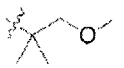
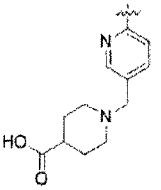
[Table 4-31]

Compound No.	L	R^1	R^2	R^3	
180					
181					
182					
183					
184					
185					

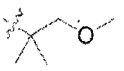
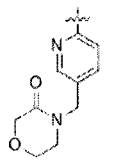
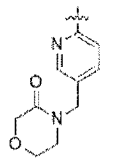
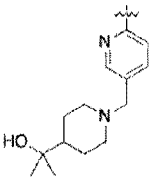
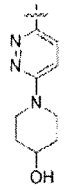
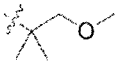
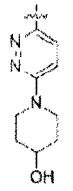
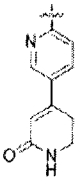
[Table 4-32]

Compound No.	L	R^1	R^2	R^3	
186					
187					
188					
189					
190					
191					

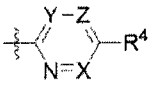
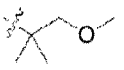
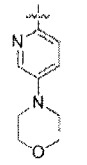
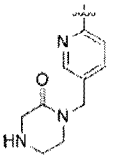
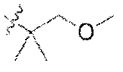
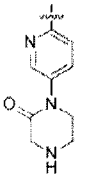
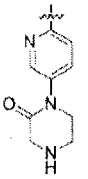
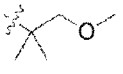
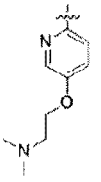
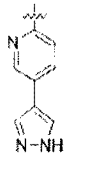
[Table 4-33]

Compound No.	L	R^1	R^2	R^3	
192					
193					
194					
195					
196					
197					

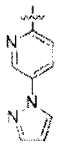
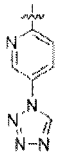
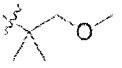
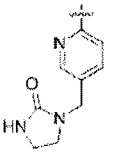
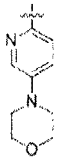
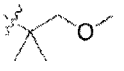
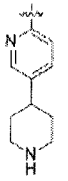
[Table 4-34]

Compound No.	L	R^1	R^2	R^3	
198					
199					
200					
201					
202					
203					

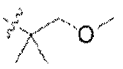
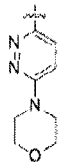
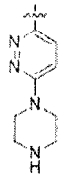
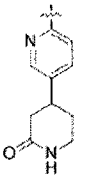
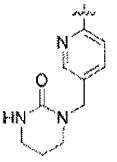
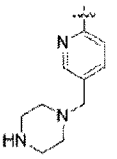
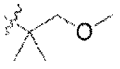
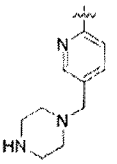
[Table 4-35]

Compound No.	L	R^1	R^2	R^3	
204					
205					
206					
207					
208					
209					

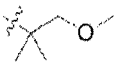
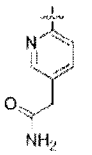
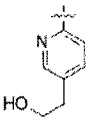
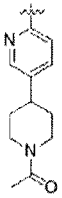
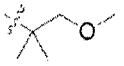
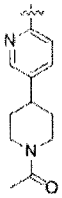
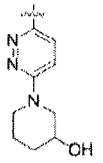
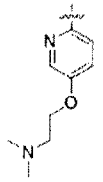
[Table 4-36]

Compound No.	L	R^1	R^2	R^3	
210					
211					
212					
213					
214					
215					

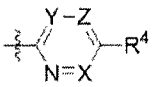
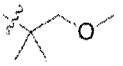
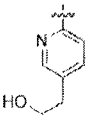
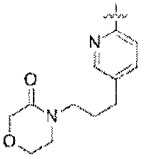
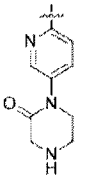
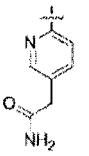
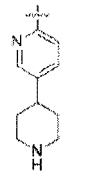
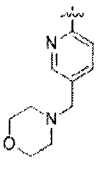
[Table 4-37]

Compound No.	L	R^1	R^2	R^3	
216					
217					
218					
219					
220					
221					

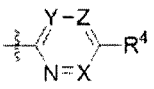
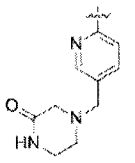
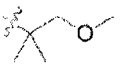
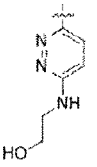
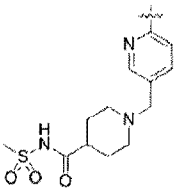
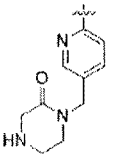
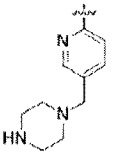
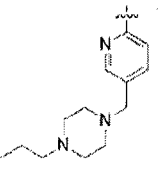
[Table 4-38]

Compound No.	L	R^1	R^2	R^3	
222					
223					
224					
225					
226					
227					

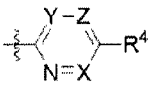
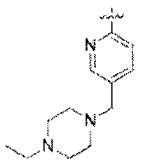
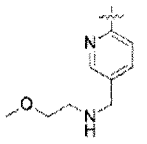
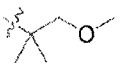
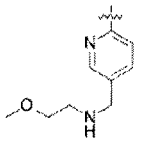
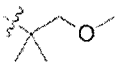
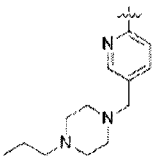
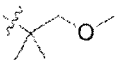
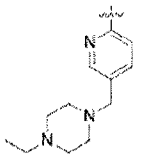
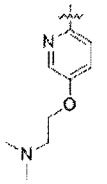
[Table 4-39]

Compound No.	L	R^1	R^2	R^3	
228					
229					
230					
231					
232					
233					

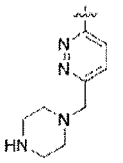
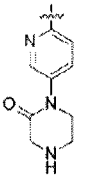
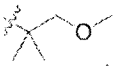
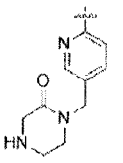
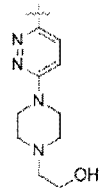
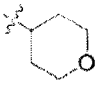
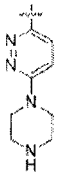
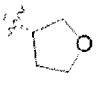
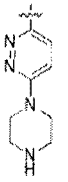
[Table 4-40]

Compound No.	L	R^1	R^2	R^3	
234					
235					
236					
237					
238					
239					

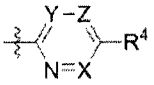
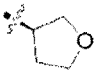
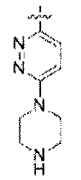
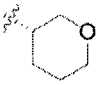
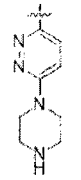
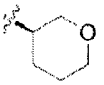
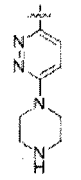
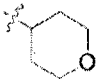
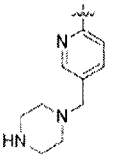
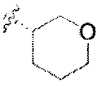
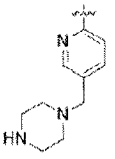
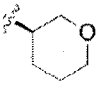
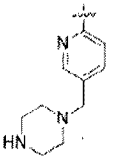
[Table 4-41]

Compound No.	L	R^1	R^2	R^3	
240					
241					
242					
243					
244					
245					

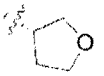
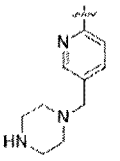
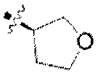
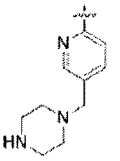
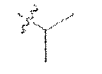
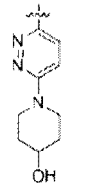
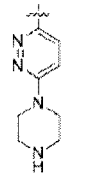
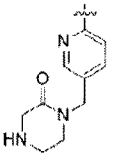
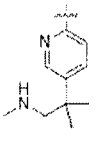
[Table 4-42]

Compound No.	L	R^1	R^2	R^3	
246					
247					
248					
249					
250					
251					

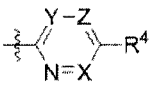
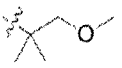
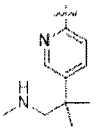
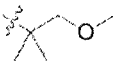
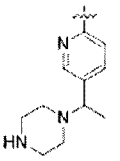
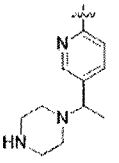
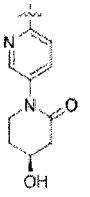
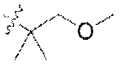
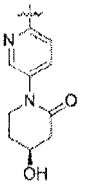
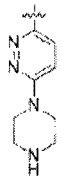
[Table 4-43]

Compound No.	L	R^1	R^2	R^3	
252					
253					
254					
255					
256					
257					

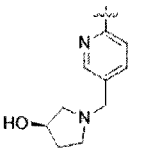
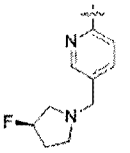
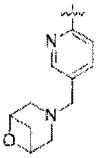
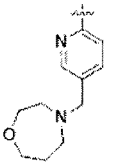
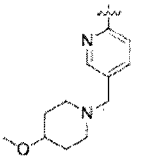
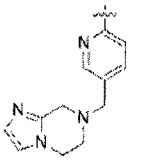
[Table 4-44]

Compound No.	L	R^1	R^2	R^3	
258					
259					
260					
261					
262					
263					

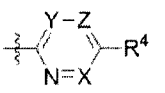
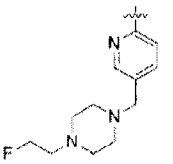
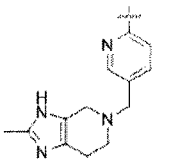
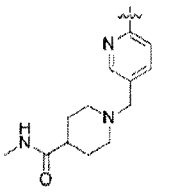
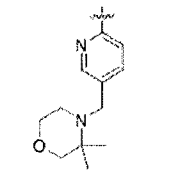
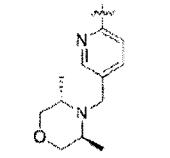
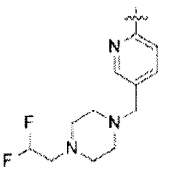
[Table 4-45]

Compound No.	L	R^1	R^2	R^3	
264					
265					
266					
267					
268					
269					

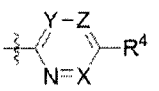
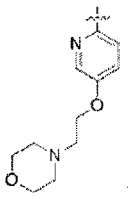
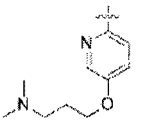
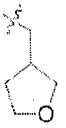
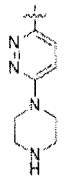
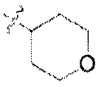
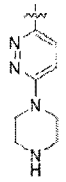
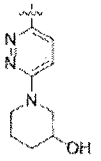
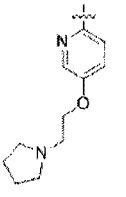
[Table 4-46]

Compound No.	L	R^1	R^2	R^3	
270					
271					
272					
273					
274					
275					

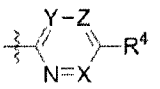
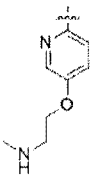
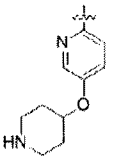
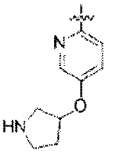
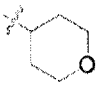
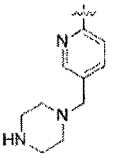
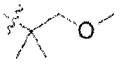
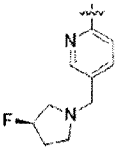
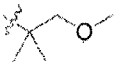
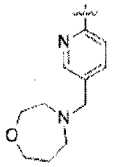
[Table 4-47]

Compound No.	L	R^1	R^2	R^3	
276					
277					
278					
279					
280					
281					

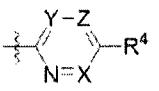
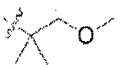
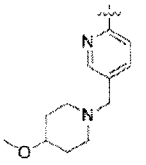
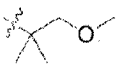
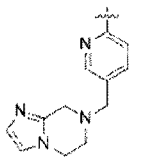
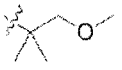
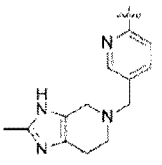
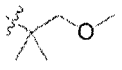
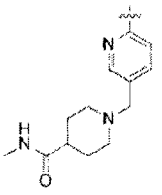
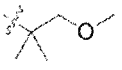
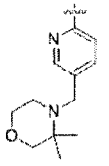
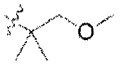
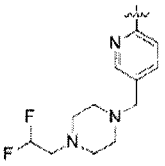
[Table 4-48]

Compound No.	L	R^1	R^2	R^3	
282					
283					
284					
285					
286					
287					

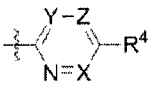
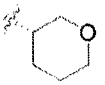
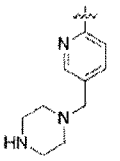
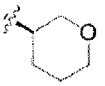
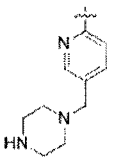
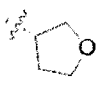
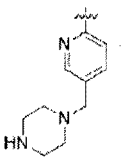
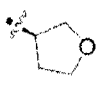
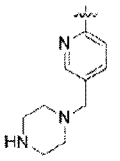
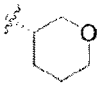
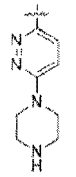
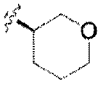
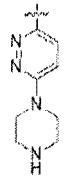
[Table 4-49]

Compound No.	L	R^1	R^2	R^3	
288					
289					
290					
291					
292					
293					

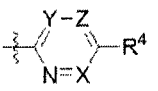
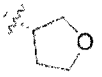
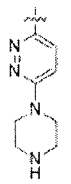
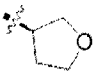
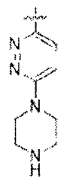
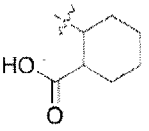
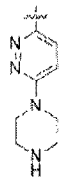
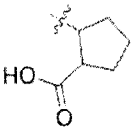
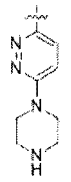
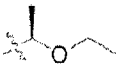
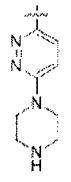
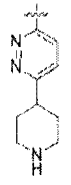
[Table 4-50]

Compound No.	L	R^1	R^2	R^3	
294					
295					
296					
297					
298					
299					

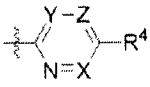
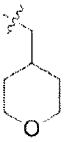
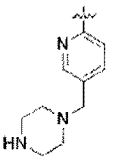
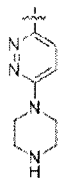
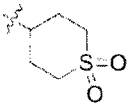
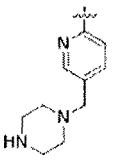
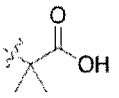
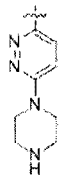
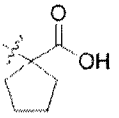
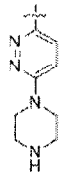
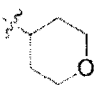
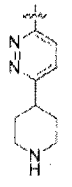
[Table 4-51]

Compound No.	L	R^1	R^2	R^3	
300					
301					
302					
303					
304					
305					

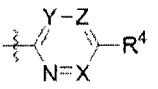
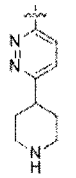
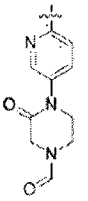
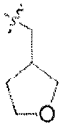
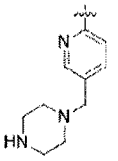
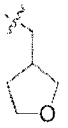
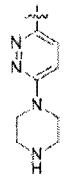
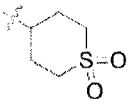
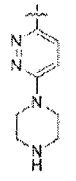
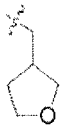
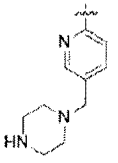
[Table 4-52]

Compound No.	L	R^1	R^2	R^3	
306					
307					
308					
309					
310					
311					

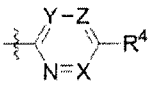
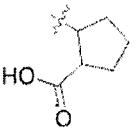
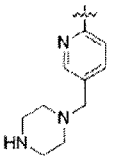
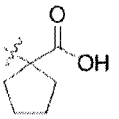
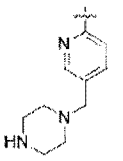
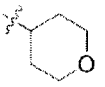
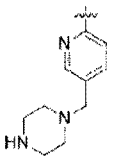
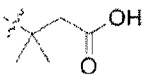
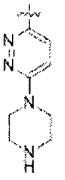
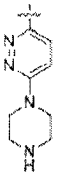
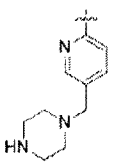
[Table 4-53]

Compound No.	L	R^1	R^2	R^3	
312					
313					
314					
315					
316					
317					

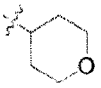
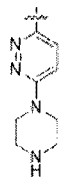
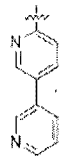
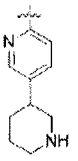
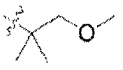
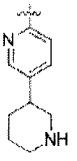
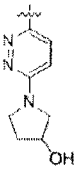
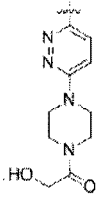
[Table 4-54]

Compound No.	L	R^1	R^2	R^3	
318					
319					
320					
321					
322					
323					

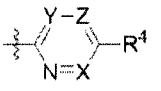
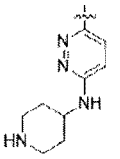
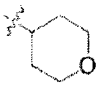
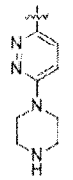
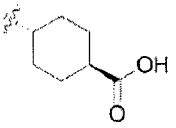
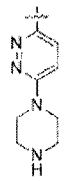
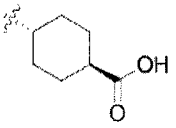
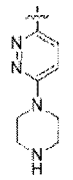
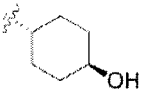
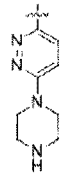
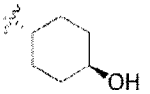
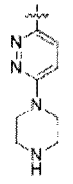
[Table 4-55]

Compound No.	L	R^1	R^2	R^3	
324					
325					
326					
327					
328					
329					

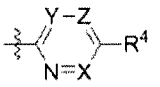
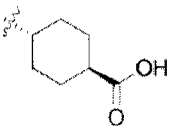
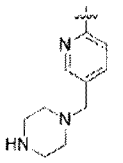
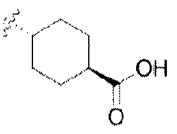
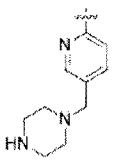
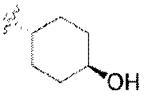
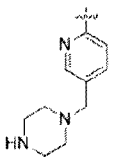
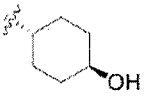
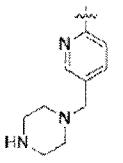
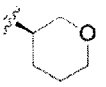
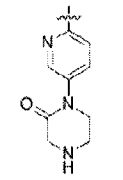
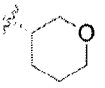
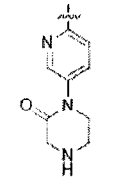
[Table 4-56]

Compound No.	L	R^1	R^2	R^3	
330					
331					
332					
333					
334					
335					

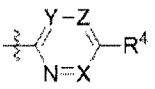
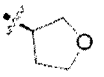
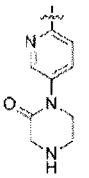
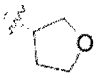
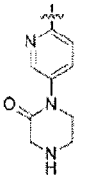
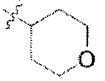
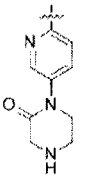
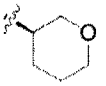
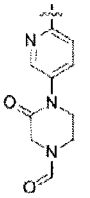
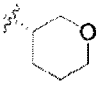
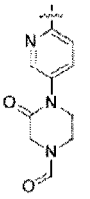
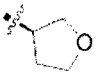
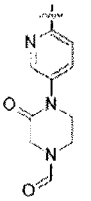
[Table 4-57]

Compound No.	L	R^1	R^2	R^3	
336					
337					
338					
339					
340					
341					

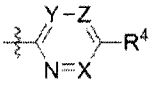
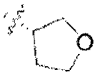
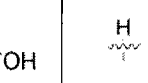
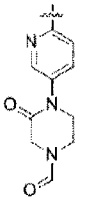
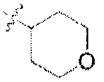
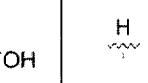
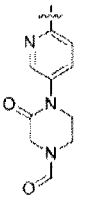
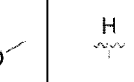
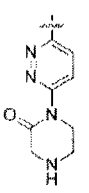
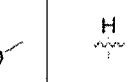
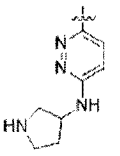
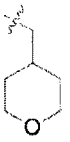
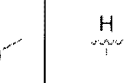
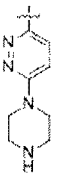
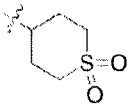
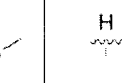
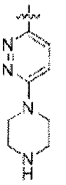
[Table 4-58]

Compound No.	L	R^1	R^2	R^3	
342					
343					
344					
345					
346					
347					

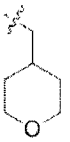
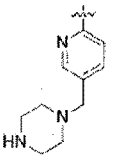
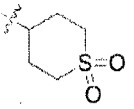
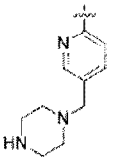
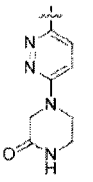
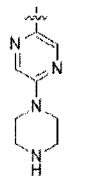
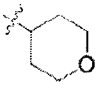
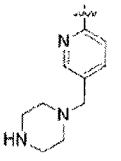
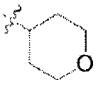
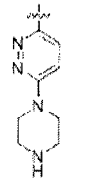
[Table 4-59]

Compound No.	L	R^1	R^2	R^3	
348					
349					
350					
351					
352					
353					

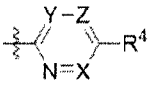
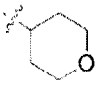
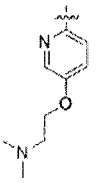
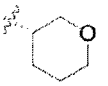
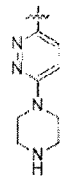
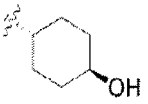
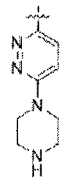
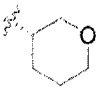
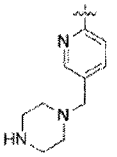
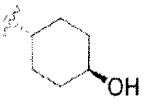
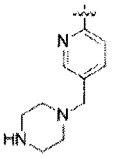
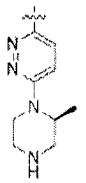
[Table 4-60]

Compound No.	L	R^1	R^2	R^3	
354					
355					
356					
357					
358					
359					

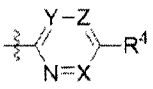
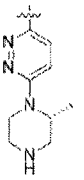
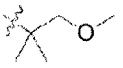
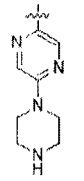
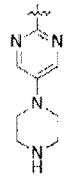
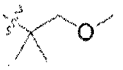
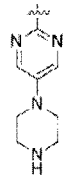
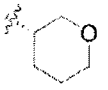
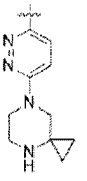
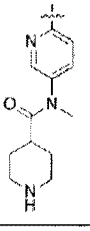
[Table 4-61]

Compound No.	L	R^1	R^2	R^3	
360					
361					
362					
363					
364					
365					

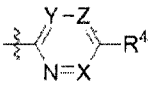
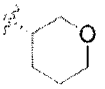
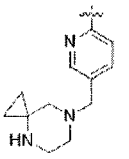
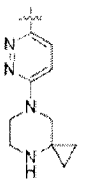
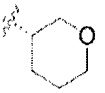
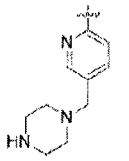
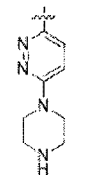
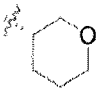
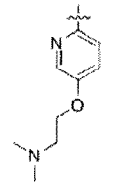
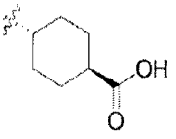
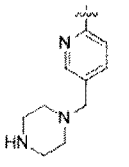
[Table 4-62]

Compound No.	L	R^1	R^2	R^3	
366					
367					
368					
369					
370					
371					

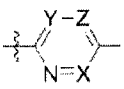
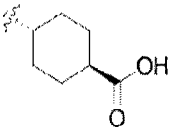
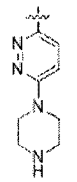
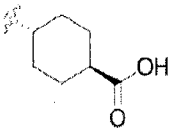
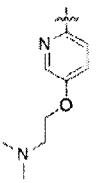
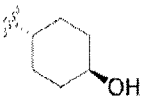
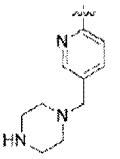
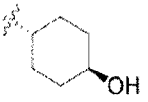
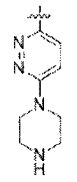
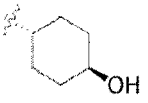
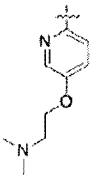
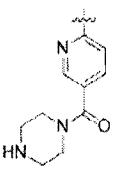
[Table 4-63]

Compound No.	L	R^1	R^2	R^3	
372					
373					
374					
375					
376					
377					

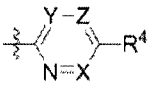
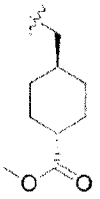
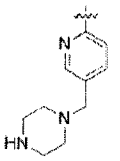
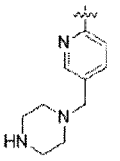
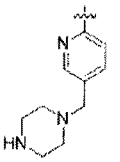
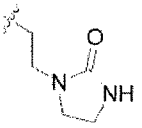
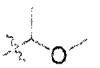
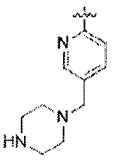
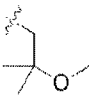
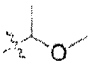
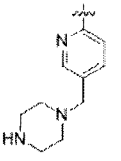
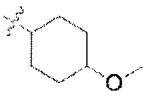
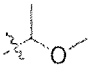
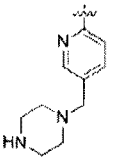
[Table 4-64]

Compound No.	L	R^1	R^2	R^3	
378					
379					
380					
381					
382					
383					

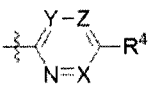
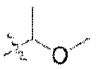
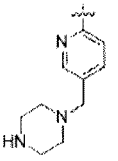
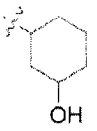
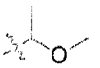
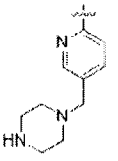
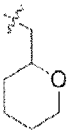
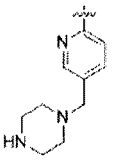
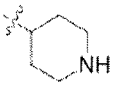
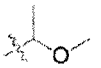
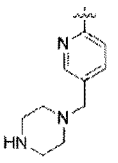
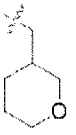
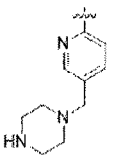
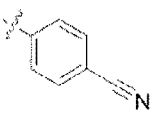
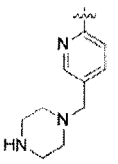
[Table 4-65]

Compound No.	L	R^1	R^2	R^3	
384					
385					
386					
387					
388					
389					

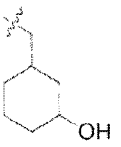
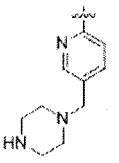
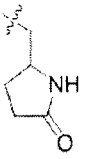
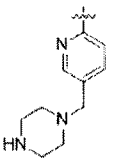
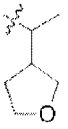
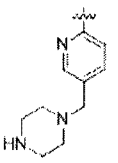
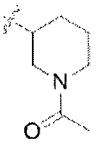
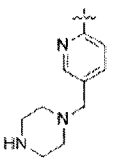
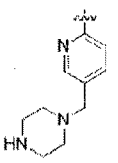
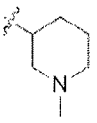
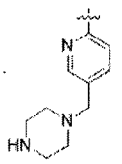
[Table 4-66]

Compound No.	L	R^1	R^2	R^3	
390					
391					
392					
393					
394					
395					

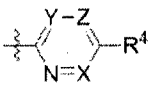
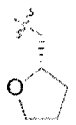
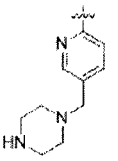
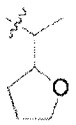
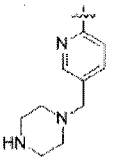
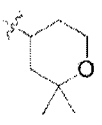
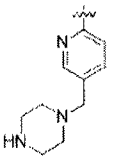
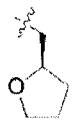
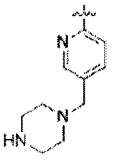
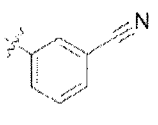
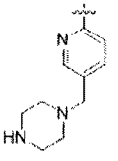
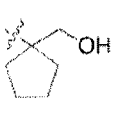
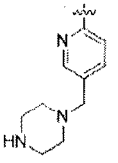
[Table 4-67]

Compound No.	L	R^1	R^2	R^3	
396					
397					
398					
399					
400					
401					

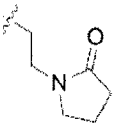
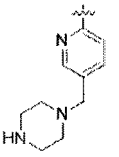
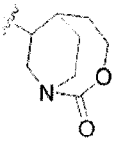
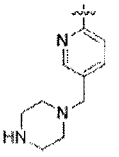
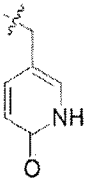
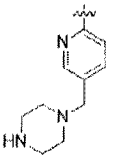
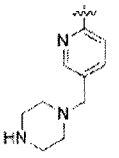
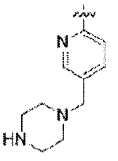
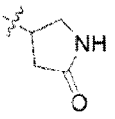
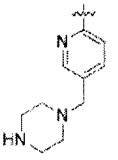
[Table 4-68]

Compound No.	L	R^1	R^2	R^3	
402					
403					
404					
405					
406					
407					

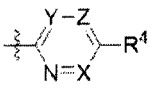
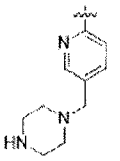
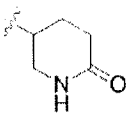
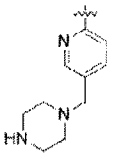
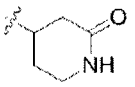
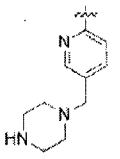
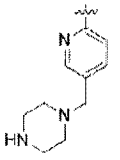
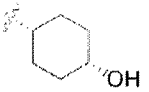
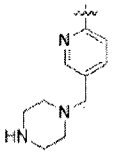
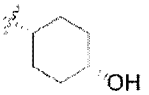
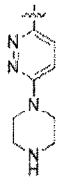
[Table 4-69]

Compound No.	L	R^1	R^2	R^3	
408					
409					
410					
411					
412					
413					

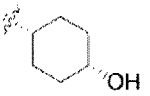
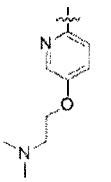
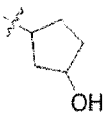
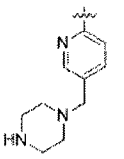
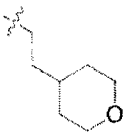
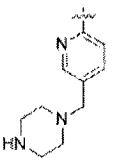
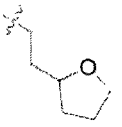
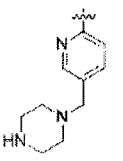
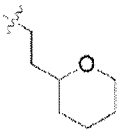
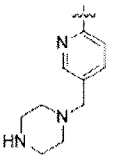
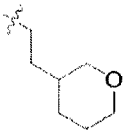
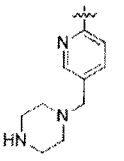
[Table 4-70]

Compound No.	L	R^1	R^2	R^3	
414					
415					
416					
417					
418					
419					

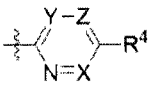
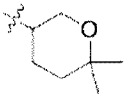
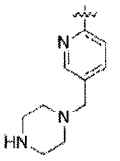
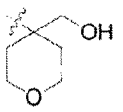
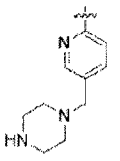
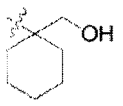
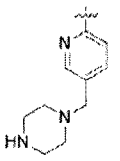
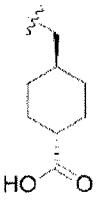
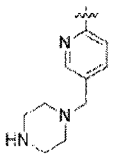
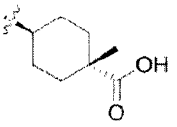
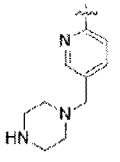
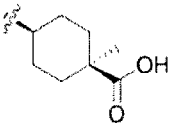
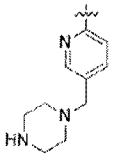
[Table 4-71]

Compound No.	L	R^1	R^2	R^3	
420					
421					
422					
423					
424					
425					

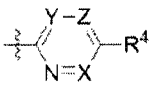
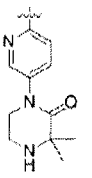
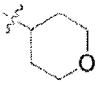
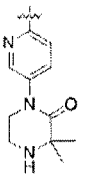
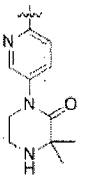
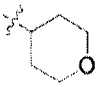
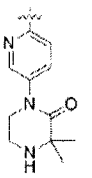
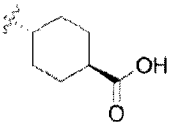
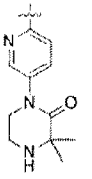
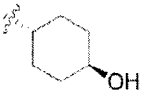
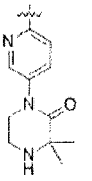
[Table 4-72]

Compound No.	L	R^1	R^2	R^3	
426					
427					
428					
429					
430					
431					

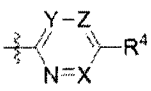
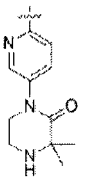
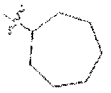
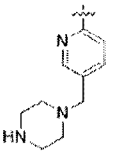
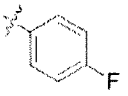
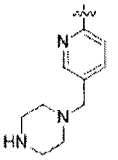
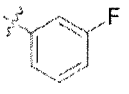
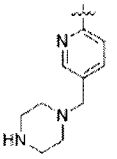
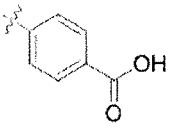
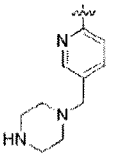
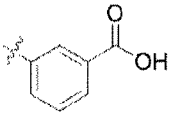
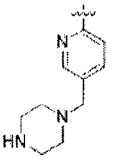
[Table 4-73]

Compound No.	L	R^1	R^2	R^3	
432					
433					
434					
435					
436					
437					

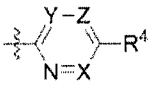
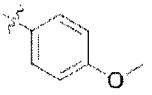
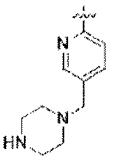
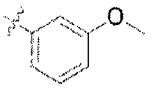
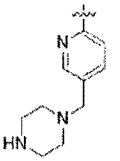
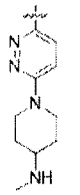
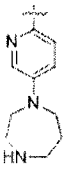
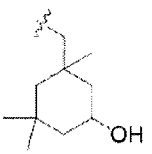
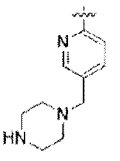
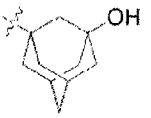
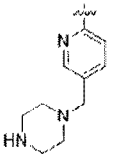
[Table 4-74]

Compound No.	L	R^1	R^2	R^3	
438					
439					
440					
441					
442					
443					

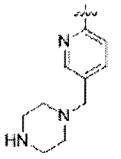
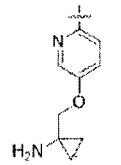
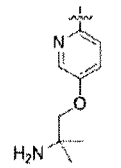
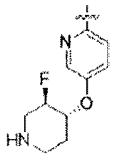
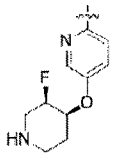
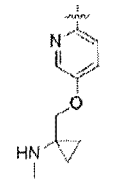
[Table 4-75]

Compound No.	L	R^1	R^2	R^3	
444					
445					
446					
447					
448					
449					

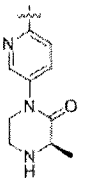
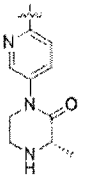
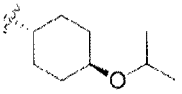
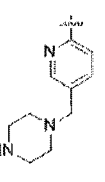
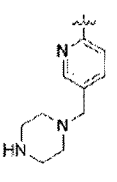
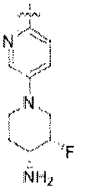
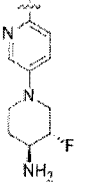
[Table 4-76]

Compound No.	L	R^1	R^2	R^3	
450					
451					
452					
453					
454					
455					

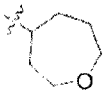
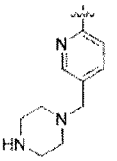
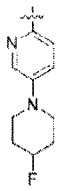
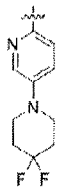
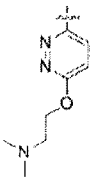
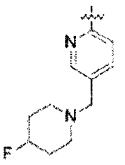
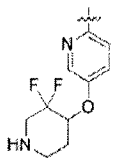
[Table 4-77]

Compound No.	L	R^1	R^2	R^3	
456					
457					
458					
459					
460					
461					

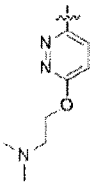
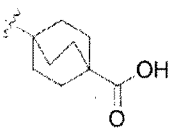
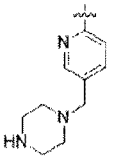
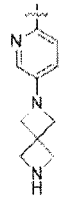
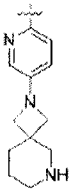
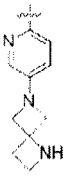
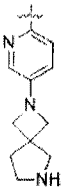
[Table 4-78]

Compound No.	L	R^1	R^2	R^3	
462					
463					
464					
465					
466					
467					

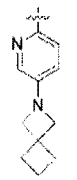
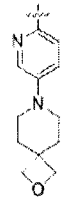
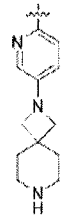
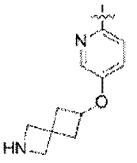
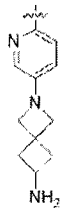
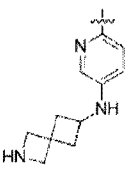
[Table 4-79]

Compound No.	L	R^1	R^2	R^3	
468					
469					
470					
471					
472					
473					

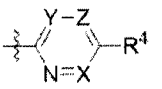
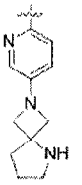
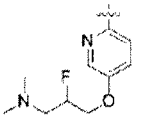
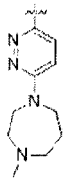
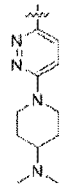
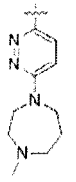
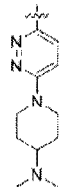
[Table 4-80]

Compound No.	L	R^1	R^2	R^3	
474					
475					
476					
477					
478					
479					

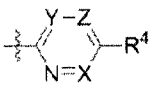
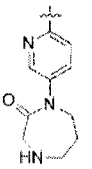
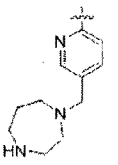
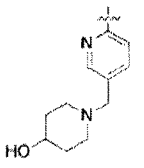
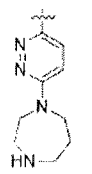
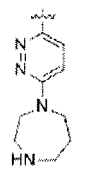
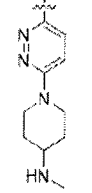
[Table 4-81]

Compound No.	L	R^1	R^2	R^3	
480					
481					
482					
483					
484					
485					

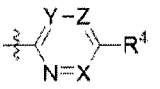
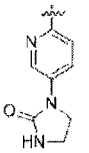
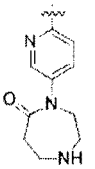
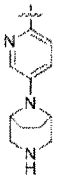
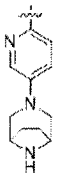
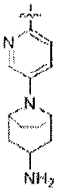
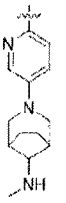
[Table 4-82]

Compound No.	L	R^1	R^2	R^3	
486					
487					
488					
489					
490					
491					

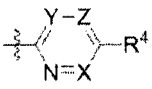
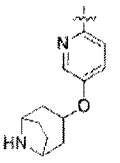
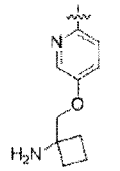
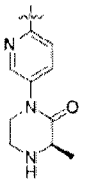
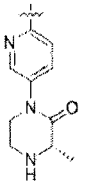
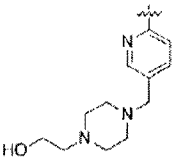
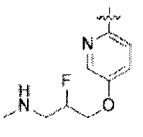
[Table 4-83]

Compound No.	L	R^1	R^2	R^3	
492					
493					
494					
495					
496					
497					

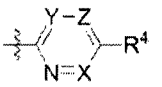
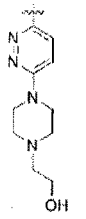
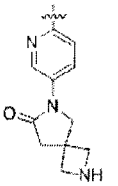
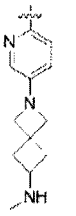
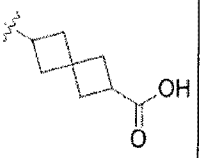
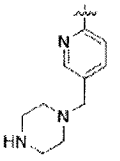
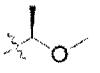
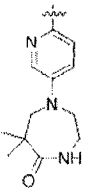
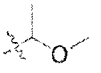
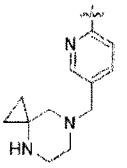
[Table 4-84]

Compound No.	L	R^1	R^2	R^3	
498					
499					
500					
501					
502					
503					

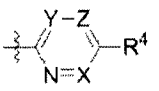
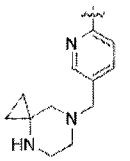
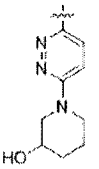
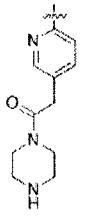
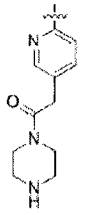
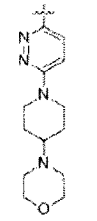
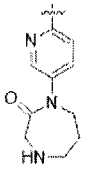
[Table 4-85]

Compound No.	L	R^1	R^2	R^3	
504					
505					
506					
507					
508					
509					

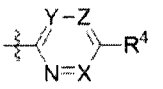
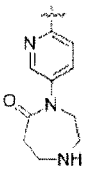
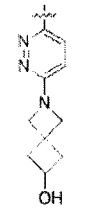
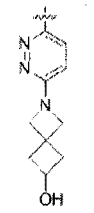
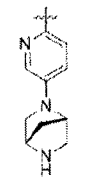
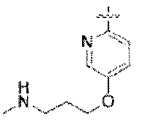
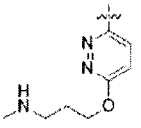
[Table 4-86]

Compound No.	L	R^1	R^2	R^3	
510					
511					
512					
513					
514					
515					

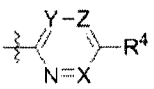
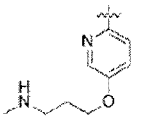
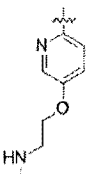
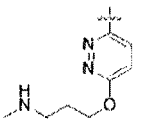
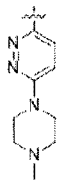
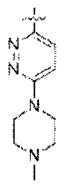
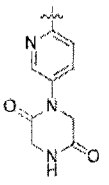
[Table 4-87]

Compound No.	L	R^1	R^2	R^3	
516					
517					
518					
519					
520					
521					

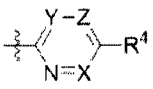
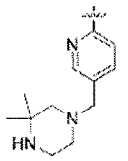
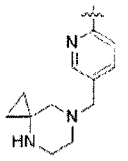
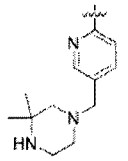
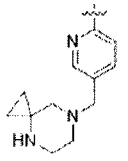
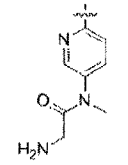
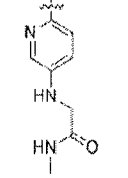
[Table 4-88]

Compound No.	L	R^1	R^2	R^3	
522					
523					
524					
525					
526					
527					

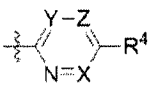
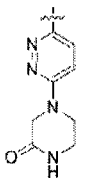
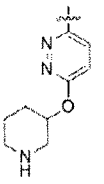
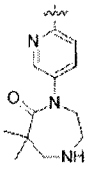
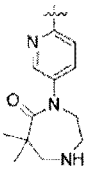
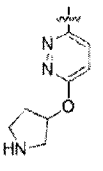
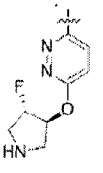
[Table 4-89]

Compound No.	L	R^1	R^2	R^3	
528					
529					
530					
531					
532					
533					

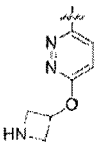
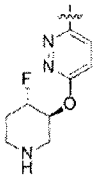
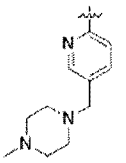
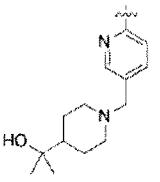
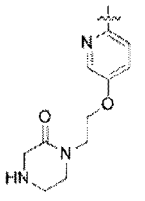
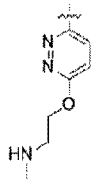
[Table 4-90]

Compound No.	L	R^1	R^2	R^3	
534					
535					
536					
537					
538					
539					

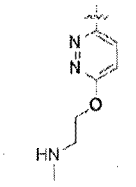
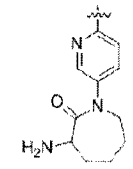
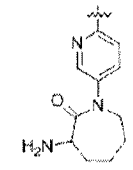
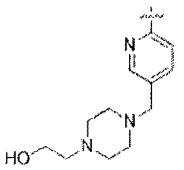
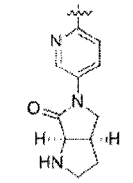
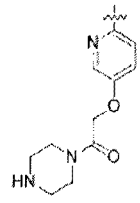
[Table 4-91]

Compound No.	L	R^1	R^2	R^3	
540					
541					
542					
543					
544					
545					

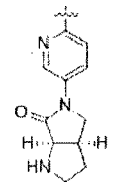
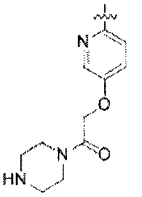
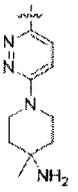
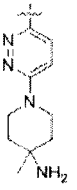
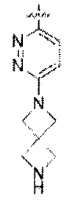
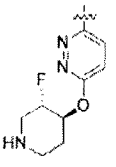
[Table 4-92]

Compound No.	L	R^1	R^2	R^3	
546					
547					
548					
549					
550					
551					

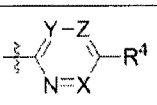
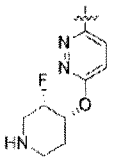
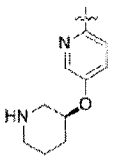
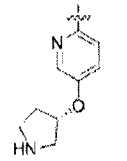
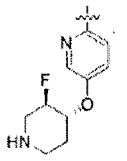
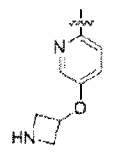
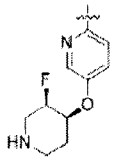
[Table 4-93]

Compound No.	L	R^1	R^2	R^3	
552					
553					
554					
555					
556					
557					

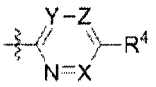
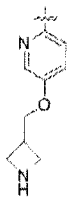
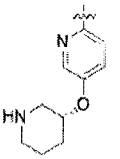
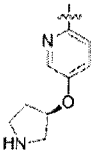
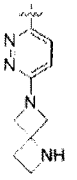
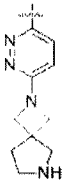
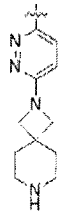
[Table 4-94]

Compound No.	L	R^1	R^2	R^3	
558					
559					
560					
561					
562					
563					

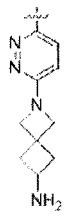
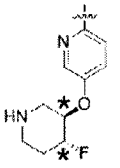
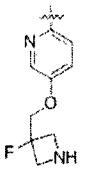
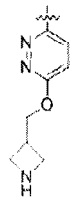
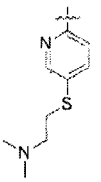
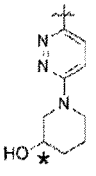
[Table 4-95]

Compound No.	L	R^1	R^2	R^3	
564					
565					
566					
567					
568					
569					

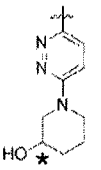
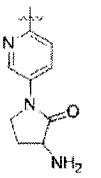
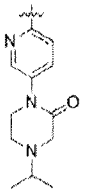
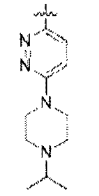
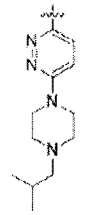
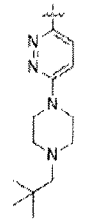
[Table 4-96]

Compound No.	L	R^1	R^2	R^3	
570					
571					
572					
573					
574					
575					

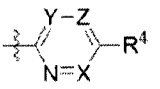
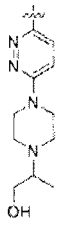
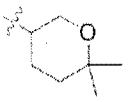
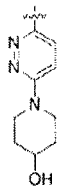
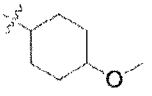
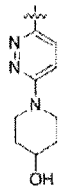
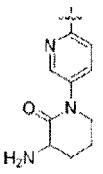
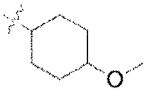
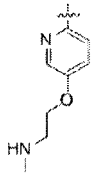
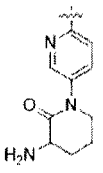
[Table 4-97]

Compound No.	L	R^1	R^2	R^3	
576					
577					
578					
579					
580					
581					*faster isomer 

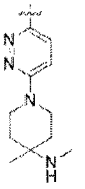
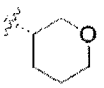
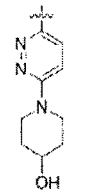
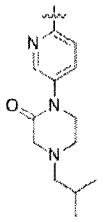
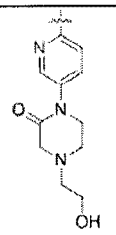
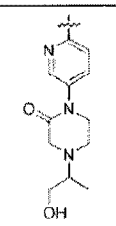
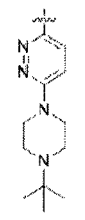
[Table 4-98]

Compound No.	L	R^1	R^2	R^3	
582					*later isomer 
583					
584					
585					
586					
587					

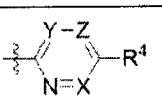
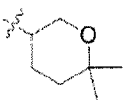
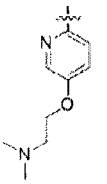
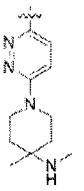
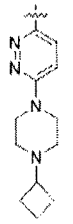
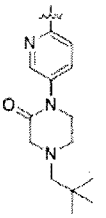
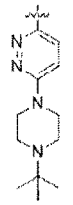
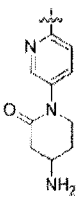
[Table 4-99]

Compound No.	L	R^1	R^2	R^3	
588					
589					
590					
591					
592					
593					

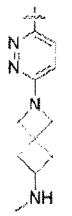
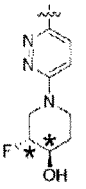
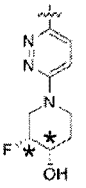
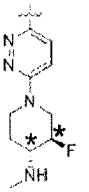
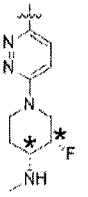
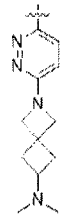
[Table 4-100]

Compound No.	L	R^1	R^2	R^3	
594					
595					
596					
597					
598					
599					

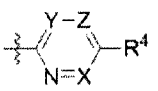
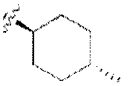
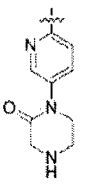
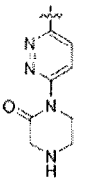
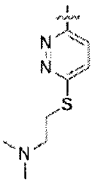
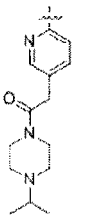
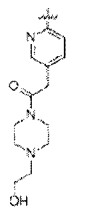
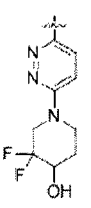
[Table 4-101]

Compound No.	L	R^1	R^2	R^3	
600					
601					
602					
603					
604					
605					

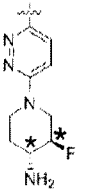
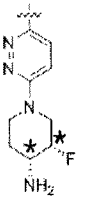
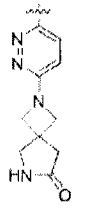
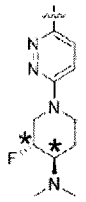
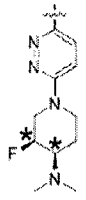
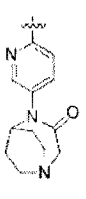
[Table 4-102]

Compound No.	L	R^1	R^2	R^3	
606					
607					
608					
609					
610					
611					

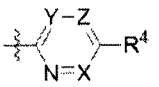
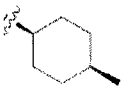
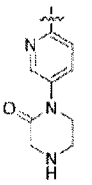
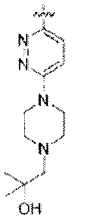
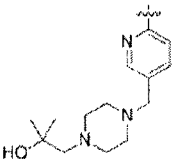
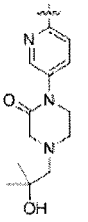
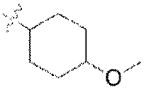
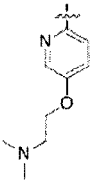
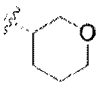
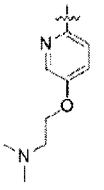
[Table 4-103]

Compound No.	L	R^1	R^2	R^3	
612					
613					
614					
615					
616					
617					

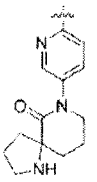
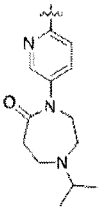
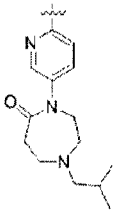
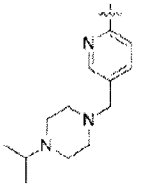
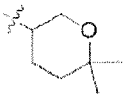
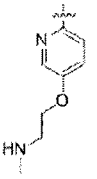
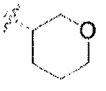
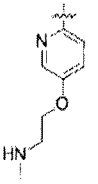
[Table 4-104]

Compound No.	L	R^1	R^2	R^3	
618					
619					
620					
621					
622					
623					

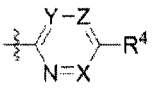
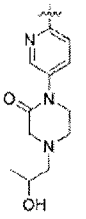
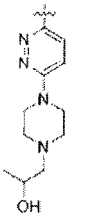
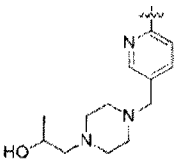
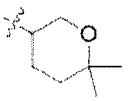
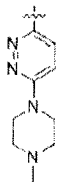
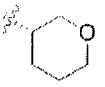
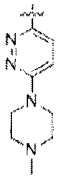
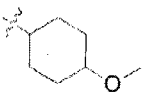
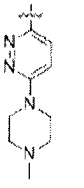
[Table 4-105]

Compound No.	L	R^1	R^2	R^3	
624					
625					
626					
627					
628					
629					

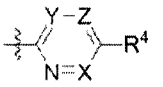
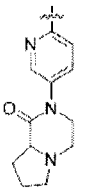
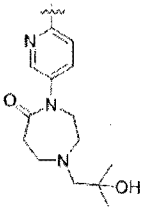
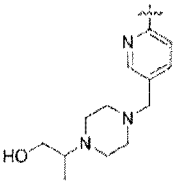
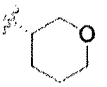
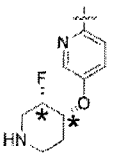
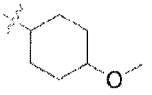
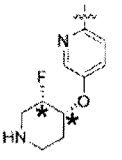
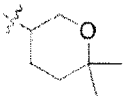
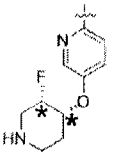
[Table 4-106]

Compound No.	L	R^1	R^2	R^3	
630					
631					
632					
633					
634					
635					

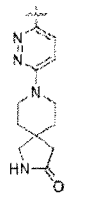
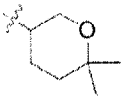
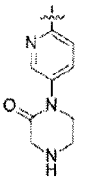
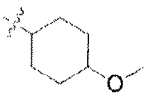
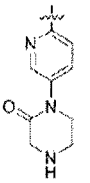
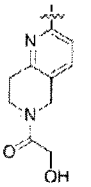
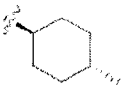
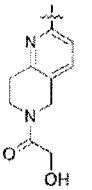
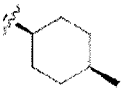
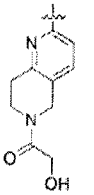
[Table 4-107]

Compound No.	L	R^1	R^2	R^3	
636					
637					
638					
639					
640					
641					

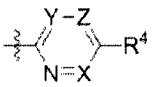
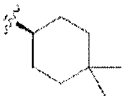
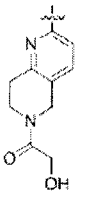
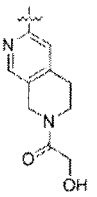
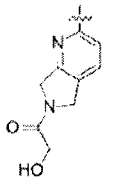
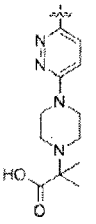
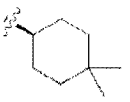
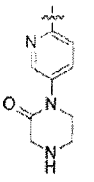
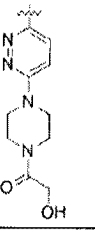
[Table 4-108]

Compound No.	L	R^1	R^2	R^3	
642					
643					
644					
645					
646					
647					

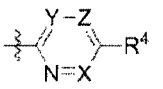
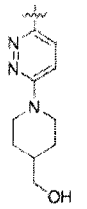
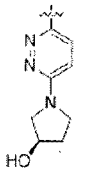
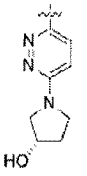
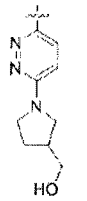
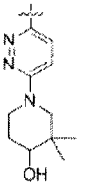
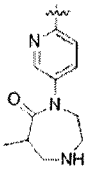
[Table 4-109]

Compound No.	L	R^1	R^2	R^3	
648					
649					
650					
651					
652					
653					

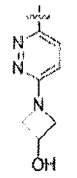
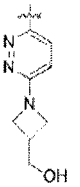
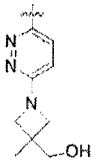
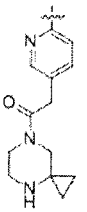
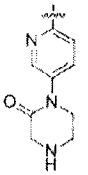
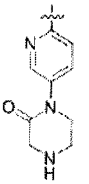
[Table 4-110]

Compound No.	L	R^1	R^2	R^3	
654					
655					
656					
657					
658					
659					

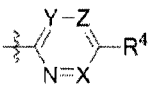
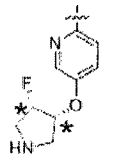
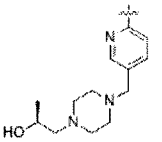
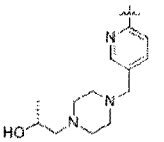
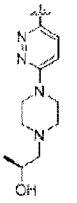
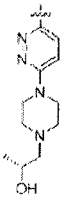
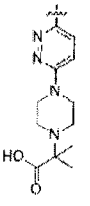
[Table 4-111]

Compound No.	L	R^1	R^2	R^3	
660					
661					
662					
663					
664					
665					

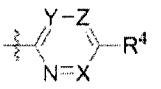
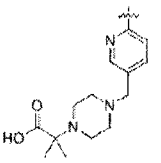
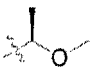
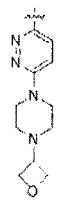
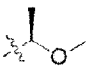
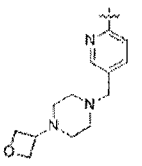
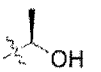
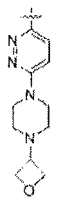
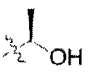
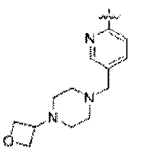
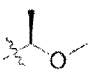
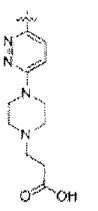
[Table 4-112]

Compound No.	L	R^1	R^2	R^3	
666					
667					
668					
669					
670			*faster isomer 		
672			*later isomer 		

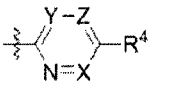
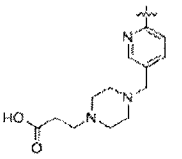
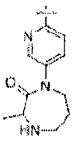
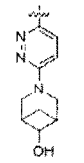
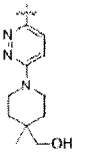
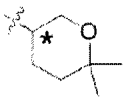
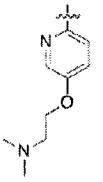
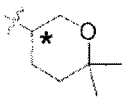
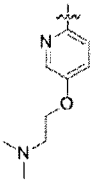
[Table 4-113]

Compound No.	L	R^1	R^2	R^3	
673					
674					
675					
676					
677					
678					

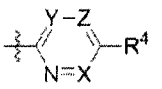
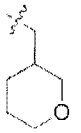
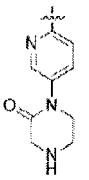
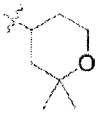
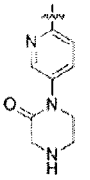
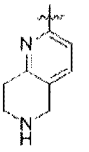
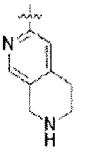
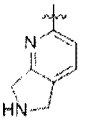
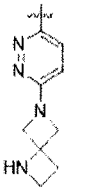
[Table 4-114]

Compound No.	L	R^1	R^2	R^3	
679					
680					
681					
682					
683					
684					

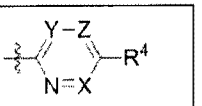
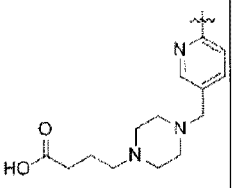
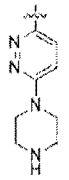
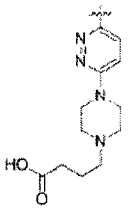
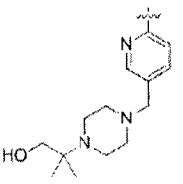
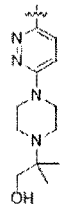
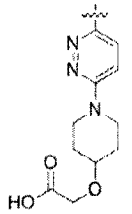
[Table 4-115]

Compound No.	L	R^1	R^2	R^3	
685					
686					
687					
688					
689		*faster isomer 			
690		*later isomer 			

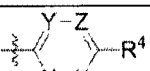
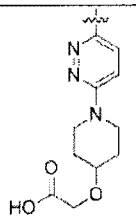
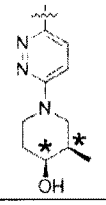
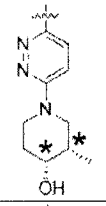
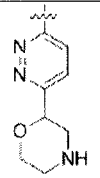
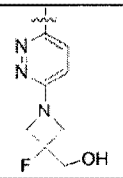
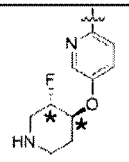
[Table 4-116]

Compound No.	L	R^1	R^2	R^3	
691					
692					
693					
694					
695					
696					

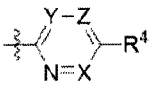
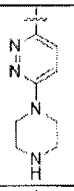
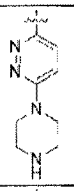
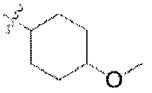
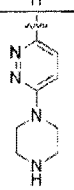
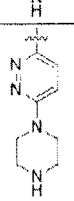
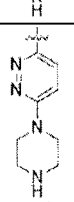
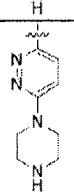
[Table 4-117]

Compound No.	L	R^1	R^2	R^3	
697					
698					
699					
700					
701					
702					

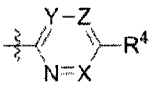
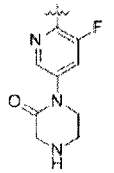
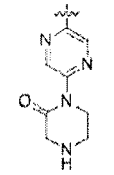
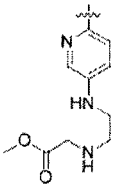
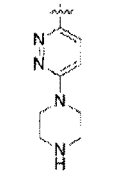
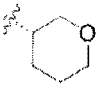
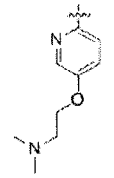
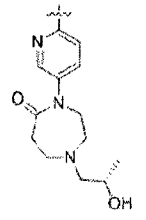
[Table 4-118]

Compound No.	L	R^1	R^2	R^3	
703					
704					*later isomer 
705					*faster isomer 
706					
707					
708					

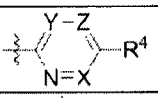
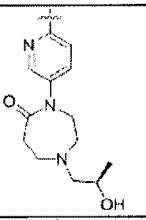
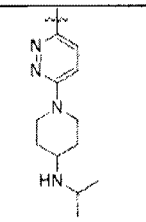
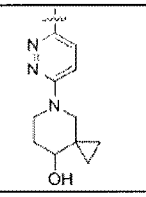
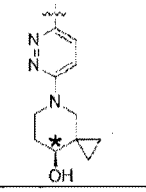
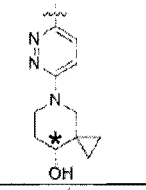
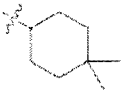
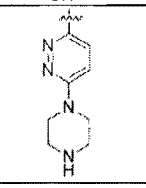
[Table 4-119]

Compound No.	L	R^1	R^2	R^3	
709					
710					
711					
712					
713			*later isomer 		
714			*faster isomer 		

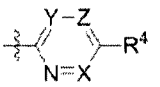
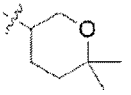
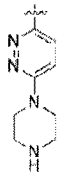
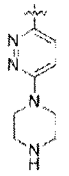
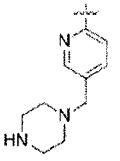
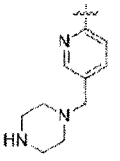
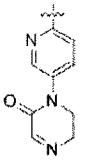
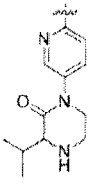
[Table 4-120]

Compound No.	L	R^1	R^2	R^3	
715					
716					
717					
718					
719					
720					

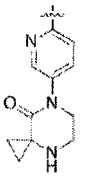
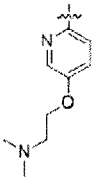
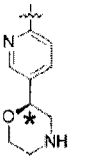
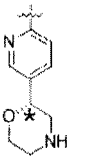
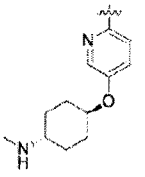
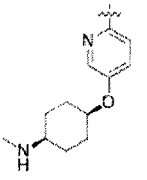
[Table 4-121]

Compound No.	L	R^1	R^2	R^3	
721					
722					
723					
724					*faster isomer 
725					*later isomer 
726					

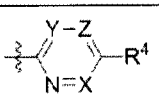
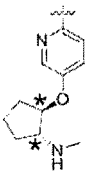
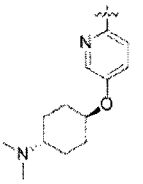
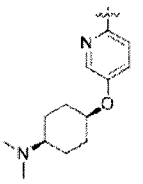
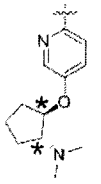
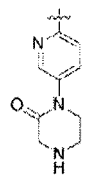
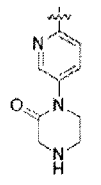
[Table 4-122]

Compound No.	L	R^1	R^2	R^3	
727					
728					
729			*later isomer 		
730			*faster isomer 		
731					
732					

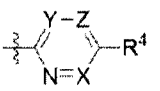
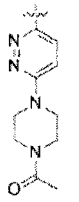
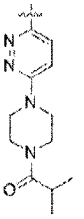
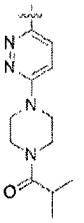
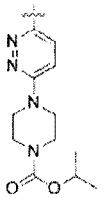
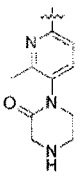
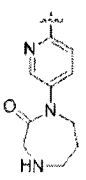
[Table 4-123]

Compound No.	L	R^1	R^2	R^3	
733					
734					
735					*faster isomer 
736					*later isomer 
737					
738					

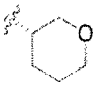
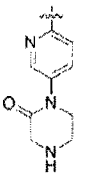
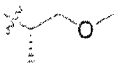
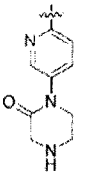
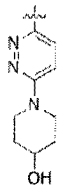
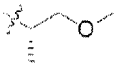
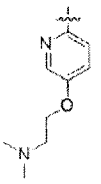
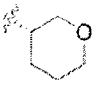
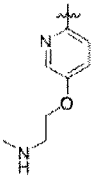
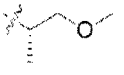
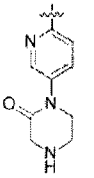
[Table 4-124]

Compound No.	L	R^1	R^2	R^3	
739					
740					
741					
742					
743					
744					

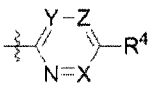
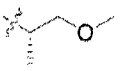
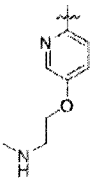
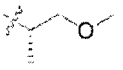
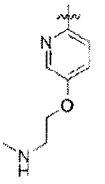
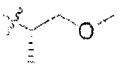
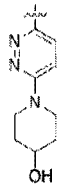
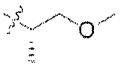
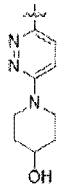
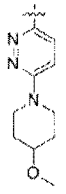
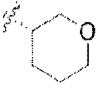
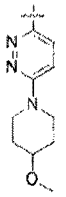
[Table 4-125]

Compound No.	L	R^1	R^2	R^3	
745					
746					
747					
748					
749					
750					

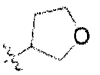
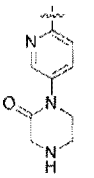
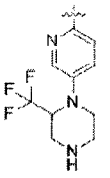
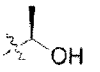
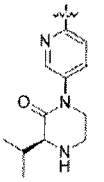
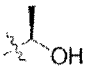
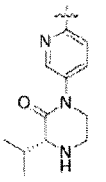
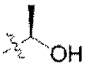
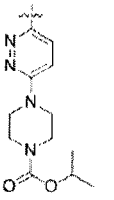
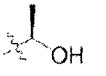
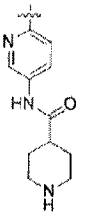
[Table 4-126]

Compound No.	L	R^1	R^2	R^3	
751					
752					
753					
754					
755					
756					

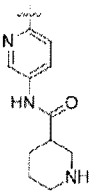
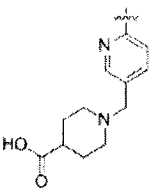
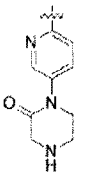
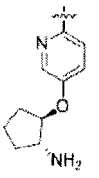
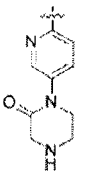
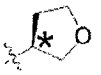
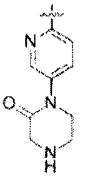
[Table 4-127]

Compound No.	L	R^1	R^2	R^3	
757					
758					
759					
760					
761					
762					

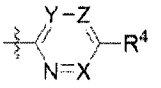
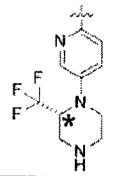
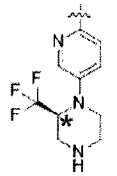
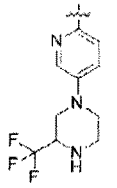
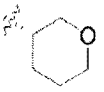
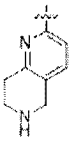
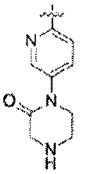
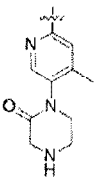
[Table 4-128]

Compound No.	L	R^1	R^2	R^3	
763					
764					
765					
766					
767					
768					

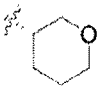
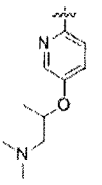
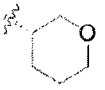
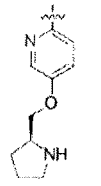
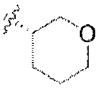
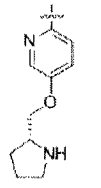
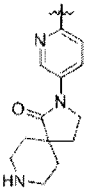
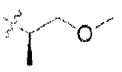
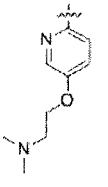
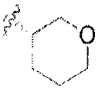
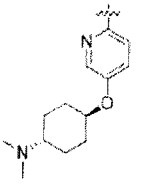
[Table 4-129]

Compound No.	L	R^1	R^2	R^3	
769					
770					
771					
772					
773			*faster isomer 		
774			*later isomer 		

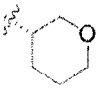
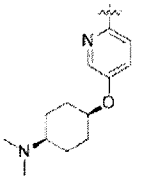
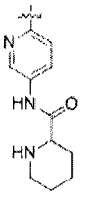
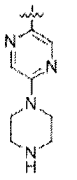
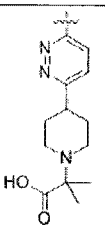
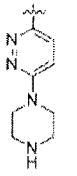
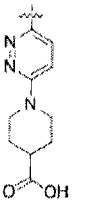
[Table 4-130]

Compound No.	L	R^1	R^2	R^3	
775					*faster isomer 
776					*later isomer 
777					
778					
779					
780					

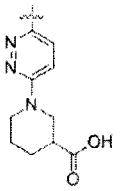
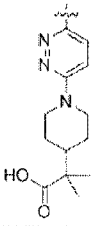
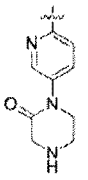
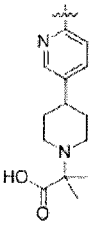
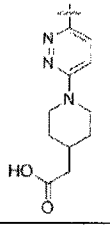
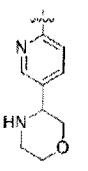
[Table 4-131]

Compound No.	L	R^1	R^2	R^3	
781					
782					
783					
784					
785					
786					

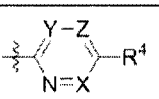
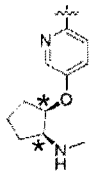
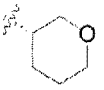
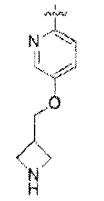
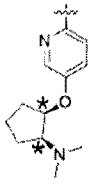
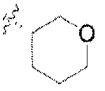
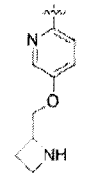
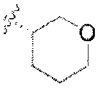
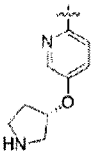
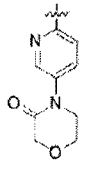
[Table 4-132]

Compound No.	L	R^1	R^2	R^3	
787					
788					
789					
790					
791					
792					

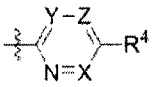
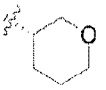
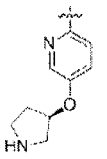
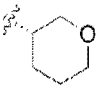
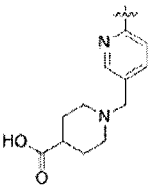
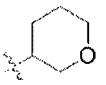
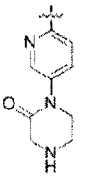
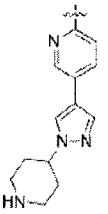
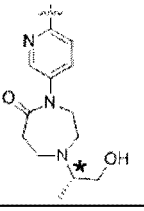
[Table 4-133]

Compound No.	L	R^1	R^2	R^3	
793					
794					
795					
796					
797					
798					

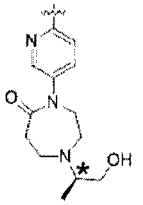
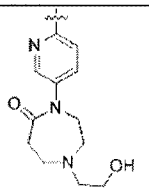
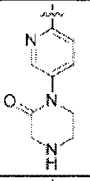
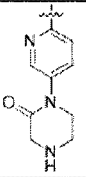
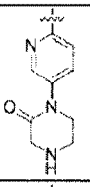
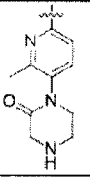
[Table 4-134]

Compound No.	L	R^1	R^2	R^3	
799					
800					
801					
802					
803					
804					

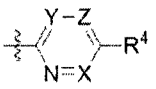
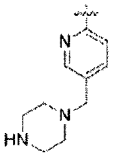
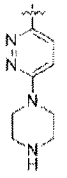
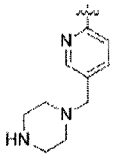
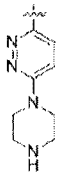
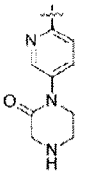
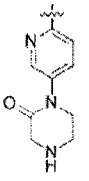
[Table 4-135]

Compound No.	L	R^1	R^2	R^3	
805					
806					
807					
808					
809					*faster isomer 

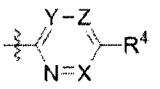
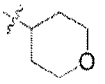
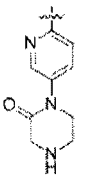
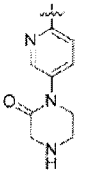
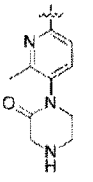
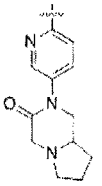
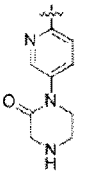
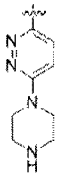
[Table 4-136]

Compound No.	L	R^1	R^2	R^3	
810					*later isomer 
811					
812					
813					
814					
815					

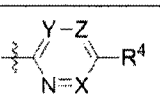
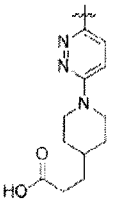
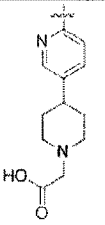
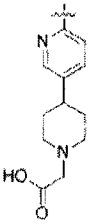
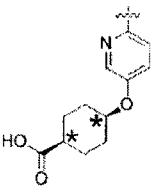
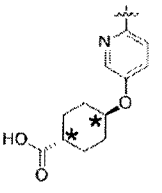
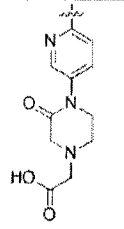
[Table 4-137]

Compound No.	L	R^1	R^2	R^3	
816					
817					
818					
819					
820					
821					

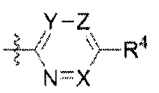
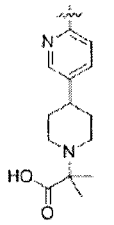
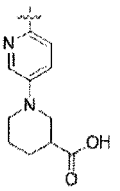
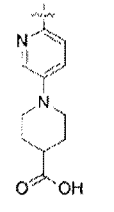
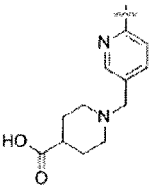
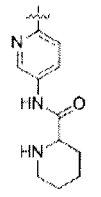
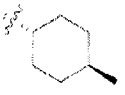
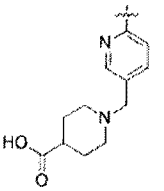
[Table 4-138]

Compound No.	L	R^1	R^2	R^3	
822					
823					
824					
825					
826					
827					

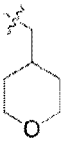
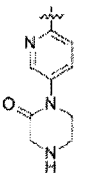
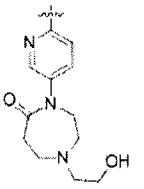
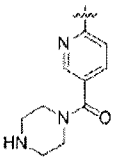
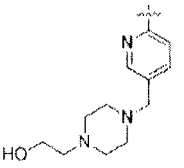
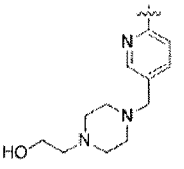
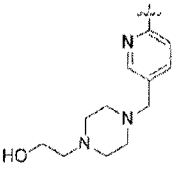
[Table 4-139]

Compound No.	L	R^1	R^2	R^3	
828					
829					
830					
831					
832					
833					

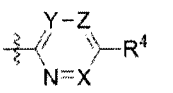
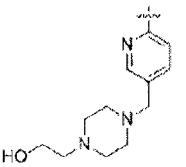
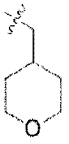
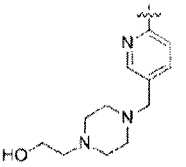
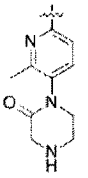
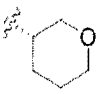
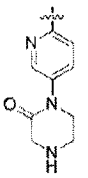
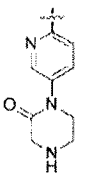
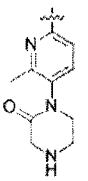
[Table 4-140]

Compound No.	L	R^1	R^2	R^3	
834					
835					
836					
837					
838					
839					

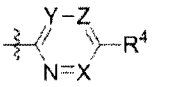
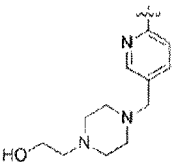
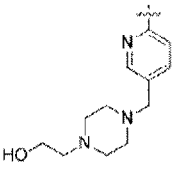
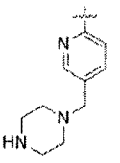
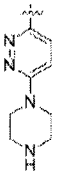
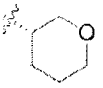
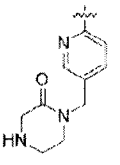
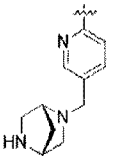
[Table 4-141]

Compound No.	L	R^1	R^2	R^3	
840					
841					
842					
843					
844					
845					

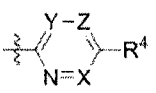
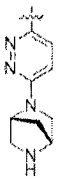
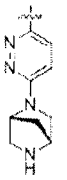
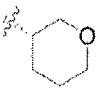
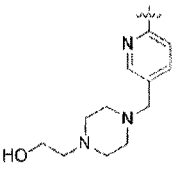
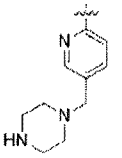
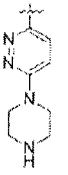
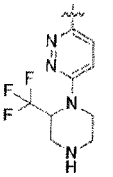
[Table 4-142]

Compound No.	L	R^1	R^2	R^3	
846					
847					
848					
849					
850					
851					

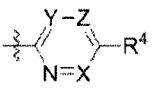
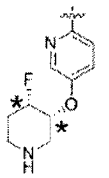
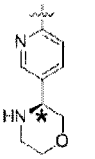
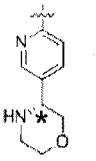
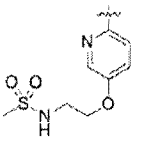
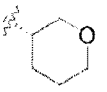
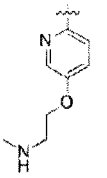
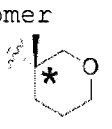
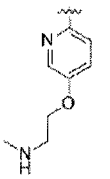
[Table 4-143]

Compound No.	L	R^1	R^2	R^3	
852					
853					
854					
855					
856					
857					

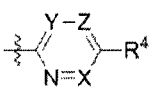
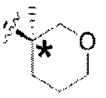
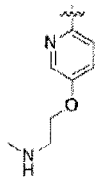
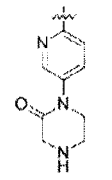
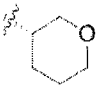
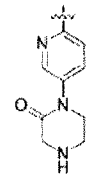
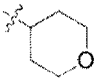
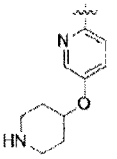
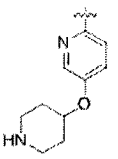
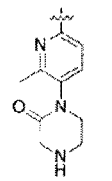
[Table 4-144]

Compound No.	L	R^1	R^2	R^3	
858					
859					
860					
861					
862					
863					

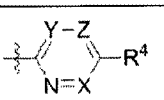
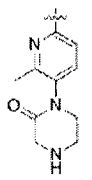
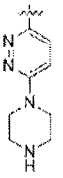
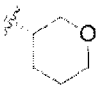
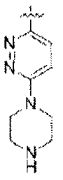
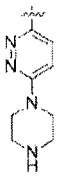
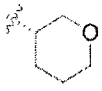
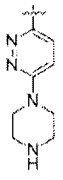
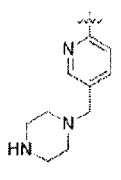
[Table 4-145]

Compound No.	L	R^1	R^2	R^3	
864					
865					*faster isomer 
866					*later isomer 
867					
868					
869		faster isomer 			

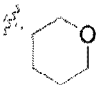
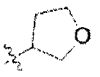
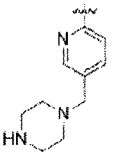
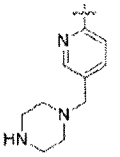
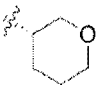
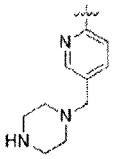
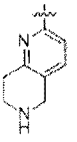
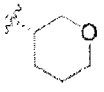
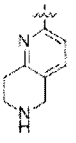
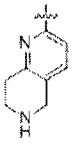
[Table 4-146]

Compound No.	L	R^1	R^2	R^3	
870		later isomer 			
871					
872					
873					
874					
875			*faster isomer 		

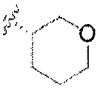
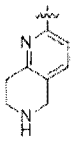
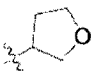
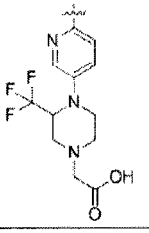
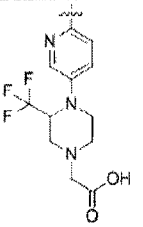
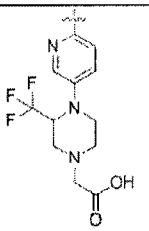
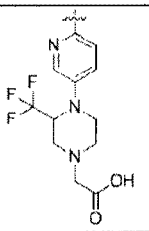
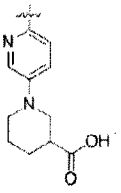
[Table 4-147]

Compound No.	L	R^1	R^2	R^3	
876			*later isomer 		
877					
878					
879					
880					
881					

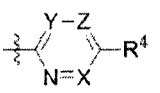
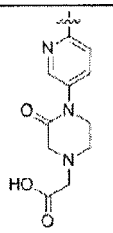
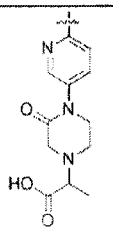
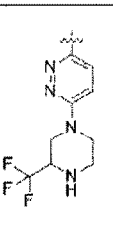
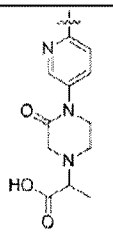
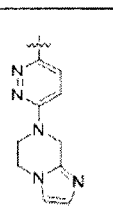
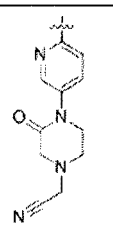
[Table 4-148]

Compound No.	L	R^1	R^2	R^3	
882					
883					
884					
885					
886					
887					

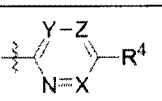
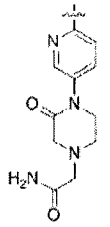
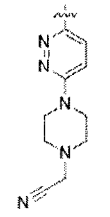
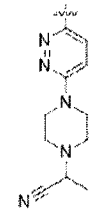
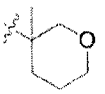
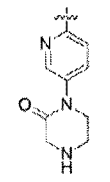
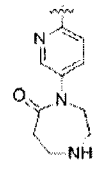
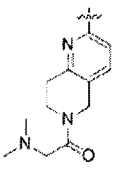
[Table 4-149]

Compound No.	L	R^1	R^2	R^3	
888					
889					
890					
891					
892					
893					

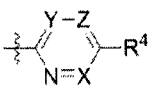
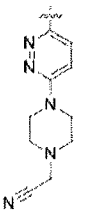
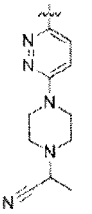
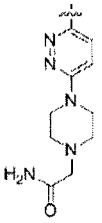
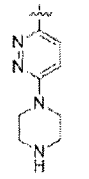
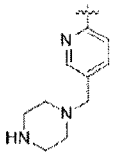
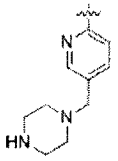
[Table 4-150]

Compound No.	L	R^1	R^2	R^3	
894					
895					
896					
897					
898					
899					

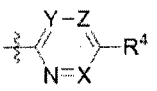
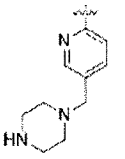
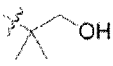
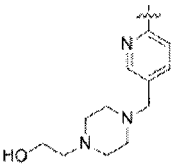
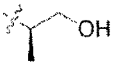
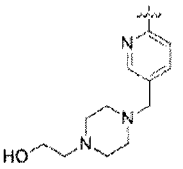
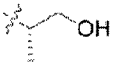
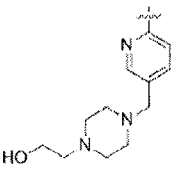
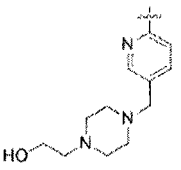
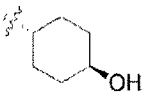
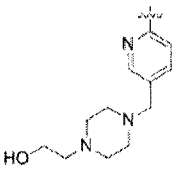
[Table 4-151]

Compound No.	L	R^1	R^2	R^3	
900					
901					
902					
903					
904					
905					

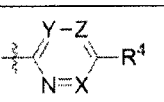
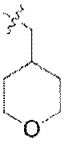
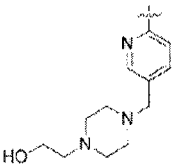
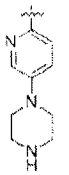
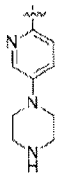
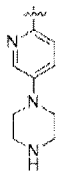
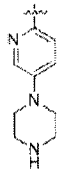
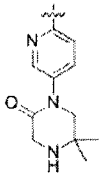
[Table 4-152]

Compound No.	L	R^1	R^2	R^3	
906					
907					
908					
909					
910					
911					

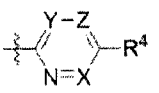
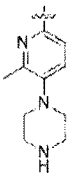
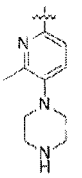
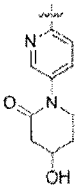
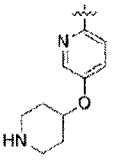
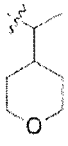
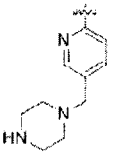
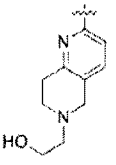
[Table 4-153]

Compound No.	L	R^1	R^2	R^3	
912					
913					
914					
915					
916					
917					

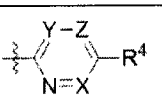
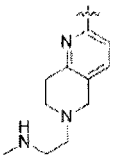
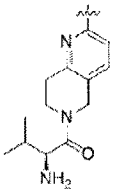
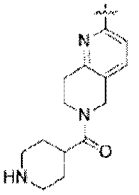
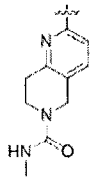
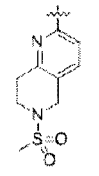
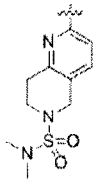
[Table 4-154]

Compound No.	L	R^1	R^2	R^3	
918					
919					
920					
921					
922					
923					

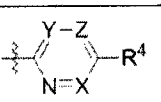
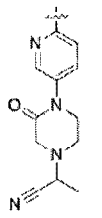
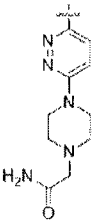
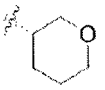
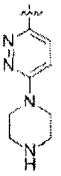
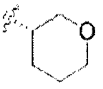
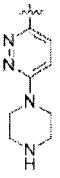
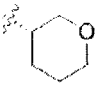
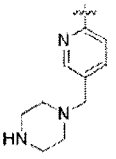
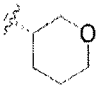
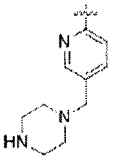
[Table 4-155]

Compound No.	L	R^1	R^2	R^3	
924					
925					
926					
927					
928					
929					

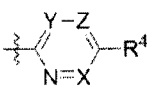
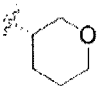
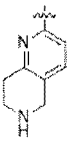
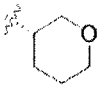
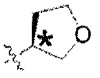
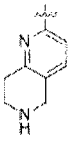
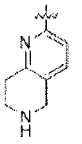
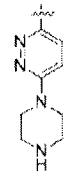
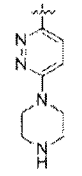
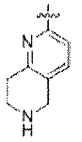
[Table 4-156]

Compound No.	L	R^1	R^2	R^3	
930					
931					
932					
933					
934					
935					

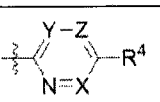
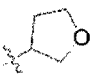
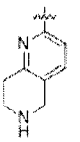
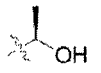
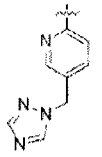
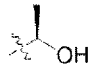
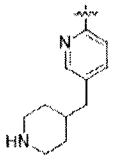
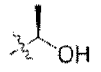
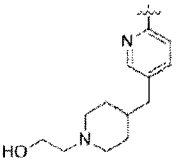
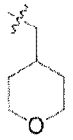
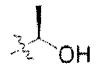
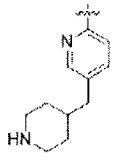
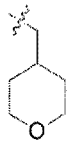
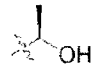
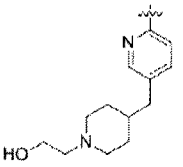
[Table 4-157]

Compound No.	L	R^1	R^2	R^3	
936					
937					
938			*faster isomer 		
939			*later isomer 		
940			*faster isomer 		
941			*later isomer 		

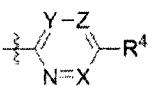
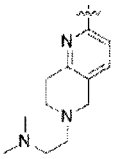
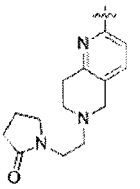
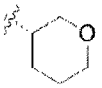
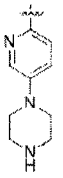
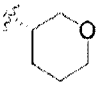
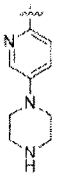
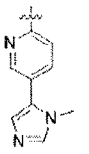
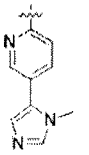
[Table 4-158]

Compound No.	L	R^1	R^2	R^3	
942			*faster isomer 		
943			*later isomer 		
944					
945					
946					
947					

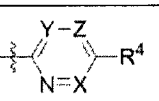
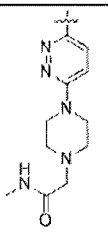
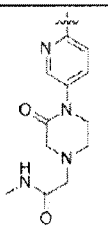
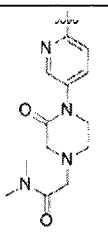
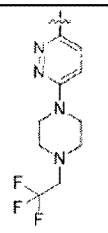
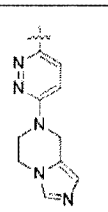
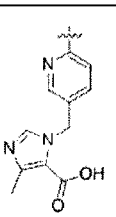
[Table 4-159]

Compound No.	L	R^1	R^2	R^3	
948					
949					
950					
951					
952					
953					

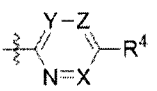
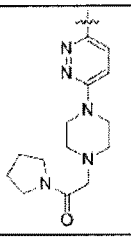
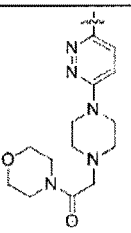
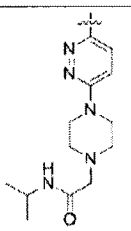
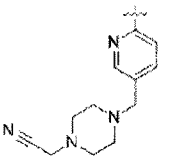
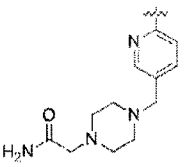
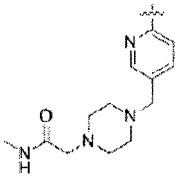
[Table 4-160]

Compound No.	L	R^1	R^2	R^3	
954					
955					
956					
957					
958					
959					

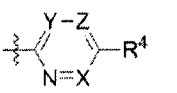
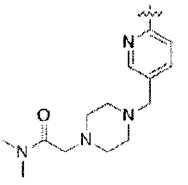
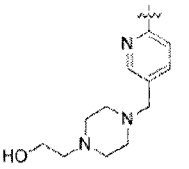
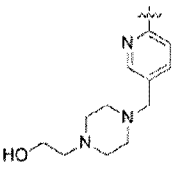
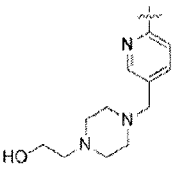
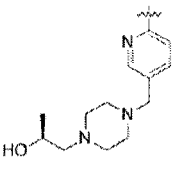
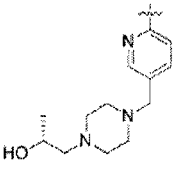
[Table 4-161]

Compound No.	L	R^1	R^2	R^3	
960					
961					
962					
963					
964					
965					

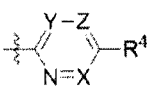
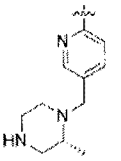
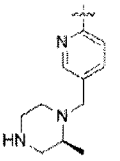
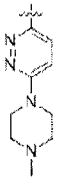
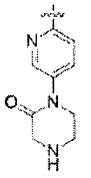
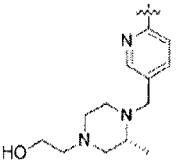
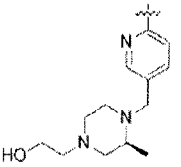
[Table 4-162]

Compound No.	L	R^1	R^2	R^3	
966					
967					
968					
969					
970					
971					

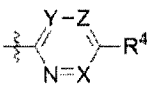
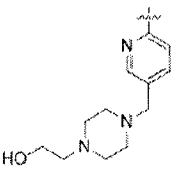
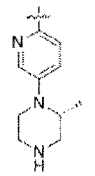
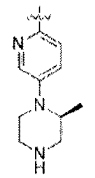
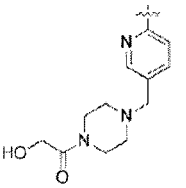
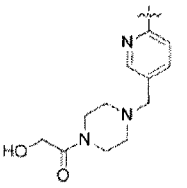
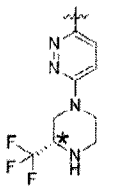
[Table 4-163]

Compound No.	L	R^1	R^2	R^3	
972					
973					
974					
975					
976					
977					

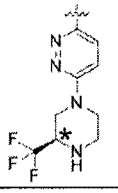
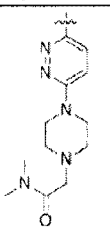
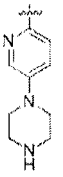
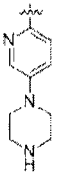
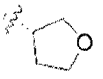
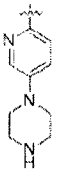
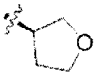
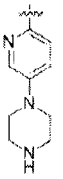
[Table 4-164]

Compound No.	L	R^1	R^2	R^3	
978					
979					
980					
981					
982					
983					

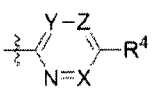
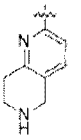
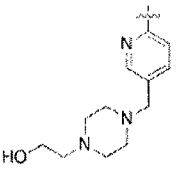
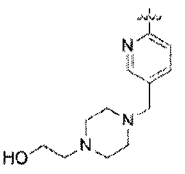
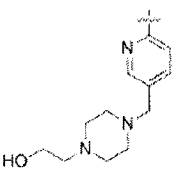
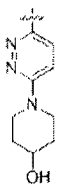
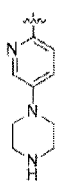
[Table 4-165]

Compound No.	L	R^1	R^2	R^3	
984					
985					
986					
987					
988					
989					*faster isomer 

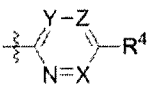
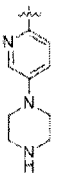
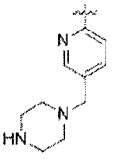
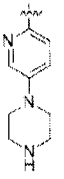
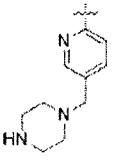
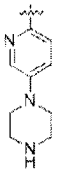
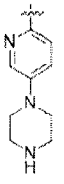
[Table 4-166]

Compound No.	L	R^1	R^2	R^3	
990					*later isomer 
991					
992			*faster isomer 		
993			*later isomer 		
994					
995					

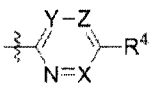
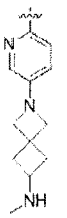
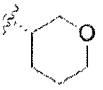
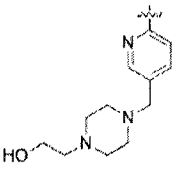
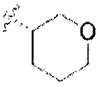
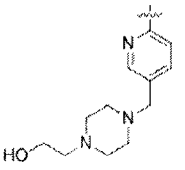
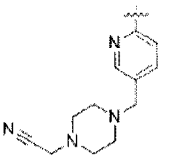
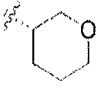
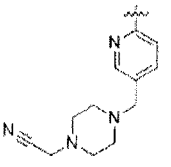
[Table 4-167]

Compound No.	L	R^1	R^2	R^3	
996					
997					
998					
999					
1000					
1001					

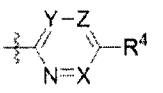
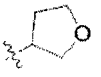
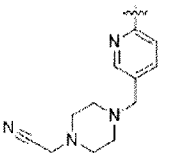
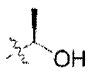
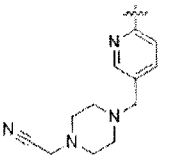
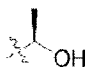
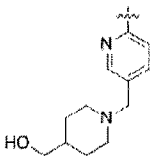
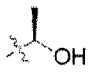
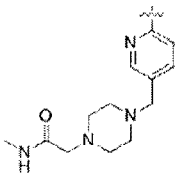
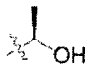
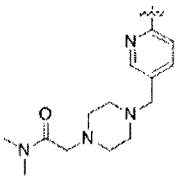
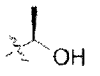
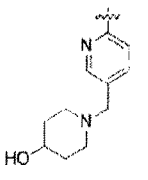
[Table 4-168]

Compound No.	L	R^1	R^2	R^3	
1002					
1003					
1004					
1005					
1006					
1007					

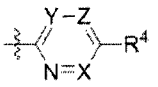
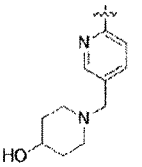
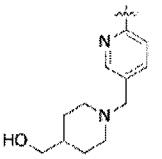
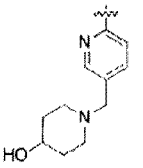
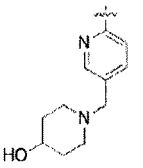
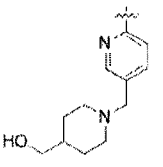
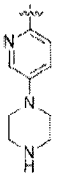
[Table 4-169]

Compound No.	L	R^1	R^2	R^3	
1008					
1009					
1010					
1011					
1012					
1013					

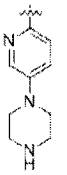
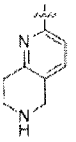
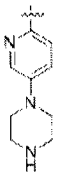
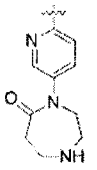
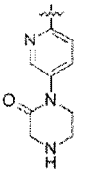
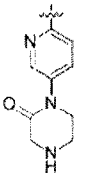
[Table 4-170]

Compound No.	L	R^1	R^2	R^3	
1014					
1015					
1016					
1017					
1018					
1019					

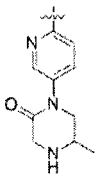
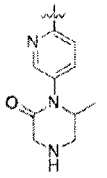
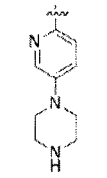
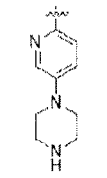
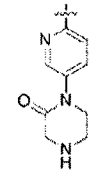
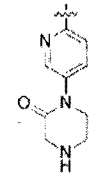
[Table 4-171]

Compound No.	L	R^1	R^2	R^3	
1020					
1021					
1022					
1023					
1024					
1025			*faster isomer 		

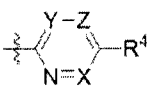
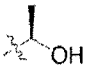
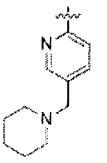
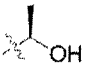
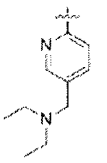
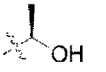
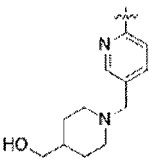
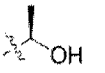
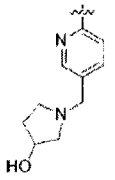
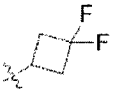
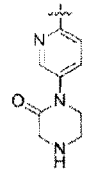
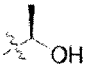
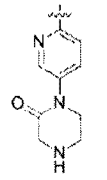
[Table 4-172]

Compound No.	L	R^1	R^2	R^3	
1026			*later isomer 		
1027					
1028					
1029					
1030					
1031					

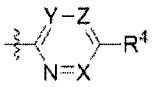
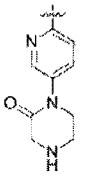
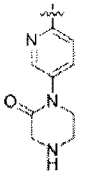
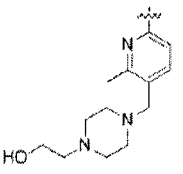
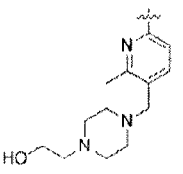
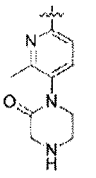
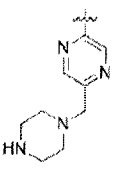
[Table 4-173]

Compound No.	L	R^1	R^2	R^3	
1032					
1033					
1034			*faster isomer 		
1035			*later isomer 		
1036			*faster isomer 		
1037			*later isomer 		

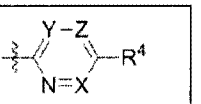
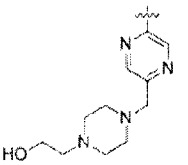
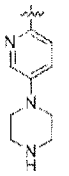
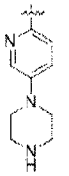
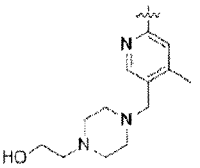
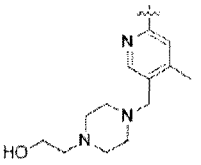
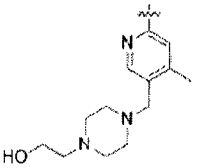
[Table 4-174]

Compound No.	L	R^1	R^2	R^3	
1038					
1039					
1040					
1041					
1042					
1043					

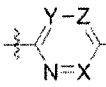
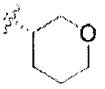
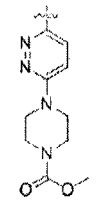
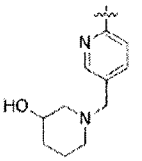
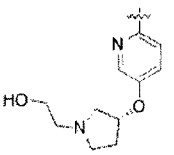
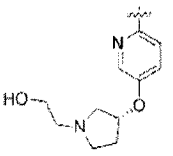
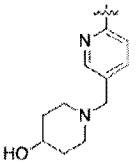
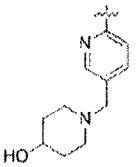
[Table 4-175]

Compound No.	L	R^1	R^2	R^3	
1044					
1045					
1046					
1047					
1048					
1049					

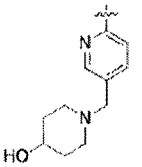
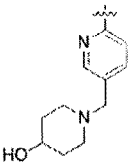
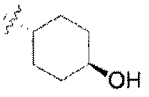
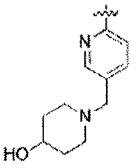
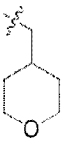
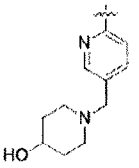
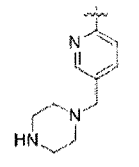
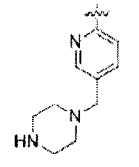
[Table 4-176]

Compound No.	L	R^1	R^2	R^3	
1050					
1051					
1052					
1053					
1054					
1055					

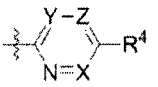
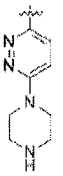
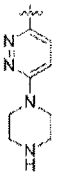
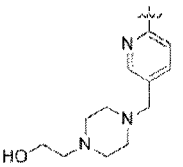
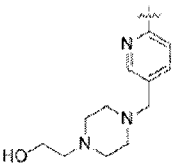
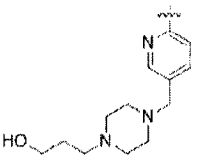
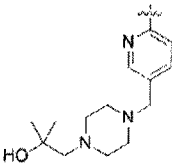
[Table 4-177]

Compound No.	L	R^1	R^2	R^3	
1056					
1057					
1058					
1059					
1060					
1061					

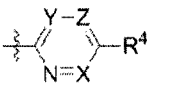
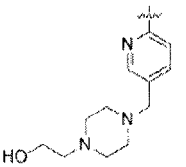
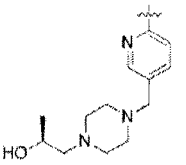
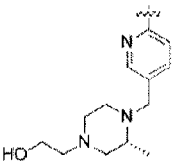
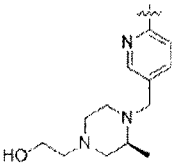
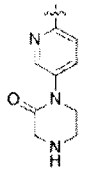
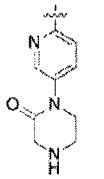
[Table 4-178]

Compound No.	L	R^1	R^2	R^3	
1062					
1063					
1064					
1065					
1066			*faster isomer 		
1067			*later isomer 		

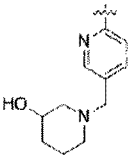
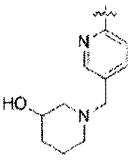
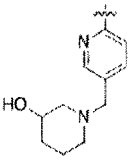
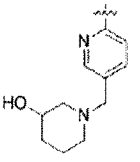
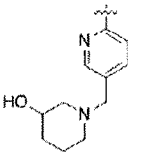
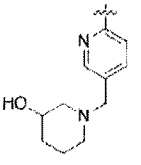
[Table 4-179]

Compound No.	L	R^1	R^2	R^3	
1068			*faster isomer 		
1069			*later isomer 		
1070					
1071					
1072					
1073					

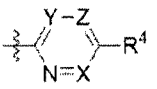
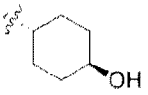
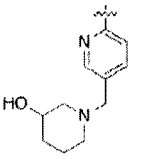
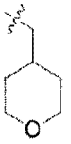
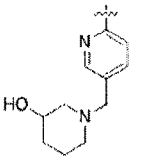
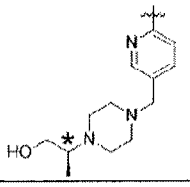
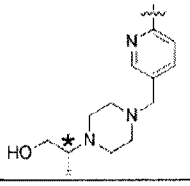
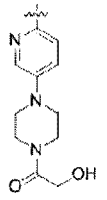
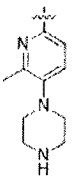
[Table 4-180]

Compound No.	L	R^1	R^2	R^3	
1074					
1075					
1076					
1077					
1078					
1079					

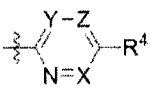
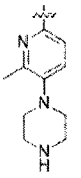
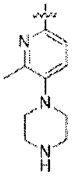
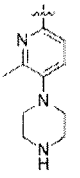
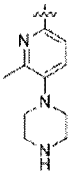
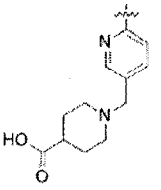
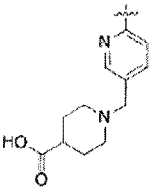
[Table 4-181]

Compound No.	L	R^1	R^2	R^3	
1080					
1081					
1082					
1083					
1084					
1085					

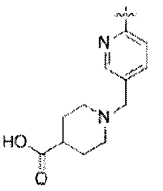
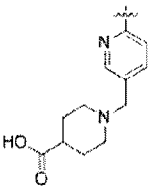
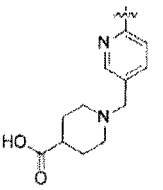
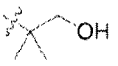
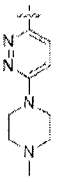
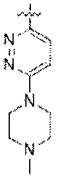
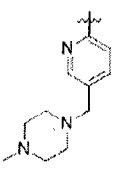
[Table 4-182]

Compound No.	L	R^1	R^2	R^3	
1086					
1087					
1088					*faster isomer 
1089					*later isomer 
1090					
1091					

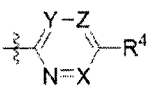
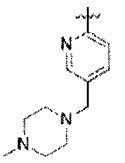
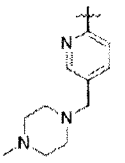
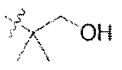
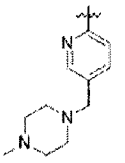
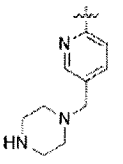
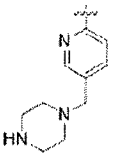
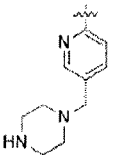
[Table 4-183]

Compound No.	L	R^1	R^2	R^3	
1092					
1093					
1094					
1095					
1096					
1097					

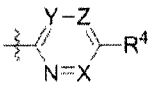
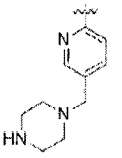
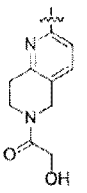
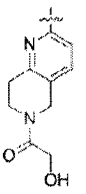
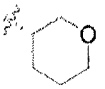
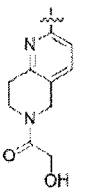
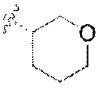
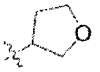
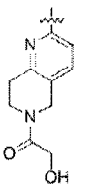
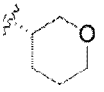
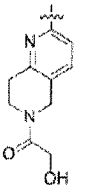
[Table 4-184]

Compound No.	L	R^1	R^2	R^3	
1098					
1099					
1100					
1101					
1102					
1103					

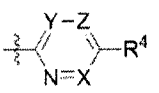
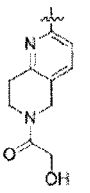
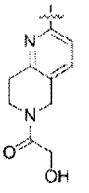
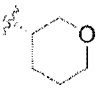
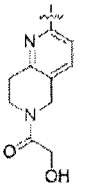
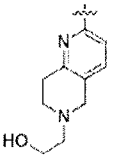
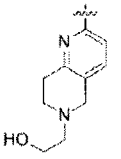
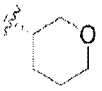
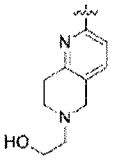
[Table 4-185]

Compound No.	L	R^1	R^2	R^3	
1104					
1105					
1106					
1107					
1108					
1109					

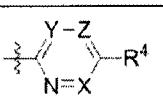
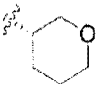
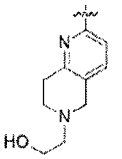
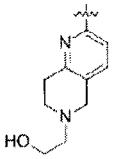
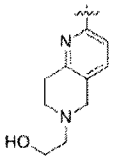
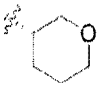
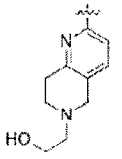
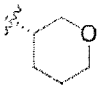
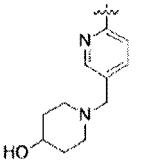
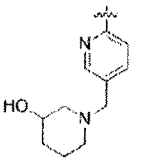
[Table 4-186]

Compound No.	L	R^1	R^2	R^3	
1110					
1111					
1112					
1113					
1114					
1115					

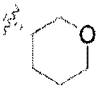
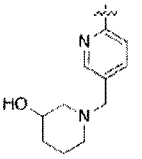
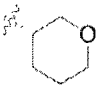
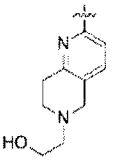
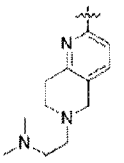
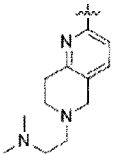
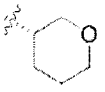
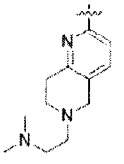
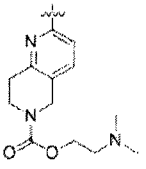
[Table 4-187]

Compound No.	L	R^1	R^2	R^3	
1116					
1117					
1118					
1119					
1120					
1121					

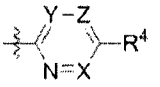
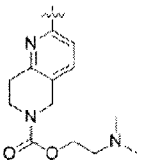
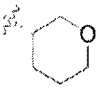
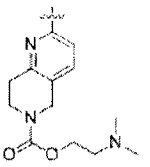
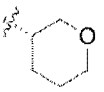
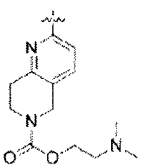
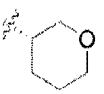
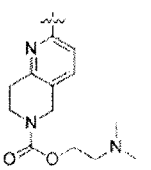
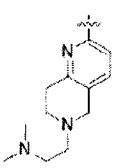
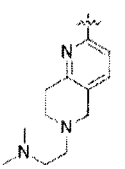
[Table 4-188]

Compound No.	L	R^1	R^2	R^3	
1122					
1123					
1124					
1125					
1126					
1127					

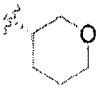
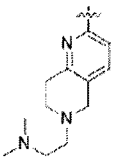
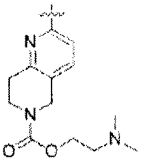
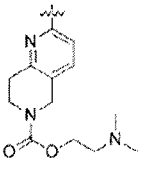
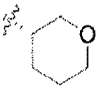
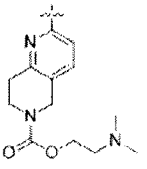
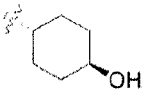
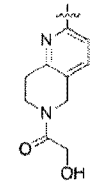
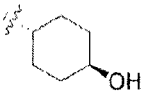
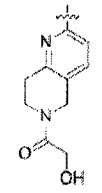
[Table 4-189]

Compound No.	L	R^1	R^2	R^3	
1128					
1129					
1130					
1131					
1132					
1133					

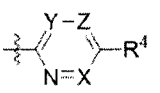
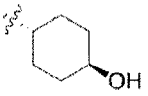
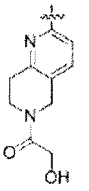
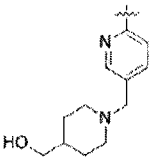
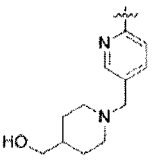
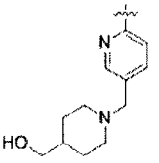
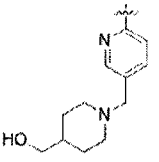
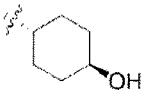
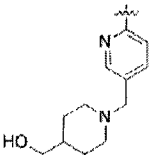
[Table 4-190]

Compound No.	L	R^1	R^2	R^3	
1134					
1135					
1136					
1137					
1138					
1139					

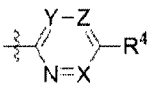
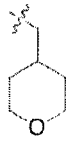
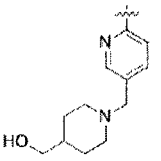
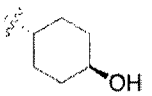
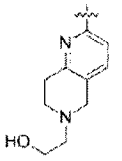
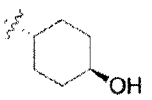
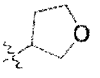
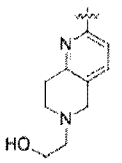
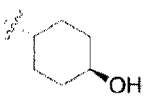
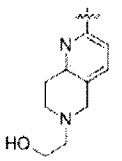
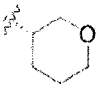
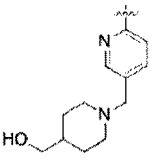
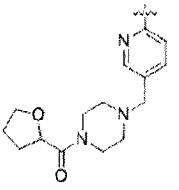
[Table 4-191]

Compound No.	L	R^1	R^2	R^3	
1140					
1141					
1142					
1143					
1144					
1145					

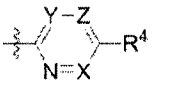
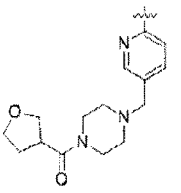
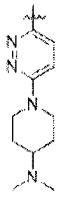
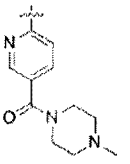
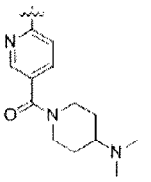
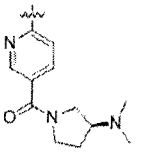
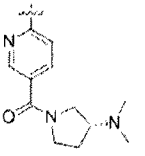
[Table 4-192]

Compound No.	L	R^1	R^2	R^3	
1146					
1147					
1148					
1149					
1150					
1151					

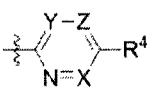
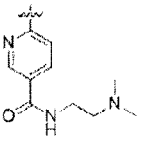
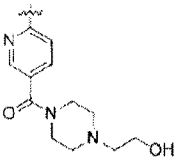
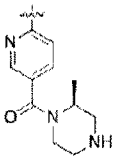
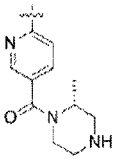
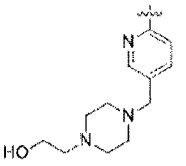
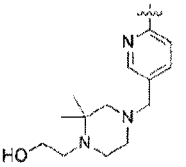
[Table 4-193]

Compound No.	L	R^1	R^2	R^3	
1152					
1153					
1154					
1155					
1156					
1157					

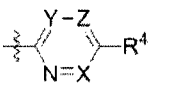
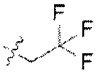
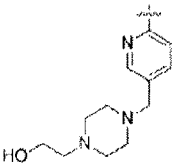
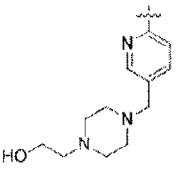
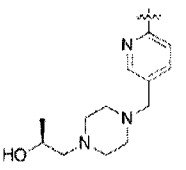
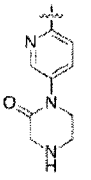
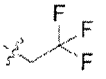
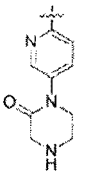
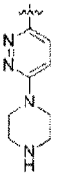
[Table 4-194]

Compound No.	L	R^1	R^2	R^3	
1158					
1159					
1160					
1161					
1162					
1163					

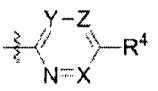
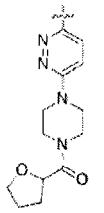
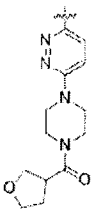
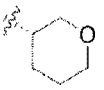
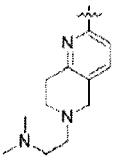
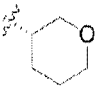
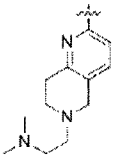
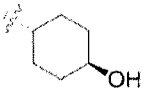
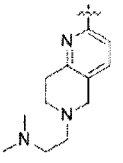
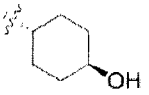
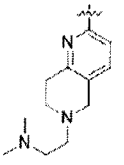
[Table 4-195]

Compound No.	L	R^1	R^2	R^3	
1164					
1165					
1166					
1167					
1168					
1169					

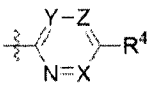
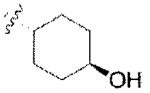
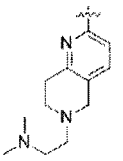
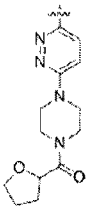
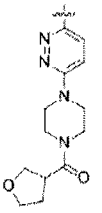
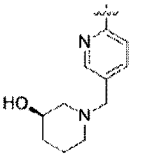
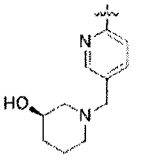
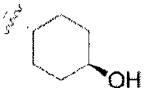
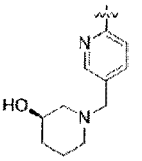
[Table 4-196]

Compound No.	L	R^1	R^2	R^3	
1170					
1171					
1172					
1173					
1174					
1175					

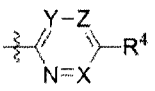
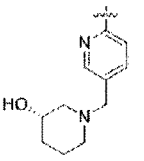
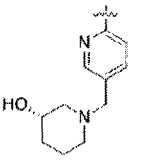
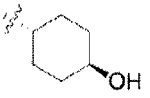
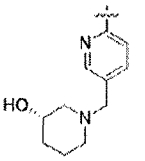
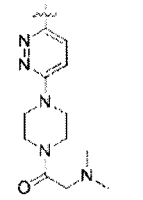
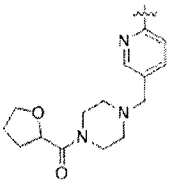
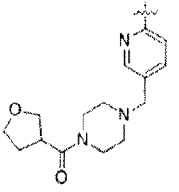
[Table 4-197]

Compound No.	L	R^1	R^2	R^3	
1176					
1177					
1178					
1179					
1180					
1181					

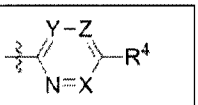
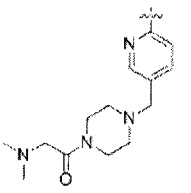
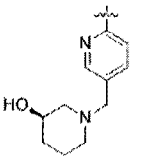
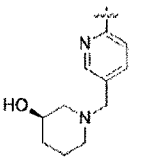
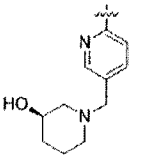
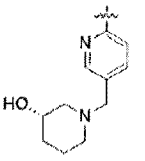
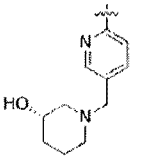
[Table 4-198]

Compound No.	L	R^1	R^2	R^3	
1182					
1183					
1184					
1185					
1186					
1187					

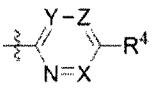
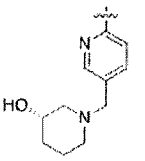
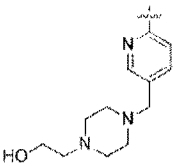
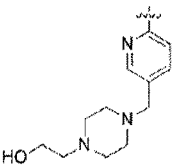
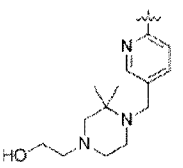
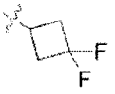
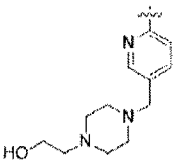
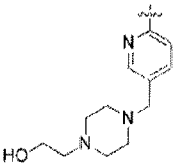
[Table 4-199]

Compound No.	L	R^1	R^2	R^3	
1188					
1189					
1190					
1191					
1192					
1193					

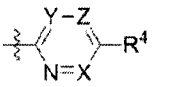
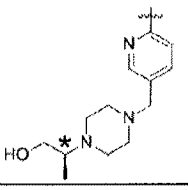
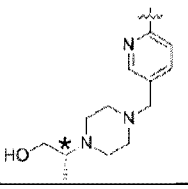
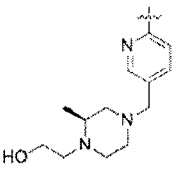
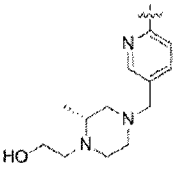
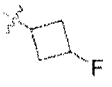
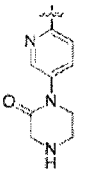
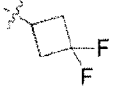
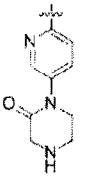
[Table 4-200]

Compound No.	L	R^1	R^2	R^3	
1194					
1195					
1196					
1197					
1198					
1199					

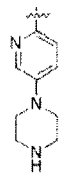
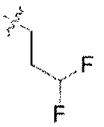
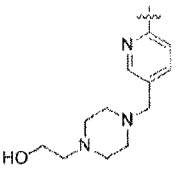
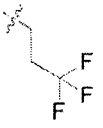
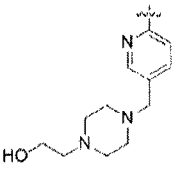
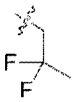
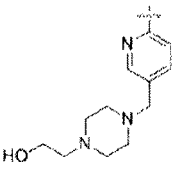
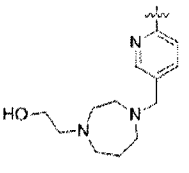
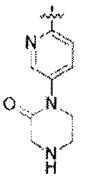
[Table 4-201]

Compound No.	L	R^1	R^2	R^3	
1200					
1201					
1202					
1203					
1204					
1205					

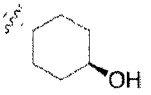
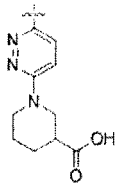
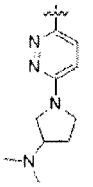
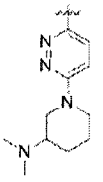
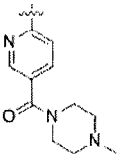
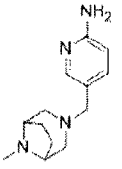
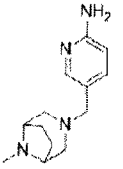
[Table 4-202]

Compound No.	L	R^1	R^2	R^3	
1206					*faster isomer 
1207					*later isomer 
1208					
1209					
1210					
1211					

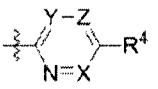
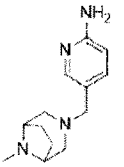
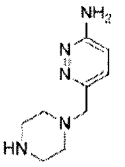
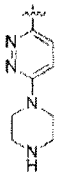
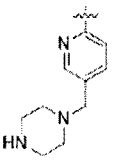
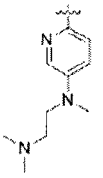
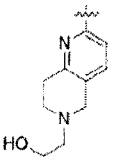
[Table 4-203]

Compound No.	L	R^1	R^2	R^3	
1212					
1213					
1214					
1215					
1216					
1217					

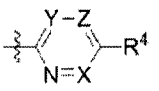
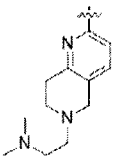
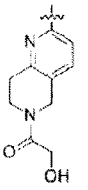
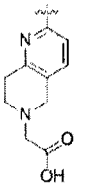
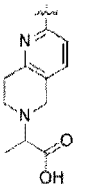
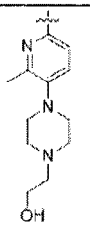
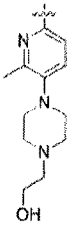
[Table 4-204]

Compound No.	L	R^1	R^2	R^3	
1218					
1219					
1220					
1221					
1222					
1223					

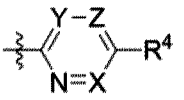
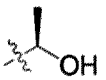
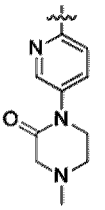
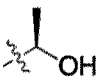
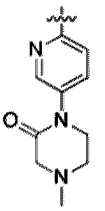
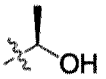
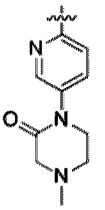
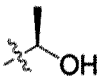
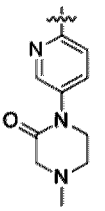
[Table 4-205]

Compound No.	L	R^1	R^2	R^3	
1224					
1225					
1226					
1227					
1228					
1229					

[Table 4-206]

Compound No.	L	R^1	R^2	R^3	
1230					
1231					
1232					
1233					
1234					
1235					

[Table 4-207]

Compound No.	L	R^1	R^2	R^3	
1236					
1237					
1238					
1239					

[0289] *: The compounds separated as optically active isomers by HPLC purification with a chiral column (note: absolute configuration is not determined).

Abbrebiations:

DEA: diethylamine, TEA = triethylamine, DCM: dichloromethane, IPA: isopropylalcohol

(1) Compound 581: DAICEL® CHIRALPAK® AD 5μm, n-hexane/MeOH/IPA, RT = 12.31 min.: optically active isomer

with shorter retention time.

(1) Compound 582: DAICEL® CHIRALPAK® AD 5μm, n-hexane/MeOH/IPA, RT = 15.35 min.: optically active isomer with longer retention time.

(2) Compound 671: CHIRALPAK® IA-3μm, 100%EtOH, RT= 4.388min.: optically active isomer with shorter retention time.

(2) Compound 672: CHIRALPAK® IA-3μm, 100%EtOH, RT= 6.490 min.: optically active isomer with longer retention time.

(3) Compound 689: DAICEL® CHIRALPAK® AD-H 5μm, n-hexane/EtOH, RT = 17.61 min.: optically active isomer with shorter retention time.

(3) Compound 690: DAICEL® CHIRALPAK® AD-H 5μm, n-hexane/EtOH, RT = 20.71 min.: optically active isomer with longer retention time.

(4) Compound 704: CHIRALPAK® AD-3μm, Hexane (0.2%TEA)/EtOH=50:50, RT = 6.446 min.: optically active isomer with longer retention time.

(4) Compound 705: CHIRALPAK® AD-3μm, Hexane (0.2%TEA)/EtOH=50:50, RT = 4.679 min.: optically active isomer with shorter retention time.

(5) Compound 713: CHIRALPAK® IA-3μm, 100%MeOH (0.1%DEA), RT = 3.628 min.: optically active isomer with longer retention time.

(5) Compound 714: CHIRALPAK® IA-3μm, 100%MeOH (0.1%DEA), RT = 2.533 min.: optically active isomer with shorter retention time.

(6) Compound 724: CHIRALPAK® AD-3, Hexane (0.1%DEA)/EtOH = 50:50, RT = 4.32 min.: optically active isomer with shorter retention time.

(6) Compound 725: CHIRALPAK® AD-3, Hexane (0.1%DEA)/EtOH = 50:50, RT = 5.06 min.: optically active isomer with longer retention time.

(7) Compound 729: CHIRALPAK® IA-3, 0.46*5cm; 3μm, Hexane

(0.1%IPA)/EtOH = 50:50, RT = 4.01 min.: optically active isomer with longer retention time.

(7) Compound 730: CHIRALPAK® IA-3, 0.46*5cm; 3μm, Hexane (0.1%IPA)/EtOH = 50:50, RT = 1.68 min.: optically active isomer with shorter retention time.

(8) Compound 735: DAICEL® CHIRALPAK® AD-H 5μm, Hexane/IPA = 90/10, RT = 9.18 min.: optically active isomer with shorter retention time.

(8) Compound 736: DAICEL® CHIRALPAK® AD-H 5μm, Hexane/IPA = 90/10, RT = 10.65 min.: optically active isomer with longer retention time.

(9) Compound 773: DAICEL® CHIRALPAK® IA 5μm, MeOH/IPA = 6/4, RT = 17.90 min.: optically active isomer with shorter retention time.

(9) Compound774: DAICEL® CHIRALPAK® IA 5μm, MeOH/IPA = 6/4, RT = 21.84 min.: optically active isomer with longer retention time.

(10) Compound 775: DAICEL® CHIRALPAK® IA 5μm, Hexane/MeOH/IPA = 6/1/1, RT = 10.25 min.: optically active isomer with shorter retention time.

(10) Compound776: DAICEL® CHIRALPAK® IA 5μm, Hexane/MeOH/IPA = 6/1/1, RT = 14.71 min.: optically active isomer with longer retention time.

(11) Compound 809: DAICEL® CHIRALPAK® AD-H 5μm, 4.6*250mm, n-Hexane/EtOH/MeOH = 70/15/15, RT = 21.62 min.: optically active isomer with shorter retention time.

(11) Compound 810: DAICEL® CHIRALPAK® AD-H 5μm, 4.6*250mm, n-Hexane/EtOH/MeOH = 70/15/15, RT = 25.87 min.: optically active isomer with longer retention time.

(12) Compound 865: CHIRALPAK® IA-3; 0.46*5cm; 3μm; Hexane (0.1%DEA)/EtOH = 70:30, RT = 4.81 min.: optically active isomer with shorter retention time.

(12) Compound 866: CHIRALPAK® IA-3; 0.46*5cm; 3μm; Hexane

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(0.1%DEA)/EtOH = 70:30, RT = 5.48 min.: optically active isomer with longer retention time.

(13) Compound 869: CHIRALPAK® IA-3; 0.46*5cm; 3μm; Hexane (0.1%DEA)/EtOH = 60:40, RT = 2.27 min.: optically active isomer with shorter retention time.

(13) Compound 870: CHIRALPAK® IA-3; 0.46*5cm; 3μm; Hexane (0.1%DEA)/EtOH = 60:40, RT = 2.93 min.: optically active isomer with longer retention time.

(14) Compound 875: DAICEL® CHIRALPAK® AD-H 5μm, Hexane/MeOH/EtOH = 80/10/10, RT = 22.30 min.: optically active isomer with shorter retention time.

(14) Compound 876: DAICEL® CHIRALPAK® AD-H 5μm, Hexane/MeOH/EtOH = 80/10/10, RT = 29.24 min.: optically active isomer with longer retention time.

(15) Compound 938: DAICEL® CHIRALPAK® AD-H 5μm, (100%EtOH+0.1%DEA), RT = 33.58 min.: optically active isomer with shorter retention time.

(15) Compound939: DAICEL® CHIRALPAK® AD-H 5μm, (100%EtOH+0.1%DEA), RT = 42.68 min.: optically active isomer with longer retention time.

(16) Compound 940: DAICEL® CHIRALPAK® AD-H 5μm, (Hexane/MeOH/EtOH +0.1%DEA = 6/2/2), RT = 20.23 min.: optically active isomer with shorter retention time.

(16) Compound 941: DAICEL® CHIRALPAK® AD-H 5μm, (Hexane/MeOH/EtOH +0.1%DEA = 6/2/2), RT = 22.07 min.: optically active isomer with longer retention time.

(17) Compound 942: DAICEL® CHIRALPAK® AD-H 5μm, (Hexane/MeOH/EtOH +0.1%DEA = 6/2/2), RT = 13.99 min.: optically active isomer with shorter retention time.

(17) Compound 943: DAICEL® CHIRALPAK® AD-H 5μm, (Hexane/MeOH/EtOH +0.1%DEA = 6/2/2), RT = 15.66 min.: optically active isomer with longer retention time.

(18) Compound 989: CHIRALPAK® IA, n-Hexane/EtOH = 70/30,

RT = 13.32 min.: optically active isomer with shorter retention time.

(18) Compound 990: CHIRALPAK® IA, n-Hexane/EtOH = 70/30, RT = 16.69 min.: optically active isomer with longer retention time.

(19) Compound 992: CHIRALPAK® IA-3: 0.46*5cm; 3μm, Hexane (0.1%DEA)/EtOH = 50:50, 1.5ml/min, RT = 1.87 min.: optically active isomer with shorter retention time.

(19) Compound 993: CHIRALPAK® IA-3: 0.46*5cm; 3μm, Hexane (0.1%DEA)/EtOH = 50:50, 1.5ml/min, RT = 3.56 min.: optically active isomer with longer retention time.

(20) Compound 1025: CHIRALPAK® IA, 0.46*25cm; 5μm, MeOH (0.1%DEA)/DCM = 75:25, 1.0mL/min., RT = 6.597 min.: optically active isomer with shorter retention time.

(20) Compound 1026: CHIRALPAK® IA, 0.46*25cm; 5μm, MeOH (0.1%DEA)/DCM = 75:25, 1.0mL/min., RT = 8.199 min.: optically active isomer with longer retention time.

(21) Compound 1034: CHIRALPAK® AS-3, 0.46*10cm; 3μm, Hexane (0.1%DEA)/(MeOH/EtOH = 1:1) = 70:30, 1.0mL/min., RT = 6.23 min.: optically active isomer with shorter retention time.

(21) Compound 1035: CHIRALPAK® AS-3, 0.46*10cm; 3μm, Hexane (0.1%DEA)/(MeOH/EtOH = 1:1) = 70:30, 1.0mL/min., RT = 9.94 min.: optically active isomer with longer retention time.

(22) Compound 1036: CHIRALPAK® IC-3, 0.46*10cm; 3μm, DCM (0.1%DEA)/MeOH = 20:80, 1.0mL/min., RT = 5.10 min.: optically active isomer with shorter retention time.

(22) Compound 1037: CHIRALPAK® IC-3, 0.46*10cm; 3μm, DCM (0.1%DEA)/MeOH = 20:80, 1.0mL/min., RT = 5.95 min.: optically active isomer with longer retention time.

(23) Compound 1066: CHIRALPAK® IC-3, 0.46*10cm; 3μm, MeOH (0.1%DEA)/DCM = 95:5, 1.0ml/min., RT = 5.421 min.: optically active isomer with shorter retention time.

(23) Compound 1067: CHIRALPAK® IC-3, 0.46*10cm; 3μm, MeOH

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(0.1%DEA)/DCM = 95:5, 1.0ml/min., RT = 6.00 min.: optically active isomer with longer retention time.

(24) Compound 1068: CHIRALPAK® IC, 0.46*25cm; 5μm, MeOH (0.1%DEA)/DCM = 90:10, 1.0ml/min., RT = 17.429 min.: optically active isomer with shorter retention time.

(24) Compound 1069: CHIRALPAK® IC, 0.46*25cm; 5μm, MeOH (0.1%DEA)/DCM = 90:10, 1.0ml/min., RT = 20.57 min.: optically active isomer with longer retention time.

(25) Compound 1088: CHIRALPAK® IA, n-Hexane/EtOH/MeOH = 50/25/25, 1.0 mL/min., RT = 15.21 min.: optically active isomer with shorter retention time.

(25) Compound 1089: CHIRALPAK® IA, n-Hexane/EtOH/MeOH = 50/25/25, 1.0 mL/min., RT = 18.59 min.: optically active isomer with longer retention time.

[0290] *: Compound separated as diastereomers by reversed phase HPLC purification (note: absolute configuration is not determined).

(1) Compound 831: C-18: RT = 1.67 min.: diastereomer with shorter retention time.

(1) Compound 832: C-18: RT = 1.71 min.: diastereomer with longer retention time.

[0291] *: Compound represented its relative configurations of two substituents.

Compound#: 577, 607, 608, 609, 610, 618, 619, 621, 622, 645, 646, 647, 673, 708, 739, 742, 799, 801, and 864.

[0292]

[Table 5-1]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
1	1H-NMR (DMSO-D6) δ: 10.33 (1H, s), 9.32 (1H, s), 8.74 (1H, br s), 8.09-8.11 (2H, m), 7.59-7.62 (1H, m), 7.22 (1H, s), 6.96 (1H, t, J = 51.1 Hz), 6.67-6.94 (2H,m), 4.38-4.43 (1H, m), 3.36-3.37 (4H, br m), 3.28 (4H, br s), 2.05-2.10 (2H, m), 1.60-1.67 (2H, m), 1.71-1.76 (2H, m), 1.60-1.67 (4H, m).	441.42	440.22
2	1H-NMR (CD3OD) δ: 9.45 (1H, s), 8.14(1H, dd, J = 9.60, 2.68 Hz), 8.00 (1H, d, J = 2.76Hz), 7.72 (1H, d, J = 23.5Hz), 7.39 (1H, s), 6.64 (1H, t, J = 55.6 Hz), 4.57 (1H, br m), 3.69 (1H, dd, J = 12.2, 3.44 Hz), 3.51-3.54 (3H, m), 3.35-3.47 (6H, m), 3.08-3.15 (2H, m), 2.14-2.21 (2H, br m), 1.94-1.96 (2H, br m).	456.38	455.24
3	1H-NMR (CD3OD) δ: 9.37 (1H, s), 8.16 (1H, d, J = 9.1 Hz), 7.92 (1H, br, s), 7.63 (1H, d, J = 9.1 Hz), 7.24 (1H, s), 6.58 (1H, t, J = 55.7 Hz), 4.41-4.45 (1H, m), 3.52 (4H, br s), 3.44 (4H, br, s), 2.65 (2H, s), 1.35 (6H, d, J = 6.5 Hz).	415.36	414.21
4	1H-NMR (CD3OD) δ: 9.41 (1H, s), 8.22(1H, dd, J = 9.44, 2.72 Hz), 7.94 (1H, d, J = 2.68Hz), 7.60 (1H, d, J = 9.56 Hz), 7.30 (1H, s), 6.60 (1H, t, J = 55.7 Hz), 4.36-4.41 (1H, m), 3.94-4.04 (2H, br m), 3.58-3.64 (2H, m), 3.53-3.58 (4H, m), 3.39-3.45 (4H, m), 2.10-2.13 (2H, br m), 1.69-1.79 (2H, m), 1.14 (2H, d, J = 6.04Hz).	457.39	456.22
6	1H-NMR (CD3OD) δ: 9.05 (1H, s), 8.10 (1H, d, J = 9.1 Hz), 8.00 (1H, d, 2.9 Hz), 7.51 (1H, dd, J = 9.1, 2.9 Hz), 6.90 (1H, s), 4.59 (2H, s), 4.48-4.52 (1H, m), 3.15-3.16 (4H, m), 3.01-3.04 (4H, m), 2.11-2.14 (2H, m), 1.80-1.83 (2H, m), 1.70-1.73 (2H, m), 1.61-1.64 (2H, m).	421.2	420.24
7		416.22	415.19

[Table 5-2]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
8	1H-NMR (CD3OD) δ: 9.06 (1H, s), 8.15 (1H, d, J = 9.1 Hz), 8.02 (1H, d, 2.9 Hz), 7.55 (1H, dd, J = 9.1, 2.9 Hz), 6.91 (1H, s), 4.58 (5H, s), 4.48-4.50 (1H, m),3.20-3.22 (4H, m), 2.13-2.15 (2H, m), 1.92 (3H, s), 1.62-1.82 (6H, m),1.50 (3H, d, J = 6.6 Hz).	435.21	434.25
9	1H-NMR (CD3OD) δ: 9.05 (1H, s), 8.14(1H, br s), 8.01 (1H,br s), 7.53 (1H, d, J = 9.0 Hz), 6.90 (1H, s), 4.72-4.77 (1H, m), 4.35-4.42 (1H, m), 3.18-3.20 (4H, br m), 3.07 (4H, br s), 1.49 (3H, d, J = 6.52 Hz), 1.33 (6H, dd, J = 6.48, 2.24 Hz)	409.35	408.24
12	1H-NMR (CD3OD) δ: 9.17 (1H, s), 7.98-8.01(2H, br m), 7.78-7.80(1H, br m), 7.01 (1H, s), 4.77-4.86 (1H, m), 4.36 (1H, br m), 4.00-4.03 (2H, br m), 3.63 (2H, apparent t, J = 11.3 Hz), 3.43-3.44 (8H, br m), 2.11-2.14 (2H, br m), 1.70-1.73 (2H, br m), 1.50 (3H, d, J = 6.52 Hz)	451.31	450.25
13	1H-NMR (CD3OD) δ: 9.36 (1H, s), 8.12(1H, dd, J = 9.52, 2.84 Hz), 7.93 (1H, d, J = 2.72Hz), 7.67 (1H, d, J = 9.48 Hz), 7.26 (1H, s), 6.60 (1H, t, J = 55.76 Hz), 3.43-3.52 (8H, m), 1.59 (9H, s).	429.32	428.22
15	1H-NMR (CD3OD) δ: 9.40 (1H, s), 8.16(1H, dd, J = 9.48, 2.84 Hz), 7.97 (1H, d, J = 2.88Hz), 7.66 (1H, d, J = 9.52 Hz), 7.30 (1H, s), 6.61 (1H, t, J = 55.72 Hz), 3.83-3.85 (2H, m), 3.69-3.72 (2H, m), 3.42-3.53 (8H, m), 3.42 (3H, s).	431.27	430.20
16	1H-NMR (CD3OD) δ: 9.05 (1H, s), 8.14(1H, br s), 8.01 (1H,br s), 7.53 (1H, d, J = 9.0 Hz), 6.90 (1H, s), 4.72-4.77 (1H, m), 4.35-4.42 (1H, m), 3.18-3.20 (4H, br m), 3.07 (4H, br s), 1.49 (3H, d, J = 6.52 Hz), 1.33 (6H, dd, J = 6.48, 2.24 Hz)		

[Table 5-3]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
17	1H-NMR (CD3OD) δ: 9.05 (1H, s), 8.14(1H, br s), 8.01 (1H,br s), 7.53 (1H, d, J = 9.0 Hz), 6.90 (1H, s), 4.72-4.77 (1H, m), 4.35-4.42 (1H, m), 3.18-3.20 (4H, br m), 3.07 (4H, br s), 1.49 (3H, d, J = 6.52 Hz), 1.33 (6H, dd, J = 6.48, 2.24 Hz)		
18	1H-NMR (CD3OD) δ: 9.42 (1H, s), 8.20(1H, dd, J = 9.64, 2.68 Hz), 7.96 (1H, d, J = 2.48Hz), 7.60 (1H, d, J = 9.56 Hz), 7.36 (1H, s), 6.66 (1H, t, J = 55.64 Hz), 3.43-3.55 (8H, m), 2.98-3.00(1H, m), 0.90-0.93(2H, m), 0.70-0.72(2H, m).	413.32	412.19
19	1H-NMR (DMSO) δ: 9.98 (1H, s), 9.26 (1H, s), 8.28(1H, d, J = 9.04 Hz), 8.04 (1H, d, J = 2.84Hz), 7.43 (1H, dd, J = 9.08, 2.88 Hz), 7.16-7.18 (2H, br m), 6.81 (1H, t, J = 55.64 Hz), 3.05-3.06 (7H, m), 2.85-2.87 (4H, m), 1.23(1H, s).	387.22	386.18
20	1H-NMR (DMSO) δ: 9.99 (1H, s), 9.26 (1H, s), 8.21(1H, d, J = 9.08 Hz), 8.03 (1H, d, J = 2.80Hz), 7.45 (1H, dd, J = 9.04, 2.92 Hz), 7.17 (1H, s), 7.07 (1H, t, J = 5.72), 6.79(1H, t, J = 55.56 Hz), 3.56(1H, q, J =6.6 Hz), 3.05-3.07 (4H, m), 2.85-2.87 (4H, m), 1.25(3H, t, 7.08 Hz).	401.32	400.19
21	1H-NMR (CD3OD) δ: 9.07 (1H, s), 8.13 (1H, d, J = 9.08 Hz), 7.99 (1H, d, J = 2.84Hz), 7.54 (1H, dd, J = 9.08, 2.96 Hz), 6.98 (1H, s), 4.79-4.82 (1H, m), 3.15-3.21 (4H, m), 3.02-3.04 (3H, m), 2.93-2.95 (1H, m), 2.86-2.89 (1H, m), 1.51 (1H, d, J = 6.52 Hz), 0.85-0.88 (2H, m), 0.62 (2H, br s).	407.37	406.22
22	1H-NMR (CD3OD) δ: 9.07 (1H, s), 8.30 (1H, d, J = 9.16 Hz), 8.03-8.09 (2H, br m), 7.95 (1H, d, J = 7.48 Hz), 7.58-7.59 (1H, br m), 7.50-7.54 (1H, br m), 6.91 (1H, s), 4.75-4.79 (1H, m), 3.30 (8H, br s), 3.12 (3H, s), 1.50 (3H, d, J = 6.48 Hz).	381.24	380.21

[Table 5-4]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
23	1H-NMR (DMSO-d6) δ: 9.73 (1H, s), 9.19 (1H, s), 8.24 (1H, d, J = 9.04 Hz), 8.03 (1H, d, J = 2.72 Hz), 7.45 (1H, dd, J = 9.12, 2.84 Hz), 6.91 (1H, s), 6.79 (1H, t, J = 5.64 Hz), 5.16 (1H, Br m), 4.60-4.62 (1H, m), 3.54-3.57 (2H, m), 3.08-3.10 (4H, m), 2.91-2.93 (4H, m), 1.38 (3H, d, 6.48 Hz), 1.25 (3H, t, J = 7.08 Hz).	395.33	394.22
24	1H-NMR (DMSO-d6) δ: 9.86 (1H, s), 9.17 (1H, s), 8.01-8.06 (2H, m), 7.45 (1H, d, J = 9.24 Hz), 6.95 (1H, s), 6.40 (1H, s), 5.17 (1H, d, J = 4.72 Hz), 4.62-4.64 (1H, m), 3.05-3.06 (4H, m), 2.87 (4H, br s), 1.53 (9H, s), 1.40 (3H, d, 6.40 Hz), 1.05 (2H, br s).	423.3	422.25
25	1H-NMR (CD3OD) δ: 8.81 (1H, s), 8.37 (1H, d, J = 8.28 Hz), 7.98 (1H, br s), 7.46 (1H, d, J = 6.68 Hz), 6.29 (1H, br s), 4.67 (1H, br s), 4.41-4.51 (2H, br m), 4.28 (1H, br s), 3.75 (2H, br s), 3.12 (4H, br s), 2.99 (4H, br s), 1.50 (3H, br s).	423.4	422.22
26	1H-NMR (DMSO-d6) δ: 9.97 (1H, s), 9.33 (1H, s), 8.79 (1H, s), 8.24 (1H, d, J = 7.6 Hz), 7.99-8.21 (3H, m), 7.55 (1H, dd, J = 12.4, 4.0 Hz), 7.36-7.42 (2H, m), 7.25 (1H, s), 7.00-7.05 (1H, m), 5.35 (1H, d, J = 6.0 Hz), 4.70-4.76 (1H, m), 3.06-3.09 (4H, m), 2.85-2.95 (4H, m), 1.47 (3H, d, J = 8.8 Hz).	443.2	442.22
27	1H-NMR (DMSO-d6) δ: 12.35 (1H, s), 10.05 (1H, s), 9.33 (1H, s), 8.79 (1H, s), 8.07 (2H, br s), 7.73 (1H, s), 7.50 (1H, d, J = 5.6 Hz), 7.22 (1H, s), 7.00 (1H, s), 5.33 (1H, s), 4.75 (1H, br s), 3.236-3.26 (4H, m), 2.97 (4H, br s), 1.48 (3H, d, J = 8.8 Hz).	433.2	432.21

[Table 5-5]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
28	1H-NMR (DMSO-d6) δ: 9.84 (1H, s), 9.20 (1H, s), 8.02-8.10 (2H, m), 7.42 (1H, d, J = 12 Hz), 6.98 (1H, s), 6.56 (1H, t, J = 10.4 Hz), 5.18 (1H, t, J = 5.6 Hz), 4.60-4.63 (1H, m), 4.28-4.35 (1H, m), 3.51-3.57 (2H, m), 3.33-3.37 (3H, m), 3.03-3.06 (4H, m), 2.84-2.87 (4H, m), 1.44 (3H, d, J = 8.8 Hz), 1.30 (3H, d, J = 8.8 Hz).	439.3	438.25
29	1H-NMR (DMSO-d6) δ: 9.89 (1H, s), 9.18 (1H, s), 8.03-8.08 (2H, m), 7.41 (1H, dd, J = 12.0, 3.6 Hz), 6.97 (1H, s), 6.67 (1H, s), 5.18 (1H, d, J = 6.0 Hz), 4.58-4.64 (1H, m), 3.57-3.60 (2H, m), 3.28-3.38 (3H, m), 3.02-3.06 (4H, m), 2.84-2.87 (4H, m), 1.51 (6H,s), 1.39 (3H, d, J = 8.4 Hz).	453.4	452.26
30	1H-NMR (DMSO-d6) δ: 10.15 (1H, s), 9.29 (1H, s), 8.05-8.08 (2H, m), 7.44 (1H, dd, J = 12.0, 3.6 Hz), 7.21 (1H, s), 6.62-6.98 (2H, m), 4.34-4.38 (1H, m), 3.55-3.58 (2H, m), 3.22-3.40 (3H, m), 3.12-3.16 (4H, m), 2.91-2.97 (4H, m),1.28 (3H, d, J = 8.8 Hz).	445.2	444.22
31	1H-NMR (DMSO-d6) δ: 10.17 (1H, s), 9.26 (1H, s), 8.00-8.06 (2H, m), 7.42 (1H, dd, J = 12.0, 3.6 Hz), 7.19 (1H, s), 6.62-6.99 (2H, m), 3.56 (2H, s), 3.29-3.38 (3H, m), 3.04-3.07 (4H, m), 2.84-2.87 (4H, m), 1.51 (6H, s).	459.15	458.24
32	1H-NMR (DMSO-d6) δ: 12.56 (1H, br s), 9.69 (1H, s), 9.25 (1H, s), 8.78 (1H, s), 8.25-8.28 (2H, m), 8.02-8.03 (1H, m), 7.50 (1H, d, J = 5.6 Hz), 7.09 (1H, s), 5.26 (1H, d, J = 6 Hz), 4.75 (1H, br s), 3.05-3.08 (4H, m), 2.86-2.89 (4H, m), 1.45 (3H, d, J = 8.4 Hz).	433.1	432.21

[Table 5-6]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
33	1H-NMR (CD3OD) δ: 9.45 (1H, s), 8.82 (1H, d, J = 9.56 Hz), 8.17-8.20 (2H, m), 7.35 (1H, s), 6.60 (1H, t, J = 55.56 Hz), 5.47 (1H, dd, J = 9.80, 2.24 Hz), 5.09 (1H, t, J = 12.64 Hz), 4.89-4.90 (1H, m), 4.29 (1H, dd, J = 12.00, 3.08 Hz), 3.86 (1H, dd, J = 12.04, 1.72 Hz), 3.30-3.34 (4H, m), 3.07-3.10 (4H, m).	429.25	428.19
34	1H-NMR (DMSO-d6) δ: 9.96 (1H, s), 9.18 (1H, s), 8.04 (1H, d, J = 9.2 Hz), 7.98 (1H, d, J = 2.8 Hz), 7.43 (1H, dd, J = 8.8, 2.8 Hz), 7.046 (1H, s), 6.47 (1H, d, J = 7.6 Hz), 4.16-4.21 (1H, m), 3.09 (6H, br s), 2.99 (4H, br s), 2.93 (9H, br s), 1.23 (6H, d, J = 6.8 Hz).	436.2	435.25
36	1H-NMR (CD3OD) δ: 9.14 (1H, s), 8.25 (1H, d, J = 2.9 Hz), 7.59 (1H, dd, J = 8.9, 3.0 Hz), 7.49 (1H, d, J = 8.9 Hz), 7.09 (1H, s), 6.21-6.48 (2H, m), 4.91-4.96 (1H, m), 4.67-4.75 (2H, m), 3.50-3571 (4H, m), 3.43-3.46 (4H, m), 1.56 (1H, d, J = 6.5 Hz).	431.35	430.20
37	1H-NMR (DMSO-d6) δ: 9.92 (1H, s), 9.20 (1H, s), 8.64 (1H, s), 8.15 (1H, d, J = 9.3 Hz), 8.08 (1H, d, J = 2.9 Hz), 7.53 (1H, dd, J = 9.3, 2.9 Hz), 6.87 (1H, s), 6.38 (1H, d, J = 7.8 Hz), 4.25 (2H, td, J = 12.4, 6.5 Hz), 3.31 (10H, s), 3.26 (4H, s), 3.23 (4H, d, J = 5.4 Hz), 1.38 (3H, d, J = 6.3 Hz), 1.29 (6H, dd, J = 6.3, 3.4 Hz).	423.2	422.25
38	1H-NMR (DMSO-d6) δ: 9.92 (1H, s), 9.20 (1H, s), 8.64 (1H, s), 8.15 (1H, d, J = 9.3 Hz), 8.08 (1H, d, J = 2.9 Hz), 7.53 (1H, dd, J = 9.3, 2.9 Hz), 6.87 (1H, s), 6.38 (1H, d, J = 7.8 Hz), 4.25 (2H, td, J = 12.4, 6.5 Hz), 3.31 (10H, s), 3.26 (4H, s), 3.23 (4H, d, J = 5.4 Hz), 1.38 (3H, d, J = 6.3 Hz), 1.29 (6H, dd, J = 6.3, 3.4 Hz).		

[Table 5-7]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
39	1H-NMR (DMSO-d6) δ: 9.92 (1.0H, s), 9.20 (1.0H, s), 8.64 (1.1H, s), 8.15 (1.2H, d, J = 9.3 Hz), 8.08 (1.1H, d, J = 2.9 Hz), 7.53 (1.0H, dd, J = 9.3, 2.9 Hz), 6.87 (1.0H, s), 6.38 (1.0H, d, J = 7.8 Hz), 4.25 (2.1H, td, J = 12.4, 6.5 Hz), 3.31 (9.8H, s), 3.26 (3.6H, s), 3.23 (4.5H, d, J = 5.4 Hz), 1.38 (3.1H, d, J = 6.3 Hz), 1.29 (6.7H, dd, J = 6.3, 3.4 Hz).	423.25	422.25
40	1H-NMR (DMSO-d6) δ: 9.80 (1H, s), 9.26 (1H, s), 8.26 (1H, d, J = 12.0 Hz), 8.03 (1H, d, J = 4.0 Hz), 7.40 (1H, dd, J = 12.0, 4.0 Hz), 7.20 (1H, d, J = 9.2 Hz), 7.12 (1H, s), 5.34 (1H, d, J = 6.4 Hz), 4.62-4.66 (1H, m), 4.38-4.45 (2H, br m), 3.03-3.06 (4H, m), 2.84-2.87 (4H, m), 1.38 (3H, d, J = 8.8 Hz).	449.2	448.19
41	1H-NMR (DMSO-d6) δ: 9.82 (1H, s), 9.19 (1H, s), 8.13 (1H, d, J = 12.4 Hz), 8.01 (1H, d, J = 4.0 Hz), 7.42 (1H, dd, J = 12.4, 4.0 Hz), 6.97 (1H, s), 6.58 (1H, t, J = 10.4 Hz), 5.17 (1H, t, J = 6.4 Hz), 4.97-5.00 (1H, m), 4.59-4.62 (1H, m), 4.17-4.19 (1H, br m), 3.57-3.60 (1H, m), 3.03-3.06 (4H, m), 2.84-2.87 (4H, m), 1.38 (3H, dd, J = 8.4, 1.6 Hz), 1.25 (3H, d, J = 4.8 Hz).	425.4	424.23
42	1H-NMR (DMSO-d6) δ: 10.05 (1H, s), 9.27 (1H, s), 8.04-8.10 (2H, m), 7.49 (1H, dd, J = 12.0, 4.0 Hz), 7.19 (1H, s), 6.79 (1H, t, J = 62.8 Hz), 6.61 (1H, s), 4.21-4.32 (1H, m), 3.14-3.17 (1H, m), 3.03-3.06 (4H, m), 2.46-2.50 (4H, m), 2.20 (3H, s), 1.30 (6H, d, J = 8.4 Hz).	429.15	428.22
43	1H-NMR (DMSO-d6) δ: 10.08 (1H, s), 9.28 (1H, s), 8.06-8.12 (2H, m), 7.50 (1H, dd, J = 12.0, 4.4 Hz), 7.19 (1H, s), 6.79 (1H, t, J = 74.4 Hz), 6.61 (1H, s), 4.21-4.32 (1H, m), 3.75-3.79 (4H, m), 3.10-3.15 (4H, m), 1.30 (6H, d, J = 8.0 Hz).	416	415.19

[Table 5-8]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
44	1H-NMR (DMSO-d6) δ: 9.82 (1H, s), 9.19 (1H, s), 8.08 (1H, d, J = 12.4 Hz), 8.01 (1H, d, J = 4.0 Hz), 7.46 (1H, dd, J = 12.8, 4.4 Hz), 6.88 (1H, s), 6.61 (1H, d, J = 10.0 Hz), 4.38 (2H, s), 4.25 (1H, br m), 3.40 (3H, s), 3.03-3.06 (4H, m), 2.84-2.87 (4H, m), 1.28 (6H, d, J = 8.8 Hz).	409.2	408.24
45	1H-NMR (DMSO-d6) δ: 9.87 (1H, s), 9.17 (1H, s), 8.10 (1H, d, J = 12.4 Hz), 8.02 (1H, d, J = 4.0 Hz), 7.46 (1H, dd, J = 12.8, 4.4 Hz), 6.95 (1H, s), 6.87 (1H, s), 5.39 (1H, br m), 5.17 (1H, d, J = 6.0 Hz), 4.62 (1H, br m), 3.57 (1H, d, J = 6.4 Hz), 3.08-3.10 (4H, m), 2.93 (4H, br m), 1.46 (6H, s), 1.38 (3H, d, J = 8.8 Hz).	439.2	438.25
46	1H-NMR (DMSO-d6) δ: 10.27 (1H, s), 9.36 (1H, s), 8.24-8.26 (2H, m), 7.76 (1H, m), 7.25 (1H, s), 6.72 (1H, t, J = 42.0 Hz), 6.71 (1H, m), 4.25-4.35 (1H, m), 3.17-3.20 (2H, m), 2.73-2.76 (3H, m), 1.81 (2H, m), 1.67 (2H, m), 1.34 (6H, d, J = 6.4 Hz).	414.3	413.21
47	1H-NMR (DMSO-d6) δ: 10.32 (1H, s), 9.37 (1H, s), 8.25-8.30 (2H, m), 7.80 (1H, dd, J = 8.4, 2.4 Hz), 7.25 (1H, s), 6.74 (1H, t, J = 40.0 Hz), 6.70 (1H, m), 4.25-4.35 (1H, m), 3.48 (2H, s), 2.78 (4H, br m), 2.35-2.38 (4H, br m), 1.34 (6H, d, J = 6.4 Hz).	429.4	428.22
48	1H-NMR (DMSO-d6) δ: 9.75 (1H, s), 9.22 (1H, s), 8.20 (1H, d, J = 9.2 Hz), 8.04 (1H, d, J = 2.8 Hz), 7.50 (1H, dd, J = 9.2, 3.2 Hz), 7.00 (1H, s), 6.75 (1H, d, J = 7.6 Hz), 5.19 (1H, d, J = 4.4 Hz), 4.60-4.66 (1H, br m), 3.06-3.09 (4H, m), 2.87-2.90 (4H, m), 2.36-2.41 (2H, m), 2.08-2.15 (2H, m), 1.76-1.80 (2H, m), 1.38 (3H, d, J = 8.8 Hz).	421.1	420.24

[Table 5-9]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
49	1H-NMR (DMSO-d6) δ: 10.04 (1H, s), 9.27 (1H, s), 8.04-8.09 (2H, m), 7.49 (1H, d, J = 4.0 Hz), 7.18 (1H, s), 6.61 (1H, t, J = 70.8 Hz), 6.58 (1H, m), 4.41-4.45 (1H, m), 4.25-4.35 (1H, m), 3.53-3.57 (2H, m), 3.13-3.16 (4H, m), 2.56-2.60 (4H, m), 2.42-2.46 (2H, m), 1.29 (6H, d, J = 8.8 Hz).	459.2	458.24
50	1H-NMR (DMSO-d6) δ: 10.01 (1H, s), 9.27 (1H, s), 8.04-8.07 (2H, m), 7.48 (1H, dd, J = 12.0, 4.8 Hz), 7.18 (1H, s), 6.79 (1H, t, J = 74.0 Hz), 6.58 (1H, m), 4.68 (1H, d, J = 5.6 Hz), 4.23-4.31 (1H, m), 3.63-3.64 (1H, m), 3.49-3.55 (2H, m), 2.86-2.90 (2H, m), 1.82-1.85 (2H, m), 1.49-1.52 (2H, m), 1.29 (6H, d, J = 8.8 Hz).	430.2	429.21
51	1H-NMR (DMSO-d6) δ: 10.02 (1H, s), 9.26 (1H, s), 8.03-8.07 (2H, m), 7.47 (1H, dd, J = 12.4, 4.4 Hz), 7.18 (1H, s), 6.79 (1H, t, J = 74.4 Hz), 6.58 (1H, m), 4.35-4.39 (1H, m), 4.23-4.28 (1H, m), 3.64-3.68 (2H, m), 3.31-3.36 (2H, m), 2.60-2.72 (2H, m), 1.74-1.78 (2H, m), 1.47-1.49 (2H, m), 1.23-1.28 (11H, m).	472.3	471.26
52	1H-NMR (DMSO-d6) δ: 9.88 (1H, s), 9.23 (1H, s), 8.00 (1H, d, J = 11.6 Hz), 7.69 (1H, d, J = 4.0 Hz), 7.06 (1H, dd, J = 12.0, 4.0 Hz), 6.78 (1H, t, J = 74.0 Hz), 6.56 (1H, d, 10.4 Hz), 4.25-4.27 (1H, m), 3.67-3.69 (1H, m), 3.43-3.47 (3H, m), 2.98-3.02 (1H, m), 2.11-2.17 (1H, m), 1.82-1.85 (1H, m), 1.29 (6H, d, J = 8.8 Hz).	415.05	414.21

[Table 5-10]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
53	1H-NMR (DMSO-d6) δ: 9.87 (1H, s), 9.23 (1H, s), 7.98 (1H, d, J = 9.2 Hz), 7.69 (1H, d, J = 2.8 Hz), 7.17 (1H, s), 7.06 (1H, dd, J = 9.2, 3.2 Hz), 6.78 (1H, t, J = 55.2 Hz), 6.56 (1H, d, 7.6 Hz), 4.98 (1H, d, 4.0 Hz), 4.42 (1H, br m), 4.26-4.27-3.69 (1H, m), 3.44-3.47 (1H, m), 3.31-3.36 (2H, m), 3.10-3.13 (1H, m), 2.06-2.08 (1H, m), 1.91-1.93 (1H, m), 1.30 (6H, d, J = 6.4 Hz).	416.05	415.19
54	1H-NMR (DMSO-d6) δ: 9.81 (1H, d, J = 5.6 Hz), 9.28 (1H, s), 8.07 (1H, d, J = 12.4 Hz), 8.01 (1H, d, J = 3.6 Hz), 7.44 (1H, dd, J = 11.6, 3.6 Hz), 7.12 (1H, d, J = 5.6 Hz), 6.62 (1H, d, J = 12.8 Hz), 5.24 (1H, dd, J = 10.8, 6.0 Hz), 4.64 (1H, br m), 3.03-3.06 (4H, m), 2.84-2.87 (4H, m), 1.47 (3H, d, J = 9.2 Hz), 1.37-1.40 (3H, m).	463.2	462.21
55	1H-NMR (DMSO-d6) δ: 10.33 (1H, s), 9.39 (1H, s), 8.02-8.05 (2H, m), 7.47 (1H, dd, J = 11.6, 4.0 Hz), 7.03 (1H, t, J = 71.6 Hz), 6.46 (1H, d, J = 10.8 Hz), 4.19-4.25 (1H, m), 3.05-3.08 (4H, m), 2.84-2.87 (4H, m), 1.29 (3H, d, J = 8.4 Hz).	433.3	432.20
56	1H-NMR (DMSO-d6) δ: 10.19 (1H, s), 9.36 (1H, s), 8.12 (1H, d, J = 12 Hz), 8.03 (1H, d, J = 3.6 Hz), 7.63 (1H, s), 7.48 (1H, dd, J = 12.0, 4.0 Hz), 6.64 (1H, d, J = 8.8 Hz), 4.23 (1H, br m), 4.23 (1H, br m), 3.92-3.96 (2H, m), 3.49-3.56 (2H, m), 3.06-3.09 (4H, m), 2.86-2.88 (4H, m), 2.52 (3H ,s), 2.06-2.10 (2H, m), 1.69-1.72 (2H, m).	449.1	448.23
57	1H-NMR (DMSO-d6) δ: 10.16 (1H, s), 9.35 (1H, s), 8.08 (1H, d, J = 12 Hz), 8.03 (1H, d, J = 3.6 Hz), 7.60 (1H, s), 7.46 (1H, dd, J = 11.6, 3.6 Hz), 6.63 (1H, d, J = 9.6 Hz), 4.42-4.44 (1H, br m), 3.05-3.08 (4H, m), 2.86-2.88 (4H, m), 2.61 (3H ,s), 2.16 (2H, br m), 1.63-1.77 (6H, m).	433.15	432.24

[Table 5-11]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
58	1H-NMR (DMSO-d6) δ: 10.10 (1H, s), 9.33 (1H, s), 8.23 (1H, d, J = 12 Hz), 8.04 (1H, d, J = 3.6 Hz), 7.59 (1H, s), 7.45 (1H, dd, J = 12.0, 4.0 Hz), 7.01 (1H, m), 3.62-3.66 (2H, m), 3.05-3.08 (4H, m), 2.84-2.88 (4H, m), 1.30(3H, t, 9.6 Hz).	393.3	392.21
59	1H-NMR (DMSO-d6) δ: 10.28 (1H, s), 9.34 (1H, s), 8.03 (2H, m), 7.60 (1H, s), 7.45 (1H, dd, J = 12.0, 4.0 Hz), 6.54 (1H, m), 3.04-3.07 (4H, m), 2.83-2.87 (4H, m), 1.58(9H, s).	421.1	420.24
60	1H-NMR (DMSO-d6) δ: 10.06 (1H, s), 9.43 (1H, s), 8.03-8.09 (2H, m), 7.47 (1H, dd, J = 12.4, 4.4 Hz), 6.80 (1H, t, J = 72.8 Hz), 6.35 (1H, d, J = 9.6 Hz), 4.22-4.31 (1H, m), 3.06-3.09 (4H, m), 2.87-2.90 (4H, m), 2.50 (3H, s), 1.30 (6H, d, J = 8.4 Hz).	429.1	428.22
61	1H-NMR (DMSO-d6) δ: 9.75 (1H, s), 9.18 (1H, s), 8.08 (1H, d, J = 12.0 Hz), 8.02 (1H, d, J = 4.0 Hz), 7.45 (1H, dd, J = 9.12, 2.84 Hz), 6.96 (1H, s), 6.35 (1H, m), 5.16 (1H, d, J = 6.0 Hz), 4.69-4.70 (1H, m), 4.69-4.70 (1H, m), 4.68-4.56 (1H, m), 4.18-4.31 (1H, m), 3.58-3.62 (1H, m), 3.44-3.52 (2H, m), 2.81-2.88 (2H, m), 1.82-1.88 (2H, m), 1.45-1.54 (2H, m), 1.38 (3H, d, J = 8.40 Hz), 1.29 (6H, dd, J = 8.8, 1.6 Hz).	424.1	423.24
62	1H-NMR (DMSO-d6) δ: 9.87 (1H, s), 9.37 (1H, s), 8.11 (1H, d, J = 9.08 Hz), 8.03 (1H, d, J = 2.84 Hz), 7.49 (1H, dd, J = 9.08, 2.92 Hz), 6.25 (1H, d, J = 7.96 Hz), 4.84 (1H, br s), 4.51 (2H, s), 4.27-4.32 (1H, m), 3.13-3.15 (4H, m), 2.97-2.99 (4H, m), 2.41 (3H, s), 1.29 (6H, d, J = 6.44 Hz).	437.4	408.24

[Table 5-12]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
63	1H-NMR (DMSO-d6) δ: 10.01 (1H, s), 9.32 (1H, s), 8.09 (1H, d, J = 9.2 Hz), 8.03 (1H, d, J = 3.2 Hz), 7.47 (1H, dd, J = 9.2, 3.2 Hz), 6.25 (1H, d, J = 7.6 Hz), 4.99 (1H, m), 4.92 (1H, d, J = 5.2 Hz), 4.27-4.29 (1H, m), 3.05-3.08 (4H, m), 2.85-2.87 (4H, m), 1.42 (3H, d, J = 6.4 Hz), 1.31 (6H, apparent t, J = 6.0 Hz).	427.1	426.23
64	1H-NMR (DMSO-d6) δ: 10.01 (1H, s), 9.32 (1H, s), 8.09 (1H, d, J = 9.2 Hz), 8.03 (1H, d, J = 3.2 Hz), 7.47 (1H, dd, J = 9.2, 3.2 Hz), 6.25 (1H, d, J = 7.6 Hz), 4.99 (1H, m), 4.92 (1H, d, J = 5.2 Hz), 4.27-4.29 (1H, m), 3.05-3.08 (4H, m), 2.85-2.87 (4H, m), 1.42 (3H, d, J = 6.4 Hz), 1.31 (6H, apparent t, J = 6.0 Hz).	427.2	426.23
65	1H-NMR (DMSO-d6) δ: 9.82 (1H, s), 9.36 (1H, s), 8.09 (1H, d, J = 12.0 Hz), 8.01 (1H, d, J = 4.0 Hz), 7.46 (1H, dd, J = 12.0, 4.0 Hz), 6.28 (1H, d, J = 10.0 Hz), 4.94-4.99 (1H, m), 4.73 (1H, d, J = 9.2 Hz), 4.25-4.32 (1H, m), 3.03-3.06 (4H, m), 2.83-2.87 (4H, m), 2.41 (3H, s), 2.27 (1H, br s), 1.29-1.36 (9H, m).	423.2	422.25
66	1H-NMR (DMSO-d6) δ: 9.82 (1H, s), 9.36 (1H, s), 8.09 (1H, d, J = 12.0 Hz), 8.01 (1H, d, J = 4.0 Hz), 7.46 (1H, dd, J = 12.0, 4.0 Hz), 6.28 (1H, d, J = 10.0 Hz), 4.94-4.99 (1H, m), 4.73 (1H, d, J = 9.2 Hz), 4.25-4.32 (1H, m), 3.03-3.06 (4H, m), 2.83-2.87 (4H, m), 2.41 (3H, s), 2.27 (1H, br s), 1.29-1.36 (9H, m).	423.2	422.25
67	1H-NMR (DMSO-d6) δ: 10.40 (1H, s), 9.32 (1H, s), 7.62 (1H, dd, J = 14.8, 11.6 Hz), 7.22 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.62 (1H, d, J = 2.8 Hz), 4.24-4.35 (1H, m), 2.89-3.09 (8H, m), 1.31 (6H, d, J = 8.4 Hz).	433.1	432.20

[Table 5-13]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
68	1H-NMR (DMSO-d6) δ: 10.16 (1H, d, J = 15.6 Hz), 9.52 (1H, d, J = 15.6 Hz), 8.09 (1H, d, J = 12 Hz), 8.04 (1H, d, J = 4.0 Hz), 7.47 (1H, dd, J = 12.0, 3.6 Hz), 6.37 (1H, d, J = 9.6 Hz), 4.19-4.28 (1H, m), 3.05-3.19 (4H, m), 2.84-2.87 (4H, m), 2.63 (3H ,s), 2.59 (3H ,s), 1.33 (6H, d, J = 8.4 Hz).	421.1	420.24
69	1H-NMR (DMSO-d6) δ: 9.72 (1H, s), 9.20 (1H, s), 8.26 (1H, d, J = 12.0 Hz), 8.00 (1H, d, J = 4.0 Hz), 7.31-7.42 (6H, m), 7.19-7.28 (1H, m) ,6.98 (1H, s), 5.13 (1H, d, J = 6.0 Hz), 4.76 (1H, d, J = 8.0 Hz), 4.55-4.59 (1H, m), 3.01-3.05 (4H, m), 2.83-2.87 (4H, m), 1.31 (3H, d, J = 8.8 Hz).	457.1	456.24
71	1H-NMR (DMSO-d6) δ: 9.78 (1H, s), 9.19 (1H, s), 8.10 (1H, d, J = 12.4 Hz), 8.02 (1H, d, J = 3.6 Hz), 7.50 (1H, dd, J = 12.4, 3.6 Hz), 6.96 (1H, s), 6.32 (1H, d, J = 10.0 Hz), 5.17 (1H, d, J = 6.0 Hz), 4.55-4.59 (1H, m), 4.18-4.31 (1H, m), 3.12-3.21 (4H, m), 2.45-2.49 (4H, m), 2.23 (3H, s), 1.38 (3H, d, J = 8.4 Hz), 1.29 (6H, dd, J = 8.4, 1.6 Hz).	423.4	422.25
72	1H-NMR (DMSO-d6) δ: 9.79 (1H, s), 9.20 (1H, s), 8.13 (1H, d, J = 12.4 Hz), 8.04 (1H, d, J = 4.0 Hz), 7.49 (1H, dd, J = 12.0, 4.0 Hz), 6.97 (1H, s), 6.34 (1H, d, J = 10.0 Hz), 5.17 (1H, d, J = 6.0 Hz), 4.58-4.66 (1H, m), 4.21-4.31 (1H, m), 3.75-3.88 (4H, m), 3.11-3.25 (4H, m), 1.48 (3H, d, J = 8.4 Hz), 1.38 (6H, d, J = 8.8 Hz).	410.3	409.22

[Table 5-14]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
74	1H-NMR (DMSO-d6) δ: 9.78 (1H, s), 9.19 (1H, s), 8.11 (1H, d, J = 12.0 Hz), 8.03 (1H, d, J = 4.0 Hz), 7.48 (1H, dd, J = 12.0, 4.0 Hz), 6.96 (1H, s), 6.33 (1H, d, J = 10.0 Hz), 5.17 (1H, d, J = 6.0 Hz), 4.61 (1H, m), 4.46 (1H, m), 4.42-4.44 (1H, m), 3.33-3.57 (2H, m), 3.12-3.15 (4H, m), 2.57-2.60 (4H, m), 2.42-2.49 (2H, m), 1.38 (3H, d, J = 8.4 Hz), 1.30 (6H, dd, J = 8.4, 1.6 Hz).	453.6	452.26
75	1H-NMR (DMSO-d6) δ: 9.76 (1H, s), 9.19 (1H, s), 8.05 (1H, d, J = 12.0 Hz), 8.02 (1H, d, J = 4.0 Hz), 7.47 (1H, dd, J = 12.0, 4.0 Hz), 6.96 (1H, s), 6.34 (1H, d, J = 10.0 Hz), 5.17 (1H, d, J = 6.0 Hz), 4.61 (1H, m), 4.38 (1H, m), 4.36-4..38 (1H, m), 3.61-3.64 (2H, m), 3.37-3.40 (2H, m), 2.52-2.56 (2H, m), 1.71-1.78 (2H, m), 1.40-1.42 (2H, m), 1.38 (3H, d, J = 8.8 Hz), 1.29 (6H, dd, J = 8.8, 1.6 Hz).	466.6	465.29
76	1H-NMR (DMSO-d6) δ: 9.57 (1H, s), 9.15 (1H, s), 8.03 (1H, d, J = 12.0 Hz), 7.66 (1H, d, J = 3.6 Hz), 7.03 (1H, dd, J = 12.0, 4.0 Hz), 6.94 (1H, s), 6.31 (1H, d, J = 10.0 Hz), 5.15 (1H, d, J = 6.0 Hz), 4.60-4.62 (1H, m), 4.21-4.28 (1H, m), 3.58-3.62 (1H, m), 3.41-3.46 (2H, m), 3.23-3.24 (1H, m), 2.89-2.94 (1H, m), 2.06-2.13 (2H, m), 1.72-1.76 (1H, m), 1.38 (3H, d, J = 8.8 Hz), 1.30 (6H, dd, J = 8.8, 1.2 Hz).	409.4	408.24

[Table 5-15]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
77	1H-NMR (DMSO-d6) δ: 9.58 (1H, s), 9.15 (1H, s), 8.02 (1H, d, J = 12.0 Hz), 7.67 (1H, d, J = 4.0 Hz), 7.06 (1H, dd, J = 12.0, 4.0 Hz), 6.94 (1H, s), 6.30 (1H, d, J = 10.0 Hz), 5.15 (1H, d, J = 6.0 Hz), 4.98 (1H, d, J = 5.2 Hz), 4.60-4.62 (1H, m), 4.42 (1H, br s), 4.21-4.28 (1H, m), 3.40-3.48 (1H, m), 3.09-3.12 (1H, m), 2.00-2.08 (1H, m), 1.88-1.93 (1H, m), 1.38 (3H, d, J = 8.4 Hz), 1.29 (6H, dd, J = 8.8, 1.2 Hz).	410.2	409.22
78	1H-NMR (DMSO-d6) δ: 9.94 (1H, s), 9.23 (1H, s), 8.22 (1H, d, J = 11.2 Hz), 8.18 (1H, d, J = 2.8 Hz), 7.71 (1H, d J = 3.6 Hz), 6.99 (1H, s), 6.40 (1H, d, J = 9.6 Hz), 5.18 (1H, d, J = 6.4 Hz), 4.58-4.66 (1H, m), 4.20-4.31 (1H, m), 3.02-3.06 (2H, m), 2.51-2.59 (3H, m), 1.69 (2H, br m), 1.55-1.56 (2H, m), 1.39 (3H, d, J = 8.4 Hz), 1.30 (6H, dd, J = 8.8, 2.0 Hz).	408.4	407.24
79	1H-NMR (DMSO-d6) δ: 10.03 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 11.6 Hz), 8.19 (1H, d, J = 2.4 Hz), 7.74 (1H, dd, J = 11.6, 2.4 Hz), 6.99 (1H, s), 6.42 (1H, d, J = 10.0 Hz), 5.19 (1H, d, J = 6.0 Hz), 4.61-4.66 (1H, m), 4.22-4.31 (1H, m), 3.54 (2H, s), 2.69-2.77 (4H, m), 2.27-2.31 (4H, m), 1.39 (3H, d, J = 8.4 Hz), 1.30 (6H, dd, J = 8.8, 1.6 Hz).	423.1	422.25
90		458.53	457.20

[Table 5-16]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
92	1H-NMR (DMSO-d6) δ: 9.78 (1H, s), 9.22 (1H, s), 8.13 (1H, d, J = 11.6 Hz), 8.00 (1H, d, J = 4.0 Hz), 7.45 (1H, dd, J = 12.0, 4.0 Hz), 6.65 (1H, s), 6.31 (1H, d, J = 8.0 Hz), 5.19 (1H, d, J = 3.2 Hz), 4.61-4.64 (2H, m), 3.88-4.01 (2H, m), 3.75-3.80 (1H, m), 3.64-3.69 (1H, m), 3.03-3.06 (4H, m), 2.84-2.87 (4H, m), 2.26-2.36 (1H, m), 1.98-2.02 (1H, m), 1.29 (3H, dd, J = 8.8, 2.8 Hz).	437.2	436.23
94	1H-NMR (DMSO-d6) δ: 10.32 (1H, s), 9.34 (1H, s), 8.27 (1H, d, J = 8.4 Hz), 8.24 (1H, d, J = 1.6 Hz), 7.78 (1H, dd, J = 8.4, 1.6 Hz), 7.22 (1H, s), 6.81 (1H, t, J = 55.6 Hz), 6.68 (1H, d, J = 9.6 Hz), 4.27-4.32 (1H, m), 3.57-3.59 (4H, m), 3.65 (2H, s), 2.38 (4H, br s), 1.31 (3H, d, J = 6.4 Hz).	430.2	429.21
99	1H-NMR (DMSO-d6) δ: 10.49 (1H, s), 9.38 (1H, s), 8.69 (1H, d, J = 2.8 Hz), 8.38 (1H, d, J = 8.8 Hz), 8.18 (1H, dd, J = 8.4, 2.4 Hz), 7.75 (2H, d, J = 7.2 Hz), 7.51 (1H, apparent t, J = 7.2 Hz), 7.49 (2H, apparent t, J = 8.0 Hz), 7.25 (1H, s), 6.83 (1H, t, J = 55.2 Hz), 6.74 (1H, d, J = 8.0 Hz), 4.30-4.33 (1H, m), 1.33 (6H, d, J = 6.4 Hz).	407.1	406.17
100	1H-NMR (DMSO-d6) δ: 10.63 (1H, s), 9.40 (1H, s), 8.45 (1H, s), 8.65 (2H, apparent d, J = 6.8 Hz), 8.44 (1H, d, J = 12.0 Hz), 8.32 (1H, d, J = 11.2 Hz), 7.81 (2H, apparent d, J = 7.2 Hz), 7.25 (1H, s), 6.82 (1H, t, J = 73.6 Hz), 6.75 (1H, d, J = 10.4 Hz), 4.30-4.33 (1H, m), 1.33 (6H, d, J = 8.8 Hz).	408.1	407.17
101		449.20	448.17

[Table 5-17]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
103	1H-NMR (DMSO-D6) δ: 10.17 (1H, s), 9.29 (1H, s), 8.15 (1H, d, J = 9.3 Hz), 8.07 (1H, d, J = 3.4 Hz), 7.52 (1H, dd, J = 8.8, 2.9 Hz), 7.19 (1H, s), 6.78 (1H, t, J = 55.6 Hz), 6.61 (1H, d, J = 7.8 Hz), 4.27 (1H, dd, J = 13.4, 6.6 Hz), 4.16-4.15 (2H, m), 3.55 (2H, t, J = 5.4 Hz), 3.46 (2H, t, J = 7.1 Hz), 2.22 (3H, t, J = 8.0 Hz), 1.96-1.88 (3H, m), 1.56-1.33 (3H, m), 1.29 (6H, d, J = 6.3 Hz), 1.20 (2H, dd, J = 33.4, 6.6 Hz), 0.87 (1H, t, J = 7.1 Hz).	458.44	457.20
104	1H-NMR (DMSO-D6) δ: 10.17 (1H, s), 9.32 (1H, s), 8.03 (1H, d, J = 8.3 Hz), 7.72 (1H, t, J = 7.8 Hz), 7.20 (1H, s), 6.90-6.69 (3H, m), 4.31-4.23 (1H, m), 2.43 (3H, s), 1.30 (6H, d, J = 6.3 Hz).	345.15	344.16
105	1H-NMR (DMSO-d6) δ: 12.78 (1H, s), 9.86 (1H, s), 9.20 (1H, s), 8.20 (1H, br s), 8.00 (1H, d, J = 3.6 Hz), 7.74 (1H, br s), 7.45 (1H, d, J = 11.6 Hz), 7.23 (1H, br m), 7.00 (1H, d, J = 7.6 Hz), 6.30 (1H, br s), 5.32 (1H, br s), 5.17-5.21 (1H, m), 4.61-4.64 (1H, m), 3.04-3.06 (4H, m), 2.85-2.88 (4H, m), 1.58 (3H, d, J = 8.0 Hz), 1.29 (3H, dd, J = 15.2, 8.8 Hz).	461.2	460.24
106	1H-NMR (DMSO-d6) δ: 12.72 (1H, s), 9.82 (1H, d, J = 4.0 Hz), 9.20 (1H, s), 8.03 (1H, dd, J = 12.0, 3.6 Hz), 7.99 (1H, d, J = 4.0 Hz), 7.78 (1H, br s), 7.56 (1H, br m), 7.37 (1H, m), 6.98 (1H, d, J = 3.2 Hz), 6.56 (1H, t, J = 10.4 Hz), 5.29-5.34 (1H, m), 5.19 (1H, t, J = 6.4 Hz), 4.62-4.66 (1H, m), 3.01-3.04 (4H, m), 2.83-2.87 (4H, m), 1.59 (3H, d, J = 8.8 Hz), 1.40-1.42 (3H, m).	461.2	460.24

[Table 5-18]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
107	1H-NMR (DMSO-d6) δ: 10.20 (1H, s), 9.33 (1H, s), 8.21 (1H, dd, J = 7.6, 4.0 Hz), 7.74 (1H, d, J = 9.2 Hz), 7.21 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.68 (1H, d, J = 10.4 Hz), 4.39 (1H, d, J = 4.4 Hz), 4.24-4.35 (1H, m), 3.91 (1H, br s), 2.58-2.59 (1H, m), 1.74-1.98 (4H, m), 1.50-1.60 (4H, m), 1.31 (6H, d, J = 8.4 Hz).	429.2	428.21
108	1H-NMR (DMSO-d6) δ: 10.21 (1H, s), 9.33 (1H, s), 8.18-8.21 (2H, m), 7.69 (1H, dd, J = 11.2, 3.2 Hz), 7.21 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.68 (1H, d, J = 10.4 Hz), 4.39 (1H, t, J = 6.8 Hz), 4.25-4.32 (1H, m), 3.3.40-3.46 (2H, m), 2.56-2.61 (2H, m), 1.60-1.65 (2H, m), 1.43-1.50 (2H, m), 1.31 (6H, d, J = 8.8 Hz).	403.1	402.20
109	1H-NMR (DMSO-d6) δ: 10.74 (1H, br s), 9.34 (1H, s), 8.82 (1H, d, J = 2.8 Hz), 8.53 (1H, t, J = 6.8 Hz), 8.38 (1H, d, J = 12.0 Hz), 8.29 (1H, dd, J = 12.0, 0.8 Hz), 7.25 (1H, s), 6.82 (1H, t, J = 73.6 Hz), 6.77 (1H, d, J = 10.8 Hz), 4.76 (1H, t, J = 7.2 Hz), 4.28-4.37 (1H, m), 3.52-3.56 (2H, m), 3.31-3.33 (2H, m), 1.32 (6H, d, J = 8.8 Hz).	418.2	417.17
110	1H-NMR (DMSO-d6) δ: 10.40 (1H, s), 9.60 (1H, s), 9.36 (1H, s), 8.59 (1H, d, J = 2.4 Hz), 8.32 (1H, d, J = 8.8 Hz), 7.56 (2H, d, J = 8.8 Hz), 7.24 (1H, s), 6.82 (1H, t, J = 55.6 Hz), 6.88 (1H, d, J = 8.4 Hz), 6.70-6.72 (1H, m), 4.30 (1H, q, J = 6.4 Hz), 1.32 (6H, d, J = 6.4 Hz).	423.1	422.17
112		453.20	452.14

[Table 5-19]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
113	1H-NMR (DMSO-D6) δ: 10.49 (1H, br s), 9.35 (1H, s), 8.31-8.28 (1H, br m), 8.24 (1H, d, J = 8.8 Hz), 7.85 (1H, d, J = 8.3 Hz), 7.23 (1H, s), 6.94-6.66 (2H, m), 4.31-4.28 (1H, m), 3.74 (2H, br s), 2.96 (4H, br s), 1.31 (6H, d, J = 6.3 Hz), 1.24-1.17 (2H, m).	478.1	477.18
114	1H-NMR (DMSO-D6) δ: 10.32 (1H, br s), 9.34 (1H, s), 8.28-8.26 (2H, m), 7.79 (1H, d, J = 7.8 Hz), 7.21 (1H, s), 6.82 (1H, t, J = 45.9 Hz), 6.67 (1H, d, J = 11.2 Hz), 4.31-4.24 (1H, m), 3.53 (1H, br s), 3.31 (4H, br s), 3.16 (6H, s), 2.75 (6H, s), 1.30 (6H, d, J = 6.3 Hz), 1.26-1.16 (2H, m).	536.2	535.23
115	1H-NMR (DMSO-D6) δ: 10.43 (1H, br s), 9.35 (1H, s), 8.30 (2H, br s), 7.84 (1H, br s), 7.22 (1H, s), 6.94-6.67 (2H, m), 4.33-4.25 (1H, m), 3.63-3.59 (1H, m), 3.47-3.36 (4H, br m), 3.16-3.12 (4H, m), 2.91 (3H, br s), 1.31 (6H, d, J = 6.8 Hz), 1.26-1.24 (3H, m).	507.1	506.20
116	1H-NMR (DMSO-D6) δ: 10.35 (1H, br s), 9.34 (1H, s), 8.28-8.26 (2H, br m), 7.79 (1H, d, J = 6.8 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.30-4.27 (1H, m), 3.31 (4H, br s), 3.19-3.17 (3H, br m), 2.70-2.67 (4H, br m), 1.30 (6H, d, J = 6.3 Hz), 1.23-1.15 (2H, m).	511.2	510.23
117	1H-NMR (DMSO-D6) δ: 10.32 (1H, s), 9.33 (1H, s), 8.28-8.19 (2H, m), 7.78 (1H, dd, J = 8.5, 2.2 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.33-4.24 (1H, m), 3.42-3.40 (5H, br m), 2.39-2.37 (2H, m), 2.32-2.31 (2H, m), 1.97 (3H, s), 1.30 (6H, d, J = 6.3 Hz).	471.43	470.24

[Table 5-20]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
118	1H-NMR (DMSO-D6) δ: 10.35 (1H, s), 9.34 (1H, s), 8.28-8.24 (2H, m), 7.79 (1H, dd, J = 8.5, 2.2 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.33-4.24 (1H, m), 4.08 (1H, br s), 3.56 (2H, s), 2.98-2.95 (2H, br m), 2.03-2.00 (2H, br m), 1.68-1.66 (2H, br m), 1.30 (6H, d, J = 6.3 Hz), 1.23-1.17 (4H, m), 1.01 (6H, s).	486.48	485.27
119		445.46	444.21
120		445.41	444.21
124	1H-NMR (DMSO-D6) δ: 10.31 (1H, s), 9.33 (1H, s), 8.37 (1H, t, J = 5.6 Hz), 8.23 (2H, t, J = 4.1 Hz), 7.73 (1H, dd, J = 8.4, 2.6 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.32-4.22 (3H, m), 1.86 (3H, s), 1.30 (6H, d, J = 6.3 Hz).		
125	1H-NMR (DMSO-D6) δ: 10.28 (1H, s), 9.33 (1H, s), 8.25 (1H, d, J = 8.3 Hz), 8.21 (1H, d, J = 2.0 Hz), 7.76 (1H, dd, J = 8.3, 2.0 Hz), 7.21 (1H, s), 7.19 (1H, br s), 6.93-6.66 (3H, m), 4.31-4.24 (1H, m), 3.43 (2H, s), 3.33 (2H, br s), 2.84-2.82 (2H, m), 2.06-2.03 (1H, m), 1.93-1.90 (2H, m), 1.67-1.64 (2H, m), 1.56-1.50 (2H, m), 1.30 (6H, d, J = 6.3 Hz).	471.43	470.24
126		416.34	415.19
127	1H-NMR (DMSO-D6) δ: 10.27 (1H, s), 9.33 (1H, s), 8.27-8.22 (3H, m), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 7.21 (1H, s), 6.93-6.66 (2H, m), 4.31-4.24 (1H, m), 3.47-3.38 (2H, m), 3.29-3.25 (1H, m), 3.18-3.14 (1H, m), 2.86-2.84 (1H, m), 2.74-2.71 (1H, m), 1.91-1.88 (1H, m), 1.66-1.59 (5H, br m), 1.45-1.42 (1H, br m), 1.30 (6H, d, J = 6.3 Hz).	458.4	457.24

[Table 5-21]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
128	1H-NMR (DMSO-D6) δ: 10.29 (1H, s), 9.33 (1H, s), 8.26-8.21 (3H, m), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 7.21 (1H, s), 6.93-6.66 (2H, m), 4.33-4.24 (1H, m), 3.51-3.39 (3H, m), 2.80-2.78 (1H, m), 2.66-2.64 (1H, m), 1.88-1.86 (1H, m), 1.79-1.69 (2H, m), 1.62-1.59 (1H, m), 1.43-1.37 (1H, m), 1.30 (6H, d, J = 6.8 Hz), 1.15-1.00 (2H, m).	444.42	443.22
132	1H-NMR (DMSO-d6) δ: 10.26 (1H, br s), 9.33 (1H, s), 8.23 (1H, d, J = 11.7 Hz), 8.20 (1H, d, J = 2.8 Hz), 7.74 (1H, dd, J = 11.6, 3.2 Hz), 7.52 (1H, br s), 7.22 (1H, s), 6.94 (1H, br s), 6.81 (1H, t, J = 74.0 Hz), 6.69 (1H, d, J = 10.4 Hz), 4.23-4.33 (1H, m), 3.40 (2H, s), 1.31 (6H, d, J = 8.8 Hz).	388.3	387.16
133	1H-NMR (DMSO-d6) δ: 10.16 (1H, br s), 9.32 (1H, s), 8.16-8.19 (2H, m), 7.74 (1H, br m), 7.21 (1H, s), 6.80 (1H, t, J = 74.0 Hz), 6.68 (1H, br m), 4.23-4.33 (1H, m), 3.39 (2H, s), 1.30 (6H, d, J = 8.8 Hz).	389.1	388.15
134	1H-NMR (DMSO-d6) δ: 10.19 (1H, br s), 9.33 (1H, s), 8.17-8.20 (2H, m), 7.71-7.74 (1H, br m), 7.21 (1H, s), 6.80 (1H, t, J = 74.0 Hz), 6.67 (1H, d, J = 10.4 Hz), 4.68 (1H, t, J = 7.2 Hz), 4.23-4.33 (1H, m), 3.60-3.66 (2H, m), 2.72 (2H, t, J = 8.4 Hz), 1.31 (6H, d, J = 8.4 Hz).	375.1	374.17
135	1H-NMR (DMSO-d6) δ: 10.21 (1H, s), 9.33 (1H, s), 8.18-8.22 (2H, m), 7.69-7.71 (1H, br m), 7.27 (1H, br s), 7.21 (1H, s), 6.80 (1H, t, J = 74.4 Hz), 6.67-6.72 (2H, br m), 4.28-4.32 (1H, m), 2.59-2.73 (2H, m), 2.09 (2H, t, J = 10.0 Hz), 1.78-1.83 (2H, m), 1.31 (6H, d, J = 8.4 Hz).	416.2	415.19

[Table 5-22]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
136	1H-NMR (DMSO-d6) δ: 10.22 (1H, s), 9.33 (1H, s), 8.18-8.21 (2H, m), 7.68-7.71 (1H, br m), 7.21 (1H, s), 6.80 (1H, t, J = 74.0 Hz), 6.67-6.72 (1H, br m), 4.25-4.27 (1H, m), 2.51-2.73 (2H, m), 2.12 (2H, br m), 1.80-1.87 (2H, m), 1.30 (6H, d, J = 8.4 Hz).	417.3	416.18
138	1H-NMR (DMSO-D6) δ: 10.30 (1H, s), 9.32 (1H, s), 8.23 (2H, d, J = 8.8 Hz), 7.73 (1H, dd, J = 8.5, 2.4 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 6.46 (1H, t, J = 6.0 Hz), 5.56 (2H, s), 4.34-4.24 (1H, m), 4.16 (2H, d, J = 6.1 Hz), 1.30 (6H, d, J = 6.3 Hz).		
139	1H-NMR (DMSO-D6) δ: 10.33 (1H, s), 9.33 (1H, s), 8.29-8.27 (1H, m), 8.23-8.23 (2H, m), 7.72-7.72 (1H, m), 7.21 (3H, s), 6.78-6.73 (2H, m), 4.47 (2H, s), 4.31-4.29 (1H, m), 2.94 (3H, s), 2.05 (3H, s), 1.30 (6H, d, J = 6.6 Hz).		
140	1H-NMR (DMSO-D6) δ: 10.37 (1H, s), 9.34 (1H, s), 8.29-8.27 (2H, m), 7.82 (1H, d, J = 8.8 Hz), 7.57 (1H, t, J = 6.1 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.30-4.26 (1H, m), 4.16 (2H, d, J = 6.1 Hz), 2.91 (3H, s), 1.30 (6H, d, J = 6.3 Hz).		
141	1H-NMR (DMSO-D6) δ: 10.41 (1H, s), 9.34 (1H, s), 8.33-8.29 (2H, m), 7.82 (1H, dd, J = 8.7, 2.3 Hz), 7.22 (1H, s), 6.94-6.66 (2H, m), 4.33-4.26 (1H, m), 4.24 (2H, s), 3.32 (2H, s), 2.97 (3H, s), 2.69 (3H, s), 1.31 (6H, d, J = 6.6 Hz).		

[Table 5-23]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
142	1H-NMR (DMSO-D6) δ: 10.28 (1H, s), 9.33 (1H, s), 8.25 (1H, d, J = 8.8 Hz), 8.21 (1H, d, J = 2.4 Hz), 8.15 (1H, s), 7.76 (1H, dd, J = 8.8, 2.4 Hz), 7.21 (1H, s), 6.93-6.66 (2H, m), 4.31-4.24 (1H, m), 3.33 (1H, br s), 3.16 (2H, s), 2.69-2.66 (2H, br m), 2.09-2.04 (2H, br m), 1.71-1.69 (2H, br m), 1.42-1.33 (2H, m), 1.30 (6H, d, J = 6.8 Hz).	44.38	443.22
143	1H-NMR (DMSO-D6) δ: 10.39 (1H, s), 9.34 (1H, s), 8.49 (1H, br s), 8.33 (1H, s), 8.28 (1H, d, J = 8.8 Hz), 7.86 (1H, dd, J = 8.8, 2.4 Hz), 7.22 (1H, s), 6.94-6.66 (2H, m), 4.34 (2H, s), 4.30-4.24 (1H, m), 3.76-3.73 (2H, br m), 3.17-3.08 (2H, m), 3.02 (2H, d, J = 7.3 Hz), 2.96 (3H, s), 1.68-1.66 (1H, br m), 1.46-1.44 (2H, br m), 1.30 (6H, d, J = 6.3 Hz), 1.23-1.16 (2H, m), 1.06-0.97 (2H, m).	536.32	535.22
144	1H-NMR (DMSO-D6) δ: 10.41 (0.4H, s), 10.33 (0.6H, s), 9.34 (0.4H, s), 9.33 (0.6H, s), 8.28-8.23 (2.0H, m), 7.72 (1.0H, td, J = 9.0, 2.3 Hz), 7.21 (1.0H, s), 6.93-6.66 (2.0H, m), 4.57 (0.8H, s), 4.49 (1.3H, s), 4.32-4.22 (1.0H, m), 3.86-3.80 (2.0H, m), 3.26-3.16 (4.0H, m), 2.08 (3.0H, s), 1.92-1.87 (1.0H, m), 1.47-1.43 (2.0H, m), 1.30 (6.0H, d, J = 6.3 Hz), 1.25-1.11 (3.0H, m).	500.33	499.25
145	1H-NMR (DMSO-D6) δ: 10.38 (0.3H, s), 10.31 (0.6H, s), 9.34 (0.3H, s), 9.33 (0.6H, s), 8.28-8.22 (2.1H, m), 7.72-7.69 (1.0H, m), 7.21 (1.0H, s), 6.94-6.66 (2.0H, m), 4.66-4.53 (2.0H, m), 4.31-4.24 (1.0H, m), 4.04-3.98 (1.0H, br m), 3.80-3.74 (1.0H, m), 3.68-3.60 (1.0H, m), 3.54-3.50 (0.3H, m), 3.39-3.25 (7.5H, m), 3.12 (0.3H, dd, J = 13.7, 7.8 Hz), 2.09 (2.0H, s), 2.07 (1.0H, s), 1.95-1.75 (3.4H, m), 1.48-1.41 (1.0H, m), 1.30 (6.0H, d, J = 6.3 Hz).	486.31	485.24

[Table 5-24]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
146	1H-NMR (DMSO-D6) δ: 10.39 (0.4H, s), 10.31 (0.6H, s), 9.34 (0.4H, s), 9.33 (0.7H, s), 8.28-8.22 (2.0H, m), 7.71 (1.0H, d, J = 8.8 Hz), 7.21 (1.0H, s), 6.94-6.66 (2.0H, m), 4.66-4.53 (2.0H, m), 4.31-4.25 (1.0H, m), 4.04-4.02 (0.8H, br m), 3.80-3.74 (1.1H, m), 3.68-3.60 (1.1H, m), 3.53-3.51 (0.3H, m), 3.36-3.27 (10.0H, m), 3.14-3.10 (0.3H, m), 2.09 (2.0H, s), 2.07 (1.0H, s), 1.95-1.78 (2.0H, m), 1.48-1.41 (0.8H, m), 1.30 (6.0H, d, J = 6.3 Hz).	486.31	485.24
147	1H-NMR (DMSO-D6) δ: 10.44 (1H, s), 9.34 (1H, s), 8.32-8.28 (2H, m), 7.82 (1H, d, J = 8.3 Hz), 7.22 (1H, s), 6.94-6.67 (2H, m), 4.32-4.24 (1H, m), 3.74 (2H, s), 3.24 (2H, d, J = 6.3 Hz), 3.03-3.00 (2H, br m), 2.30-2.24 (2H, br m), 1.70-1.67 (2H, br m), 1.43 (1H, br s), 1.30 (6H, d, J = 6.3 Hz), 1.25-1.16 (3H, m).	458.36	457.24
148	1H-NMR (DMSO-D6) δ: 10.41 (1H, s), 9.34 (1H, s), 8.31-8.28 (2H, m), 7.85-7.82 (1H, m), 7.21 (1H, s), 6.94-6.67 (2H, m), 4.42 (2H, dd, J = 43.9, 15.6 Hz), 4.30-4.25 (1H, m), 4.04-4.01 (1H, m), 3.71 (1H, q, J = 7.2 Hz), 3.65-3.60 (1H, m), 3.21-3.09 (2H, m), 3.03 (3H, s), 1.83-1.72 (3H, m), 1.48-1.41 (1H, m), 1.30 (6H, d, J = 6.3 Hz).	522.3	521.20
149		522.3	521.20
150		416.15	415.19
151		452.10	451.16
152		430.15	429.21
153		466.15	465.18

[Table 5-25]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
157	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.31 (1H, s), 8.48 (1H, s), 8.17-8.15 (2H, m), 7.67 (1H, dd, J = 8.5, 2.7 Hz), 7.20 (1H, s), 6.93-6.60 (2H, m), 4.30-4.24 (1H, m), 2.27 (3H, s), 1.30 (6H, d, J = 6.3 Hz).	345.26	344.16
158	1H-NMR (DMSO-D6) δ: 9.56 (1H, s), 8.36 (1H, s), 8.21 (1H, t, J = 5.9 Hz), 7.95 (1H, d, J = 2.0 Hz), 7.44 (1H, dd, J = 8.5, 2.2 Hz), 7.35 (1H, s), 7.21 (1H, d, J = 7.8 Hz), 6.84 (1H, t, J = 55.4 Hz), 6.39 (1H, d, J = 8.3 Hz), 5.84 (2H, s), 4.46 (2H, d, J = 5.9 Hz), 4.36-4.29 (1H, m), 2.21 (3H, s), 1.26 (6H, d, J = 6.3 Hz).	441.33	440.20
159	1H-NMR (DMSO-d6) δ: 10.31 (1H, s), 9.34 (1H, s), 8.23-8.25 (2H, m), 7.79 (1H, dd, J = 11.6, 2.8 Hz), 7.22 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.68 (1H, d, J = 10 Hz), 4.26-4.33 (1H, m), 3.30-3.32 (2H, m), 3.12-3.16 (2H, m), 2.99 (1H, br m), 2.13-2.15 (4H, br s), 1.31 (6H, d, J = 8.8 Hz).	463.3	462.16
160	1H-NMR (DMSO-d6) δ: 10.24 (1H, s), 9.33 (1H, s), 8.25 (1H, d, J = 2.8 Hz), 8.21 (1H, d, J = 11.6), 7.76 (1H, dd, J = 11.6, 3.2 Hz), 7.22 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.68 (1H, d, J = 10.4 Hz), 4.23-4.35 (1H, m), 3.95-3.99 (2H, m), 3.38-3.95 (2H, m), 2.73-2.87 (1H, m), 1.64-1.74 (4H, m), 1.31 (6H, d, J = 8.8 Hz).	415.2	414.20
162	1H-NMR (DMSO-D6) δ: 10.33 (1H, s), 9.33 (1H, s), 8.27 (2H, t, J = 7.1 Hz), 7.82 (1H, dd, J = 8.5, 2.2 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.46-4.26 (3H, m), 3.88-3.83 (1H, m), 3.70-3.66 (1H, m), 3.60-3.50 (2H, m), 3.03 (3H, s), 2.22-2.12 (1H, br m), 1.89-1.82 (1H, m), 1.30 (6H, d, J = 6.3 Hz).	508.24	507.19

[Table 5-26]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
163	1H-NMR (DMSO-d6) δ: 10.42 (1H, s), 9.28 (1H, s), 8.39 (2H, s), 7.19 (1H, s), 6.80 (1H, t, J = 74.0 Hz), 6.71 (1H, d, J = 10.8 Hz), 4.20-4.31 (1H, m), 3.04-3.11 (4H, m), 2.84-2.87 (4H, m), 1.28 (6H, d, J = 8.4 Hz).	416.2	415.20
165	1H-NMR (DMSO-D6) δ: 10.31 (1H, s), 9.33 (1H, s), 8.58 (1H, t, J = 5.6 Hz), 8.25-8.23 (2H, m), 7.74-7.72 (1H, m), 7.21 (1H, s), 6.86-6.71 (2H, m), 4.32-4.25 (3H, m), 2.53 (4H, d, J = 1.2 Hz), 1.60-1.55 (1H, m), 1.30 (6H, d, J = 6.3 Hz), 0.68-0.66 (4H, m).		427.19
166	1H-NMR (DMSO-D6) δ: 10.37 (1H, s), 9.34 (1H, s), 8.28-8.27 (2H, m), 7.76 (1H, dd, J = 8.5, 2.4 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.54 (2H, s), 4.30-4.27 (1H, m), 4.10 (2H, s), 3.81 (2H, t, J = 5.1 Hz), 3.31-3.29 (2H, m), 2.53 (1H, d, J = 0.5 Hz), 1.30 (6H, d, J = 6.6 Hz).		443.19
167		456.20	455.22
168		472.2	471.22
169		444.05	443.19
170		506.2	505.21
171	1H-NMR (DMSO-D6) δ: 10.44 (1H, s), 9.27 (1H, s), 8.12 (1H, d, J = 9.8 Hz), 7.41 (1H, d, J = 9.8 Hz), 7.18 (1H, s), 6.78 (1H, t, J = 55.6 Hz), 6.58 (1H, d, J = 7.8 Hz), 4.29-4.21 (1H, m), 4.02-3.99 (2H, m), 3.74-3.70 (1H, m), 3.18-3.11 (2H, m), 1.83-1.79 (2H, m), 1.45-1.36 (2H, m), 1.27 (6H, d, J = 6.3 Hz).		

[Table 5-27]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
177	1H-NMR (DMSO-D6) δ: 10.30 (1H, s), 9.33 (1H, s), 8.26-8.22 (2H, m), 7.76 (1H, d, J = 7.8 Hz), 7.21 (1H, s), 6.93-6.66 (2H, m), 4.29-4.27 (1H, br m), 3.46 (2H, br s), 2.37 (4H, br s), 1.50 (4H, br s), 1.39 (2H, br s), 1.30 (6H, d, J = 6.3 Hz).		
178	1H-NMR (DMSO-d6) δ: 10.28 (1H, s), 9.33 (1H, s), 8.20-8.25 (2H, m), 7.75 (1H, dd, J = 11.2, 2.8 Hz), 7.22 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.68 (1H, d, J = 10.4 Hz), 4.53-4.57 (1H, m), 4.26-4.32 (1H, m), 3.92-3.97 (1H, m), 3.09-3.17 (1H, m), 2.72-2.81 (2H, m), 2.04 (3H, s), 1.46-1.85 (4H, m), 1.31 (6H, d, J = 8.8 Hz).	456.1	455.22
179	1H-NMR (DMSO-d6) δ: 10.34 (1H, s), 9.40 (1H, s), 8.33 (1H, d J = 2.8 Hz), 8.29 (1H, d, J = 11.6), 7.82 (1H, dd, J = 11.6, 2.8 Hz), 7.29 (1H, s), 6.88 (1H, t, J = 74.0 Hz), 6.73 (1H, d, J = 10 Hz), 4.36-4.48 (1H, m), 3.72-3.79 (2H, m), 3.92-3.97 (1H, m), 2.98 (3H, s), 2.76-2.90 (3H, m), 1.72-1.98 (4H, m), 1.38 (6H, d, J = 8.8 Hz).	492.3	491.19
181	1H-NMR (DMSO-D6) δ: 10.47 (1H, br s), 9.28 (1H, s), 8.31 (1H, s), 8.15 (1H, d, J = 9.8 Hz), 7.42 (1H, d, J = 10.2 Hz), 7.18 (1H, s), 6.78 (1H, t, J = 55.4 Hz), 6.59 (1H, d, J = 7.8 Hz), 4.29-4.21 (1H, m), 3.62-3.60 (2H, br m), 3.44 (2H, s), 3.04-3.03 (2H, br m), 1.27 (6H, d, J = 6.8 Hz), 1.20 (6H, s).		
185	1H-NMR (DMSO-D6) δ: 10.31 (1H, s), 9.33 (1H, s), 8.48 (1H, br s), 8.26 (1H, d, J = 8.5 Hz), 8.21 (1H, d, J = 2.0 Hz), 7.71 (1H, dd, J = 8.7, 2.3 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 5.98 (2H, s), 4.38 (2H, s), 4.31-4.26 (1H, m), 2.76 (3H, s), 1.30 (6H, d, J = 6.6 Hz).		

[Table 5-28]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
186	1H-NMR (DMSO-D6) δ: 10.28 (1H, s), 9.32 (1H, s), 8.50 (3H, s), 8.23-8.21 (2H, m), 7.73-7.72 (1H, m), 7.21 (1H, s), 6.94-6.66 (2H, m), 6.40 (1H, t, J = 6.1 Hz), 5.98 (1H, t, J = 5.7 Hz), 4.29-4.27 (1H, m), 4.18 (2H, d, J = 5.9 Hz), 3.03-2.98 (2H, m), 1.30 (6H, d, J = 6.6 Hz), 0.98 (3H, t, J = 7.2 Hz).		
187	1H-NMR (DMSO-D6) δ: 10.32 (1H, s), 9.33 (1H, s), 8.44 (2H, br s), 8.28-8.24 (2H, m), 7.82 (1H, dd, J = 8.8, 2.4 Hz), 7.21 (1H, s), 7.10 (1H, t, J = 6.2 Hz), 6.87-6.73 (4H, m), 4.30-4.28 (1H, m), 4.07 (2H, d, J = 6.3 Hz), 1.30 (7H, d, J = 6.3 Hz).		
188	1H-NMR (DMSO-D6) δ: 10.34 (1H, s), 9.33 (1H, s), 8.58 (1H, d, J = 2.2 Hz), 8.44 (1H, br s), 8.27 (1H, d, J = 8.8 Hz), 8.20 (1H, s), 8.01 (1H, dd, J = 8.8, 2.4 Hz), 7.92 (1H, s), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.31-4.27 (1H, m), 3.87 (3H, s), 1.31 (7H, d, J = 6.3 Hz).		
189	1H-NMR (DMSO-D6) δ: 10.52 (1H, s), 9.33 (1H, s), 8.38 (1H, d, J = 2.0 Hz), 8.31 (1H, d, J = 8.8 Hz), 7.93 (1H, dd, J = 8.5, 2.2 Hz), 7.19 (1H, s), 6.91-6.63 (2H, m), 4.35-4.20 (2H, m), 4.13-4.10 (1H, br m), 3.40-3.37 (1H, br m), 3.13-3.09 (1H, br m), 2.49 (2H, s), 2.40-2.31 (1H, m), 1.99-1.91 (2H, m), 1.84-1.77 (1H, m), 1.27 (6H, d, J = 6.3 Hz).	458.2	457.20
190	1H-NMR (DMSO-D6) δ: 10.63 (1H, s), 9.38 (1H, s), 8.45 (1H, d, J = 1.5 Hz), 8.38 (1H, d, J = 8.3 Hz), 8.00 (1H, dd, J = 8.8, 2.0 Hz), 7.24 (1H, s), 6.95-6.67 (2H, m), 4.40 (2H, br s), 4.33-4.25 (1H, m), 3.63-3.16 (4H, br m), 2.39-2.05 (3H, br m), 1.31 (6H, d, J = 6.3 Hz).	458.2	457.20

[Table 5-29]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
191	1H-NMR (DMSO-D6) δ: 10.42 (1H, s), 9.27 (1H, s), 8.11 (1H, d, J = 9.8 Hz), 7.40 (1H, d, J = 9.8 Hz), 7.18 (1H, s), 6.78 (1H, t, J = 55.6 Hz), 6.58 (1H, d, J = 7.8 Hz), 4.38 (2H, d, J = 13.7 Hz), 4.28-4.22 (1H, m), 3.33 (3H, br s), 2.76 (2H, t, J = 12.0 Hz), 1.79 (3H, d, J = 11.7 Hz), 1.45 (1H, t, J = 12.2 Hz), 1.28 (6H, d, J = 6.3 Hz), 1.05 (6H, s).	458.2	472.25
192		480.2	479.26
193		510.25	509.28
194	1H-NMR (DMSO-D6) δ: 10.34 (1H, s), 9.34 (1H, s), 8.28 (1H, d, J = 8.8 Hz), 8.25 (1H, d, J = 1.5 Hz), 7.81 (1H, dd, J = 8.3, 2.0 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.33-4.24 (1H, m), 3.88 (1H, d, J = 13.7 Hz), 3.56 (1H, d, J = 13.7 Hz), 3.15-3.06 (1H, m), 2.93-2.88 (1H, br m), 2.29-2.27 (1H, br m), 1.81 (1H, br s), 1.74-1.69 (1H, br m), 1.50 (3H, br s), 1.37-1.35 (1H, br m), 1.30 (6H, d, J = 6.3 Hz), 1.25-1.22 (1H, br m).	472.38	471.22
195	1H-NMR (DMSO-d6) δ: 9.89 (1H, s), 9.18 (1H, s), 8.06 (1H, d J = 12.4 Hz), 8.04 (1H, d, J = 4.0 Hz), 7.41 (1H, dd, J = 12.4, 4.0 Hz), 6.96 (1H, s), 6.67 (1H, s), 5.18 (1H, d, J = 6.0 Hz), 4.60-4.64 (1H, m), 3.57 (2H, s), 3.38 (3H, s), 3.02-3.05 (4H, m), 2.83-2.86 (4H, m), 1.51 (3H, s), 1.39 (6H, d, J = 8.8 Hz).	453.2	452.26

[Table 5-30]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
196	1H-NMR (DMSO-D6) δ: 10.23 (1H, s), 9.21 (1H, s), 8.24-8.19 (2H, m), 7.74 (1H, d, J = 7.3 Hz), 6.96 (1H, s), 6.66 (1H, s), 5.17 (1H, d, J = 4.4 Hz), 4.59 (1H, t, J = 5.6 Hz), 4.09 (1H, br s), 3.53 (2H, br s), 3.34 (3H, s), 3.28 (4H, br s), 3.01 (2H, br s), 2.49 (3H, d, J = 1.0 Hz), 1.68-1.66 (2H, br m), 1.47 (6H, s), 1.36 (3H, d, J = 6.3 Hz), 0.98 (6H, s).	524.4	523.33
197	1H-NMR (DMSO-D6) δ: 12.31 (1H, br s), 10.16 (1H, s), 9.23 (1H, s), 8.21-8.19 (2H, m), 7.71 (1H, dd, J = 8.5, 2.2 Hz), 6.99 (1H, s), 6.70 (1H, s), 5.20 (1H, br s), 4.62 (1H, q, J = 6.3 Hz), 3.56 (2H, s), 3.44 (2H, s), 3.38 (3H, s), 3.33-3.29 (2H, m), 2.77-2.74 (2H, br m), 2.22-2.13 (1H, m), 2.01-1.97 (2H, m), 1.79-1.76 (2H, br m), 1.50 (6H, s), 1.39 (3H, d, J = 6.3 Hz).	510.25	509.28
198	1H-NMR (DMSO-D6) δ: 11.69 (1H, s), 10.28 (1H, s), 9.24 (1H, s), 8.27-8.23 (3H, m), 7.72 (1H, dd, J = 8.5, 2.2 Hz), 7.00 (1H, s), 6.72 (1H, s), 5.36 (1H, dd, J = 6.0, 2.1 Hz), 5.21 (1H, d, J = 4.6 Hz), 4.65-4.59 (1H, m), 4.53 (3H, s), 4.08 (3H, s), 3.79-3.76 (4H, m), 3.38 (4H, s), 3.32 (3H, s), 3.30-3.29 (2H, m), 1.99-1.62 (4H, m), 1.50 (6H, s), 1.39 (3H, d, J = 6.6 Hz).		
199	1H-NMR (DMSO-D6) δ: 11.69 (1H, s), 10.15 (1H, s), 9.25 (1H, s), 8.29-8.20 (3H, m), 7.74 (1H, dd, J = 8.7, 2.3 Hz), 6.89 (1H, s), 6.48 (1H, d, J = 7.6 Hz), 5.36 (1H, dd, J = 6.1, 2.0 Hz), 4.53 (2H, s), 4.28-4.25 (2H, m), 4.10 (3H, s), 3.77 (5H, tt, J = 12.4, 5.1 Hz), 3.27 (4H, s), 1.99-1.62 (4H, m), 1.38 (4H, d, J = 6.6 Hz), 1.30 (8H, dd, J = 6.3, 3.7 Hz).		

[Table 5-31]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
200	1H-NMR (DMSO-D6) δ: 10.09 (1H, s), 9.25 (1H, s), 8.26 (1H, d, J = 8.3 Hz), 8.19 (1H, d, J = 1.5 Hz), 8.15 (1H, s), 7.74 (1H, dd, J = 8.5, 2.2 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.29-4.22 (2H, m), 3.44 (2H, s), 3.27 (3H, s), 2.89 (2H, d, J = 11.7 Hz), 1.88 (2H, t, J = 11.0 Hz), 1.64 (2H, d, J = 11.2 Hz), 1.38 (3H, d, J = 6.3 Hz), 1.30 (6H, dd, J = 6.3, 3.4 Hz), 1.24-1.14 (4H, m), 1.01 (6H, s).	494.3	493.32
201		439.2	438.25
202		469.3	468.26
203	1H-NMR (DMSO-d6) δ: 10.61 (1H, s), 9.39 (1H, s), 8.63 (1H, d J = 3.2 Hz), 8.35 (1H, d J = 11.6 Hz), 8.14 (1H, dd, J = 12.0, 3.2 Hz), 7.49 (1H, s), 7.24 (1H, s), 6.82 (1H, t, J = 74.0 Hz), 6.72 (1H, d J = 10.4 Hz), 6.25 (1H, s), 4.28-4.34 (1H, m), 3.36-3.41 (2H, m), 2.73-2.78 (2H, m), 1.32 (6H, d, J = 8.4 Hz).	426.3	425.18
209	1H-NMR (DMSO-D6) δ: 10.34 (1H, br s), 9.33 (1H, s), 8.63 (1H, d, J = 1.7 Hz), 8.27 (1H, d, J = 9.3 Hz), 8.13 (3H, s), 8.06 (1H, dd, J = 8.8, 2.4 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.32-4.27 (1H, m), 2.53 (1H, s), 1.31 (5H, d, J = 6.3 Hz).		
210	1H-NMR (DMSO-D6) δ: 10.57 (1H, s), 9.36 (1H, s), 8.83 (1H, d, J = 2.7 Hz), 8.54 (1H, d, J = 2.4 Hz), 8.42 (1H, d, J = 9.0 Hz), 8.29 (1H, dd, J = 8.8, 2.7 Hz), 7.78 (1H, d, J = 1.7 Hz), 7.23 (1H, s), 6.95-6.67 (2H, m), 6.58 (1H, t, J = 1.8 Hz), 4.32-4.27 (1H, m), 1.32 (7H, d, J = 6.6 Hz).		

[Table 5-32]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
211	1H-NMR (DMSO-D6) δ: 9.47 (1H, s), 8.14 (1H, s), 7.62 (1H, d, J = 9.0 Hz), 7.32 (1H, s), 6.98-6.69 (2H, m), 6.58-6.53 (1H, m), 6.47-6.40 (4H, m), 4.26-4.22 (2H, m), 1.23 (6H, d, J = 6.3 Hz).		
212	1H-NMR (DMSO-D6) δ: 10.73 (1H, br s), 9.25 (1H, s), 8.88 (2H, br s), 8.17 (1H, d, J = 9.8 Hz), 8.13 (1H, s), 7.58 (1H, d, J = 9.8 Hz), 7.01 (1H, s), 6.64 (1H, br s), 4.62 (1H, q, J = 6.3 Hz), 3.76-3.75 (4H, br m), 3.57 (2H, s), 3.33 (3H, s), 3.26 (4H, br s), 1.48 (6H, s), 1.39 (3H, d, J = 6.3 Hz).	454.20	453.26
213	1H-NMR (DMSO-d6) δ: 10.36 (1H, s), 9.32 (1H, s), 8.25-8.31 (2H, m), 7.74 (1H, d, J = 6.8 Hz), 7.23 (1H, s), 6.81 (1H, t, J = 55.6 Hz), 6.70 (1H, d J = 8.0 Hz), 6.47 (1H, s), 4.25-4.37 (3H, m), 3.21 (4H, s), 1.32 (6H, d, J = 6.4 Hz).	429.2	428.19
214	1H-NMR (DMSO-d6) δ: 9.86 (1H, s), 9.21 (1H, s), 8.13 (1H, d, J = 8.8 Hz), 8.05 (1H, d, J = 2.8 Hz), 7.50 (1H, dd, J = 9.2, 2.8 Hz), 6.88 (1H, s), 6.38 (1H, d J = 7.6 Hz), 4.24-4.29 (2H, m), 3.76-3.78 (4H, m), 3.28 (3H, s), 3.11-3.14 (4H, m), 1.39 (3H, d, J = 6.8 Hz), 1.31 (6H, apparent t, J = 3.2 Hz).	424.2	423.24
215	1H-NMR (DMSO-d6) δ: 10.07 (1H, s), 9.21 (1H, s), 8.15-8.21 (2H, m), 7.46-7.68 (1H,m), 6.99 (1H, s), 6.70 (1H, s), 5.19 (1H, d, J = 6.4 Hz), 4.60-4.64 (1H, m), 3.56 (2H, s), 3.39 (3H, s), 3.03-3.07 (2H, m), 2.56-2.72 (3H, m), 1.70-1.74 (2H, m), 1.51-1.55 (8H, m), 1.39 (6H, d, J = 8.4 Hz).	452.3	451.27

[Table 5-33]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
216	1H-NMR (DMSO-D6) δ: 10.36 (1H, br s), 8.90 (1H, s), 7.92 (1H, d, J = 9.8 Hz), 7.20 (1H, d, J = 8.8 Hz), 6.77 (1H, s), 6.54 (1H, s), 5.07 (1H, br s), 4.55-4.54 (1H, br m), 3.73-3.72 (4H, br m), 3.52 (2H, s), 3.39-3.38 (4H, br m), 3.30 (3H, s), 1.44 (6H, s), 1.35 (3H, d, J = 6.8 Hz).	455.20	454.24
217	1H-NMR (CDCl3) δ: 9.00 (1H, s), 8.38 (1H, d, J = 9.8 Hz), 8.16 (1H, brs), 7.07 (1H, d, J = 9.8 Hz), 6.83 (1H, s), 6.09 (1H, d, J = 7.3 Hz), 4.46-4.35 (1H, m), 4.32 (1H, q, J = 6.5 Hz), 3.58 (4H, t, J = 5.1 Hz), 3.05 (4H, t, J = 4.9 Hz), 1.50 (3H, d, J = 6.3 Hz), 1.34 (6H, dd, J = 6.3, 5.4 Hz).	424.25	423.25
218	1H-NMR (DMSO-d6) δ: 10.28 (1H, s), 9.38 (1H, s), 8.22-8.28 (2H, m), 7.80 (1H, dd, J = 11.6, 3.2 Hz), 7.60 (1H, s), 7.22 (1H, s), 6.81 (1H, t, J = 74.0 Hz), 6.69 (1H, d J = 10.4 Hz), 6.47 (1H, s), 4.24-4.35 (1H, m), 3.28-3.02 (2H, m), 3.06-3.22 (2H, m), 2.31-2.39 (2H, m), 1.82-1.90 (2H, m), 1.31 (6H, d, J = 8.4 Hz).	428.2	427.19
219	1H-NMR (DMSO-d6) δ: 10.31 (1H, s), 9.34 (1H, s), 8.26 (1H, d, J = 8.4 Hz), 8.24 (1H, d, J = 1.6 Hz), 7.74 (1H, dd, J = 8.4, 2.0 Hz), 7.22 (1H, s), 6.81 (1H, t, J = 55.6 Hz), 6.72 (1H, d J = 8.0 Hz),4.42 (1H, s), 4.27-4.32 (1H, m), 3.13-3.18 (4H, m), 1.76-1.82 (2H, m), 1.31 (6H, d, J = 6.4 Hz).	443.2	442.20
220	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.35 (1H, d, J = 8.8 Hz), 8.27 (2H, d, J = 2.4 Hz), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 6.84 (1H, s), 6.14 (1H, d, J = 7.3 Hz), 4.47-4.36 (1H, m), 4.34 (1H, q, J = 6.5 Hz), 3.49 (2H, s), 3.41 (3H, s), 2.91 (4H, t, J = 4.6 Hz), 2.46 (4H, brs), 1.51 (3H, d, J = 6.3 Hz), 1.36 (6H, t, J = 5.9 Hz).	437.35	436.27

[Table 5-34]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
221	1H-NMR (CDCl3) δ: 9.00 (1H, s), 8.36 (1H, d, J = 8.8 Hz), 8.26 (2H, d, J = 3.7 Hz), 7.73 (1H, dd, J = 8.5, 2.2 Hz), 6.91 (1H, s), 6.71 (1H, s), 4.81 (1H, q, J = 6.3 Hz), 3.62 (2H, dd, J = 10.5, 9.0 Hz), 3.50 (3H, s), 3.49 (2H, s), 2.90 (4H, t, J = 4.9 Hz), 2.44 (4H, brs), 1.60 (6H, s), 1.54 (3H, d, J = 6.3 Hz).	467.35	466.28
222	1H-NMR (DMSO-d6) δ: 10.13 (1H, s), 9.23 (1H, s), 8.16-8.20 (2H, m), 7.74 (1H, m), 7.50 (1H, br s), 7.00 (1H, s), 6.92 (1H, s), 6.71 (1H, s), 5.20 (1H, d, J = 6.4 Hz), 4.62-4.69 (1H, m), 3.57 (2H, s), 3.39 (5H, s), 1.51 (6H, s), 1.40 (3H, d, J = 8.4 Hz).	426.2	425.22
223	1H-NMR (DMSO-d6) δ: 10.00 (1H, s), 9.25 (1H, s), 8.18-8.22 (2H, m), 7.70 (1H, m), 6.89 (1H, s), 6.44 (1H, d, J = 6.8 Hz), 4.69 (1H, br s), 4.25-4.26 (2H, br m), 3.61-3.63 (2H, br m), 2.71(2H, br s), 1.39 (3H, d, J = 6.0 Hz), 1.31 (6H, br s).	383.2	382.21
224	1H-NMR (DMSO-d6) δ: 10.03 (1H, s), 9.25 (1H, s), 8.22-8.24 (2H, m), 7.74 (1H, dd, J = 8.8, 2.4 Hz), 6.90 (1H, s), 6.44 (1H, d, J = 8.0 Hz), 4.53-4.57 (1H, br m), 4.23-4.29 (2H, br m), 3.92-3.96 (1H, br m), 3.31(3H, s), 3.10-3.16 (1H, m), 2.77-2.81 (1H, m), 2.51-2.67 (1H, m), 2.04 (3H, s), 1.77-1.86 (1H, m), 1.62-1.66 (1H, m), 1.46-1.50 (1H, m), 1.39 (3H, d, J = 6.4 Hz), 1.32 (6H, m).	464.3	463.27
225	1H-NMR (DMSO-d6) δ: 10.10 (1H, s), 9.23 (1H, s), 8.24 (1H, d, J = 2.4 Hz), 8.16 (1H, d, J = 11.2 Hz), 7.72 (1H, m), 7.00 (1H, s), 6.69 (1H, s), 5.20 (1H, 6.4 Hz), 4.50-4.68 (2H, br m), 3.92-3.96 (1H, br m), 3.58 (2H, s), 3.38 (3H, s), 3.09-3.16 (1H, m), 2.71-2.81 (1H, m), 2.61-2.67 (1H, m), 2.04 (3H, s), 1.77-1.86 (2H, m), 1.51-1.62 (1H, m), 1.51 (6H, s), 1.40 (3H, d, J = 8.4 Hz).	494.2	493.28

[Table 5-35]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
226	1H-NMR (DMSO-D6) δ: 10.41 (1H, s), 9.27 (1H, s), 8.11 (1H, d, J = 9.8 Hz), 7.37 (1H, d, J = 10.2 Hz), 7.18 (1H, s), 6.78 (1H, t, J = 55.4 Hz), 6.58 (1H, d, J = 7.8 Hz), 4.87 (1H, d, J = 4.4 Hz), 4.28-4.23 (1H, m), 4.15-4.11 (1H, m), 3.95-3.92 (1H, m), 3.56-3.55 (1H, m), 3.05-3.02 (1H, m), 2.84-2.81 (1H, m), 1.89-1.87 (1H, br m), 1.76-1.73 (1H, br m), 1.49-1.38 (2H, m), 1.28 (6H, d, J = 6.8 Hz).		
227	1H-NMR (DMSO-D6) δ: 9.96 (1H, s), 9.21 (1H, d, J = 1.5 Hz), 8.17 (1H, d, J = 9.3 Hz), 8.06 (1H, d, J = 2.4 Hz), 7.51 (1H, dd, J = 9.3, 2.9 Hz), 6.87 (1H, s), 6.39 (1H, d, J = 7.3 Hz), 4.29-4.23 (2H, m), 4.15 (2H, t, J = 5.4 Hz), 3.27 (3H, d, J = 1.5 Hz), 2.77 (2H, t, J = 5.4 Hz), 2.32 (6H, s), 1.38 (3H, d, J = 6.3 Hz), 1.29 (6H, dd, J = 6.3, 3.4 Hz).	426.3	425.25
228	1H-NMR (DMSO-d6) δ: 10.52 (1H, s), 9.24 (1H, s), 8.19 (1H, s), 8.13 (1H, d, J = 8.0 Hz), 7.71 (1H, d, J = 8.8 Hz), 7.00 (1H, s), 4.60-4.65 (1H, br m), 3.57-3.63 (4H, m), 3.37 (3H, s), 2.67-2.74 (2H, m), 1.51 (6H, s), 1.40 (3H, d, J = 6.8 Hz).	413.2	412.22
229	1H-NMR (DMSO-D6) δ: 9.95 (1H, s), 9.23 (1H, s), 8.20 (1H, d, J = 8.3 Hz), 8.18 (1H, d, J = 2.0 Hz), 7.70 (1H, dd, J = 8.5, 2.2 Hz), 6.98 (1H, s), 6.39 (1H, d, J = 7.3 Hz), 5.18 (1H, d, J = 4.4 Hz), 4.64-4.58 (1H, m), 4.26 (1H, td, J = 13.3, 6.2 Hz), 4.00 (2H, s), 3.79 (2H, t, J = 5.1 Hz), 3.38-3.32 (4H, m), 2.55 (2H, t, J = 7.6 Hz), 1.85-1.78 (2H, m), 1.38 (3H, d, J = 6.8 Hz), 1.29 (6H, dd, J = 6.6, 1.7 Hz).	466.25	465.25

[Table 5-36]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
230	1H-NMR (DMSO-D6) δ: 10.17 (1H, s), 9.26 (1H, s), 8.33-8.26 (2H, m), 7.80 (1H, dd, J = 8.8, 2.4 Hz), 6.99 (1H, s), 6.42 (1H, d, J = 7.3 Hz), 5.19 (1H, d, J = 4.4 Hz), 4.68-4.55 (1H, m), 4.31-4.21 (1H, m), 3.63 (2H, t, J = 5.4 Hz), 3.40 (2H, s), 3.03 (2H, t, J = 5.1 Hz), 1.39 (3H, d, J = 6.3 Hz), 1.30 (6H, dd, J = 6.3, 2.0 Hz).	423.25	422.22
231	1H-NMR (DMSO-d6) δ: 9.25 (1H, s), 8.23 (1H, d, J = 8.4 Hz), 8.19 (1H, d, J = 2.0 Hz), 7.72 (1H, dd, J = 8.8, 2.4 Hz), 6.90 (1H, s), 6.51 (1H, d, J = 6.8 Hz), 4.24-4.30 (3H, m), 3.39 (2H, s), 3.23 (3H, s), 1.39 (6H, d, J = 6.4 Hz), 1.24-1.32 (3H, m).	396.2	395.21
232	1H-NMR (DMSO-d6) δ: 10.00 (1H, s), 9.24 (1H, s), 8.21 (1H, d, J = 8.4 Hz), 8.19 (1H, d, J = 2.0 Hz), 7.70 (1H, dd, J = 8.4, 2.4 Hz), 6.89 (1H, s), 6.45 (1H, d, J = 7.6 Hz), 4.25-4.28 (2H, m), 3.30 (3H, s), 3.02-3.04 (2H, m), 2.52-2.61(3H, m), 1.69-1.72 (2H, m), 1.52-1.55 (2H, m), 1.39 (3H, d, J = 6.8 Hz), 1.30-1.32 (6H, m).	422.2	421.26
233	1H-NMR (DMSO-D6) δ: 10.09 (1H, br s), 9.26 (1H, s), 8.25-8.17 (2H, m), 7.78 (1H, br s), 6.99 (1H, s), 6.43 (1H, d, J = 7.8 Hz), 5.21 (1H, d, J = 4.9 Hz), 4.61 (1H, t, J = 5.4 Hz), 4.28-4.25 (1H, m), 3.58-3.45 (4H, m), 2.37 (3H, br s), 1.38 (3H, d, J = 6.8 Hz), 1.30-1.29 (6H, m).		
234	1H-NMR (DMSO-D6) δ: 10.07 (1H, s), 9.25 (1H, s), 8.28-8.24 (2H, m), 7.77-7.75 (2H, m), 6.99 (1H, s), 6.42 (1H, d, J = 6.8 Hz), 5.18 (1H, s), 4.61 (1H, t, J = 5.4 Hz), 4.29-4.22 (1H, m), 3.53 (2H, s), 3.14 (2H, s), 2.93 (2H, s), 2.56 (3H, t, J = 4.9 Hz), 1.38 (4H, d, J = 6.8 Hz), 1.30 (6H, d, J = 4.9 Hz).		

[Table 5-37]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
235	1H-NMR (DMSO-D6) δ: 10.08 (1H, s), 9.15 (1H, s), 7.94 (1H, d, J = 9.3 Hz), 7.00-6.93 (2H, m), 6.66 (1H, t, J = 5.6 Hz), 6.58 (1H, s), 5.16 (1H, d, J = 4.4 Hz), 4.77 (1H, t, J = 5.4 Hz), 4.63-4.57 (1H, m), 3.58 (2H, q, J = 5.4 Hz), 3.51 (2H, s), 3.40 (2H, q, J = 5.9 Hz), 3.34 (3H, s), 1.47 (6H, s), 1.38 (3H, d, J = 6.8 Hz).	429.25	428.23
236	1H-NMR (DMSO-D6) δ: 10.33 (1H, s), 9.34 (1H, s), 8.28-8.24 (2H, m), 7.79 (1H, dd, J = 8.3, 2.0 Hz), 7.21 (1H, s), 6.94-6.66 (2H, m), 4.31-4.24 (1H, m), 3.57 (2H, br s), 3.11 (3H, s), 2.91-2.89 (2H, br m), 2.23-2.20 (1H, br m), 2.09-2.06 (2H, br m), 1.77-1.74 (2H, br m), 1.57-1.55 (2H, br m), 1.31 (6H, d, J = 6.3 Hz).	549.62	548.21
237		451.61	450.25
238	1H-NMR (DMSO-D6) δ: 10.31 (1H, s), 9.35 (1H, s), 8.26-8.17 (2H, m), 7.75 (1H, dd, J = 8.3, 2.0 Hz), 6.62 (1H, d, J = 7.8 Hz), 5.13-5.07 (1H, m), 4.79 (1H, d, J = 6.8 Hz), 4.45-4.30 (1H, m), 3.41 (2H, s), 2.67 (4H, t, J = 4.4 Hz), 2.29 (4H, brs), 1.38 (3H, d, J = 6.3 Hz), 1.31 (6H, t, J = 6.6 Hz).	457.20	456.22
239	1H-NMR (DMSO-D6) δ: 10.12 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.21-8.18 (1H, m), 7.74 (1H, d, J = 8.8 Hz), 6.89 (1H, s), 6.45 (1H, d, J = 7.3 Hz), 4.29-4.22 (2H, m), 3.47 (2H, s), 3.27 (3H, s), 2.50-2.36 (8H, m), 1.45-1.42 (2H, m), 1.38 (3H, d, J = 6.3 Hz), 1.30 (6H, t, J = 4.9 Hz), 0.82 (3H, t, J = 7.3 Hz).		

[Table 5-38]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
240	1H-NMR (DMSO-D6) δ: 10.09 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.18 (1H, d, J = 12.2 Hz), 7.74 (1H, d, J = 8.8 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.30-4.22 (2H, m), 3.45 (2H, s), 3.27 (3H, s), 2.42-2.34 (10H, m), 1.38 (3H, d, J = 6.3 Hz), 1.30 (6H, dd, J = 6.1, 3.7 Hz), 0.98 (3H, t, J = 7.1 Hz).		
241	1H-NMR (DMSO-D6) δ: 10.28 (1H, s), 9.28 (1H, s), 8.37-8.35 (2H, m), 7.94 (1H, dd, J = 8.8, 2.0 Hz), 7.01 (1H, s), 6.44 (1H, d, J = 6.8 Hz), 5.22 (1H, d, J = 3.9 Hz), 4.62 (1H, t, J = 5.4 Hz), 4.28-4.25 (1H, m), 4.13 (2H, s), 3.58 (2H, t, J = 5.4 Hz), 3.30 (6H, s), 3.09 (2H, t, J = 4.9 Hz), 1.39 (3H, d, J = 6.8 Hz), 1.30 (6H, dd, J = 6.8, 2.0 Hz).		
242	1H-NMR (DMSO-D6) δ: 10.51 (1H, s), 9.29 (1H, s), 8.93 (2H, s), 8.42 (1H, s), 8.28 (1H, d, J = 8.8 Hz), 7.95 (1H, d, J = 6.8 Hz), 7.03 (1H, s), 6.72 (1H, s), 4.64 (1H, d, J = 5.9 Hz), 4.18 (2H, s), 3.59 (4H, s), 3.40 (3H, s), 3.31 (3H, s), 3.13 (2H, s), 1.51 (6H, s), 1.40 (3H, d, J = 5.9 Hz).		
243	1H-NMR (DMSO-D6) δ: 10.20 (1H, s), 9.23 (1H, s), 8.19 (2H, t, J = 12.9 Hz), 7.71 (1H, dd, J = 8.8, 2.0 Hz), 6.99 (1H, s), 6.70 (1H, s), 4.62 (1H, q, J = 6.5 Hz), 3.56 (2H, s), 3.38 (3H, s), 3.16 (2H, s), 2.49-2.44 (8H, br m), 2.32 (2H, t, J = 7.6 Hz), 1.50 (6H, s), 1.45-1.39 (5H, m), 0.82 (3H, t, J = 7.3 Hz).		

[Table 5-39]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
244	1H-NMR (DMSO-D6) δ: 10.17 (1H, s), 9.23 (1H, d, J = 4.9 Hz), 8.19 (2H, t, J = 12.4 Hz), 7.71 (1H, dd, J = 8.5, 1.7 Hz), 6.99 (1H, s), 6.70 (1H, s), 4.62 (1H, q, J = 6.3 Hz), 3.56 (2H, s), 3.46 (2H, s), 3.38 (3H, s), 2.40-2.35 (8H, br m), 1.50 (6H, s), 1.40 (3H, d, J = 6.3 Hz), 0.99 (3H, t, J = 7.3 Hz).		
245	1H-NMR (DMSO-D6) δ: 9.89 (1H, s), 9.20 (1H, d, J = 1.0 Hz), 8.16 (2H, dd, J = 5.1, 4.1 Hz), 8.04 (1H, d, J = 2.9 Hz), 7.50 (1H, dd, J = 9.3, 2.9 Hz), 6.96 (1H, s), 6.35 (1H, d, J = 7.8 Hz), 4.60 (1H, q, J = 6.3 Hz), 4.27-4.22 (1H, m), 4.12 (2H, t, J = 5.9 Hz), 2.65 (2H, t, J = 5.6 Hz), 2.24 (6H, s), 1.38 (3H, d, J = 6.3 Hz), 1.29 (6H, d, J = 6.3 Hz).		
246	1H-NMR (DMSO-D6) δ: 10.71 (1H, brs), 9.28 (1H, s), 8.53 (1H, d, J = 9.3 Hz), 7.70 (1H, d, J = 9.3 Hz), 6.91 (1H, s), 6.50 (1H, d, J = 7.3 Hz), 4.30-4.23 (2H, m), 3.68 (2H, s), 3.28 (3H, s), 2.68 (4H, t, J = 4.6 Hz), 2.34 (4H, s), 1.39 (3H, d, J = 6.3 Hz), 1.30 (6H, dd, J = 6.3, 3.9 Hz).	438.30	437.27
247	1H-NMR (DMSO-D6) δ: 10.45 (1H, s), 9.36 (1H, s), 8.37-8.25 (2H, m), 7.82 (1H, dd, J = 8.8, 2.4 Hz), 6.64 (1H, d, J = 7.3 Hz), 5.14-5.07 (1H, m), 4.80 (1H, d, J = 6.3 Hz), 4.42-4.30 (1H, m), 3.64 (2H, t, J = 5.4 Hz), 3.41 (2H, s), 3.03 (2H, t, J = 5.4 Hz), 1.38 (3H, d, J = 6.3 Hz), 1.31 (6H, t, J = 6.6 Hz).	457.20	456.18

[Table 5-40]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
249	1H-NMR (DMSO-D6) δ: 10.22 (1H, s), 9.20 (1H, s), 8.17 (1H, d, J = 9.8 Hz), 7.39 (1H, d, J = 9.8 Hz), 6.87 (1H, s), 6.36 (1H, d, J = 7.3 Hz), 4.43 (1H, t, J = 5.4 Hz), 4.28-4.17 (2H, m), 3.55 (2H, t, J = 5.9 Hz), 3.50 (4H, t, J = 5.1 Hz), 3.26 (3H, s), 2.55 (4H, t, J = 4.9 Hz), 2.44 (2H, t, J = 6.3 Hz), 1.37 (3H, d, J = 6.3 Hz), 1.27 (6H, dd, J = 6.3, 3.4 Hz).	468.25	467.28
250	1H-NMR (CDCl3) δ: 9.02 (1H, s), 8.34 (1H, d, J = 9.8 Hz), 8.28 (1H, br s), 7.07 (1H, d, J = 10.2 Hz), 6.74 (1H, s), 6.30 (1H, d, J = 7.8 Hz), 4.80 (1H, q, J = 6.3 Hz), 4.38-4.27 (1H, m), 4.08-4.02 (2H, m), 3.67-3.57 (6H, m), 3.07-3.02 (4H, m), 2.18-2.12 (2H, m), 1.74-1.63 (2H, m), 1.53 (3H, d, J = 6.3 Hz).		
251	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.33 (1H, d, J = 10.2 Hz), 8.27 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.77 (1H, s), 6.46 (1H, d, J = 6.8 Hz), 4.84-4.77 (2H, m), 4.12-4.03 (2H, m), 3.96-3.84 (2H, m), 3.61-3.57 (4H, m), 3.06-3.03 (4H, m), 2.49-2.39 (1H, m), 2.07-1.98 (1H, m), 1.54 (3H, d, J = 6.8 Hz).		
252	1H-NMR (CDCl3) δ: 9.02 (1H, s), 8.34 (1H, d, J = 10.2 Hz), 8.27 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.76 (1H, s), 6.46 (1H, d, J = 6.8 Hz), 4.84-4.76 (2H, m), 4.12-4.03 (2H, m), 3.96-3.84 (2H, m), 3.62-3.58 (4H, m), 3.07-3.04 (4H, m), 2.48-2.39 (1H, m), 2.07-1.97 (1H, m), 1.53 (3H, d, J = 6.3 Hz).		

[Table 5-41]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
253	1H-NMR (CDCl3) δ: 9.02 (1H, s), 8.40 (1H, d, J = 9.8 Hz), 8.30 (1H, br s), 7.07 (1H, d, J = 10.2 Hz), 6.73 (1H, s), 6.65 (1H, d, J = 8.3 Hz), 4.79 (1H, q, J = 6.3 Hz), 4.36-4.29 (1H, m), 4.01 (1H, dd, J = 11.2, 2.9 Hz), 3.78-3.74 (2H, m), 3.66-3.58 (5H, m), 3.08-3.04 (4H, m), 2.09-2.01 (1H, m), 1.93-1.84 (2H, m), 1.73-1.66 (1H, m), 1.53 (3H, d, J = 6.3 Hz).		
254	1H-NMR (DMSO-D6) δ: 10.22 (1H, s), 9.20 (1H, s), 8.17 (1H, d, J = 9.8 Hz), 7.39 (1H, d, J = 9.8 Hz), 6.87 (1H, s), 6.36 (1H, d, J = 7.3 Hz), 4.43 (1H, t, J = 5.4 Hz), 4.28-4.17 (2H, m), 3.55 (2H, t, J = 5.9 Hz), 3.50 (4H, t, J = 5.1 Hz), 3.26 (3H, s), 2.55 (4H, t, J = 4.9 Hz), 2.44 (2H, t, J = 6.3 Hz), 1.37 (3H, d, J = 6.3 Hz), 1.27 (6H, dd, J = 6.3, 3.4 Hz).		
255	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.48 (1H, br s), 8.33 (1H, d, J = 8.8 Hz), 8.30 (1H, d, J = 2.4 Hz), 7.73 (1H, dd, J = 8.8, 2.4 Hz), 6.76 (1H, s), 6.36 (1H, d, J = 7.3 Hz), 4.82 (1H, q, J = 6.3 Hz), 4.39-4.29 (1H, m), 4.10-4.03 (2H, m), 3.69-3.61 (2H, m), 3.54 (2H, s), 3.09-3.04 (4H, m), 2.65-2.57 (4H, m), 2.21-2.15 (2H, m), 1.76-1.65 (2H, m), 1.54 (3H, d, J = 6.3 Hz).		
256	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.38 (1H, d, J = 8.8 Hz), 8.28-8.24 (2H, m), 7.71 (1H, dd, J = 8.5, 2.2 Hz), 6.75 (1H, s), 6.70 (1H, d, J = 8.3 Hz), 4.80 (1H, q, J = 6.2 Hz), 4.39-4.31 (1H, m), 4.02 (1H, dd, J = 11.2, 2.9 Hz), 3.80-3.75 (2H, m), 3.65 (1H, dd, J = 11.0, 5.6 Hz), 3.56 (2H, s), 3.19-3.10 (4H, m), 2.74-2.64 (4H, m), 2.09-2.02 (1H, m), 1.95-1.85 (2H, m), 1.76-1.67 (1H, m), 1.53 (3H, d, J = 6.3 Hz).	465.35	464.26

[Table 5-42]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
257	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.44 (1H, br s), 8.37 (1H, d, J = 8.3 Hz), 8.29 (1H, d, J = 2.0 Hz), 7.73 (1H, dd, J = 8.3, 2.4 Hz), 6.74 (1H, s), 6.69 (1H, d, J = 8.3 Hz), 4.80 (1H, q, J = 6.3 Hz), 4.38-4.31 (1H, m), 4.03 (1H, dd, J = 11.2, 2.9 Hz), 3.80-3.75 (2H, m), 3.64 (1H, dd, J = 11.2, 5.9 Hz), 3.52 (2H, s), 3.04-3.00 (4H, m), 2.62-2.51 (4H, m), 2.11-2.03 (1H, m), 1.95-1.84 (2H, m), 1.76-1.68 (1H, m), 1.53 (3H, d, J = 6.8 Hz).		
258	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.39 (1H, br s), 8.31 (1H, d, J = 8.8 Hz), 8.28 (1H, d, J = 2.0 Hz), 7.74 (1H, dd, J = 8.5, 2.2 Hz), 6.79 (1H, s), 6.50 (1H, d, J = 6.8 Hz), 4.86-4.78 (2H, m), 4.14-4.05 (2H, m), 3.97-3.85 (2H, m), 3.51 (2H, s), 2.99-2.95 (4H, m), 2.55-2.41 (5H, m), 2.08-2.00 (1H, m), 1.54 (3H, d, J = 6.3 Hz).		
259	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.42 (1H, br s), 8.31 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 2.4 Hz), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 6.78 (1H, s), 6.50 (1H, d, J = 6.8 Hz), 4.85-4.78 (2H, m), 4.14-4.05 (2H, m), 3.98-3.86 (2H, m), 3.51 (2H, s), 2.98-2.93 (4H, m), 2.55-2.41 (5H, m), 2.08-1.99 (1H, m), 1.54 (3H, d, J = 6.3 Hz).		
260	1H-NMR (DMSO-D6) δ: 10.14 (1H, s), 9.19 (1H, s), 8.14 (1H, t, J = 4.9 Hz), 7.40 (1H, d, J = 9.8 Hz), 6.96 (1H, s), 6.31 (1H, d, J = 7.8 Hz), 4.60 (1H, q, J = 6.5 Hz), 4.23 (1H, dd, J = 13.4, 6.6 Hz), 4.02-3.99 (2H, br m), 3.72-3.70 (1H, br m), 3.17-3.10 (2H, m), 1.83-1.80 (2H, br m), 1.43 (2H, dd, J = 16.1, 6.8 Hz), 1.37 (3H, d, J = 6.3 Hz), 1.27 (6H, d, J = 6.3 Hz).		

[Table 5-43]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
261	1H-NMR (DMSO-D6) δ: 10.15 (1H, brs), 9.17 (1H, s), 8.14 (1H, d, J = 9.8 Hz), 7.34 (1H, d, J = 9.8 Hz), 6.94 (1H, s), 6.31 (1H, d, J = 7.8 Hz), 5.15 (1H, d, J = 3.4 Hz), 4.60 (1H, dt, J = 11.1, 4.6 Hz), 4.27-4.18 (1H, m), 3.42 (4H, t, J = 5.1 Hz), 2.81 (4H, brs), 2.29 (1H, s), 1.37 (3H, d, J = 6.3 Hz), 1.27 (6H, d, J = 6.3 Hz).	410.25	409.23
263	1H-NMR (DMSO-D6) δ: 10.05 (1H, s), 9.24 (1H, s), 8.29-8.25 (3H, m), 7.83 (1H, d, J = 8.8 Hz), 6.99 (1H, s), 6.40 (1H, d, J = 6.8 Hz), 4.61 (1H, q, J = 6.2 Hz), 4.29-4.25 (1H, m), 2.87 (2H, s), 2.35 (4H, s), 1.38 (3H, d, J = 6.8 Hz), 1.34 (6H, s), 1.30 (8H, d, J = 5.9 Hz).		
264	1H-NMR (DMSO-D6) δ: 10.18 (1H, s), 9.23 (1H, s), 8.33 (1H, d, J = 2.0 Hz), 8.26 (1H, s), 8.19 (1H, d, J = 8.8 Hz), 7.79 (1H, dd, J = 8.8, 2.0 Hz), 6.99 (1H, s), 6.72 (1H, s), 4.62 (1H, q, J = 6.2 Hz), 3.55 (3H, s), 2.77 (2H, s), 2.30 (3H, s), 1.51 (6H, s), 1.39 (3H, d, J = 6.8 Hz), 1.31 (6H, s).		
265	1H-NMR (DMSO-D6) δ: 10.22 (1H, s), 9.23 (1H, s), 8.23-8.21 (3H, m), 7.72 (1H, d, J = 8.8 Hz), 6.99 (1H, s), 6.71 (1H, s), 5.23 (1H, s), 4.63-4.61 (1H, m), 3.58-3.56 (4H, m), 3.38 (3H, s), 2.88-2.86 (4H, m), 1.50 (6H, s), 1.39 (3H, d, J = 6.8 Hz), 1.33 (3H, d, J = 6.8 Hz).		
266	1H-NMR (DMSO-D6) δ: 10.11 (1H, s), 9.25 (1H, s), 8.36 (2H, s), 8.26 (1H, d, J = 8.8 Hz), 8.20 (1H, s), 7.75 (1H, d, J = 8.8 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 6.8 Hz), 4.29-4.22 (3H, m), 3.50 (7H, d, J = 6.8 Hz), 3.27 (6H, s), 2.80 (4H, s), 2.38-2.36 (6H, br m), 1.38 (3H, d, J = 5.9 Hz), 1.33-1.29 (6H, m).		

[Table 5-44]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
269	1H-NMR (DMSO-D6) δ: 10.38 (1H, s), 9.33 (1H, s), 8.49 (1H, d, J = 9.8 Hz), 7.40-7.33 (2H, m), 5.46-5.39 (1H, m), 5.36 (1H, d, J = 4.4 Hz), 4.72-4.64 (1H, m), 3.43 (4H, dd, J = 5.6, 4.1 Hz), 2.81 (4H, dd, J = 5.9, 3.9 Hz), 1.41 (9H, dd, J = 5.9, 2.4 Hz).	411.20	410.22
270	1H-NMR (DMSO-D6) δ: 10.11 (1H, s), 9.25 (1H, s), 8.26 (1H, d, J = 8.8 Hz), 8.20 (1H, t, J = 6.3 Hz), 7.75 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.27-4.20 (2H, m), 3.56-3.53 (2H, m), 3.27 (5H, s), 2.70-2.67 (1H, m), 2.59-2.57 (1H, m), 2.44-2.41 (1H, m), 2.33-2.30 (1H, m), 2.01-1.97 (1H, m), 1.57-1.52 (1H, m), 1.38 (3H, d, J = 5.9 Hz), 1.30 (6H, dd, J = 5.9, 3.9 Hz).		
271	1H-NMR (DMSO-D6) δ: 10.12 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.22 (1H, br s), 7.77 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 5.27-5.11 (1H, br m), 4.27-4.24 (2H, m), 3.59 (2H, s), 3.27 (3H, s), 2.83-2.74 (2H, m), 2.62-2.57 (1H, m), 2.32-2.30 (1H, m), 2.22-2.06 (1H, m), 1.91-1.83 (1H, m), 1.38 (3H, d, J = 6.8 Hz), 1.29 (6H, dd, J = 6.3, 3.4 Hz).		
272	1H-NMR (DMSO-D6) δ: 10.11 (1H, s), 9.25 (1H, s), 8.28-8.26 (2H, m), 7.79 (1H, d, J = 9.8 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 6.8 Hz), 4.41 (2H, d, J = 5.9 Hz), 4.30-4.22 (2H, m), 3.70 (2H, s), 3.26 (3H, s), 2.97 (2H, d, J = 10.7 Hz), 2.84 (1H, q, J = 6.5 Hz), 2.67 (2H, d, J = 11.7 Hz), 2.25 (1H, d, J = 7.8 Hz), 1.38 (3H, d, J = 5.9 Hz), 1.29 (6H, dd, J = 6.3, 3.4 Hz).		

[Table 5-45]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
273	1H-NMR (DMSO-D6) δ: 10.11 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.22 (1H, s), 7.78 (1H, d, J = 8.8 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.30-4.22 (2H, m), 3.68 (2H, t, J = 5.9 Hz), 3.62-3.60 (4H, br m), 3.27 (3H, s), 2.64-2.62 (4H, m), 1.83-1.79 (2H, m), 1.38 (3H, d, J = 5.9 Hz), 1.30 (6H, dd, J = 5.9, 3.9 Hz).		
274	1H-NMR (DMSO-D6) δ: 10.12 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.17 (1H, d, J = 14.6 Hz), 7.74 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.30-4.22 (2H, m), 3.44 (3H, s), 3.27 (3H, s), 3.17-3.16 (1H, m), 2.66-2.64 (2H, br m), 2.11-2.09 (2H, br m), 1.82-1.80 (2H, br m), 1.43-1.41 (2H, br m), 1.38 (3H, d, J = 5.9 Hz), 1.30 (6H, dd, J = 5.9, 3.9 Hz).		
276	1H-NMR (DMSO-D6) δ: 10.12 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.19 (1H, d, J = 2.0 Hz), 8.15 (1H, s), 7.74 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.50 (2H, dt, J = 47.8, 4.9 Hz), 4.30-4.22 (2H, m), 3.44 (2H, s), 3.27 (3H, s), 2.66-2.60 (1H, m), 2.56-2.53 (1H, m), 2.41-2.38 (8H, br m), 1.38 (3H, d, J = 6.8 Hz), 1.30 (6H, dd, J = 5.9, 3.9 Hz).		
277	1H-NMR (DMSO-D6) δ: 9.51 (1H, s), 8.19 (1H, s), 7.78 (1H, s), 7.30 (1H, dd, J = 8.8, 2.0 Hz), 7.02 (1H, s), 6.85 (1H, d, J = 7.8 Hz), 6.36 (1H, d, J = 7.8 Hz), 5.79 (1H, s), 4.36-4.26 (2H, m), 3.72 (2H, s), 3.49 (2H, s), 3.30 (3H, s), 2.75-2.74 (2H, m), 2.60 (3H, s), 1.38 (3H, d, J = 5.9 Hz), 1.29 (6H, t, J = 5.9 Hz).		

[Table 5-46]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
278	1H-NMR (DMSO-D6) δ: 10.11 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 7.8 Hz), 8.18 (1H, d, J = 2.0 Hz), 7.74 (1H, dd, J = 8.3, 2.4 Hz), 7.68 (1H, d, J = 4.9 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.30-4.22 (2H, m), 3.42 (2H, s), 3.27 (3H, s), 2.82 (2H, d, J = 10.7 Hz), 2.53 (3H, d, J = 4.9 Hz), 2.07-2.01 (1H, m), 1.93-1.87 (2H, m), 1.63-1.50 (4H, m), 1.38 (3H, d, J = 5.9 Hz), 1.30 (6H, dd, J = 6.8, 3.9 Hz).		
279	1H-NMR (DMSO-D6) δ: 10.06 (1H, s), 9.24 (1H, s), 8.25 (1H, d, J = 8.8 Hz), 8.20 (1H, s), 7.74 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.47 (1H, d, J = 7.8 Hz), 4.30-4.22 (2H, m), 3.51-3.45 (4H, br m), 3.27 (5H, s), 2.31 (2H, t, J = 4.4 Hz), 1.38 (3H, d, J = 6.8 Hz), 1.30 (6H, dd, J = 6.8, 3.9 Hz), 1.07 (6H, s).		
280	1H-NMR (DMSO-D6) δ: 10.07 (1H, s), 9.24 (1H, s), 8.26-8.25 (2H, m), 7.78 (1H, d, J = 9.8 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 4.30-4.22 (2H, m), 3.89 (1H, d, J = 13.7 Hz), 3.57 (2H, dd, J = 10.7, 2.0 Hz), 3.30-3.24 (6H, m), 2.73-2.69 (2H, m), 1.38 (3H, d, J = 5.9 Hz), 1.30 (6H, dd, J = 6.3, 3.4 Hz), 0.96 (6H, d, J = 6.8 Hz).		
281	1H-NMR (DMSO-D6) δ: 10.12 (1H, s), 9.25 (1H, s), 8.27 (1H, d, J = 7.8 Hz), 8.19 (1H, d, J = 2.0 Hz), 8.15 (1H, s), 7.74 (1H, dd, J = 8.3, 2.4 Hz), 6.89 (1H, s), 6.46 (1H, d, J = 7.8 Hz), 6.11 (1H, tt, J = 55.6, 4.1 Hz), 4.30-4.22 (2H, m), 3.44 (2H, s), 3.27 (3H, s), 2.69 (2H, td, J = 15.9, 4.2 Hz), 2.54-2.52 (2H, br m), 2.40-2.37 (4H, br m), 1.38 (3H, d, J = 5.9 Hz), 1.30 (6H, dd, J = 5.9, 3.9 Hz).		

[Table 5-47]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
282	1H-NMR (DMSO-d6) δ: 9.93 (1H, s), 9.22 (1H, s), 8.17 (1H, d, J = 12.4 Hz), 8.06 (1H, d, J = 4.0 Hz), 7.51 (1H, dd, J = 12.0, 4.0 Hz), 6.88 (1H, s), 6.39 (1H, d, J = 10.4 Hz), 4.24-4.29 (2H, m), 4.16 (2H, t, J = 15.2 Hz), 3.57-3.60 (4H, m), 3.21(6H, m), 2.69-2.73 (2H, m), 1.38 (3H, d, J = 8.4 Hz), 1.29-1.32 (6H, m).		
284	1H-NMR (DMSO-D6) δ: 10.18 (1H, s), 9.20 (1H, s), 8.28 (1H, d, J = 9.8 Hz), 7.31 (1H, d, J = 10.2 Hz), 6.96 (1H, s), 6.89 (1H, t, J = 5.9 Hz), 5.17 (1H, d, J = 2.9 Hz), 4.62-4.56 (1H, m), 3.81-3.75 (1H, m), 3.72-3.46 (5H, m), 3.45-3.40 (4H, m), 2.85-2.79 (4H, m), 2.69-2.62 (1H, m), 2.00-1.91 (1H, m), 1.71-1.62 (1H, m), 1.37 (3H, d, J = 6.3 Hz).		
285	1H-NMR (DMSO-D6) δ: 10.26 (1H, s), 9.21 (1H, s), 8.20 (1H, d, J = 9.8 Hz), 7.38 (1H, d, J = 10.2 Hz), 6.89 (1H, s), 6.48 (1H, d, J = 7.3 Hz), 4.26-4.11 (2H, m), 3.92-3.86 (2H, m), 3.51-3.42 (6H, m), 3.26 (3H, s), 2.86-2.82 (4H, m), 2.03-1.96 (2H, m), 1.68-1.55 (2H, m), 1.36 (3H, d, J = 6.3 Hz).		
286	1H-NMR (DMSO-D6) δ: 10.20 (1H, s), 9.20 (1H, s), 8.17 (1H, d, J = 13.2 Hz), 7.38 (1H, d, J = 13.2 Hz), 6.87 (1H, s), 6.36 (1H, d, J = 10.0 Hz), 4.87 (1H, d, J = 6.0 Hz), 4.21-4.28 (2H, m), 4.11-4.17 (1H, m), 3.92-3.96 (1H, m), 3.92-3.96 (1H, m), 3.56-3.61 (1H, m), 3.00 (3H, s), 2.98-3.03 (1H, m), 2.79-2.86 (1H, m), 1.91-1.94 (1H, m), 1.75-1.80 (1H, m), 1.40-1.51 (2H, m), 1.38 (3H, d, J = 10.0 Hz), 1.23-1.29 (6H, m).	439.4	438.25

[Table 5-48]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
287	1H-NMR (DMSO-D6) δ: 9.95 (1H, s), 9.22 (1H, s), 8.16 (1H, d, J = 8.8 Hz), 8.06 (1H, d, J = 2.8 Hz), 7.51 (1H, dd, J = 9.2, 3.2 Hz), 6.88 (1H, s), 6.39 (1H, d, J = 7.6 Hz), 5.31-5.34 (1H, m), 4.24-4.50 (2H, m), 4.15 (2H, br s), 2.83 (2H, br s), 1.96-2.03 (2H, m), 1.71 (4H, br s), 1.39 (3H, d, J = 6.4 Hz), 1.27-1.33 (6H, m).	452.2	451.27
288	1H-NMR (DMSO-D6) δ: 9.94 (1H, s), 9.22 (1H, s), 8.17 (1H, d, J = 8.8 Hz), 8.07 (1H, d, J = 2.8 Hz), 7.51 (1H, dd, J = 9.2, 3.2 Hz), 6.89 (1H, s), 6.39 (1H, d, J = 7.6 Hz), 4.22-4.30 (2H, m), 4.08-4.11 (2H, m), 3.28-3.30 (3H, m), 2.84-2.86 (2H, m), 2.36 (3H, s), 1.39 (3H, d, J = 6.4 Hz), 1.27-1.33 (6H, m).	412.1	411.24
289	1H-NMR (DMSO-D6) δ: 9.93 (1H, s), 9.22 (1H, s), 8.15 (1H, d, J = 9.2 Hz), 8.05 (1H, d, J = 3.2 Hz), 7.52 (1H, dd, J = 9.2, 2.8 Hz), 6.88 (1H, s), 6.39 (1H, d, J = 7.6 Hz), 4.40-4.48 (1H, m), 4.24-4.27 (2H, m), 3.28 (3H, s), 3.0 (2H, br s), 2.52-2.67 (2H, m), 1.93-1.95 (2H, m), 1.48-1.50 (2H, m), 1.39 (3H, d, J = 6.4 Hz), 1.30 (6H, dd, J = 6.4, 3.6 Hz).	438.2	437.25
290	1H-NMR (DMSO-D6) δ: 9.94 (1H, s), 9.22 (1H, s), 8.16 (1H, d, J = 8.8 Hz), 8.03 (1H, d, J = 3.2 Hz), 7.48 (1H, dd, J = 8.8 2.8 Hz), 6.89 (1H, s), 6.41 (1H, d, J = 7.2 Hz), 4.93-4.94 (1H, m), 4.25-4.29 (2H, m), 3.28 (3H, s), 3.11-3.12 (1H, m), 2.92-2.98 (2H, m), 2.85-2.86 (1H, m), 2.02-2.07 (1H, m), 1.83-1.85 (1H, m), 1.39 (3H, d, J = 6.4 Hz), 1.30 (6H, dd, J = 6.4, 3.6 Hz).	424.2	423.24

[Table 5-49]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
291	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.34-8.28 (3H, m), 7.74 (1H, dd, J = 8.8, 2.4 Hz), 6.88 (1H, s), 6.24 (1H, d, J = 7.8 Hz), 4.42-4.30 (2H, m), 4.09-4.03 (2H, m), 3.70-3.61 (2H, m), 3.50 (2H, s), 3.41 (3H, s), 3.00-2.90 (4H, m), 2.49 (4H, br s), 2.22-2.15 (2H, m), 1.73-1.61 (2H, m), 1.50 (3H, d, J = 6.3 Hz).		
292	1H-NMR (DMSO-D6) δ: 10.27 (1H, s), 9.24 (1H, s), 8.28 (1H, s), 8.23 (1H, d, J = 8.8 Hz), 8.12 (1H, s), 7.77 (1H, d, J = 7.8 Hz), 7.00 (1H, s), 6.70 (1H, s), 5.27-5.20 (2H, m), 4.63-4.61 (1H, m), 3.73 (1H, br s), 3.56 (2H, br s), 3.38 (2H, s), 2.98-2.88 (2H, br m), 2.19-2.13 (1H, m), 1.95-1.89 (1H, m), 1.50 (6H, s), 1.39 (3H, d, J = 5.9 Hz).		
293	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.23 (1H, s), 8.24-8.21 (2H, m), 8.14 (1H, s), 7.75 (1H, dd, J = 8.8, 2.0 Hz), 6.99 (1H, s), 6.71 (1H, s), 5.23 (1H, br s), 4.62 (1H, q, J = 6.5 Hz), 3.68 (2H, t, J = 5.9 Hz), 3.60-3.56 (5H, m), 3.38 (3H, s), 3.15 (1H, s), 2.64-2.62 (4H, m), 1.83-1.77 (2H, m), 1.50 (6H, s), 1.39 (3H, d, J = 6.8 Hz).		
294	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.23 (1H, s), 8.21-8.19 (2H, m), 8.14 (2H, s), 7.72 (1H, d, J = 10.7 Hz), 6.99 (1H, s), 6.71 (1H, s), 5.23 (1H, br s), 4.62 (1H, q, J = 6.2 Hz), 3.51 (3H, d, J = 33.2 Hz), 3.38 (3H, s), 3.18 (5H, d, J = 18.5 Hz), 2.66 (2H, br s), 2.12 (2H, t, J = 9.3 Hz), 1.51-1.49 (6H, m), 1.50 (6H, s), 1.39 (3H, d, J = 6.8 Hz).		

[Table 5-50]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
295	1H-NMR (DMSO-D6) δ: 10.26 (1H, s), 9.24 (1H, s), 8.30 (1H, d, J = 2.0 Hz), 8.24 (1H, d, J = 8.8 Hz), 7.79-7.78 (1H, m), 7.01 (2H, d, J = 14.6 Hz), 6.82 (1H, s), 6.70 (1H, s), 5.23 (1H, br s), 4.62 (1H, s), 3.94 (2H, t, J = 5.4 Hz), 3.70 (2H, s), 3.57 (3H, d, J = 10.7 Hz), 2.88-2.80 (2H, m), 1.49 (6H, d, J = 7.8 Hz), 1.39 (3H, d, J = 6.8 Hz).		
296	1H-NMR (DMSO-D6) δ: 9.50 (1H, s), 7.80 (1H, s), 7.31 (1H, dd, J = 7.8, 2.0 Hz), 7.15 (1H, s), 6.85 (1H, s), 6.36 (1H, d, J = 7.8 Hz), 5.79 (2H, s), 5.39 (1H, s), 4.66 (1H, d, J = 5.9 Hz), 4.11 (1H, s), 3.72 (2H, s), 3.60-3.46 (4H, m), 3.38 (2H, s), 3.15 (4H, s), 2.73 (2H, d, J = 4.9 Hz), 2.62 (3H, s), 2.49 (7H, s), 1.76-1.73 (1H, m), 1.51 (6H, s), 1.41 (3H, d, J = 5.9 Hz).		
297	1H-NMR (DMSO-D6) δ: 10.25 (1H, s), 9.24 (1H, s), 8.23-8.21 (2H, m), 8.13 (1H, s), 7.75-7.70 (2H, m), 7.00 (1H, s), 6.71 (1H, s), 5.23 (1H, s), 4.63-4.61 (1H, m), 3.57 (4H, d, J = 9.8 Hz), 3.38 (2H, s), 3.15 (1H, s), 2.96-2.91 (2H, m), 2.53 (3H, d, J = 3.9 Hz), 2.08-2.05 (3H, m), 1.65-1.56 (4H, m), 1.50 (6H, s), 1.39 (3H, d, J = 6.8 Hz).		
298	1H-NMR (DMSO-D6) δ: 10.18 (1H, s), 9.22 (1H, s), 8.21-8.19 (2H, m), 8.13 (1H, s), 7.74 (1H, dd, J = 8.3, 2.4 Hz), 6.99 (1H, s), 6.73 (1H, s), 5.23 (1H, br s), 4.62-4.60 (1H, m), 3.54 (1H, s), 3.48 (2H, t, J = 7.3 Hz), 3.40 (2H, s), 3.26 (1H, s), 2.32 (2H, t, J = 4.4 Hz), 1.50 (6H, s), 1.39 (3H, d, J = 5.9 Hz), 1.06 (6H, s).		

[Table 5-51]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
299	1H-NMR (DMSO-D6) δ: 10.22 (1H, s), 9.23 (1H, s), 8.21-8.20 (2H, m), 8.13 (1H, s), 7.72-7.71 (1H, m), 6.99 (1H, s), 6.71 (1H, s), 6.11 (1H, tt, J = 55.6, 4.1 Hz), 5.23 (1H, s), 4.63-4.61 (1H, m), 3.56 (1H, s), 3.47 (2H, s), 3.38 (3H, s), 3.15 (1H, s), 2.69 (2H, td, J = 15.6, 3.9 Hz), 2.53-2.51 (2H, m), 2.40 (4H, s), 1.50 (6H, s), 1.39 (3H, d, J = 6.8 Hz).		
300	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.38 (1H, d, J = 8.8 Hz), 8.29-8.24 (2H, m), 7.74 (1H, dd, J = 8.5, 2.2 Hz), 6.88 (1H, s), 6.53 (1H, d, J = 7.8 Hz), 4.40-4.29 (2H, m), 4.06 (1H, dd, J = 11.0, 2.7 Hz), 3.81-3.70 (2H, m), 3.58 (1H, dd, J = 11.2, 5.9 Hz), 3.49 (2H, s), 3.41 (3H, s), 2.95-2.87 (4H, m), 2.49-2.42 (4H, br m), 2.10-2.02 (1H, m), 1.96-1.67 (3H, m), 1.49 (3H, d, J = 6.3 Hz).		
301	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.38 (1H, d, J = 8.8 Hz), 8.31 (1H, br s), 8.27 (1H, d, J = 2.0 Hz), 7.74 (1H, dd, J = 8.5, 2.2 Hz), 6.88 (1H, s), 6.55 (1H, d, J = 8.3 Hz), 4.40-4.30 (2H, m), 4.06 (1H, dd, J = 10.7, 2.9 Hz), 3.81-3.72 (2H, m), 3.60 (1H, dd, J = 11.0, 6.1 Hz), 3.49 (2H, s), 3.41 (3H, s), 2.95-2.88 (4H, m), 2.53-2.37 (4H, m), 2.09-2.03 (1H, m), 1.95-1.82 (2H, m), 1.76-1.68 (1H, m), 1.49 (3H, d, J = 6.3 Hz).		
302	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.34-8.26 (3H, m), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 6.91 (1H, s), 6.39 (1H, d, J = 6.8 Hz), 4.86-4.80 (1H, m), 4.34 (1H, q, J = 6.5 Hz), 4.14-4.05 (2H, m), 3.97-3.90 (1H, m), 3.86-3.81 (1H, m), 3.49 (2H, s), 3.41 (3H, s), 2.94-2.89 (4H, m), 2.50-2.40 (5H, m), 2.06-1.76 (2H, m), 1.50 (3H, d, J = 6.3 Hz).		

[Table 5-52]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
303	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.36 (1H, br s), 8.33 (1H, d, J = 8.3 Hz), 8.28 (1H, d, J = 2.0 Hz), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 6.90 (1H, s), 6.39 (1H, d, J = 6.3 Hz), 4.87-4.81 (1H, m), 4.34 (1H, q, J = 6.3 Hz), 4.15-4.04 (2H, m), 3.97-3.90 (1H, m), 3.85 (1H, dd, J = 9.3, 3.9 Hz), 3.49 (2H, s), 3.41 (3H, s), 2.95-2.90 (4H, m), 2.50-2.39 (5H, m), 2.05-1.86 (2H, m), 1.51 (3H, d, J = 6.3 Hz).		
304	1H-NMR (CDCl3) δ: 9.02 (1H, s), 8.42 (1H, d, J = 9.8 Hz), 8.22 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.86 (1H, s), 6.49 (1H, d, J = 7.8 Hz), 4.38-4.28 (2H, m), 4.03 (1H, dd, J = 11.2, 2.9 Hz), 3.81-3.69 (2H, m), 3.61-3.55 (5H, m), 3.40 (3H, s), 3.08-3.02 (4H, m), 2.09-2.01 (1H, m), 1.91-1.70 (3H, m), 1.48 (3H, d, J = 6.3 Hz).		
305	1H-NMR (CDCl3) δ: 9.02 (1H, s), 8.42 (1H, d, J = 9.8 Hz), 8.24 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.87 (1H, s), 6.51 (1H, d, J = 8.3 Hz), 4.37-4.29 (2H, m), 4.04 (1H, dd, J = 10.7, 2.9 Hz), 3.79-3.71 (2H, m), 3.63-3.55 (5H, m), 3.40 (3H, s), 3.08-3.02 (4H, m), 2.08-1.99 (1H, m), 1.91-1.67 (3H, m), 1.48 (3H, d, J = 6.3 Hz).		
306	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.36 (1H, d, J = 9.8 Hz), 8.27 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.90 (1H, s), 6.35 (1H, d, J = 6.8 Hz), 4.86-4.79 (1H, m), 4.33 (1H, q, J = 6.3 Hz), 4.12-4.03 (2H, m), 3.96-3.89 (1H, m), 3.83 (1H, dd, J = 9.3, 3.4 Hz), 3.62-3.56 (4H, m), 3.41 (3H, s), 3.08-3.02 (4H, m), 2.48-2.38 (1H, m), 2.04-1.96 (1H, m), 1.49 (3H, d, J = 6.3 Hz).		

[Table 5-53]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
307	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.36 (1H, d, J = 9.8 Hz), 8.26 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.89 (1H, s), 6.35 (1H, d, J = 6.8 Hz), 4.87-4.80 (1H, m), 4.33 (1H, q, J = 6.5 Hz), 4.13-4.02 (2H, m), 3.95-3.89 (1H, m), 3.84 (1H, dd, J = 9.3, 3.4 Hz), 3.62-3.58 (4H, m), 3.40 (3H, s), 3.08-3.04 (4H, m), 2.47-2.37 (1H, m), 2.04-1.95 (1H, m), 1.50 (3H, d, J = 6.3 Hz).		
308	1H-NMR (DMSO-D6) δ: 10.08 (1.0H, br s), 9.40-9.08 (2.0H, m), 8.94-8.86 (1.0H, br m), 7.46-7.37 (1.0H, m), 6.83-6.78 (1.0H, m), 5.17-5.09 (1.0H, m), 4.58-4.54 (1.0H, br m), 4.20-4.09 (1.0H, br m), 3.44-3.37 (5.8H, m), 2.85-2.79 (2.2H, m), 2.36-2.20 (2.4H, m), 1.71-1.33 (9.6H, m).		
309	1H-NMR (DMSO-D6) δ: 10.10 (1H, br s), 9.33-8.93 (3H, m), 7.40-7.34 (1H, m), 6.84-6.78 (1H, m), 5.16-5.06 (1H, m), 4.59-4.54 (1H, m), 4.29-4.19 (1H, m), 3.41-3.35 (5H, m), 2.86-2.78 (3H, m), 2.39-2.27 (1H, m), 2.14-1.98 (2H, m), 1.82-1.33 (7H, m).		
310	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.20 (1H, s), 8.16 (1H, d, J = 9.8 Hz), 7.36 (1H, d, J = 9.8 Hz), 6.88 (1H, s), 6.35 (1H, d, J = 7.8 Hz), 4.34 (1H, q, J = 6.3 Hz), 4.29-4.16 (1H, m), 3.46 (2H, t, J = 7.1 Hz), 3.43 (4H, t, J = 4.9 Hz), 2.81 (4H, t, J = 4.9 Hz), 1.37 (3H, d, J = 6.3 Hz), 1.27 (6H, dd, J = 6.3, 3.9 Hz), 1.15 (3H, t, J = 7.1 Hz).	438.30	437.27

[Table 5-54]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
311	1H-NMR (DMSO-D6) δ: 10.62 (1H, brs), 9.27 (1H, s), 8.44 (1H, d, J = 9.3 Hz), 7.60 (1H, d, J = 9.3 Hz), 6.90 (1H, s), 6.48 (1H, d, J = 7.3 Hz), 4.32-4.20 (2H, m), 3.27 (3H, s), 3.04 (2H, dt, J = 12.4, 3.0 Hz), 2.92 (1H, tt, J = 12.0, 3.7 Hz), 2.61 (2H, td, J = 12.2, 2.4 Hz), 1.79 (2H, dt, J = 14.0, 1.6 Hz), 1.64 (2H, ddd, J = 24.4, 12.2, 3.9 Hz), 1.38 (3H, d, J = 6.8 Hz), 1.29 (6H, dd, J = 6.6, 3.7 Hz).	423.30	422.25
312	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.46 (1H, br s), 8.31 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 2.0 Hz), 7.74 (1H, dd, J = 8.8, 2.0 Hz), 6.74 (1H, s), 6.55 (1H, t, J = 6.1 Hz), 4.82 (1H, q, J = 6.3 Hz), 4.07-3.98 (2H, m), 3.59 (2H, t, J = 6.6 Hz), 3.50 (2H, s), 3.47-3.38 (2H, m), 2.93-2.87 (4H, m), 2.45 (4H, br s), 2.06-1.96 (1H, m), 1.78-1.73 (2H, m), 1.56-1.44 (5H, m).		
313	1H-NMR (CDCl3) δ: 9.00 (1H, s), 8.34 (1H, d, J = 9.8 Hz), 8.14 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.72 (1H, s), 6.50 (1H, t, J = 8.0 Hz), 4.80 (1H, q, J = 6.3 Hz), 4.03-3.37 (2H, m), 3.60-3.53 (6H, m), 3.45-3.38 (2H, m), 3.07-3.03 (4H, m), 2.04-1.96 (1H, m), 1.76-1.71 (2H, m), 1.57-1.45 (5H, m).		
314	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.27 (1H, d, J = 2.4 Hz), 8.24 (1H, d, J = 8.8 Hz), 8.12 (1H, br s), 7.78 (1H, dd, J = 8.8, 2.4 Hz), 6.85 (1H, s), 6.37 (1H, d, J = 7.8 Hz), 4.84 (1H, q, J = 6.3 Hz), 4.46-4.40 (1H, m), 3.51 (2H, s), 3.23-3.21 (4H, m), 2.92-2.91 (4H, m), 2.61-2.54 (2H, m), 2.46-2.33 (6H, m), 1.54 (3H, d, J = 6.3 Hz).		

[Table 5-55]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
315	1H-NMR (DMSO-D6) δ: 10.47 (1H, s), 9.18 (1H, s), 8.83 (1H, d, J = 9.8 Hz), 8.41 (1H, br s), 7.37 (1H, d, J = 9.8 Hz), 6.90 (1H, s), 5.14 (1H, br s), 4.64-4.56 (1H, m), 3.76-3.01 (8H, m), 1.67 (6H, s), 1.39 (3H, d, J = 6.3 Hz).		
316	1H-NMR (DMSO-D6) δ: 10.16 (1H, s), 9.10 (1H, s), 8.80 (1H, br s), 8.77 (1H, d, J = 9.8 Hz), 7.29 (1H, d, J = 9.8 Hz), 6.80 (1H, s), 5.12 (1H, d, J = 4.4 Hz), 4.59-4.53 (1H, m), 3.44-3.38 (4H, m), 2.85-2.80 (4H, m), 2.32-2.04 (4H, m), 1.88-1.74 (4H, m), 1.36 (3H, d, J = 6.8 Hz).		
317	1H-NMR (DMSO-D6) δ: 10.60 (1H, brs), 9.28 (1H, s), 8.48 (1H, d, J = 9.3 Hz), 7.61 (1H, d, J = 9.3 Hz), 7.02 (1H, s), 6.55 (1H, d, J = 7.3 Hz), 5.21 (1H, d, J = 4.4 Hz), 4.65-4.55 (1H, m), 4.24-4.12 (1H, m), 3.92-3.89 (2H, m), 3.48 (2H, dq, J = 16.6, 4.2 Hz), 3.04 (2H, dd, J = 10.0, 2.2 Hz), 2.92 (1H, tt, J = 12.0, 3.5 Hz), 2.61 (2H, td, J = 12.1, 2.1 Hz), 2.00 (2H, t, J = 13.7 Hz), 1.79 (2H, d, J = 12.2 Hz), 1.72-1.59 (4H, m), 1.38 (3H, d, J = 6.3 Hz).	451.30	450.25
318	1H-NMR (DMSO-D6) δ: 10.58 (1H, brs), 9.26 (1H, s), 8.44 (1H, d, J = 9.3 Hz), 7.60 (1H, d, J = 9.3 Hz), 7.00 (1H, d, J = 1.0 Hz), 6.43 (1H, d, J = 7.8 Hz), 5.20 (1H, d, J = 4.4 Hz), 4.67-4.57 (1H, m), 4.32-4.20 (1H,m), 3.06-3.03 (2H, m), 2.92 (1H, tt, J = 12.0, 3.6 Hz), 2.60 (2H, td, J = 12.0, 2.3 Hz), 1.79 (2H, dd, J = 12.7, 2.4 Hz), 1.64 (2H, ddd, J = 24.4, 12.2, 3.9 Hz), 1.38 (3H, d, J = 6.3 Hz), 1.29 (6H, dd, J = 6.3, 2.0 Hz).	409.30	408.24

[Table 5-56]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
319	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.26 (1H, s), 8.36-8.28 (2H, m), 8.15 (1H, d, J = 2.9 Hz), 7.82 (1H, dd, J = 9.0, 2.7 Hz), 6.99 (1H, s), 6.42 (1H, d, J = 7.3 Hz), 5.19 (1H, d, J = 4.4 Hz), 4.64-4.59 (1H, m), 4.32-4.13 (3H, m), 3.85-3.70 (4H, m), 1.39 (3H, d, J = 6.3 Hz), 1.29 (6H, dd, J = 6.3, 2.0 Hz).	451.30	450.21
320	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.39 (1H, br s), 8.36 (1H, d, J = 8.8 Hz), 8.28 (1H, d, J = 2.0 Hz), 7.76 (1H, dd, J = 8.8, 2.0 Hz), 6.88 (1H, s), 6.51 (1H, t, J = 5.4 Hz), 4.34 (1H, q, J = 5.9 Hz), 4.01-3.99 (1H, m), 3.93-3.91 (1H, m), 3.84-3.75 (2H, m), 3.71-3.67 (2H, m), 3.50 (2H, s), 3.41 (3H, s), 2.93-2.89 (4H, br m), 2.79-2.72 (1H, m), 2.46 (4H, br s), 2.19-2.11 (1H, m), 1.86-1.81 (2H, m), 1.50 (3H, d, J = 5.9 Hz).		
321	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.55 (1H, br s), 8.43 (1H, d, J = 9.8 Hz), 7.10 (1H, d, J = 9.8 Hz), 6.88 (1H, s), 6.48 (1H, t, J = 5.4 Hz), 4.33 (1H, q, J = 6.3 Hz), 4.00-3.98 (1H, m), 3.90-3.88 (1H, m), 3.82-3.77 (2H, m), 3.68-3.66 (2H, m), 3.60-3.58 (4H, m), 3.40 (3H, s), 3.06-3.05 (4H, m), 2.77-2.74 (1H, m), 2.16-2.13 (1H, m), 1.82-1.78 (2H, m), 1.50 (3H, d, J = 6.3 Hz).		
322		500.3	499.21
323	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.35-8.28 (3H, m), 7.77-7.76 (1H, m), 6.74 (1H, s), 6.65-6.62 (1H, br m), 4.82 (1H, q, J = 5.9 Hz), 4.04-4.00 (1H, m), 3.91-3.88 (1H, m), 3.83-3.79 (2H, m), 3.70-3.68 (2H, m), 3.50-3.49 (2H, m), 2.92-2.91 (4H, m), 2.76 (1H, br s), 2.46 (4H, br s), 2.18-2.15 (1H, m), 1.82-1.79 (2H, m), 1.54 (3H, d, J = 5.9 Hz).		

[Table 5-57]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
324	1H-NMR (DMSO-D6) δ: 10.10-10.02 (0.2H, m), 9.91-9.80 (0.8H, m), 9.49-9.38 (0.8H, m), 9.23-9.12 (1.0H, m), 8.96-8.88 (0.8H, m), 8.51-8.41 (0.2H, m), 8.19-8.10 (1.0H, m), 7.90-7.70 (1.0H, m), 7.33-7.23 (0.2H, m), 6.98-6.82 (1.0H, m), 5.20-5.10 (1.0H, m), 4.64-4.53 (1.0H, m), 4.34-4.21 (1.0H, m), 2.69-1.98 (10.0H, m), 1.87-1.34 (8.0H, m).		
325	1H-NMR (DMSO-D6) δ: 9.94 (1H, br s), 9.13 (1H, s), 8.91 (1H, s), 8.81 (1H, d, J = 8.3 Hz), 8.16 (1H, s), 7.75 (1H, d, J = 8.3 Hz), 6.82 (1H, s), 5.10 (1H, br s), 4.60-4.55 (1H, m), 3.41 (2H, s), 2.72-2.66 (4H, br m), 2.33-2.03 (8H, m), 1.89-1.79 (4H, br m), 1.37 (3H, d, J = 6.3 Hz).		
326	1H-NMR (CDCl3) δ: 9.42 (1H, s), 8.60 (1H, br s), 8.31 (1H, d, J = 2.0 Hz), 8.29 (1H, d, J = 8.3 Hz), 7.77 (1H, dd, J = 8.5, 2.2 Hz), 6.42 (1H, d, J = 7.8 Hz), 5.18 (1H, q, J = 6.3 Hz), 4.34-4.27 (1H, m), 4.10-4.01 (2H, m), 3.69-3.59 (2H, m), 3.51 (2H, s), 2.95-2.86 (4H, m), 2.49-2.42 (4H, br m), 2.22-2.11 (2H, m), 1.78-1.64 (2H, m), 1.47 (3H, d, J = 6.3 Hz).		
327	1H-NMR (DMSO-D6) δ: 10.19 (1H, br s), 9.16 (1H, s), 8.74 (1H, d, J = 9.8 Hz), 8.06 (1H, br s), 7.31 (1H, d, J = 9.8 Hz), 6.92 (1H, s), 4.61 (1H, q, J = 6.3 Hz), 3.46-3.40 (4H, br m), 2.88-2.79 (4H, br m), 2.53-2.42 (2H, m), 1.58 (6H, s), 1.39 (3H, d, J = 6.3 Hz).		
328	1H-NMR (DMSO-D6) δ: 10.63 (1H, s), 9.36 (1H, s), 8.23-8.20 (2H, m), 7.60 (1H, s), 7.41 (1H, d, J = 9.8 Hz), 6.52 (1H, d, J = 7.8 Hz), 4.32-4.29 (1H, m), 3.52 (7H, t, J = 4.9 Hz), 3.15 (1H, s), 2.92 (4H, t, J = 4.9 Hz), 2.59 (3H, s), 1.33 (6H, d, J = 6.8 Hz).		

[Table 5-58]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
329	1H-NMR (DMSO-D6) δ: 10.45 (1H, s), 9.41 (1H, s), 8.28-8.25 (3H, m), 7.79 (1H, t, J = 8.3 Hz), 7.62 (1H, s), 6.62 (1H, d, J = 7.8 Hz), 4.35-4.32 (1H, m), 2.82 (3H, t, J = 3.9 Hz), 2.60 (3H, s), 2.40-2.33 (4H, m), 1.35 (6H, d, J = 6.8 Hz).		
330	1H-NMR (DMSO-D6) δ: 10.65 (1H, s), 9.38 (1H, s), 8.23-8.22 (2H, m), 7.62 (1H, s), 7.41 (1H, d, J = 9.8 Hz), 6.64 (1H, d, J = 7.8 Hz), 4.23-4.21 (1H, m), 3.92 (3H, d, J = 11.7 Hz), 3.51-3.49 (9H, m), 2.91 (5H, t, J = 4.9 Hz), 2.59 (3H, s), 2.05 (2H, d, J = 12.7 Hz), 1.71-1.64 (2H, m).		
331	1H-NMR (DMSO-D6) δ: 10.39 (1H, s), 9.29 (1H, s), 8.97 (1H, s), 8.72 (1H, d, J = 2.0 Hz), 8.57 (1H, d, J = 4.9 Hz), 8.43-8.40 (2H, m), 8.23 (1H, dd, J = 8.8, 2.0 Hz), 8.16 (1H, d, J = 7.8 Hz), 7.50 (1H, dd, J = 7.8, 4.9 Hz), 6.92 (1H, s), 6.50 (1H, d, J = 6.8 Hz), 4.29-4.26 (3H, m), 3.28 (3H, s), 1.39 (3H, d, J = 5.9 Hz), 1.31 (6H, dd, J = 5.9, 3.9 Hz).		
332	1H-NMR (DMSO-D6) δ: 10.09 (1H, s), 9.24 (1H, s), 8.34 (1H, s), 8.23-8.22 (2H, m), 7.74 (1H, d, J = 8.8 Hz), 6.89 (1H, s), 6.45 (1H, d, J = 6.8 Hz), 4.28-4.24 (2H, m), 3.27 (3H, s), 3.12-3.09 (2H, m), 2.77-2.75 (2H, m), 2.67-2.64 (1H, m), 2.54-2.52 (2H, br m), 1.87-1.85 (1H, m), 1.78-1.75 (1H, m), 1.64-1.61 (2H, m), 1.38 (3H, d, J = 6.8 Hz), 1.30 (6H, dd, J = 6.8, 3.9 Hz).		

[Table 5-59]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
333	1H-NMR (DMSO-D6) δ: 10.18 (1H, s), 9.22 (1H, s), 8.28 (1H, s), 8.23 (1H, s), 8.17 (1H, d, J = 8.8 Hz), 7.70 (1H, d, J = 6.8 Hz), 6.99 (1H, s), 6.69 (1H, s), 5.23 (1H, br s), 4.63-4.61 (1H, m), 3.56 (2H, s), 3.38 (2H, s), 3.14-3.10 (2H, m), 2.79-2.77 (2H, m), 2.70-2.68 (1H, m), 2.54-2.52 (3H, m), 1.89-1.86 (1H, m), 1.79-1.76 (1H, m), 1.63-1.57 (2H, m), 1.50 (6H, s), 1.39 (3H, d, J = 6.8 Hz).		
334	1H-NMR (DMSO-D6) δ: 10.09 (1H, s), 9.19 (1H, s), 8.08 (1H, d, J = 12.8 Hz), 7.00 (1H, d, J = 12.8 Hz), 6.86 (1H, s), 6.34 (1H, d, J = 10.0 Hz), 4.99 (1H, d, J = 4.8 Hz), 4.43 (1H, br s), 4.23 (1H, q, J = 8.8 Hz), 3.50-3.59 (3H, m), 3.37-3.40 (1H, m), 3.30 (3H, s), 1.91-2.07 (2H, m), 1.38 (3H, d, J = 8.4 Hz), 1.29 (6H, d, J = 2.8 Hz).	425.3	424.23
335	1H-NMR (DMSO-D6) δ: 10.31 (1H, s), 9.22 (1H, s), 8.23 (1H, d, J = 9.6 Hz), 7.46 (1H, d, J = 9.6 Hz), 6.89 (1H, s), 6.38 (1H, d, J = 7.6 Hz), 4.65 (1H, t, J = 5.6 Hz), 4.23-4.28 (2H, m), 4.16 (2H, d, J = 5.6 Hz), 3.53-3.64 (8H, br m), 3.30 (3H, s), 1.91-2.07 (2H, m), 1.38 (3H, d, J = 6.4 Hz), 1.30 (6H, dd, J = 6.4, 3.2 Hz).	482.2	481.25
336	1H-NMR (DMSO-D6) δ: 9.99 (1H, s), 9.17 (1H, s), 7.96 (1H, d, J = 9.2 Hz), 6.90 (1H, d, J = 9.6 Hz), 6.85 (1H, s), 6.50 (1H, d, J = 7.6 Hz), 6.34 (1H, d, J = 7.6 Hz), 4.19-4.25 (2H, m), 3.80-3.86 (1H, br m), 3.29 (3H, s), 2.93-2.96 (2H, m), 2.53-2.56 (2H, m), 1.90-1.92 (2H, m), 1.37 (3H, d, J = 6.4 Hz), 1.23-1.30 (8H, m).		

[Table 5-60]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
337	1H-NMR (CDCl3) δ: 9.35 (1H, s), 8.39-8.21 (2H, m), 7.07 (1H, d, J = 9.8 Hz), 6.38 (1H, d, J = 7.3 Hz), 5.17 (1H, q, J = 6.3 Hz), 4.33-4.23 (1H, m), 4.10-4.01 (2H, m), 3.70-3.55 (6H, m), 3.10-3.00 (4H, m), 2.21-2.10 (2H, m), 1.73-1.65 (2H, m), 1.46 (3H, d, J = 6.3 Hz).		
338	1H-NMR (DMSO-D6) δ: 10.19 (1H, br s), 9.18 (1H, s), 8.15 (1H, d, J = 9.8 Hz), 7.37 (1H, d, J = 9.8 Hz), 6.94 (1H, s), 6.30 (1H, d, J = 7.8 Hz), 5.19 (1H, br s), 4.64-4.54 (1H, m), 3.92-3.81 (1H, br m), 2.85-2.75 (4H, m), 2.13-1.79 (5H, m), 1.49-1.18 (7H, m).		
339	1H-NMR (DMSO-D6) δ: 10.23 (1H, br s), 9.18 (1H, s), 8.15 (1H, d, J = 9.8 Hz), 7.37 (1H, d, J = 10.2 Hz), 6.85 (1H, s), 6.34 (1H, d, J = 6.8 Hz), 4.27-4.19 (1H, m), 3.91-3.81 (1H, m), 3.45-3.40 (4H, m), 3.26 (3H, s), 2.85-2.77 (4H, m), 2.10-1.84 (5H, m), 1.47-1.20 (7H, m).		
340	1H-NMR (DMSO-D6) δ: 10.19 (1H, s), 9.19 (1H, s), 8.15 (1H, d, J = 9.8 Hz), 7.36 (1H, d, J = 9.8 Hz), 6.95 (1H, s), 6.31 (1H, d, J = 7.3 Hz), 5.21-5.13 (1H, m), 4.63-4.51 (2H, m), 3.94-3.80 (1H, m), 3.52-3.38 (5H, m), 2.84-2.75 (4H, m), 2.32 (1H, br s), 2.12-1.79 (4H, m), 1.45-1.24 (7H, m).		
341	1H-NMR (DMSO-D6) δ: 10.23 (1H, br s), 9.19 (1H, s), 8.15 (1H, d, J = 9.8 Hz), 7.36 (1H, d, J = 10.2 Hz), 6.86 (1H, s), 6.34 (1H, d, J = 7.8 Hz), 4.57 (1H, d, J = 3.9 Hz), 4.23 (1H, q, J = 6.3 Hz), 3.94-3.79 (1H, m), 3.56-3.37 (5H, m), 3.26 (3H, s), 2.85-2.77 (4H, m), 2.32 (1H, br s), 2.11-2.00 (2H, m), 1.89-1.79 (2H, m), 1.44-1.21 (7H, m).		

[Table 5-61]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
342	1H-NMR (DMSO-D6) δ: 10.02 (1H, s), 9.22 (1H, s), 8.25-8.12 (2H, m), 7.74 (1H, d, J = 8.3 Hz), 6.96 (1H, s), 6.42-6.33 (1H, m), 5.27-5.12 (1H, m), 4.63-4.57 (1H, m), 3.93-3.84 (1H, m), 2.71-2.62 (4H, br m), 2.33-2.21 (4H, br m), 2.11-2.00 (3H, m), 1.91-1.82 (2H, m), 1.48-1.27 (7H, m).		
343	1H-NMR (DMSO-D6) δ: 10.05 (1H, s), 9.23 (1H, s), 8.25-8.18 (2H, m), 7.79-7.71 (1H, m), 6.87 (1H, s), 6.45-6.39 (1H, m), 4.29-4.20 (1H, m), 3.92-3.84 (1H, m), 2.70-2.61 (4H, m), 2.34-2.21 (4H, m), 2.11-2.00 (2H, m), 1.92-1.80 (3H, m), 1.48-1.19 (7H, m).		
344	1H-NMR (DMSO-D6) δ: 10.05 (1H, br s), 9.23 (1H, s), 8.27-8.16 (2H, m), 7.73 (1H, d, J = 8.8 Hz), 6.98 (1H, s), 6.40 (1H, d, J = 7.8 Hz), 5.20 (1H, br s), 4.67-4.52 (2H, m), 3.98-3.83 (1H, m), 3.56-3.38 (3H, m), 3.25-3.16 (1H, m), 2.71-2.61 (3H, br m), 2.31-2.19 (4H, m), 2.14-2.00 (2H, m), 1.92-1.81 (2H, m), 1.52-1.24 (7H, m).		
345	1H-NMR (DMSO-D6) δ: 10.09 (1H, br s), 9.24 (1H, s), 8.26-8.16 (2H, m), 7.73 (1H, d, J = 8.8 Hz), 6.88 (1H, s), 6.44 (1H, d, J = 7.8 Hz), 4.61-4.53 (1H, br m), 4.24 (1H, q, J = 6.3 Hz), 3.95-3.83 (1H, m), 3.55-3.45 (1H, br m), 3.40 (2H, s), 3.27 (3H, s), 2.70-2.63 (4H, m), 2.35-2.21 (4H, br m), 2.11-2.01 (2H, m), 1.91-1.83 (2H, m), 1.49-1.25 (7H, m).		
346	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.47 (1H, d, J = 8.8 Hz), 8.31 (1H, d, J = 2.9 Hz), 8.19 (1H, s), 7.76 (1H, dd, J = 8.8, 2.0 Hz), 6.75 (1H, s), 6.68 (1H, d, J = 7.8 Hz), 4.81 (1H, q, J = 6.2 Hz), 4.35 (1H, s), 4.03 (1H, dd, J = 11.2, 3.4 Hz), 3.86 (1H, s), 3.78-3.73 (7H, m), 3.67-3.61 (2H, m), 3.27 (2H, t, J = 5.4 Hz), 2.08-2.06 (1H, m), 1.90-1.87 (2H, m), 1.53 (2H, d, J = 6.8 Hz), 1.25 (2H, s).		

[Table 5-62]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
347	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.47 (1H, d, J = 8.8 Hz), 8.32 (1H, d, J = 2.9 Hz), 8.27 (1H, s), 7.76 (1H, dd, J = 8.8, 2.9 Hz), 7.26 (6H, s), 6.75 (1H, s), 6.69 (1H, d, J = 7.8 Hz), 4.81 (1H, q, J = 6.5 Hz), 4.35 (1H, s), 4.02 (1H, dd, J = 11.2, 2.4 Hz), 3.78-3.73 (7H, m), 3.65-3.62 (2H, m), 3.27 (2H, t, J = 5.4 Hz), 2.10-2.06 (1H, m), 1.89-1.88 (2H, m), 1.53 (4H, d, J = 6.8 Hz), 1.25 (1H, s).		
348	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.40 (1H, d, J = 8.8 Hz), 8.32 (1H, d, J = 2.9 Hz), 8.27 (1H, s), 7.76 (1H, dd, J = 8.8, 2.9 Hz), 6.78 (1H, s), 6.50 (1H, d, J = 6.8 Hz), 4.83-4.82 (2H, m), 4.11-4.07 (2H, m), 3.95-3.93 (1H, m), 3.87 (1H, dd, J = 9.3, 3.4 Hz), 3.75 (5H, t, J = 5.4 Hz), 3.27 (2H, t, J = 5.4 Hz), 2.47-2.43 (1H, m), 2.06-2.01 (1H, m), 1.54 (3H, d, J = 6.8 Hz).		
349	1H-NMR (CDCl3) δ: 9.06 (0H, s), 8.40 (0H, d, J = 8.8 Hz), 8.32 (0H, d, J = 2.0 Hz), 8.21 (0H, s), 7.76 (0H, dd, J = 8.8, 2.9 Hz), 6.79 (0H, s), 6.50 (0H, d, J = 6.8 Hz), 4.83-4.82 (1H, m), 4.11-4.06 (1H, m), 3.93-3.88 (1H, m), 3.74 (2H, t, J = 4.9 Hz), 3.27 (1H, t, J = 5.4 Hz), 2.50-2.03 (1H, m), 1.54 (2H, d, J = 5.9 Hz).		
350	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.41 (1H, d, J = 8.8 Hz), 8.33 (1H, d, J = 2.0 Hz), 8.26 (1H, s), 7.76 (1H, dd, J = 8.8, 2.9 Hz), 6.76 (1H, s), 6.35 (1H, d, J = 7.8 Hz), 4.82 (1H, q, J = 6.5 Hz), 4.34-4.33 (1H, m), 4.07-4.05 (2H, m), 3.75 (4H, t, J = 4.9 Hz), 3.67-3.61 (2H, m), 3.28 (2H, t, J = 5.4 Hz), 2.18-2.16 (2H, m), 1.53 (2H, d, J = 6.8 Hz).		

[Table 5-63]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
351	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.50 (1H, dd, J = 8.8, 2.0 Hz), 8.42 (1H, d, J = 2.0 Hz), 8.31 (1H, d, J = 2.9 Hz), 8.21 (1H, s), 7.74-7.70 (1H, m), 6.76 (1H, s), 6.70 (1H, d, J = 7.8 Hz), 4.82-4.80 (1H, br m), 4.41 (1H, s), 4.35 (1H, br s), 4.28 (1H, s), 4.04-3.98 (2H, m), 3.86 (2H, s), 3.83-3.77 (4H, m), 3.67-3.64 (1H, m), 2.10-2.02 (1H, m), 1.90-1.89 (2H, m), 1.53 (3H, d, J = 6.8 Hz).		
352	1H-NMR (CDCl3) δ: 9.08 (1H, s), 8.60 (1H, d, J = 7.8 Hz), 8.50 (1H, dd, J = 9.3, 2.4 Hz), 8.32 (1H, d, J = 2.9 Hz), 8.21 (1H, s), 7.74-7.70 (1H, m), 6.76 (1H, s), 6.70 (1H, d, J = 8.8 Hz), 4.82-4.80 (1H, m), 4.41 (1H, s), 4.35 (1H, br s), 4.28 (1H, s), 4.03-3.98 (2H, m), 3.86 (3H, s), 3.80-3.77 (3H, m), 3.67-3.64 (1H, m), 2.08-2.05 (1H, m), 1.97-1.80 (2H, m), 1.53 (3H, d, J = 6.8 Hz).		
353	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.43 (1H, dd, J = 8.8, 2.0 Hz), 8.34 (1H, s), 8.30 (1H, d, J = 2.9 Hz), 8.21 (1H, s), 7.75-7.69 (1H, m), 6.79 (1H, s), 6.50 (1H, d, J = 6.8 Hz), 4.82 (2H, br s), 4.41 (1H, s), 4.28 (1H, s), 4.14-4.04 (2H, m), 4.02-3.88 (3H, m), 3.86 (3H, s), 3.50-3.40 (2H, m), 2.50-2.40 (1H, m), 2.15-1.95 (1H, m), 1.54 (4H, d, J = 6.8 Hz).		
354	1H-NMR (CDCl3) δ: 9.08 (1H, s), 8.42 (2H, td, J = 9.0, 3.3 Hz), 8.31 (1H, d, J = 2.0 Hz), 8.21 (1H, s), 7.74-7.70 (1H, m), 6.80 (1H, s), 6.50 (1H, d, J = 6.8 Hz), 4.88-4.77 (2H, m), 4.42 (1H, s), 4.28 (1H, s), 4.12-4.05 (2H, m), 4.01-3.88 (3H, m), 3.86 (3H, s), 3.81 (2H, t, J = 5.4 Hz), 2.52-2.40 (1H, m), 2.12-1.97 (1H, m), 1.55 (3H, d, J = 6.8 Hz).		

[Table 5-64]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
355	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.60 (1H, d, J = 4.9 Hz), 8.45 (1H, dd, J = 8.8, 2.9 Hz), 8.33 (1H, d, J = 2.0 Hz), 8.21 (1H, s), 7.73 (1H, td, J = 6.1, 3.3 Hz), 6.77 (1H, s), 6.34 (1H, d, J = 7.8 Hz), 4.88-4.77 (1H, m), 4.42 (1H, s), 4.40-4.31 (1H, m), 4.29 (1H, s), 4.06 (2H, td, J = 7.6, 3.6 Hz), 4.00 (1H, t, J = 5.4 Hz), 3.91 (1H, s), 3.87 (2H, s), 3.81 (1H, t, J = 5.9 Hz), 3.67-3.61 (2H, m), 2.25-2.10 (2H, m), 1.76-1.67 (2H, m), 1.54 (3H, d, J = 5.9 Hz).		
356	1H-NMR (DMSO-D6) δ: 10.79 (1H, br s), 9.30 (1H, s), 8.55 (1H, d, J = 12.8 Hz), 8.06 (1H, d, J = 12.8 Hz), 6.93 (1H, s), 6.52 (1H, d, J = 10.0 Hz), 4.25-4.29 (2H, br m), 3.95 (2H, t, J = 6.8 Hz), 3.51 (2H, s), 3.28 (3H, s), 3.10 (2H, t, J = 7.2 Hz), 1.39 (3H, d, J = 8.8 Hz), 1.30 (6H, dd, J = 8.8, 3.6).	438.4	437.23
357	1H-NMR (DMSO-D6) δ: 10.01 (1H, br s), 9.19 (1H, s), 8.02 (1H, d, J = 12.8 Hz), 6.93 (1H, d, J = 12.8 Hz), 6.87 (1H, s), 6.80 (1H, d, J = 7.2 Hz), 6.35 (1H, d, J = 10.0 Hz), 4.34-4.38 (1H, br m), 4.19-4.26 (2H, br m), 3.27 (3H, s), 2.90-3.20 (3H, br m), 1.65-2.20 (3H, br m), 1.38 (3H, d, J = 8.4 Hz), 1.27 (6H, dd, J = 8.4, 2.8 Hz).	424.3	423.25
358	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.38-8.35 (2H, m), 7.07 (1H, d, J = 9.8 Hz), 6.86 (1H, s), 6.39 (1H, t, J = 6.1 Hz), 4.32 (1H, q, J = 6.3 Hz), 4.03-4.00 (2H, m), 3.58-3.55 (6H, m), 3.42-3.38 (5H, m), 3.06-3.05 (4H, m), 2.05-2.03 (2H, m), 2.04-1.95 (2H, m), 1.52-1.45 (5H, m).		

[Table 5-65]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
359	1H-NMR (CDCl3) δ: 9.10 (1H, s), 8.57 (1H, br s), 8.30 (1H, d, J = 10.2 Hz), 7.13 (1H, d, J = 10.2 Hz), 6.94 (1H, s), 6.22 (1H, d, J = 7.8 Hz), 4.47-4.43 (1H, m), 4.32 (1H, q, J = 6.3 Hz), 3.61-3.60 (4H, m), 3.39 (3H, s), 3.22-3.21 (4H, m), 3.06-3.05 (4H, m), 2.58-2.54 (2H, m), 2.36-2.32 (2H, m), 1.49 (3H, d, J = 6.3 Hz).		
360	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.34-8.28 (3H, m), 7.73 (1H, dd, J = 8.5, 4.3 Hz), 6.87 (1H, s), 6.44 (1H, t, J = 6.1 Hz), 4.34 (1H, q, J = 6.5 Hz), 4.04-4.01 (2H, m), 3.60-3.57 (2H, m), 3.49 (2H, br s), 3.44-3.41 (5H, m), 2.93-2.91 (4H, m), 2.45-2.42 (4H, m), 2.01-1.98 (1H, m), 1.76-1.74 (3H, m), 1.52-1.46 (5H, m).		
361	1H-NMR (CDCl3) δ: 9.10 (1H, s), 8.44 (1H, s), 8.29-8.27 (2H, m), 7.79-7.77 (1H, m), 6.95 (1H, s), 6.26 (1H, d, J = 7.3 Hz), 4.47-4.31 (2H, m), 3.51 (2H, br s), 3.40 (3H, s), 3.22-3.21 (4H, m), 2.92-2.91 (4H, m), 2.56-2.32 (8H, m), 1.50 (3H, d, J = 6.3 Hz).		
362	1H-NMR (DMSO-D6) δ: 10.30 (1H, s), 9.22 (1H, s), 8.23 (1H, d, J = 12.8 Hz) 8.11 (1H, br s), 7.43 (1H, d, J = 13.2 Hz), 6.88 (1H, s), 6.37 (1H, d, J = 10.8 Hz), 4.34-4.38 (1H, br m), 4.22-4.26 (2H, br m), 4.07 (2H, s), 3.72-3.79 (3H, m), 3.27 (4H, apparent s), 1.38 (3H, d, J = 8.8 Hz), 1.30 (6H, d, J = 5.2 Hz).	438.4	437.23
363	1H-NMR (DMSO-D6) δ: 9.95 (1H, s), 9.19 (1H, s), 8.92 (1H, d, J = 1.2 Hz), 8.06 (1H, d, J = 1.2 Hz), 6.87 (1H, s), 6.37 (1H, d, J = 7.6 Hz), 4.22-4.26 (2H, br m), 3.29-3.41 (4H, m), 3.26 (3H, s), 2.80-2.83 (4H, m), 1.38 (3H, d, J = 6.4 Hz), 1.28 (6H, dd, J = 6.4, 3.2 Hz).	424.3	423.25

[Table 5-66]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
364	1H-NMR (DMSO-D6) δ: 10.33 (1H, s), 9.34 (1H, s), 8.28 (1H, d, J = 8.8 Hz), 8.21 (1H, s), 7.77 (1H, d, J = 7.8 Hz), 7.24 (1H, s), 6.96-6.65 (2H, m), 4.20 (1H, br s), 3.91 (2H, d, J = 11.7 Hz), 3.49 (2H, t, J = 11.2 Hz), 3.42 (3H, s), 2.68 (4H, t, J = 4.4 Hz), 2.53 (2H, s), 2.29 (4H, s), 2.00 (2H, d, J = 10.7 Hz), 1.77-1.63 (2H, m).		
365	1H-NMR (DMSO-D6) δ: 10.53 (1H, s), 9.30 (1H, s), 8.26-8.18 (2H, m), 7.41 (1H, d, J = 9.8 Hz), 7.22 (1H, s), 6.95-6.64 (2H, m), 4.17 (1H, br s), 3.89 (2H, d, J = 11.7 Hz), 3.57-3.50 (3H, m), 3.49-3.42 (2H, m), 2.98-2.87 (4H, m), 2.55-2.50 (3H, m), 1.98 (2H, d, J = 10.7 Hz), 1.70-1.55 (2H, m).		
366	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.30 (1H, s), 8.25-8.00 (3H, m), 7.52 (1H, d, J = 7.8 Hz), 7.22 (1H, s), 6.97-6.63 (2H, m), 4.30-4.07 (3H, br m), 3.90 (2H, d, J = 9.8 Hz), 3.48 (1H, t, J = 10.7 Hz), 2.70-2.64 (2H, br m), 2.25 (6H, s), 2.05-1.96 (2H, m), 1.75-1.58 (2H, m).		
367	1H-NMR (CDCl3) δ: 9.34 (1H, s), 8.36 (1H, d, J = 9.8 Hz), 8.28 (1H, br s), 7.06 (1H, d, J = 9.8 Hz), 6.76 (1H, d, J = 7.3 Hz), 5.16 (1H, q, J = 6.3 Hz), 4.34-4.22 (1H, m), 3.96 (1H, dd, J = 11.2, 2.9 Hz), 3.84-3.56 (7H, m), 3.08-3.01 (4H, m), 2.09-1.59 (4H, m), 1.45 (3H, d, J = 6.3 Hz).		
368	1H-NMR (CDCl3) δ: 9.34 (1H, s), 8.31 (1H, d, J = 9.8 Hz), 8.22 (1H, br s), 7.07 (1H, d, J = 9.8 Hz), 6.30 (1H, d, J = 7.3 Hz), 5.16 (1H, q, J = 6.2 Hz), 4.08-3.97 (1H, m), 3.79-3.70 (1H, m), 3.63-3.52 (4H, m), 3.07-2.98 (4H, m), 2.32-2.01 (4H, m), 1.60-1.36 (7H, m).		

[Table 5-67]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
369	1H-NMR (CDCl3) δ: 9.40 (1H, s), 8.50 (1H, br s), 8.33 (1H, d, J = 8.3 Hz), 8.30 (1H, d, J = 2.4 Hz), 7.76 (1H, dd, J = 8.5, 2.2 Hz), 6.80 (1H, d, J = 7.8 Hz), 5.17 (1H, q, J = 6.3 Hz), 4.34-4.28 (1H, br m), 3.98 (1H, dd, J = 11.2, 2.9 Hz), 3.84-3.63 (3H, m), 3.50 (2H, s), 2.94-2.86 (4H, m), 2.50-2.39 (4H, br m), 2.10-1.84 (3H, m), 1.46 (3H, d, J = 6.3 Hz).		
370	1H-NMR (CDCl3) δ: 9.40 (1H, s), 8.43 (1H, br s), 8.31-8.24 (2H, m), 7.80-7.72 (1H, m), 6.33 (1H, d, J = 7.8 Hz), 5.17 (1H, q, J = 6.2 Hz), 4.09-3.99 (1H, m), 3.82-3.72 (1H, m), 3.50 (2H, s), 2.95-2.86 (4H, m), 2.57-2.20 (6H, m), 2.16-2.01 (2H, m), 1.59-1.40 (7H, m).		
371	1H-NMR (DMSO-D6) δ: 10.17 (1H, s), 9.19 (1H, s), 8.13 (1H, d, J = 9.8 Hz), 7.30 (1H, d, J = 9.8 Hz), 6.86 (1H, s), 6.35 (1H, d, J = 7.3 Hz), 4.35-4.29 (1H, m), 4.29-4.16 (2H, m), 3.89 (1H, dd, J = 12.9, 3.7 Hz), 3.26 (3H, s), 2.96 (2H, dt, J = 18.2, 6.5 Hz), 2.88 (1H, dd, J = 12.2, 3.4 Hz), 2.80 (1H, d, J = 11.7 Hz), 2.66 (1H, dt, J = 20.2, 8.3 Hz), 1.37 (3H, d, J = 6.8 Hz), 1.27 (6H, dd, J = 6.3, 3.4 Hz), 1.13 (3H, d, J = 6.8 Hz).	438.35	437.27
372	1H-NMR (DMSO-D6) δ: 10.17 (1H, s), 9.19 (1H, s), 8.13 (1H, d, J = 10.2 Hz), 7.30 (1H, d, J = 9.8 Hz), 6.86 (1H, s), 6.35 (1H, d, J = 7.3 Hz), 4.33 (1H, dt, J = 11.7, 5.0 Hz), 4.23 (2H, td, J = 13.2, 6.8 Hz), 3.90 (1H, dd, J = 13.2, 4.4 Hz), 3.26 (3H, s), 2.99-2.92 (2H, m), 2.88 (1H, dd, J = 12.0, 3.7 Hz), 2.80 (1H, d, J = 11.7 Hz), 2.64 (1H, td, J = 12.1, 3.6 Hz), 1.37 (3H, d, J = 6.3 Hz), 1.27 (6H, dd, J = 6.3, 2.9 Hz), 1.13 (3H, d, J = 6.8 Hz).	438.35	437.27

[Table 5-68]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
373	1H-NMR (DMSO-D6) δ: 10.02 (1H, s), 9.17 (1H, s), 8.97 (1H, d, J = 1.2 Hz), 8.08 (1H, d, J = 1.2 Hz), 6.96 (1H, s), 6.76 (1H, s), 5.18 (1H, d, J = 4.4 Hz), 4.60-4.63 (1H, m), 3.50 (2H, s), 3.43 (3H, s), 3.38-3.41 (4H, m), 2.79-2.81 (4H, m), 1.49 (6H, s), 1.39 (3H, d, J = 6.4 Hz).	454.3	453.26
374	1H-NMR (DMSO-D6) δ: 10.19 (1H, s), 9.20 (1H, s), 8.37 (2H, s), 6.86 (1H, s), 6.51 (1H, d, 7.8 Hz), 4.20-4.30 (2H, m), 3.30 (3H, s), 3.01-3.11 (4H, m), 2.86-2.89 (4H, m), 1.38 (3H, d, J = 8.8 Hz), 1.27 (6H, dd, J = 8.8, 3.2 Hz).	424.4	423.25
375	1H-NMR (DMSO-D6) δ: 10.24 (1H, s), 9.17 (1H, s), 8.38 (2H, s), 6.95 (1H, s), 6.78 (1H, s), 5.18 (1H, d, J = 4.4 Hz), 4.60-4.62 (1H, m), 3.57 (2H, s), 3.30 (3H, s), 3.11-3.12 (4H, m), 2.91-2.92 (4H, m), 1.47 (6H, s), 1.39 (3H, d, J = 6.4 Hz).	454.2	453.26
376	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.52 (1H, brs), 8.42 (1H, d, J = 9.8 Hz), 7.04 (1H, d, J = 9.8 Hz), 6.88 (1H, s), 6.49 (1H, d, J = 7.8 Hz), 4.33 (2H, dq, J = 19.1, 5.0 Hz), 4.04 (1H, dd, J = 11.2, 2.9 Hz), 3.75 (2H, ddt, J = 21.5, 12.1, 3.8 Hz), 3.57 (3H, dq, J = 15.5, 4.2 Hz), 3.48 (2H, d, J = 2.4 Hz), 3.40 (3H, s), 3.14 (2H, dd, J = 6.1, 4.1 Hz), 2.04 (1H, td, J = 8.8, 4.6 Hz), 1.91-1.83 (3H, m), 1.74-1.68 (1H, m), 1.48 (3H, d, J = 6.3 Hz), 0.68 (4H, dt, J = 21.6, 5.5 Hz).	492.40	491.28

[Table 5-69]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
377	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.51-8.50 (2H, m), 8.24 (1H, d, J = 2.9 Hz), 7.59 (1H, dd, J = 8.8, 2.9 Hz), 6.88 (1H, s), 6.13 (1H, d, J = 7.8 Hz), 4.47-4.33 (2H, m), 3.42 (3H, s), 3.28 (3H, s), 3.06-3.02 (2H, br m), 2.42-2.39 (3H, br m), 1.77-1.71 (4H, m), 1.51 (3H, d, J = 6.3 Hz), 1.37 (3H, d, J = 6.3 Hz), 1.37 (3H, d, J = 6.3 Hz).		
378	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.62 (1H, brs), 8.39 (1H, d, J = 8.3 Hz), 8.29 (1H, d, J = 2.0 Hz), 7.76 (1H, dd, J = 8.5, 2.2 Hz), 6.89 (1H, s), 6.53 (1H, d, J = 7.8 Hz), 4.40-4.30 (2H, m), 4.06 (1H, dd, J = 10.7, 2.9 Hz), 3.82-3.71 (2H, m), 3.58 (1H, dd, J = 11.0, 6.1 Hz), 3.52 (2H, s), 3.41 (3H, s), 3.04 (2H, t, J = 4.9 Hz), 2.55 (3H, brs), 2.31 (2H, s), 2.08 (1H, td, J = 9.5, 4.6 Hz), 1.88 (2H, dtd, J = 28.8, 8.5, 4.2 Hz), 1.74 (1H, tt, J = 11.7, 3.7 Hz), 1.49 (3H, d, J = 6.3 Hz), 0.69 (2H, t, J = 5.1 Hz), 0.49 (2H, t, J = 5.6 Hz).	505.40	504.30
379	1H-NMR (CDCl3) δ: 8.99 (1H, s), 8.35 (1H, d, J = 9.8 Hz), 8.17 (1H, brs), 7.04 (1H, d, J = 9.8 Hz), 6.68 (1H, s), 6.21 (1H, d, J = 7.8 Hz), 4.80 (1H, q, J = 6.5 Hz), 4.48-4.32 (1H, m), 4.05 (1H, brs), 3.55 (2H, t, J = 5.1 Hz), 3.48 (2H, s), 3.14 (2H, t, J = 5.1 Hz), 1.53 (3H, d, J = 6.8 Hz), 1.37 (6H, d, J = 6.3 Hz), 0.67 (4H, dt, J = 20.2, 5.6 Hz).	436.35	435.25
380	1H-NMR (DMSO-D6) δ: 10.46 (1H, s), 9.35 (1H, s), 8.31-8.22 (3H, m), 7.78-7.72 (1H, m), 7.25 (1H, s), 6.98-6.66 (2H, m), 4.25-4.10 (1H, m), 3.90 (1H, dd, J = 10.7, 2.9 Hz), 3.72-3.64 (1H, m), 3.61-3.53 (1H, m), 3.52-3.42 (3H, m), 3.40-3.33 (1H, m), 2.92-2.85 (3H, m), 2.48-2.25 (4H, m), 2.04-1.94 (1H, m), 1.90-1.70 (2H, m), 1.67-1.55 (1H, m).		

[Table 5-70]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
381	1H-NMR (DMSO-D6) δ: 10.56 (1H, s), 9.30 (1H, s), 8.26 (1H, s), 8.20-8.10 (1H, m), 7.37 (1H, d, J = 9.8 Hz), 7.23 (1H, s), 6.95-6.63 (2H, m), 4.19-4.08 (1H, m), 3.88 (1H, dd, J = 10.7, 2.9 Hz), 3.71-3.63 (1H, m), 3.58-3.47 (3H, m), 3.45-3.36 (1H, m), 2.93-2.85 (3H, m), 2.03-1.90 (1H, m), 1.83-1.69 (2H, m), 1.66-1.53 (1H, m).		
382	1H-NMR (DMSO-D6) δ: 10.29 (1H, s), 9.31 (1H, s), 8.19-8.05 (3H, m), 7.47 (1H, dd, J = 9.8, 2.9 Hz), 7.23 (1H, s), 6.97-6.65 (2H, m), 4.13 (3H, t, J = 5.4 Hz), 3.93-3.86 (1H, m), 3.73-3.64 (1H, m), 3.61-3.53 (1H, m), 3.48-3.40 (1H, m), 2.67 (2H, t, J = 5.9 Hz), 2.25 (6H, s), 2.05-1.92 (1H, m), 1.86-1.69 (2H, m), 1.65-1.53 (1H, m).		
383		513.88	512.25
384	1H-NMR (DMSO-D6) δ: 10.03 (1H, s), 9.26 (1H, s), 8.10 (1H, d, J = 9.8 Hz), 7.32 (1H, d, J = 8.8 Hz), 7.19 (1H, s), 6.89-6.50 (2H, m), 3.95 (1H, br s), 3.53-3.45 (4H, m), 2.91-2.83 (3H, m), 2.35-2.22 (2H, m), 2.18-2.10 (2H, m), 2.04-1.94 (2H, m), 1.58-1.37 (4H, m).		
385	1H-NMR (DMSO-D6) δ: 9.88 (1H, s), 9.27 (1H, s), 8.11-8.05 (2H, m), 7.50 (1H, dd, J = 9.3, 3.4 Hz), 7.19 (1H, s), 6.90-6.57 (2H, m), 4.13 (2H, t, J = 5.9 Hz), 4.00-3.91 (1H, m), 2.65 (2H, t, J = 5.9 Hz), 2.24 (6H, s), 2.18-2.10 (2H, m), 2.04-1.95 (2H, m), 1.58-1.37 (4H, m).		

[Table 5-71]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
386	1H-NMR (DMSO-D6) δ: 10.02 (1H, s), 9.31 (1H, s), 8.28-8.15 (3H, m), 7.99 (1H, s), 7.77 (1H, dd, J = 8.3, 2.4 Hz), 7.21 (1H, s), 6.92-6.60 (2H, m), 5.70 (1H, s), 4.04-3.90 (1H, m), 3.58-3.50 (3H, m), 3.46 (1H, s), 3.42-3.34 (3H, m), 2.76 (1H, t, J = 4.9 Hz), 2.41 (2H, t, J = 4.9 Hz), 2.39-2.33 (3H, m), 2.13-2.05 (2H, m), 1.93-1.84 (2H, m), 1.52-1.27 (5H, m).		
387	1H-NMR (DMSO-D6) δ: 10.49 (1H, s), 9.27 (1H, s), 8.13 (1H, d, J = 9.8 Hz), 7.37 (1H, d, J = 9.8 Hz), 7.18 (1H, s), 6.79 (1H, t, J = 55.6 Hz), 6.57 (1H, d, J = 7.8 Hz), 4.60 (1H, br s), 3.89 (1H, br s), 3.61-3.40 (5H, m), 2.81 (4H, s), 2.56-2.50 (2H, m), 2.08-1.98 (2H, br m), 1.90-1.81 (2H, br m), 1.47-1.12 (5H, m).		
388	1H-NMR (DMSO-D6) δ: 10.21 (1H, s), 9.29 (1H, s), 8.20 (1H, s), 8.12 (1H, d, J = 9.8 Hz), 8.07 (1H, d, J = 2.9 Hz), 7.51 (1H, dd, J = 8.8, 2.9 Hz), 7.19 (1H, s), 6.80 (1H, t, J = 55.6 Hz), 6.60 (1H, d, J = 7.8 Hz), 4.12 (2H, t, J = 5.9 Hz), 3.95-3.85 (1H, m), 3.53-3.48 (1H, m), 2.64 (2H, t, J = 5.4 Hz), 2.23 (6H, s), 2.05 (2H, d, J = 9.8 Hz), 1.87 (2H, d, J = 10.7 Hz), 1.50-1.25 (4H, m).		
389	1H-NMR (CDCl3) δ: 9.10 (1H, s), 8.77 (1H, s), 8.49-8.45 (2H, m), 7.88-7.87 (1H, m), 6.87 (1H, s), 6.14 (1H, d, J = 7.8 Hz), 4.42-4.35 (2H, m), 3.66 (4H, br s), 3.42 (3H, s), 2.93 (4H, br s), 1.51 (3H, d, J = 5.9 Hz), 1.37 (3H, d, J = 5.4 Hz), 1.36 (3H, d, J = 5.4 Hz).		

[Table 5-72]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
390	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.68 (1H, s), 8.35-8.32 (2H, m), 7.73 (1H, dd, J = 8.5, 2.2 Hz), 6.86 (1H, s), 6.41 (1H, t, J = 5.9 Hz), 4.33 (1H, q, J = 6.5 Hz), 3.68 (3H, s), 3.54-3.50 (4H, m), 3.41 (3H, s), 2.92-2.90 (4H, m), 2.46 (4H, br s), 2.32-2.29 (1H, m), 2.07-1.97 (4H, m), 1.81-1.70 (2H, m), 1.52-1.46 (5H, m), 1.18-1.12 (2H, m).		
391	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.41 (1H, d, J = 8.8 Hz), 8.23 (1H, d, J = 2.0 Hz), 8.10 (1H, s), 7.71 (1H, dd, J = 8.5, 2.2 Hz), 6.99 (1H, s), 5.44-5.37 (1H, m), 4.36 (1H, q, J = 6.3 Hz), 3.48 (2H, s), 3.41 (3H, s), 3.17 (3H, s), 2.90 (4H, t, J = 4.9 Hz), 2.44 (4H, s), 1.48 (3H, t, J = 9.8 Hz), 1.30 (6H, t, J = 7.1 Hz).		
392	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.36 (1H, d, J = 8.3 Hz), 8.27-8.24 (2H, m), 7.73 (1H, dd, J = 8.3, 2.2 Hz), 6.84 (1H, s), 6.43 (1H, t, J = 5.9 Hz), 4.34 (1H, q, J = 6.5 Hz), 3.51-3.47 (4H, m), 3.41 (3H, s), 2.93-2.89 (4H, m), 2.45 (4H, br s), 2.07-1.98 (1H, m), 1.50 (3H, d, J = 6.3 Hz), 1.07 (6H, d, J = 6.3 Hz).		
393	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.43 (1H, d, J = 8.8 Hz), 8.32 (1H, s), 8.22 (1H, d, J = 2.4 Hz), 7.92 (1H, dd, J = 8.5, 2.2 Hz), 6.87 (1H, s), 6.65 (1H, t, J = 5.1 Hz), 4.75 (1H, s), 4.33 (1H, q, J = 6.3 Hz), 3.82-3.77 (2H, m), 3.63-3.58 (2H, m), 3.57-3.52 (2H, m), 3.49 (2H, s), 3.40-3.35 (5H, m), 2.91-2.89 (4H, m), 2.46 (4H, br s), 1.51 (3H, d, J = 6.8 Hz).		

[Table 5-73]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
394	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.42 (1H, d, J = 8.3 Hz), 8.26 (1H, d, J = 2.0 Hz), 8.21 (1H, s), 7.73 (1H, dd, J = 8.5, 2.0 Hz), 6.84 (1H, s), 6.74 (1H, t, J = 5.4 Hz), 4.32 (1H, q, J = 6.3 Hz), 3.70-3.68 (2H, m), 3.48 (2H, s), 3.40 (3H, s), 3.34 (3H, s), 2.92-2.87 (4H, m), 2.44 (4H, br s), 1.50 (3H, d, J = 6.8 Hz), 1.30 (6H, d, J = 2.4 Hz).		
395	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.33 (1H, d, J = 8.8 Hz), 8.26 (2H, d, J = 1.5 Hz), 7.74 (1H, dd, J = 8.5, 2.2 Hz), 6.86 (1H, s), 6.18 (1H, d, J = 7.3 Hz), 4.34 (1H, q, J = 6.3 Hz), 4.15-4.07 (1H, m), 3.49 (2H, s), 3.42 (3H, s), 3.41 (3H, s), 3.31-3.24 (1H, m), 2.93-2.88 (4H, m), 2.45 (4H, br s), 2.32-2.26 (2H, m), 2.16-2.10 (2H, m), 1.54-1.33 (8H, m).		
397	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.60 (1H, s), 8.45 (1H, d, J = 8.5 Hz), 8.27 (1H, d, J = 2.0 Hz), 7.75 (1H, dd, J = 8.5, 2.0 Hz), 6.89-6.82 (2H, m), 4.35-4.29 (2H, m), 4.02 (1H, br s), 3.48 (3H, s), 3.41 (3H, d, J = 7.3 Hz), 2.91-2.87 (4H, m), 2.45 (4H, br s), 2.33-2.28 (1H, m), 1.93-1.85 (3H, m), 1.65-1.47 (7H, m).		
398	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.40 (1H, d, J = 8.3 Hz), 8.26 (2H, d, J = 1.5 Hz), 7.72 (1H, dd, J = 8.5, 2.2 Hz), 6.85 (1H, s), 6.79 (1H, s), 4.33 (1H, q, J = 6.3 Hz), 4.15-4.08 (1H, m), 3.97-3.88 (1H, m), 3.69-3.61 (1H, m), 3.55 (1H, td, J = 11.5, 5.7 Hz), 3.49-3.41 (3H, m), 3.40 (3H, d, J = 1.5 Hz), 2.90-2.88 (4H, m), 2.44 (4H, br s), 1.93-1.87 (1H, br m), 1.73-1.43 (8H, m).		

[Table 5-74]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
399	1H-NMR (CDCl3) δ: 9.06 (1H, d, J = 5.9 Hz), 8.40 (1H, s), 8.35 (1H, d, J = 8.8 Hz), 8.28 (1H, d, J = 2.0 Hz), 7.74 (1H, dd, J = 8.8, 2.0 Hz), 6.86 (1H, s), 6.26 (1H, d, J = 7.8 Hz), 4.36-4.21 (2H, m), 3.50 (2H, s), 3.41 (3H, s), 3.19-3.15 (2H, m), 2.92-2.83 (6H, m), 2.45 (4H, br s), 2.22-2.16 (2H, m), 1.60-1.49 (5H, m).		
400	1H-NMR (CDCl3) δ: 9.12 (1H, d, J = 6.1 Hz), 8.91 (1H, s), 8.34 (2H, t, J = 6.1 Hz), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 6.87 (1H, s), 6.39 (1H, t, J = 6.1 Hz), 4.34 (1H, q, J = 6.5 Hz), 4.03-3.99 (1H, m), 3.91-3.86 (1H, m), 3.64-3.33 (9H, m), 2.91 (4H, t, J = 4.6 Hz), 2.46 (4H, s), 2.00-1.95 (1H, m), 1.74-1.61 (2H, m), 1.51-1.37 (5H, m).		
401	1H-NMR (CDCl3) δ: 9.23 (1H, s), 8.89 (1H, s), 8.80 (1H, s), 8.37 (1H, s), 8.36 (1H, d, J = 8.8 Hz), 8.08 (2H, d, J = 8.8 Hz), 7.84 (1H, dd, J = 8.8, 2.2 Hz), 7.69 (2H, d, J = 8.8 Hz), 7.22 (1H, s), 4.49 (1H, q, J = 6.3 Hz), 3.53 (2H, s), 3.45 (3H, s), 2.94-2.90 (4H, m), 2.48 (4H, br s), 1.59 (3H, d, J = 6.3 Hz).		
402	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.33 (1H, d, J = 8.3 Hz), 8.25 (1H, d, J = 2.0 Hz), 8.21 (1H, s), 7.78 (1H, dd, J = 8.3, 2.0 Hz), 6.85 (1H, s), 6.48 (1H, t, J = 6.1 Hz), 4.33 (1H, q, J = 6.3 Hz), 3.69-3.45 (5H, m), 3.40 (3H, d, J = 1.6 Hz), 2.92-2.88 (4H, m), 2.46 (4H, br s), 2.19-2.13 (1H, m), 2.02-1.97 (1H, m), 1.88-1.80 (3H, m), 1.50 (3H, d, J = 6.3 Hz), 1.39-1.00 (5H, m).		

[Table 5-75]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
403	1H-NMR (CDCl3) δ: 9.12 (1H, s), 9.09 (1H, s), 8.28 (1H, d, J = 8.8 Hz), 8.25 (1H, d, J = 1.5 Hz), 7.78 (1H, dd, J = 8.8, 1.5 Hz), 7.00 (1H, d, J = 20.8 Hz), 6.91 (1H, d, J = 4.4 Hz), 6.57 (1H, t, J = 5.4 Hz), 4.35 (1H, q, J = 6.3 Hz), 4.14-4.05 (1H, m), 3.85-3.67 (2H, m), 3.43 (2H, s), 3.41 (3H, s), 2.91-0.00 (4H, m), 2.44-2.27 (7H, m), 2.03-1.91 (1H, m), 1.52 (3H, d, J = 6.3 Hz).		
404	1H-NMR (CDCl3) δ: 9.10 (1H, d, J = 3.9 Hz), 8.79 (1H, s), 8.39 (1H, dd, J = 20.7, 8.5 Hz), 8.32 (1H, s), 7.79-7.73 (1H, m), 6.86-6.86 (1H, m), 6.47-6.29 (1H, m), 4.49-4.30 (2H, m), 4.04-3.88 (3H, m), 3.83-3.74 (1H, m), 3.50 (2H, br s), 3.41 (3H, t, J = 2.7 Hz), 2.94-2.88 (4H, m), 2.62-2.44 (5H, m), 2.19-2.03 (1H, m), 1.95-1.78 (1H, m), 1.50 (3H, dd, J = 6.6, 3.7 Hz), 1.37-1.30 (3H, m).		
405	1H-NMR (CDCl3) δ: 9.21-8.98 (2H, m), 8.48-8.30 (2H, m), 7.80-7.73 (1H, m), 7.14 (1H, d, J = 12.7 Hz), 6.96-6.87 (1H, m), 4.41-4.23 (3H, m), 4.00-3.97 (1H, m), 3.79-3.61 (1H, m), 3.51-3.20 (6H, m), 2.90 (4H, br s), 2.46 (4H, br s), 2.18-1.74 (8H, m), 1.53-1.48 (3H, m).		
406	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.30-8.24 (3H, m), 7.79-7.77 (1H, m), 7.28 (1H, s), 6.93-6.91 (1H, m), 6.49-6.47 (1H, m), 5.61 (1H, br s), 4.36-4.30 (1H, m), 3.84-3.71 (2H, m), 3.59 (1H, t, J = 8.8 Hz), 3.51-3.48 (2H, m), 3.42-3.40 (3H, m), 3.34-3.31 (1H, m), 3.05-2.90 (5H, m), 2.59-2.44 (5H, m), 2.32-2.26 (1H, m), 1.52-1.45 (3H, m).		
407		492.4	491.31

[Table 5-76]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
408	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.58 (1H, s), 8.41 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 1.5 Hz), 7.75 (1H, dd, J = 8.8, 1.5 Hz), 6.86 (1H, s), 6.70 (1H, t, J = 5.6 Hz), 4.33 (1H, q, J = 6.5 Hz), 4.25-4.21 (1H, m), 4.02-3.97 (1H, m), 3.93-3.82 (2H, m), 3.72-3.62 (1H, m), 3.50 (2H, s), 3.40 (3H, s), 2.94-2.90 (4H, m), 2.46 (4H, br s), 2.10-1.92 (4H, m), 1.77-1.67 (1H, m), 1.50 (3H, d, J = 6.3 Hz).		
409	1H-NMR (CDCl3) δ: 9.11 (1H, s), 8.94-8.91 (1H, m), 8.42-8.40 (1H, m), 8.33 (1H, s), 7.76-7.72 (1H, m), 6.85 (1H, d, J = 5.9 Hz), 6.62-6.59 (1H, m), 4.54-4.45 (1H, m), 4.33 (1H, q, J = 6.3 Hz), 4.14-3.96 (2H, m), 3.91-3.81 (1H, m), 3.49 (2H, s), 3.41-3.41 (3H, m), 2.90 (4H, d, J = 4.9 Hz), 2.46 (4H, s), 2.05-1.71 (5H, m), 1.50 (3H, d, J = 6.8 Hz), 1.41-1.31 (3H, m).		
410	1H-NMR (CDCl3) δ: 9.12 (1H, s), 8.94 (1H, s), 8.35 (2H, d, J = 8.8 Hz), 7.76 (1H, dd, J = 8.5, 2.9 Hz), 6.89 (1H, d, J = 2.9 Hz), 6.10 (1H, d, J = 7.3 Hz), 4.56-4.46 (1H, m), 4.34 (1H, q, J = 6.3 Hz), 3.89-3.86 (2H, m), 3.51 (2H, s), 3.43 (3H, s), 2.94-2.90 (4H, m), 2.47 (4H, br s), 2.22-2.10 (3H, m), 1.57-1.33 (11H, m).		
411	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.39 (1H, d, J = 8.3 Hz), 8.25 (1H, d, J = 2.0 Hz), 8.19 (1H, s), 7.75 (1H, dd, J = 8.3, 2.0 Hz), 6.86 (1H, s), 6.69 (1H, t, J = 5.6 Hz), 4.33 (1H, q, J = 6.3 Hz), 4.26-4.22 (1H, m), 4.00-3.98 (1H, m), 3.90-3.82 (2H, m), 3.72-3.62 (1H, m), 3.49 (2H, s), 3.40 (3H, s), 2.91-2.88 (4H, m), 2.45 (4H, br s), 2.06-2.01 (1H, m), 1.97-1.93 (2H, m), 1.77-1.68 (1H, m), 1.50 (3H, d, J = 6.3 Hz).		

[Table 5-77]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
412	1H-NMR (CDCl3) δ: 9.18 (1H, s), 8.65 (1H, s), 8.51-8.48 (2H, m), 8.36-8.33 (2H, m), 8.05 (1H, dd, J = 7.8, 1.5 Hz), 7.84 (1H, dd, J = 8.3, 2.0 Hz), 7.49 (1H, t, J = 7.8 Hz), 7.35 (1H, d, J = 7.8 Hz), 7.19 (1H, s), 4.49 (1H, q, J = 6.3 Hz), 3.53 (2H, s), 3.47 (3H, s), 2.93-2.90 (4H, m), 2.47 (4H, br s), 1.59 (3H, d, J = 6.3 Hz).		
413	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.50 (1H, br s), 8.31-8.29 (2H, m), 7.72 (1H, d, J = 8.8 Hz), 6.88 (1H, s), 6.71 (1H, s), 4.31 (1H, q, J = 6.5 Hz), 3.83 (2H, s), 3.49 (2H, s), 3.39 (3H, s), 2.96-2.88 (4H, m), 2.47 (4H, br s), 2.10 (3H, t, J = 6.6 Hz), 1.96-1.93 (4H, m), 1.49 (3H, d, J = 6.5 Hz), 1.24-1.16 (1H, m).		
414	1H-NMR (CDCl3) δ: 9.11 (1H, s), 8.93 (1H, br s), 8.44 (1H, d, J = 8.8 Hz), 8.32 (1H, d, J = 2.0 Hz), 7.90 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.57 (1H, t, J = 5.4 Hz), 4.34 (1H, q, J = 6.3 Hz), 3.86-3.81 (2H, m), 3.71-3.67 (2H, m), 3.54-3.47 (4H, m), 3.40 (3H, s), 2.91-2.87 (4H, m), 2.47-2.36 (6H, m), 2.05-1.98 (2H, m), 1.51 (3H, d, J = 6.3 Hz).		
416	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.64 (1H, s), 8.29 (2H, d, J = 8.8 Hz), 7.73 (1H, d, J = 9.8 Hz), 7.62 (1H, d, J = 9.2 Hz), 7.46 (1H, s), 6.92 (1H, s), 6.58-6.56 (2H, m), 4.63-4.61 (2H, m), 4.33 (1H, q, J = 6.3 Hz), 3.48 (2H, s), 3.39 (3H, s), 2.90-2.87 (4H, m), 2.44 (4H, br s), 1.48 (3H, d, J = 5.9 Hz), 1.26 (1H, s).		

[Table 5-78]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
417	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.34 (1H, d, J = 8.8 Hz), 8.28-8.24 (2H, m), 7.74 (1H, dd, J = 8.5, 2.2 Hz), 6.84 (1H, s), 6.29 (1H, d, J = 6.8 Hz), 4.58-4.48 (1H, m), 4.34 (1H, q, J = 6.5 Hz), 3.49 (2H, s), 3.41 (3H, s), 2.93-2.87 (4H, m), 2.49-2.40 (4H, m), 2.24-2.13 (2H, m), 1.86-1.55 (6H, m), 1.51 (3H, d, J = 6.3 Hz).		
418	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.38 (1H, d, J = 8.8 Hz), 8.34 (1H, s), 8.28 (1H, d, J = 2.0 Hz), 7.70 (1H, dd, J = 8.5, 2.2 Hz), 6.84 (1H, s), 6.51 (1H, t, J = 6.1 Hz), 4.33 (1H, q, J = 6.3 Hz), 3.56-3.42 (4H, m), 3.40 (3H, s), 2.93-2.87 (4H, m), 2.49-2.39 (4H, br m), 1.50 (3H, d, J = 6.3 Hz), 1.07 (9H, s).		
419	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.41 (1H, br s), 8.32-8.25 (2H, m), 7.76 (1H, dd, J = 8.3, 2.4 Hz), 6.98-6.93 (1H, m), 6.46-6.41 (1H, m), 5.88 (1H, br s), 5.03-4.96 (1H, m), 4.37-4.29 (1H, m), 4.01-3.94 (1H, m), 3.51-3.37 (6H, m), 2.98-2.84 (5H, m), 2.51-2.38 (5H, m), 1.52-1.47 (3H, m).		
420	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.42 (1H, br s), 8.36-8.27 (2H, m), 7.69 (1H, dd, J = 8.8, 2.0 Hz), 6.86 (1H, s), 6.40 (1H, s), 4.32 (1H, q, J = 6.3 Hz), 3.85-3.77 (4H, m), 3.49 (2H, s), 3.40 (3H, s), 2.94-2.87 (4H, m), 2.48-2.33 (6H, m), 1.94-1.87 (2H, m), 1.66 (3H, s), 1.48 (3H, d, J = 6.3 Hz).		
421	1H-NMR (CDCl3) δ: 9.11-9.07 (1.0H, m), 8.53 (1.0H, br s), 8.30-8.25 (2.0H, m), 7.80-7.74 (1.0H, m), 6.95-6.90 (1.0H, m), 6.67-6.43 (1.6H, m), 6.00 (0.4H, br s), 4.65 (0.4H, br s), 4.38-4.31 (1.0H, m), 4.07 (0.6H, br s), 3.85-3.65 (1.6H, m), 3.49-3.39 (5.4H, m), 2.93-2.87 (4.0H, m), 2.64-1.88 (8.0H, m), 1.54-1.48 (3.0H, m).		

[Table 5-79]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
422	1H-NMR (CDCl3) δ: 9.08 (1H, s), 8.43 (1H, s), 8.32-8.26 (2H, m), 7.75 (1H, dd, J = 8.3, 2.0 Hz), 6.93 (1H, s), 6.29 (1H, d, J = 6.8 Hz), 6.08 (1H, s), 4.63 (1H, br s), 4.33 (1H, q, J = 6.2 Hz), 3.54-3.45 (4H, m), 3.40 (3H, s), 3.04-2.87 (5H, m), 2.57-2.30 (6H, m), 2.08-1.97 (1H, m), 1.50 (3H, d, J = 6.3 Hz).		
423	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.38-8.33 (2H, m), 8.27 (1H, d, J = 2.0 Hz), 7.73 (1H, dd, J = 8.5, 2.2 Hz), 6.83 (1H, s), 6.18 (1H, d, J = 6.8 Hz), 4.36-4.24 (2H, m), 3.49 (2H, s), 3.41 (3H, s), 2.94-2.88 (4H, m), 2.45 (4H, br s), 1.78-1.66 (2H, m), 1.53-1.48 (3H, m), 1.35-1.29 (3H, m), 1.07-1.00 (3H, m).		
424	1H-NMR (DMSO-D6) δ: 10.46 (1H, s), 9.32 (1H, s), 8.26-8.17 (2H, m), 7.74 (1H, d, J = 7.8 Hz), 7.20 (1H, s), 6.95-6.60 (2H, m), 4.59 (1H, s), 4.09 (1H, s), 3.68 (1H, s), 3.43 (4H, s), 3.15 (1H, s), 2.72 (4H, s), 2.32 (4H, s), 1.90-1.50 (9H, m).		
425	1H-NMR (DMSO-D6) δ: 10.61 (1H, s), 9.28 (1H, d, J = 5.9 Hz), 8.15 (1H, dd, J = 9.8, 4.9 Hz), 7.41 (1H, d, J = 9.8 Hz), 7.18 (1H, d, J = 5.9 Hz), 6.92-6.63 (2H, m), 4.70-4.53 (1H, m), 4.08 (1H, br s), 3.80-3.45 (7H, m), 3.16 (1H, d, J = 3.9 Hz), 2.96 (2H, br s), 2.85-2.75 (1H, m), 2.64-2.55 (1H, m), 1.95-1.45 (11H, m).		
426	1H-NMR (DMSO-D6) δ: 9.16 (1H, s), 8.17 (1H, s), 8.06 (1H, s), 7.94 (1H, s), 7.44 (1H, s), 7.06 (1H, s), 6.69 (1H, s), 6.56 (1H, s), 4.64 (1H, s), 4.32 (2H, s), 4.00 (1H, s), 3.67 (1H, s), 2.88 (2H, s), 2.78-2.60 (10H, m), 1.85-1.20 (12H, m).		

[Table 5-80]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
427	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.40 (1H, dd, J = 8.5, 3.7 Hz), 8.34 (1H, br s), 8.25 (1H, s), 7.74 (1H, d, J = 8.5 Hz), 7.06 (1H, d, J = 8.5 Hz), 6.85 (1H, s), 4.62-4.56 (1H, m), 4.50 (1H, br s), 4.36-4.32 (1H, m), 3.48 (2H, s), 3.41 (3H, s), 2.92-2.87 (4H, m), 2.62 (1H, s), 2.45 (4H, br s), 2.28-2.21 (2H, m), 2.12-2.05 (1H, m), 1.99-1.85 (4H, m), 1.50 (3H, d, J = 6.3 Hz).		
428	1H-NMR (CDCl3) δ: 9.08 (1H, s), 8.55 (1H, s), 8.35 (1H, d, J = 8.3 Hz), 8.30 (1H, d, J = 2.4 Hz), 7.75 (1H, dd, J = 8.3, 2.4 Hz), 6.87 (1H, s), 6.28 (1H, t, J = 5.6 Hz), 4.33 (1H, q, J = 6.5 Hz), 4.01-3.97 (2H, m), 3.73-3.68 (2H, m), 3.50 (2H, s), 3.43-3.37 (5H, m), 2.93-2.88 (4H, m), 2.46 (4H, br s), 1.77-1.69 (4H, m), 1.50 (3H, d, J = 6.3 Hz), 1.43 (3H, dd, J = 19.0, 5.9 Hz).		
429	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.45-8.43 (2H, m), 8.27 (1H, d, J = 2.0 Hz), 7.75 (1H, dd, J = 8.5, 2.0 Hz), 6.89 (1H, br s), 6.84 (1H, s), 4.34 (1H, q, J = 6.3 Hz), 4.08-4.02 (1H, m), 3.96-3.66 (4H, m), 3.49 (2H, s), 3.41 (3H, s), 2.91-2.87 (4H, m), 2.45 (4H, br s), 2.09-2.03 (2H, m), 1.96-1.86 (3H, m), 1.66-1.55 (1H, m), 1.51 (3H, d, J = 6.3 Hz).		
430	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.57 (1H, s), 8.43 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 2.0 Hz), 7.76 (1H, dd, J = 8.8, 2.0 Hz), 6.86-6.83 (2H, m), 4.34 (1H, q, J = 6.2 Hz), 4.02-3.97 (1H, m), 3.87-3.77 (1H, m), 3.70-3.62 (1H, m), 3.49-3.43 (4H, m), 3.41 (3H, s), 2.91-2.87 (4H, m), 2.45 (4H, br s), 1.94-1.82 (3H, m), 1.67-1.38 (8H, m).		

[Table 5-81]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
431	1H-NMR (CDCl3) δ: 9.10 (1H, s), 8.72 (1H, s), 8.35 (1H, d, J = 8.8 Hz), 8.31 (1H, d, J = 2.4 Hz), 7.77 (1H, dd, J = 8.8, 2.4 Hz), 6.87 (1H, s), 6.29 (1H, t, J = 5.6 Hz), 4.34 (1H, q, J = 6.3 Hz), 3.98-3.89 (2H, m), 3.73-3.64 (2H, m), 3.50 (2H, s), 3.44-3.38 (4H, m), 3.19 (1H, t, J = 10.5 Hz), 2.92-2.89 (4H, m), 2.46 (4H, br s), 2.01 (1H, t, J = 6.6 Hz), 1.69-1.55 (5H, m), 1.51 (3H, d, J = 6.3 Hz), 1.32-1.22 (1H, m).		
432	1H-NMR (CDCl3) δ: 9.10 (1H, s), 8.73 (1H, s), 8.42 (1H, d, J = 8.3 Hz), 8.32 (1H, d, J = 2.4 Hz), 7.76 (1H, dd, J = 8.3, 2.4 Hz), 6.87 (1H, s), 6.67 (1H, t, J = 7.8 Hz), 4.35-4.30 (2H, m), 4.11-4.06 (1H, m), 3.70-3.64 (1H, m), 3.49 (2H, s), 3.40 (3H, s), 2.93-2.88 (4H, m), 2.45 (4H, br s), 2.06-2.00 (1H, m), 1.94-1.75 (2H, m), 1.62-1.54 (1H, m), 1.50-1.46 (3H, m), 1.33 (6H, s).		
433	1H-NMR (CDCl3) δ: 9.09 (1H, s), 8.50 (1H, s), 8.32-8.29 (2H, m), 7.72 (1H, dd, J = 8.5, 2.7 Hz), 6.92 (1H, s), 6.81 (1H, s), 4.33-4.28 (1H, m), 3.92-3.70 (6H, m), 3.49 (2H, s), 3.39 (3H, s), 2.92-2.89 (4H, m), 2.46 (4H, br s), 2.17-2.02 (5H, m), 1.51-1.47 (3H, m).		
434	1H-NMR (CDCl3) δ: 9.14 (1H, s), 9.14 (1H, s), 8.38-8.35 (2H, m), 7.71 (1H, dd, J = 8.8, 2.0 Hz), 6.89 (1H, s), 6.82 (1H, s), 4.32 (1H, q, J = 6.3 Hz), 3.80 (2H, s), 3.51 (2H, s), 3.40 (3H, s), 2.93-2.88 (4H, m), 2.46 (4H, br s), 2.16-2.11 (2H, m), 1.89 (2H, br s), 1.67-1.41 (9H, m).		
435		535.4	534.31

[Table 5-82]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
436	1H-NMR (DMSO-D6) δ: 8.93 (1H, s), 8.08-7.93 (2H, m), 7.47 (1H, d, J = 8.3 Hz), 6.68-6.62 (2H, m), 4.19-4.02 (2H, m), 3.22 (3H, s), 3.16 (2H, s), 2.68-2.62 (3H, m), 2.29-2.20 (4H, br m), 1.95-1.77 (5H, m), 1.59-1.50 (2H, br m), 1.37-1.24 (5H, m), 1.03 (3H, s).		
437	1H-NMR (DMSO-D6) δ: 8.79-8.66 (1.0H, m), 7.98-7.87 (1.0H, m), 7.77-7.60 (0.5H, m), 7.52-7.20 (1.5H, m), 6.60-6.46 (1.0H, m), 6.27-6.01 (1.0H, m), 4.15-4.07 (1.0H, m), 3.83-3.57 (1.0H, m), 3.28-3.14 (5.0H, m), 2.64 (2.0H, br s), 2.37-2.02 (6.0H, m), 1.92-1.77 (2.0H, br m), 1.52-1.19 (5.0H, m), 1.14-0.85 (5.0H, m).	535.4	534.31
438	1H-NMR (CDCl3) δ: 9.11 (1H, s), 8.57 (1H, s), 8.39 (1H, d, J = 8.8 Hz), 8.33 (1H, d, J = 2.4 Hz), 7.75 (1H, dd, J = 9.0, 2.7 Hz), 7.10 (1H, s), 6.54 (1H, t, J = 56.1 Hz), 6.27 (1H, d, J = 7.8 Hz), 4.43 (1H, td, J = 13.4, 6.5 Hz), 3.77 (2H, t, J = 5.4 Hz), 3.29 (2H, t, J = 5.4 Hz), 1.51 (6H, s), 1.36 (6H, d, J = 6.8 Hz).		
439	1H-NMR (CDCl3) δ: 9.13 (1H, s), 8.61 (1H, s), 8.37 (1H, d, J = 8.8 Hz), 8.34 (1H, d, J = 2.4 Hz), 7.75 (1H, dd, J = 9.0, 2.7 Hz), 7.26 (1H, s), 7.13 (1H, s), 6.54 (1H, t, J = 55.9 Hz), 6.36 (1H, d, J = 7.8 Hz), 4.36 (1H, tt, J = 14.1, 5.2 Hz), 4.05 (2H, td, J = 7.6, 4.1 Hz), 3.77 (2H, t, J = 5.4 Hz), 3.64 (2H, td, J = 11.3, 2.1 Hz), 3.30 (2H, t, J = 5.4 Hz), 2.17 (2H, dd, J = 12.9, 2.7 Hz), 1.71 (2H, dd, J = 10.7, 4.4 Hz), 1.52 (6H, s).		

[Table 5-83]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
440	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.39 (1H, d, J = 9.3 Hz), 8.28 (2H, d, J = 2.4 Hz), 7.74 (1H, dd, J = 9.0, 2.7 Hz), 7.26 (3H, s), 6.70 (1H, s), 6.24 (1H, d, J = 7.8 Hz), 4.81 (1H, q, J = 6.3 Hz), 4.41 (1H, td, J = 13.3, 6.7 Hz), 3.76 (2H, t, J = 5.6 Hz), 3.29 (2H, t, J = 5.4 Hz), 1.53 (4H, d, J = 6.3 Hz), 1.51 (6H, s), 1.38 (6H, d, J = 6.3 Hz).		
441	1H-NMR (DMSO-D6) δ: 10.22 (1H, s), 9.27 (1H, s), 8.34 (1H, d, J = 8.8 Hz), 8.24 (1H, s), 7.77 (1H, d, J = 7.8 Hz), 7.02 (1H, s), 6.53 (1H, d, J = 7.8 Hz), 5.24 (0H, s), 4.61 (1H, d, J = 6.8 Hz), 4.14 (5H, s), 3.90 (2H, d, J = 10.7 Hz), 3.65 (2H, t, J = 4.9 Hz), 3.50 (4H, d, J = 11.7 Hz), 3.15 (12H, s), 3.06 (2H, d, J = 4.9 Hz), 2.01 (2H, t, J = 13.2 Hz), 1.37 (3H, d, J = 5.9 Hz), 1.30 (6H, s), 1.22 (4H, s).		
442	1H-NMR (DMSO-D6) δ: 10.22 (0H, s), 9.27 (0H, s), 8.34 (0H, d, J = 8.8 Hz), 8.23 (0H, s), 7.77 (0H, d, J = 8.8 Hz), 7.01 (1H, s), 6.52 (0H, d, J = 7.8 Hz), 5.25 (0H, s), 4.61 (1H, d, J = 5.9 Hz), 4.14 (2H, s), 3.90 (1H, d, J = 8.8 Hz), 3.65 (1H, t, J = 4.9 Hz), 3.55-3.44 (2H, m), 3.15 (6H, s), 3.05 (2H, d, J = 4.9 Hz), 2.01 (1H, t, J = 11.7 Hz), 1.37 (2H, d, J = 5.9 Hz), 1.30 (3H, s), 1.22 (2H, s).		
443	1H-NMR (DMSO-D6) δ: 10.47 (1H, s), 9.34 (1H, s), 8.31-8.25 (2H, m), 7.79 (1H, dd, J = 8.8, 2.9 Hz), 7.22 (1H, s), 6.96-6.62 (2H, m), 4.62 (1H, d, J = 4.9 Hz), 3.92 (1H, t, J = 3.9 Hz), 3.65 (2H, t, J = 5.4 Hz), 3.48 (1H, t, J = 6.8 Hz), 3.06 (2H, t, J = 4.9 Hz), 2.05 (2H, d, J = 9.8 Hz), 1.87 (2H, d, J = 9.8 Hz), 1.45 (2H, q, J = 11.4 Hz), 1.33 (9H, d, J = 18.5 Hz).		

[Table 5-84]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
444	1H-NMR (DMSO-D6) δ: 10.24 (0H, s), 9.26 (0H, s), 8.31 (1H, d, J = 8.8 Hz), 8.23 (1H, s), 7.77 (0H, dd, J = 8.8, 2.0 Hz), 6.90 (0H, s), 6.45 (0H, d, J = 7.8 Hz), 4.29-4.22 (1H, m), 3.65 (1H, t, J = 5.4 Hz), 3.27 (2H, s), 3.15 (1H, d, J = 3.9 Hz), 3.05 (1H, d, J = 5.9 Hz), 2.63 (1H, d, J = 22.4 Hz), 1.38 (2H, d, J = 5.9 Hz), 1.29 (6H, d, J = 6.8 Hz), 1.25 (3H, d, J = 26.3 Hz).		
445	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.54 (1H, s), 8.37 (1H, d, J = 8.3 Hz), 8.30 (1H, s), 7.73 (1H, dd, J = 8.8, 2.0 Hz), 6.83 (1H, s), 6.33 (1H, d, J = 7.8 Hz), 4.37-4.31 (2H, m), 3.55 (2H, s), 3.42 (3H, s), 2.93-2.88 (4H, m), 2.47 (4H, br s), 2.11-2.06 (2H, m), 1.92-1.87 (2H, m), 1.70-1.65 (8H, m), 1.51 (3H, d, J = 6.3 Hz).		
446	1H-NMR (CDCl3) δ: 9.16 (1H, s), 8.64 (1H, s), 8.51 (1H, s), 8.39 (1H, d, J = 8.3 Hz), 8.34 (1H, d, J = 2.0 Hz), 7.95-7.90 (2H, m), 7.82 (1H, dd, J = 8.3, 2.0 Hz), 7.15-7.06 (3H, m), 4.45 (1H, q, J = 6.3 Hz), 3.52 (2H, s), 3.44 (3H, s), 2.93-2.90 (4H, m), 2.47 (4H, br s), 1.57 (3H, d, J = 6.3 Hz).		
447	1H-NMR (CDCl3) δ: 9.14 (1H, s), 8.63 (1H, s), 8.37 (1H, d, J = 8.3 Hz), 8.30 (1H, s), 8.23 (1H, s), 8.13-8.10 (1H, m), 7.85-7.82 (1H, m), 7.45 (1H, d, J = 8.3 Hz), 7.36-7.34 (1H, m), 7.14 (1H, s), 6.80-6.74 (1H, m), 4.48 (1H, q, J = 6.3 Hz), 3.52 (2H, s), 3.46 (3H, s), 2.93-2.89 (4H, m), 2.47 (4H, br s), 1.59 (3H, d, J = 6.3 Hz).		
448		515.3	514.24
449		515.3	514.24

[Table 5-85]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
450	1H-NMR (CDCl3) δ: 9.15 (1H, s), 8.83 (1H, s), 8.43-8.35 (3H, m), 7.88 (2H, d, J = 8.8 Hz), 7.81 (1H, dd, J = 8.8, 2.2 Hz), 7.05 (1H, s), 6.97 (2H, d, J = 8.8 Hz), 4.44 (1H, q, J = 6.3 Hz), 3.86 (3H, s), 3.52 (2H, s), 3.45 (3H, s), 2.93-2.89 (4H, m), 2.47 (4H, br s), 1.57 (3H, d, J = 6.3 Hz).		
451	1H-NMR (CDCl3) δ: 9.13 (1H, s), 8.58 (1H, s), 8.39 (1H, d, J = 8.8 Hz), 8.34-8.30 (2H, m), 8.02 (1H, d, J = 2.0 Hz), 7.82 (1H, dd, J = 8.8, 2.0 Hz), 7.32-7.25 (2H, m), 7.10 (1H, s), 6.65 (1H, d, J = 7.8 Hz), 4.47 (1H, q, J = 6.3 Hz), 3.90 (3H, s), 3.52 (2H, s), 3.44 (3H, s), 2.93-2.89 (4H, m), 2.47 (4H, br s), 1.59 (3H, d, J = 6.3 Hz).		
452	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.37-8.33 (2H, m), 7.10 (1H, d, J = 10.2 Hz), 6.83 (1H, s), 6.09 (1H, d, J = 7.3 Hz), 4.44-4.24 (4H, m), 3.41 (3H, s), 3.08-3.01 (2H, m), 2.66-2.64 (1H, m), 2.49 (3H, s), 2.04-2.00 (2H, m), 1.58-1.25 (11H, m).		
453	1H-NMR (CDCl3) δ: 8.96 (1H, s), 8.15 (1H, d, J = 8.8 Hz), 7.93-7.87 (2H, m), 7.13 (1H, dd, J = 8.8, 3.2 Hz), 6.80 (1H, s), 6.14 (1H, d, J = 7.8 Hz), 4.44-4.30 (2H, m), 3.63-3.56 (4H, m), 3.40 (3H, s), 3.08 (2H, t, J = 5.1 Hz), 2.87 (2H, t, J = 5.1 Hz), 1.98-1.92 (2H, m), 1.50 (3H, d, J = 6.8 Hz), 1.35 (6H, t, J = 5.9 Hz).		
454	1H-NMR (CDCl3) δ: 9.06 (1H, d, J = 2.9 Hz), 8.51 (1H, s), 8.38-8.34 (1H, m), 8.29 (1H, s), 7.72 (1H, d, J = 8.3 Hz), 6.84-6.79 (1H, m), 6.55-6.45 (1H, m), 4.40-3.99 (3H, m), 3.49-3.12 (6H, m), 2.92-2.89 (4H, m), 2.46 (4H, br s), 1.96-1.84 (2H, m), 1.59-1.51 (4H, m), 1.25-0.95 (14H, m).		

[Table 5-86]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
455	1H-NMR (CDCl3) δ: 9.05 (1H, s), 8.65 (1H, s), 8.35-8.29 (2H, m), 7.74 (1H, d, J = 6.8 Hz), 6.85 (1H, s), 6.33 (1H, s), 4.33 (1H, q, J = 6.3 Hz), 3.49 (2H, s), 3.42 (3H, s), 2.93-2.89 (4H, m), 2.46-2.17 (6H, m), 1.80-1.65 (13H, m), 1.51 (3H, d, J = 6.3 Hz).		
456	1H-NMR (CDCl3) δ: 9.31 (1H, br s), 9.28 (1H, s), 8.80 (1H, d, J = 8.3 Hz), 8.37 (1H, d, J = 2.0 Hz), 7.88 (1H, dd, J = 8.3, 2.0 Hz), 7.33 (1H, s), 4.52 (1H, q, J = 6.3 Hz), 4.25-4.19 (1H, m), 3.52 (2H, s), 3.42 (3H, s), 2.93-2.89 (4H, m), 2.47 (4H, br s), 1.56-1.52 (9H, m).		
457	1H-NMR (CDCl3) δ: 9.01 (1H, s), 8.29 (1H, d, J = 9.3 Hz), 8.18 (1H, s), 8.07 (1H, d, J = 2.9 Hz), 7.35 (1H, dd, J = 8.8, 2.9 Hz), 6.83 (1H, s), 6.12 (1H, d, J = 7.3 Hz), 4.45-4.29 (2H, m), 3.91 (2H, s), 3.41 (3H, s), 1.50 (3H, d, J = 6.3 Hz), 1.38-1.32 (6H, m), 0.81-0.76 (2H, m), 0.69-0.65 (2H, m).		
458	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.61 (1H, br s), 8.29 (1H, d, J = 8.8 Hz), 8.17 (1H, d, J = 2.4 Hz), 7.36 (1H, dd, J = 9.3, 2.9 Hz), 6.83 (1H, s), 6.12 (1H, d, J = 7.3 Hz), 4.45-4.29 (2H, m), 3.84 (2H, s), 3.41 (3H, s), 1.51 (3H, d, J = 6.3 Hz), 1.39-1.21 (12H, m).		
459	1H-NMR (CDCl3) δ: 9.02 (1.0H, s), 8.33-8.25 (2.0H, m), 8.13 (1.0H, d, J = 2.4 Hz), 7.42 (1.0H, dd, J = 8.8, 2.9 Hz), 6.83 (1.0H, s), 6.13 (1.0H, d, J = 7.8 Hz), 4.69-4.63 (0.5H, m), 4.57-4.51 (0.5H, m), 4.45-4.31 (3.0H, m), 3.44-3.34 (4.0H, m), 3.12-3.04 (1.0H, m), 2.92-2.84 (1.0H, m), 2.75-2.68 (1.0H, m), 2.20-2.11 (1.0H, m), 1.78-1.68 (1.0H, m), 1.51 (3.0H, d, J = 6.8 Hz), 1.38-1.34 (6.0H, m).		

[Table 5-87]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
460	1H-NMR (CDCl3) δ: 9.03 (1.0H, s), 8.31 (1.0H, d, J = 9.3 Hz), 8.26 (1.0H, br s), 8.14 (1.0H, d, J = 2.9 Hz), 7.43 (1.0H, dd, J = 9.3, 2.9 Hz), 6.84 (1.0H, s), 6.12 (1.0H, d, J = 7.8 Hz), 4.90-4.86 (0.5H, m), 4.78-4.73 (0.5H, m), 4.46-4.24 (3.0H, m), 3.44-3.34 (4.0H, m), 3.22-3.15 (1.0H, m), 2.93-2.67 (2.0H, m), 2.03-1.92 (2.0H, m), 1.51 (3.0H, d, J = 6.8 Hz), 1.38-1.33 (6.0H, m).		
461	1H-NMR (CDCl3) δ: 8.97 (1H, s), 8.15 (1H, d, J = 9.3 Hz), 8.07 (1H, s), 8.03 (1H, d, J = 3.4 Hz), 7.31 (1H, dd, J = 9.0, 3.2 Hz), 6.80 (1H, s), 6.15 (1H, d, J = 7.8 Hz), 4.45-4.29 (2H, m), 3.77 (2H, s), 3.40 (3H, s), 3.08 (3H, s), 1.50 (3H, d, J = 6.8 Hz), 1.38-1.33 (6H, m), 1.01-0.94 (4H, m).		
462	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.45 (2H, t, J = 8.8 Hz), 8.32 (1H, d, J = 2.9 Hz), 7.75 (1H, dd, J = 9.3, 2.4 Hz), 6.85 (1H, s), 6.13 (1H, d, J = 6.8 Hz), 4.42 (1H, td, J = 13.4, 6.5 Hz), 4.34 (1H, q, J = 6.5 Hz), 3.90 (1H, td, J = 10.5, 4.2 Hz), 3.76 (1H, q, J = 6.8 Hz), 3.64-3.61 (1H, m), 3.41 (3H, s), 3.37-3.23 (2H, m), 1.47 (7H, t, J = 17.1 Hz), 1.35 (7H, t, J = 5.9 Hz).		
463	1H-NMR (CDCl3) δ: 9.06 (1H, s), 8.48-8.37 (2H, m), 8.31 (1H, s), 7.75 (1H, dd, J = 8.8, 2.9 Hz), 6.85 (1H, s), 6.13 (1H, d, J = 7.8 Hz), 4.42 (1H, td, J = 13.7, 6.8 Hz), 4.34 (1H, q, J = 6.5 Hz), 3.93-3.87 (1H, m), 3.76 (1H, q, J = 6.8 Hz), 3.63 (1H, td, J = 7.3, 4.2 Hz), 3.41 (3H, s), 3.36-3.23 (2H, m), 1.51 (6H, d, J = 6.8 Hz), 1.35 (7H, t, J = 5.9 Hz).		

[Table 5-88]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
464	1H-NMR (CDCl3) δ: 9.04 (1H, s), 8.37-8.32 (1H, m), 8.29-8.24 (2H, br m), 7.76-7.70 (1H, m), 6.86 (1H, s), 6.15 (1H, d, J = 7.3 Hz), 4.39-4.31 (1H, m), 4.15-4.03 (1H, br m), 3.79-3.71 (1H, m), 3.52 (2H, s), 3.46-3.39 (4H, br m), 3.05-2.98 (4H, br m), 2.61-2.52 (4H, br m), 2.34-2.26 (2H, m), 2.09-2.02 (2H, m), 1.58-1.46 (5H, m), 1.45-1.31 (2H, m), 1.18 (6H, d, J = 5.9 Hz).		
465	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.37-8.26 (3H, m), 7.75 (1H, dd, J = 8.5, 2.2 Hz), 6.90 (1H, s), 6.40 (1H, t, J = 6.1 Hz), 4.33 (1H, q, J = 6.5 Hz), 3.80 (2H, t, J = 6.3 Hz), 3.51 (2H, s), 3.40 (3H, s), 2.97-2.91 (4H, m), 2.79-2.38 (9H, m), 1.50 (3H, d, J = 6.3 Hz).		
466	1H-NMR (CDCl3) δ: 8.99 (1H, s), 8.24 (1H, d, J = 9.3 Hz), 8.08-8.00 (2H, m), 7.40 (1H, dd, J = 9.3, 2.9 Hz), 6.82 (1H, s), 6.13 (1H, d, J = 7.3 Hz), 4.83-4.66 (1H, m), 4.45-4.29 (2H, m), 3.87-3.79 (1H, m), 3.59-3.53 (1H, m), 3.41 (3H, s), 3.11-2.87 (3H, m), 1.99-1.85 (2H, m), 1.62-1.47 (5H, m), 1.38-1.32 (6H, m).		
467	1H-NMR (CDCl3) δ: 9.00 (1H, s), 8.26 (1H, d, J = 9.3 Hz), 8.08-8.03 (2H, m), 7.38 (1H, dd, J = 9.0, 3.2 Hz), 6.82 (1H, s), 6.13 (1H, d, J = 7.3 Hz), 4.46-4.28 (3H, m), 3.87-3.79 (1H, m), 3.56-3.49 (1H, m), 3.41 (3H, s), 3.01-2.75 (3H, m), 2.09-2.00 (1H, m), 1.68-1.49 (6H, m), 1.39-1.31 (6H, m).		
468		493.4	492.30

[Table 5-89]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
469	1H-NMR (CDCl3) δ: 8.99 (1H, s), 8.24 (1H, d, J = 8.8 Hz), 8.06-8.06 (2H, m), 7.40 (1H, dd, J = 8.8, 3.2 Hz), 6.82 (1H, s), 6.15 (1H, d, J = 7.8 Hz), 4.91-4.77 (1H, m), 4.41-4.30 (2H, m), 3.55 (3H, s), 3.39-3.31 (2H, m), 3.20-3.14 (2H, m), 2.11-2.07 (4H, m), 1.50 (3H, d, J = 6.3 Hz), 1.35 (6H, d, J = 6.1 Hz).		
470	1H-NMR (CDCl3) δ: 9.00 (1H, s), 8.27 (1H, d, J = 8.8 Hz), 8.19 (1H, s), 8.07 (1H, d, J = 2.9 Hz), 7.41 (1H, dd, J = 8.8, 2.9 Hz), 6.82 (1H, s), 6.14 (1H, d, J = 7.8 Hz), 4.45-4.31 (2H, m), 3.41 (3H, s), 3.34-3.26 (4H, m), 2.21-2.11 (4H, m), 1.50 (3H, d, J = 6.3 Hz), 1.36 (6H, dd, J = 6.6, 5.1 Hz).		
471	1H-NMR (CDCl3) δ: 9.08 (1H, s), 8.95 (1H, br s), 8.54 (1H, d, J = 9.8 Hz), 7.15 (1H, d, J = 9.8 Hz), 6.85 (1H, s), 6.15 (1H, d, J = 7.3 Hz), 4.59 (2H, t, J = 5.4 Hz), 4.37-4.33 (2H, m), 3.41 (3H, s), 2.82 (2H, t, J = 5.4 Hz), 2.39 (6H, s), 1.51 (3H, d, J = 6.3 Hz), 1.34 (3H, d, J = 5.9 Hz), 1.33 (3H, d, J = 5.9 Hz).		
472	1H-NMR (CDCl3) δ: 9.07 (1H, s), 8.58 (1H, s), 8.36 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 1.5 Hz), 7.74 (1H, dd, J = 8.8, 1.5 Hz), 6.85 (1H, s), 6.14 (1H, d, J = 7.8 Hz), 4.76-4.63 (1H, m), 4.46-4.31 (2H, m), 3.51 (2H, s), 3.42 (3H, s), 2.64-2.58 (2H, m), 2.46-2.40 (2H, m), 1.98-1.86 (4H, m), 1.51 (3H, d, J = 6.3 Hz), 1.36 (3H, d, J = 6.1 Hz), 1.35 (3H, d, J = 5.1 Hz).		

[Table 5-90]

Compound No.	NMR	LC/MS $(M+H)^+$	Exact Mass
473	1H-NMR (CDCl3) δ: 9.03 (1H, s), 8.32-8.30 (2H, m), 8.16 (1H, d, J = 2.9 Hz), 7.44 (1H, dd, J = 8.8, 2.9 Hz), 6.84 (1H, s), 6.12 (1H, d, J = 7.3 Hz), 4.48-4.31 (3H, m), 3.41-3.29 (5H, m), 3.11-2.98 (2H, m), 2.82 (1H, d, J = 14.1 Hz), 2.08-2.04 (2H, m), 1.51 (3H, d, J = 6.3 Hz), 1.36 (6H, t, J = 5.9 Hz).		
474	1H-NMR (CDCl3) δ: 9.10 (1H, s), 8.91 (1H, s), 8.49 (1H, d, J = 9.8 Hz), 7.12 (1H, d, J = 9.8 Hz), 6.73 (1H, s), 6.19 (1H, d, J = 7.3 Hz), 4.81 (1H, d, J = 5.4 Hz), 4.60 (2H, t, J = 5.6 Hz), 4.42-4.32 (1H, m), 4.14 (1H, s), 2.79 (2H, t, J = 5.6 Hz), 2.36 (6H, s), 1.53 (3H, d, J = 6.3 Hz), 1.36 (3H, d, J = 6.3 Hz), 1.35 (3H, d, J = 6.3 Hz).		
475	1H-NMR (CD3OD) δ: 9.07 (1H, s), 8.28-8.21 (2H, m), 7.81 (1H, dd, J = 8.5, 2.2 Hz), 6.84 (1H, s), 4.32 (1H, q, J = 6.3 Hz), 3.53 (2H, s), 3.37 (3H, s), 2.87-2.80 (4H, m), 2.51-2.41 (4H, br m), 2.21-2.14 (6H, m), 1.99-1.92 (6H, m), 1.47 (3H, d, J = 6.3 Hz).		
476	1H-NMR (DMSO-D6) δ: 9.87 (1H, s), 9.12 (1H, s), 8.02 (1H, d, J = 8.3 Hz), 7.69-6.75 (4H, m), 6.38-6.22 (1H, br m), 4.22-3.89 (10H, m), 3.32 (3H, s), 1.41-1.14 (9H, m).		
477	1H-NMR (CDCl3) δ: 8.96 (1H, s), 8.16 (1H, d, J = 8.8 Hz), 7.95 (1H, s), 7.64 (1H, d, J = 2.9 Hz), 6.90 (1H, dd, J = 8.8, 2.9 Hz), 6.80 (1H, s), 6.13 (1H, d, J = 7.8 Hz), 4.44-4.30 (2H, m), 3.69 (2H, d, J = 6.8 Hz), 3.59 (2H, d, J = 6.8 Hz), 3.40 (3H, s), 2.98 (2H, s), 2.81-2.75 (2H, m), 1.83-1.76 (2H, m), 1.59-1.47 (5H, m), 1.38-1.31 (6H, m).		

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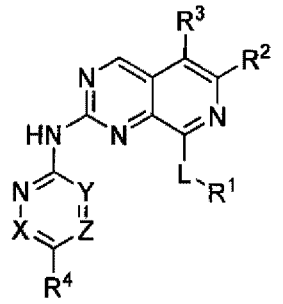
CLAIMS

1. A compound represented by Formula (I) or a pharmaceutically acceptable salt thereof:

[Formula 1]



(I)

where

L represents $-NR^5-$, -O-, or -S-;

R^5 represents a hydrogen atom or a C_{1-6} alkyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms;

R^1 represents a C_{1-8} alkyl, C_{3-12} cycloalkyl, (C_{3-12} cycloalkyl)-C_{1-6} alkyl, 4- to 12-membered heterocyclyl, (4- to 12-membered heterocyclyl)-C_{1-6} alkyl, C_{6-10} aryl, (C_{6-10} aryl)-C_{1-6} alkyl, 5- to 10-membered heteroaryl, (5- to 10-membered heteroaryl)-C_{1-6} alkyl, C_{1-8} alkylsulfonyl, or C_{1-8} acyl group;

each of the heterocyclyl and heteroaryl represented by R^1 contains one to four heteroatoms selected from oxygen, sulfur, and nitrogen atoms;

R^1 is optionally substituted with one to six substituents selected from the group consisting of a halogen atom, =O, -OH, -CN, -COOH, $-COOR^6$, $-R^7$, a C_{3-6} cycloalkyl group, a 3- to 10-membered heterocyclyl group, a C_{1-8} acyl group, and a C_{1-8} alkoxy group, wherein each of the C_{3-6} cycloalkyl, 3- to 10-membered heterocyclyl, C_{1-8} acyl, and C_{1-8} alkoxy groups is substituted with zero to two -OH groups,

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zero to two C_{1-8} alkoxy groups, and/or zero to six fluorine atoms;

R^6 and R^7 each independently represent a C_{1-6} alkyl group substituted with zero to two -OH groups, zero to two C_{1-8} alkoxy groups, and zero to six fluorine atoms;

R^2 represents a C_{1-8} alkyl, C_{3-8} cycloalkyl, 4- to 6-membered heterocyclyl, or C_{1-8} acyl group, $-COOR^8$, or $-CONR^9R^{10}$;

each of the C_{1-8} alkyl and C_{3-8} cycloalkyl groups represented by R^2 is substituted with zero or one -OH group, zero to two C_{1-8} alkoxy groups substituted with zero or one -OH group, zero or one C_{1-4} alkoxy group, and zero to three fluorine atoms, and zero to five fluorine atoms;

R^2 is neither an unsubstituted C_{1-8} alkyl, nor unsubstituted C_{3-8} cycloalkyl, nor trifluoromethyl group;

R^8, R^9, and R^{10} each independently represent a hydrogen atom or a C_{1-8} alkyl group;

the 4- to 6-membered heterocyclyl group represented by R^2 is optionally substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and C_{1-4} alkyl and C_{1-4} alkoxy groups;

each of the C_{1-8} acyl group, $-COOR^8$, and $-CONR^9R^{10}$ represented by R^2 is optionally substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and a C_{1-4} alkoxy group;

R^9 and R^{10} of $-CONR^9R^{10}$ represented by R^2 are optionally bonded via a single bond or -O- to form a ring including the nitrogen atom bonded to R^9 and R^{10};

the heterocyclyl group represented by R^2 having a 4- or 5-membered ring contains one oxygen heteroatom, and the heterocyclyl group having a 6-membered ring contains one or two oxygen heteroatoms;

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R^3 represents a hydrogen atom, a C_{1-8} alkyl group, or a halogen atom;

X represents CR^{11} or a nitrogen atom;

Y represents CR^{12} or a nitrogen atom;

Z represents CR^{13} or a nitrogen atom;

R^{11} to R^{13} each independently represent a hydrogen, fluorine, or chlorine atom or a C_{1-6} alkyl or C_{1-6} alkoxy group;

R^4 represents $-A^1-A^2-A^3$;

A^1 represents a single bond or a C_{1-8} alkylene, C_{2-8} alkenylene, or C_{2-8} alkynylene group;

one or two sp^3 carbon atoms at any positions of A^1 are optionally replaced with one or two structures selected from the group consisting of $-O-$, $-NR^{14}-$, $-C(=O)-$, $-C(=O)-O-$, $-O-C(=O)-$, $-O-C(=O)-O-$, $-C(=O)-NR^{15}-$, $-O-C(=O)-NR^{16}-$, $-NR^{17}-C(=O)-$, $-NR^{18}-C(=O)-O-$, $-NR^{19}-C(=O)-NR^{20}-$, $-S(=O)_p-$, $-S(=O)_2-NR^{21}-$, $-NR^{22}-S(=O)_2-$, and $-NR^{23}-S(=O)_2-NR^{24}-$, and a structure of $-O-O-$, $-O-NR^{14}-$, $-NR^{14}-O-$, $-O-CH_2-O-$, $-O-CH_2-NR^{14}-$, or $-NR^{14}-CH_2-O-$ is not formed in the case of replacement of two sp^3 carbon atoms;

A^2 represents a single bond or a C_{1-7} alkylene, C_{3-12} cycloalkylene, C_{3-12} cycloalkylidene, 4- to 12-membered heterocyclylene, 4- to 12-membered heterocyclylidene, C_{6-10} arylene, or 5- to 10-membered heteroarylene group;

A^3 represents a halogen atom, $-CN$, $-NO_2$, $-R^{25}$, $-OR^{26}$, $-NR^{27}R^{28}$, $-C(=O)R^{29}$, $-C(=O)-OR^{30}$, $-O-C(=O)R^{31}$, $-O-C(=O)-NR^{32}R^{33}$, $-C(=O)-NR^{34}R^{35}$, $-NR^{36}-C(=O)R^{37}$, $-NR^{38}-C(=O)-OR^{39}$, $-S(=O)_2-R^{40}$, $-S(=O)_2-NR^{41}R^{42}$, or $-NR^{43}-S(=O)_2R^{44}$;

A^3 represents $-R^{25}$, if the A^1 end on the A^2 side has a structure selected from the group consisting of $-O-$, $-NR^{14}-$, $-C(=O)-$, $-C(=O)-O-$, $-O-C(=O)-$, $-O-C(=O)-O-$, $-C(=O)-NR^{15}-$,

$-O-C(=O)-NR^{16}-$, $-NR^{17}-C(=O)-$, $-NR^{18}-C(=O)-O-$, $-NR^{19}-C(=O)-NR^{20}-$, $-S(=O)_p-$, $-S(=O)_2-NR^{21}-$, $-NR^{22}-S(=O)_2-$, and $-NR^{23}-S(=O)_2-NR^{24}-$ and A^2 is a single bond;

R^{14}, R^{32}, R^{34}, R^{36}, R^{38}, R^{41}, and R^{43} each independently represent a hydrogen atom or a C_{1-8} alkyl, C_{1-8} acyl, C_{1-8} alkylsulfonyl, 4- to 12-membered heterocyclyl, C_{3-12} cycloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, (4- to 12-membered heterocyclyl)-C_{1-3} alkyl, (C_{3-12} cycloalkyl)-C_{1-3} alkyl, (C_{6-10} aryl)-C_{1-3} alkyl, or (5- to 10-membered heteroaryl)-C_{1-3} alkyl group;

R^{15} to R^{31}, R^{33}, R^{35}, R^{37}, R^{39}, R^{40}, R^{42}, and R^{44} each independently represent a hydrogen atom or a C_{1-8} alkyl, 4- to 12-membered heterocyclyl, C_{3-12} cycloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, (4- to 12-membered heterocyclyl)-C_{1-3} alkyl, (C_{3-12} cycloalkyl)-C_{1-3} alkyl, (C_{6-10} aryl)-C_{1-3} alkyl, or (5- to 10-membered heteroaryl)-C_{1-3} alkyl group;

A^1, A^2, A^3, and R^{14} to R^{44} in A^1 and A^3 are each optionally substituted with one to four substituents selected from the group consisting of -OH, =O, -COOH, $-SO_3H$, $-PO_3H$, -CN, $-NO_2$, a halogen atom, a C_{1-8} alkyl group substituted with zero to two -OH groups, zero to two $-OR^{45}$ groups, and zero to six fluorine atoms, a C_{3-12} cycloalkyl group substituted with zero to two -OH groups, zero to two $-OR^{46}$ groups, and zero to six fluorine atoms, a C_{1-8} alkoxy group substituted with zero to two -OH groups, zero to two $-OR^{47}$ groups, and zero to six fluorine atoms, and a 4- to 12-membered heterocyclyl group substituted with zero to two -OH groups, zero to two $-OR^{49}$ groups, and zero to six fluorine atoms;

R^{14} to R^{44} are optionally bonded in A^1 or A^3 or between A^1 and A^2, between A^1 and A^3, or between A^2 and A^3 via a single bond, -O-, $-NR^{50}-$, or $-S(=O)_p-$ to form a ring;

R^{11} or R^{13} is optionally bonded to A^1, A^2, or A^3 via a single bond, -O-, $-NR^{51}-$, or $-S(=O)_p-$ to form a ring;

R^{45}, R^{46}, R^{47}, R^{49}, R^{50}, and R^{51} each represent a hydrogen atom or a C_{1-4} alkyl group substituted with zero or one -OH group and zero to six fluorine atoms;

p represents an integer of 0 to 2; and

each of the heteroatom-containing groups represented by A^1, A^2, and A^3 contains one to four heteroatoms selected from oxygen, sulfur, and nitrogen atoms.

2. The compound or pharmaceutically acceptable salt thereof according to claim 1, wherein L represents -NH-.

3. The compound or pharmaceutically acceptable salt thereof according to claim 1 or 2, wherein R^1 represents a C_{1-8} alkyl, C_{3-12} cycloalkyl, (C_{3-12} cycloalkyl)-C_{1-6} alkyl, 4- to 12-membered heterocyclyl, or (4- to 12-membered heterocyclyl)-C_{1-6} alkyl group.

4. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein R^2 is a C_{1-8} alkyl group substituted with one to four fluorine atoms.

5. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein R^2 is a C_{1-8} alkyl group substituted with zero or one -OH group and zero to two C_{1-8} alkoxy groups substituted with zero or one -OH group, zero or one C_{1-4} alkoxy group, and zero to three fluorine atoms.

6. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein R^2 is a 4- to

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6-membered heterocyclyl group optionally substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and C_{1-4} alkyl and C_{1-4} alkoxy groups.

7. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein R^2 is $-COOR^8$, $-CONR^9R^{10}$, or a C_{1-8} acyl group, optionally each group being substituted with one to four substituents selected from the group consisting of a fluorine atom, -OH, and a C_{1-4} alkoxy group.

8. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X represents CR^{11}, Y represents CR^{12}, and Z represents CR^{13}.

9. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X represents a nitrogen atom, Y represents CR^{12}, and Z represents CR^{13}.

10. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X represents CR^{11}, Y represents a nitrogen atom, and Z represents CR^{13}.

11. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X represents CR^{11}, Y represents CR^{12}, and Z represents a nitrogen atom.

12. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, wherein A^1 is a single bond.

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13. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, wherein A^1 represents a C_{1-8} alkylene group, and no sp^3 carbon atom in A^1 is replaced with another structure.

14. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, wherein A^1 represents a C_{1-8} alkylene group, and one sp^3 carbon atom at any position of A^1 is replaced with -O-.

15. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, wherein A^1 represents a C_{1-8} alkylene group, and one sp^3 carbon atom at any position of A^1 is replaced with $-NR^{14}-$.

16. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, wherein A^1 represents a C_{1-8} alkylene group, one sp^3 carbon atom at any position of A^1 is replaced with $-NR^{14}-$, and one sp^3 carbon atom at any other position of A^1 is optionally replaced with -O-.

17. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 16, wherein A^2 represents a 4- to 12-membered heterocyclylene group; and A^2 is optionally substituted with one to four substituents selected from the group consisting of -OH, -COOH, $-SO_3H$, $-PO_3H$, -CN, $-NO_2$, a halogen atom, a C_{1-8} alkyl group substituted with zero to two -OH groups, zero to two $-OR^{45}$ groups, and zero to six fluorine atoms, a C_{3-12} cycloalkyl group substituted with zero to two -OH groups, zero to two $-OR^{46}$ groups, and zero to six fluorine atoms, a C_{1-8} alkoxy group substituted with zero to two -OH groups, zero to two $-OR^{47}$ groups, and zero to six

fluorine atoms, and a 4- to 12-membered heterocyclyl group substituted with zero to two -OH groups, zero to two $-OR^{49}$ groups, and zero to six fluorine atoms.

18. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 16, wherein A^2 represents a 4- to 12-membered heterocyclylene group substituted with =O; and A^2 is optionally substituted with one to four substituents selected from the group consisting of -OH, =O, -COOH, $-SO_3H$, $-PO_3H$, -CN, $-NO_2$, a halogen atom, a C_{1-8} alkyl group substituted with zero to two -OH groups, zero to two $-OR^{45}$ groups, and zero to six fluorine atoms, a C_{3-12} cycloalkyl group substituted with zero to two -OH groups, zero to two $-OR^{46}$ groups, and zero to six fluorine atoms, a C_{1-8} alkoxy group substituted with zero to two -OH groups, zero to two $-OR^{47}$ groups, and zero to six fluorine atoms, and a 4- to 12-membered heterocyclyl group substituted with zero to two -OH groups, zero to two $-OR^{49}$ groups, and zero to six fluorine atoms.

19. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 18, wherein X represents CR^{11}, Y represents CR^{12}, Z represents CR^{13}, and R^{11} or R^{13} is bonded to A^1, A^2, or A^3 via a single bond, -O-, $-NR^{51}-$, or $-S(=O)_p-$ to form a ring.

20. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 19, wherein A^3 is a hydrogen atom.

21. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 19, wherein A^3 is a

halogen atom, -CN, -R^{25}, -OR^{26}, -$NR^{27}R^{28}$, -C(=O)R^{29}, or -C(=O)-OR^{30}, and R^{25} to R^{30} each independently represent a hydrogen atom, an optionally substituted C_{1-8} alkyl group, an optionally substituted 4- to 12-membered heterocyclyl group, an optionally substituted C_{3-12} cycloalkyl group, an optionally substituted (4- to 12-membered heterocyclyl)-C_{1-3} alkyl group, or an optionally substituted (C_{3-12} cycloalkyl)-C_{1-3} alkyl group.

22. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 21, wherein R^3 is a hydrogen atom.

23. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 21, wherein R^3 represents a C_{1-4} alkyl group, a fluorine atom, or a chlorine atom.

24. The compound, or pharmaceutically acceptable salt thereof, selected from;
6-(difluoromethyl)-N8-isopropyl-N2-(5-piperazin-1-yl-2-pyridyl)pyrido[3,4-d]pyrimidine-2,8-diamine;
(1R)-1-[8-(isopropylamino)-2-[(5-piperazin-1-yl-2-pyridyl)amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[2-[(5-piperazin-1-yl-2-pyridyl)amino]-8-(tetrahydrofuran-3-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[2-[(5-piperazin-1-yl-2-pyridyl)amino]-8-(tetrahydropyran-3-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-(6-piperazin-1-ylpyridazin-3-yl)pyrido[3,4-d]pyrimidine-2,8-diamine;
N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]pyrido[3,4-d]pyrimidine-2,8-diamine;

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1-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one;
1-[6-[[5-chloro-6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one;
(1R)-1-[2-[(6-piperazin-1-ylpyridazin-3-yl)amino]-8-(tetrahydropyran-4-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[(6-piperazin-1-ylpyridazin-3-yl)amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[(6-piperazin-1-ylpyridazin-3-yl)amino]-8-[[(3R)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[[5-(piperazin-1-ylmethyl)-2-pyridyl]amino]-8-(tetrahydropyran-4-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[[5-(piperazin-1-ylmethyl)-2-pyridyl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[[5-(piperazin-1-ylmethyl)-2-pyridyl]amino]-8-[[(3R)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]pyridazin-3-yl]piperidin-4-ol;
(1R)-1-[8-(isopropylamino)-2-[(6-piperazin-1-ylpyridazin-3-yl)amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-2-one;
6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;

6-[(1R)-1-methoxyethyl]-N2-(6-piperazin-1-ylpyridazin-3-yl)-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;

6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-(tetrahydropyran-4-ylmethyl)pyrido[3,4-d]pyrimidine-2,8-diamine;

N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-(5-piperazin-1-ylpyrazin-2-yl)pyrido[3,4-d]pyrimidine-2,8-diamine;

N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-[6-[(2S)-2-methylpiperazin-1-yl]pyridazin-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;

N8-isopropyl-6-[(1R)-1-methoxyethyl]-N2-[6-[(2R)-2-methylpiperazin-1-yl]pyridazin-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;

(1R)-1-[2-[[6-(4,7-diazaspiro[2.5]octan-7-yl)pyridazin-3-yl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;

(1R)-1-[2-[[5-(4,7-diazaspiro[2.5]octan-7-ylmethyl)-2-pyridyl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;

2-[1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]-4-piperidyl]propan-2-ol;

(1R)-1-[2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;

(1R)-1-[2-[[5-[2-(dimethylamino)ethoxy]-2-pyridyl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;

(1R)-1-[2-[[6-(4-methylpiperazin-1-yl)pyridazin-3-yl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;

2-hydroxy-1-[4-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]pyridazin-3-yl]piperazin-1-yl]ethanone;
1-[6-[[8-(isopropylamino)-6-[(2S)-tetrahydrofuran-2-yl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one;
(1R)-1-[8-(isopropylamino)-2-(5,6,7,8-tetrahydro-1,6-naphthyridin-2-ylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
2-[4-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]-2-methyl-propan-1-ol;
4-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]-1-[(2S)-2-hydroxypropyl]-1,4-diazepan-5-one;
4-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]-1-[(2R)-2-hydroxypropyl]-1,4-diazepan-5-one;
N8-isopropyl-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-6-[(2S)-tetrahydrofuran-2-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;
1-[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-2-methyl-3-pyridyl]piperazin-2-one;
1-[6-[[8-(isopropylamino)-6-[(3S)-tetrahydrofuran-3-yl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one;
(1R)-1-[2-(5,6,7,8-tetrahydro-1,6-naphthyridin-2-ylamino)-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[6-[[8-(isopropylamino)-6-(3-methyloxetan-3-yl)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one;
(1R)-1-[2-[[5-[4-(dimethylamino)cyclohexoxy]-2-pyridyl]amino]-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;

6-[(1R)-1-methoxyethyl]-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine;
6-[(1R)-1-methoxyethyl]-N2-(6-piperazin-1-ylpyridazin-3-yl)-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine;
1-[[6-[[6-(difluoromethyl)-8-[(4-methylcyclohexyl)amino]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidine-4-carboxylic acid;
(1R)-1-[8-(ethylamino)-2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]-8-(propylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
N8-isopropyl-6-(3-methyloxetan-3-yl)-N2-(6-piperazin-1-ylpyridazin-3-yl)pyrido[3,4-d]pyrimidine-2,8-diamine;
N8-isopropyl-6-(3-methyloxetan-3-yl)-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]pyrido[3,4-d]pyrimidine-2,8-diamine;
6-(3-methyloxetan-3-yl)-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;
4-[6-[[6-[(1R)-1-hydroxyethyl]-8-[isopropyl(methyl)amino]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]-1,4-diazepan-5-one;
(1R)-1-[8-(isopropylamino)-2-[(6-methyl-5-piperazin-1-yl-2-pyridyl)amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[2-[[6-(2-hydroxyethyl)-7,8-dihydro-5H-1,6-naphthyridin-2-yl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[8-(isopropylamino)-2-[[6-[2-(methylamino)ethyl]-7,8-dihydro-5H-1,6-naphthyridin-2-yl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;

N2-(6-piperazin-1-ylpyridazin-3-yl)-6-[(3S)-tetrahydrofuran-3-yl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;
N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-6-[(3R)-tetrahydrofuran-3-yl]-N8-[(3S)-tetrahydropyran-3-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;
(1R)-1-[2-[[6-[2-(dimethylamino)ethyl]-7,8-dihydro-5H-1,6-naphthyridin-2-yl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(2S)-1-[4-[[6-[[8-(ethylamino)-6-[(1R)-1-hydroxyethyl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]propan-2-ol;
(2R)-1-[4-[[6-[[8-(ethylamino)-6-[(1R)-1-hydroxyethyl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]propan-2-ol;
(1R)-1-[8-(isopropylamino)-2-[[5-[(2R)-2-methylpiperazin-1-yl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[8-(isopropylamino)-2-[[5-[(2S)-2-methylpiperazin-1-yl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
N8-isopropyl-N2-(5-piperazin-1-yl-2-pyridyl)-6-[(2S)-tetrahydrofuran-2-yl]pyrido[3,4-d]pyrimidine-2,8-diamine;
(1R)-1-[8-(cyclobutylamino)-2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
(1R)-1-[8-(cyclopropylmethylamino)-2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
6-(3-methyloxetan-3-yl)-N2-(5-piperazin-1-yl-2-pyridyl)-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine;
6-(3-methyloxetan-3-yl)-N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-propyl-pyrido[3,4-d]pyrimidine-2,8-diamine;

N2-(5-piperazin-1-yl-2-pyridyl)-N8-propyl-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidine-2,8-diamine;
N2-[5-(piperazin-1-ylmethyl)-2-pyridyl]-N8-propyl-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidine-2,8-diamine;
N8-isopropyl-6-(3-methyloxetan-3-yl)-N2-(5-piperazin-1-yl-2-pyridyl)pyrido[3,4-d]pyrimidine-2,8-diamine;
N8-isopropyl-N2-(5-piperazin-1-yl-2-pyridyl)-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidine-2,8-diamine;
2-[4-[[6-[[8-(isopropylamino)-6-tetrahydrofuran-3-yl-pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]ethanol;
2-[4-[[6-[[6-tetrahydrofuran-3-yl-8-[[(3S)-tetrahydropyran-3-yl]amino]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperazin-1-yl]ethanol;
(1R)-1-[2-[[5-[[4-(hydroxymethyl)-1-piperidyl]methyl]-2-pyridyl]amino]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidin-4-ol;
1-[[6-[[8-(tert-butylamino)-6-[(1R)-1-hydroxyethyl]pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidin-4-ol;
(1R)-1-[8-(tert-butylamino)-2-[[5-[[4-(hydroxymethyl)-1-piperidyl]methyl]-2-pyridyl]amino]pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[[6-[[6-[(1R)-1-hydroxyethyl]-8-(isobutylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]methyl]piperidin-4-ol;
(1R)-1-[2-[[5-[[4-(hydroxymethyl)-1-piperidyl]methyl]-2-pyridyl]amino]-8-(isobutylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol;
1-[6-[[6-[(1R)-1-hydroxypropyl]-8-(isopropylamino)pyrido[3,4-d]pyrimidin-2-yl]amino]-3-pyridyl]piperazin-2-one; and

(1R)-1-[2-[[5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]-6-methyl-2-pyridyl]amino]-8-(propylamino)pyrido[3,4-d]pyrimidin-6-yl]ethanol.

25. A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 24 and a pharmaceutically acceptable carrier.

26. A pharmaceutical composition exhibiting a CDK4/6 inhibitory activity, comprising the compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 24 and an additive.

27. A drug for prevention or treatment of rheumatoid arthritis, arteriosclerosis, pulmonary fibrosis, cerebral infarction, or cancer, the drug comprising the compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 24 and an additive.

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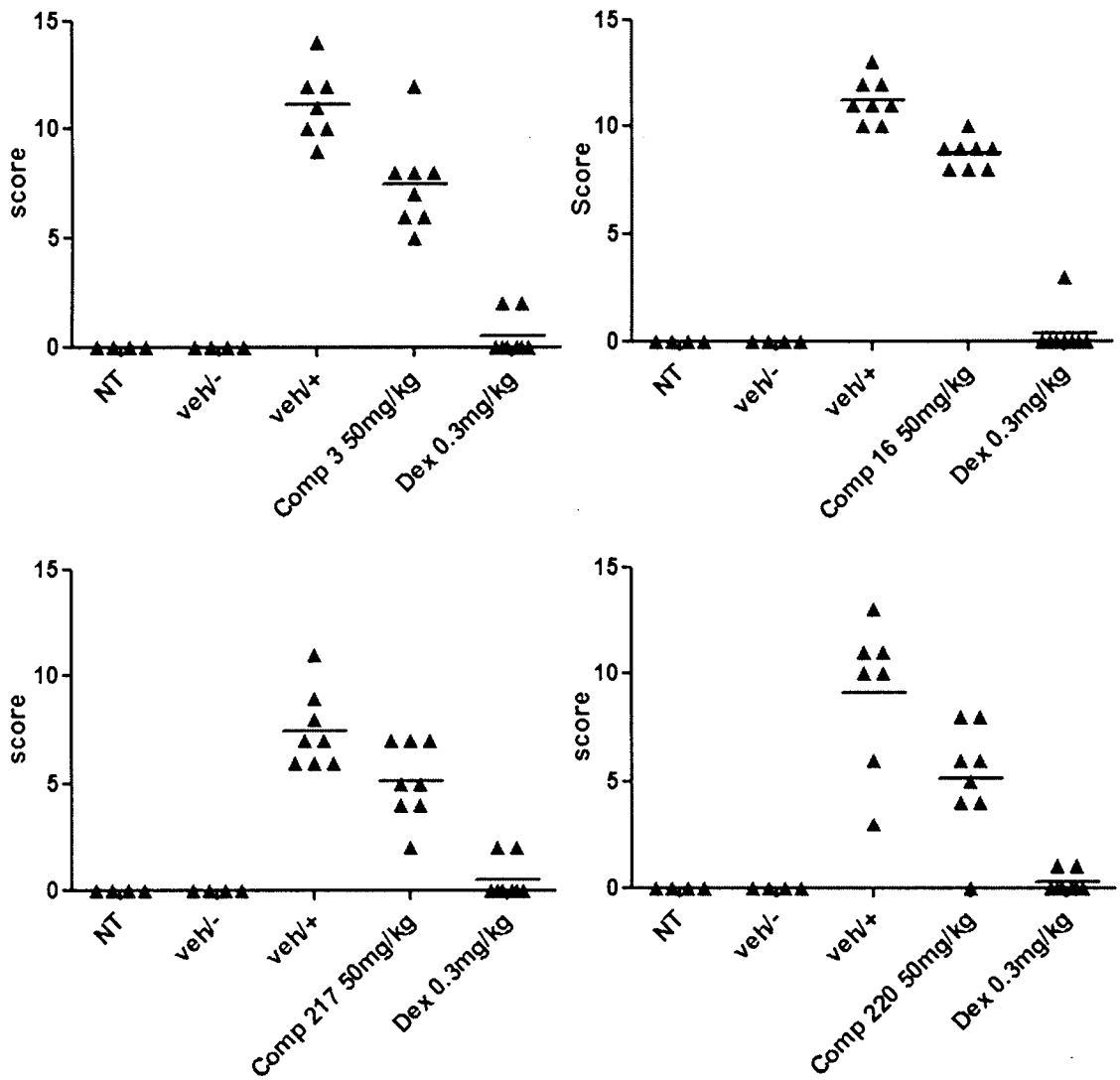
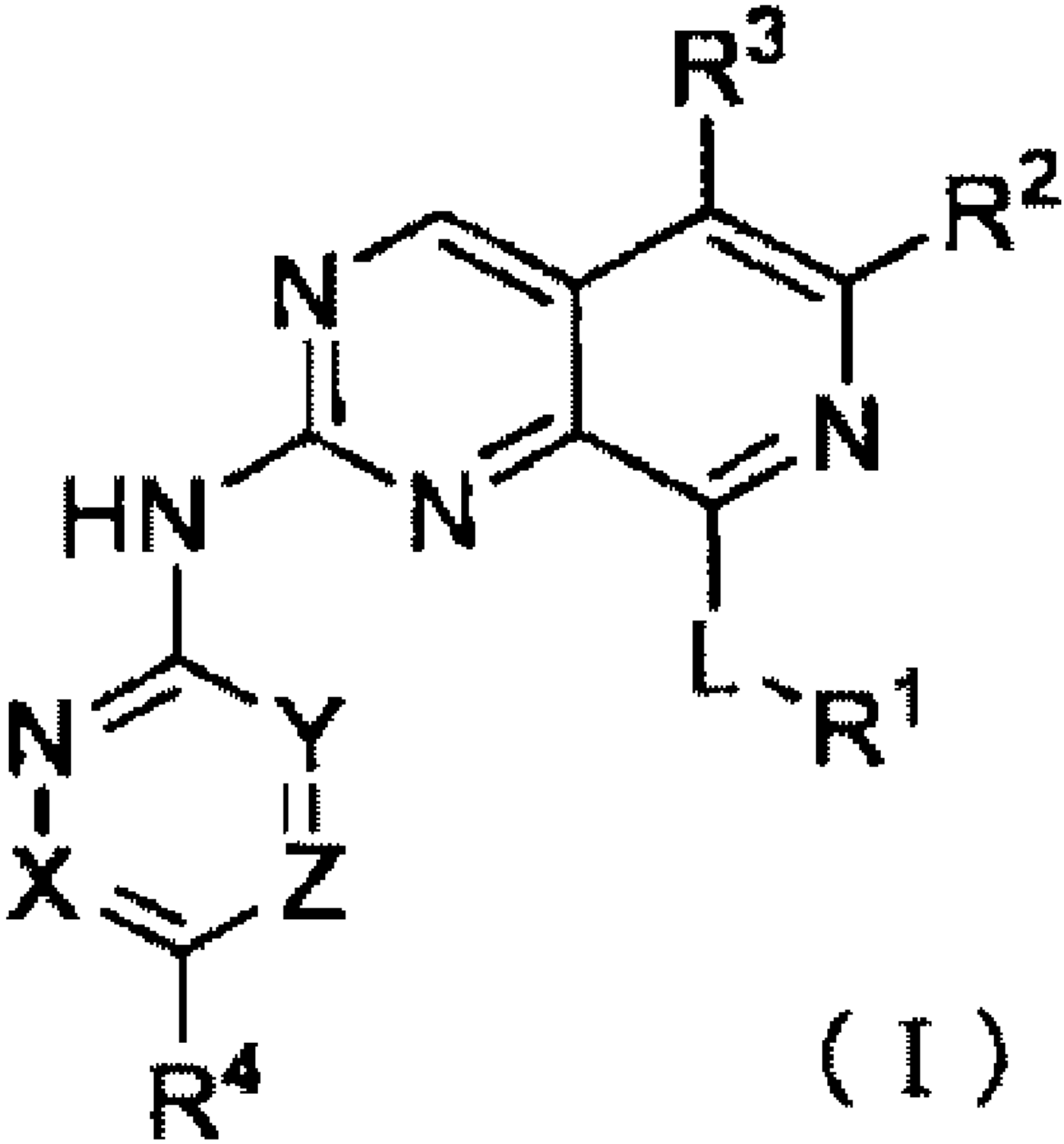
FIG. 1



*Abbreviations
NT: no treatment group, Veh/-: group of no disease induction/solvent administration,
Veh/+: group of disease induction/solvent administration,
Comp: group of disease induction/example compound administration,
Dex: group of disease induction/dexamethasone administration



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