DESCRIPTION

CARBOXAMIDE COMPOUND

Technical Field

[0001] The present invention relates to a carboxamide compound and a pharmaceutical composition containing the same, and in particular to a carboxamide compound for the prevention, amelioration, and/or treatment of diseases by which symptoms are ameliorated of antagonizing a lysophosphatidic acid (LPA) receptor and a pharmaceutical composition containing the same.

Background Art

[0002] Lysophosphatidic acid (LPA) is an endogenous bioactive phospholipid. As LPA receptors, six subtypes of LPA1 through LPA6 receptors, which are G protein-coupled receptors, are known. LPA binds to these receptors, transmits signals into cells, and regulates the proliferation, differentiation, survival, migration, adhesion, invasion, and morphogenesis of the cells. LPA is also known to be involved in fibrotic diseases in various organs.

As for lungs, there have been reports of elevated LPA levels in bronchoalveolar lavage fluids from patients with idiopathic pulmonary fibrosis (IPF). It has been also shown that in patient-derived fibroblasts, LPA1 receptors are highly expressed compared with other subtypes, and LPA induces fibroblast migration through the LPA1 receptors, and in bleomycin-induced pulmonary fibrosis mouse models as well, the LPA levels in bronchoalveolar lavage fluids are elevated, and fibrosis is inhibited by LPA1 receptor deficiency or the administration of LPA1 receptor antagonists (see NPL 1 and 2). In recent years, there has been a report that BMS-986020, which is an LPA1 receptor antagonist, significantly reduces the percentage of predicted forced vital capacity in 26-week clinical trials of IPF patients (see NPL 3).

As for skins, there have been reports that the LPA levels in serum are elevated in patients with systemic sclerosis, and in bleomycin-induced scleroderma mouse models, skin fibrosis is inhibited by LPA1 receptor deficiency or the administration of LPA1 receptor antagonists (see NPL 4 to 6).

As for livers, it is known that LPA promotes the proliferation of stellate cells playing an important role in the process of liver fibrosis and migration of myofibroblasts (see NPL 7 and 8). In addition, there has been a report that LPA levels are elevated in plasmas from patients with chronic hepatitis C and there is a correlation between LPA levels and the degree of liver fibrosis (see NPL 9).

As for kidneys, there have been reports that the production of LPA or the expression of LPA1 receptors is enhanced in unilateral ureteral obstruction model mice which are animal models of renal fibrosis and renal fibrosis is inhibited by LPA1 receptor deficiency or the administration of LPA1 receptor antagonists (see NPL 10 and 11).

[0003] In addition, LPA is known to be involved in acute and chronic pain. It has been reported that LPA1 receptors are expressed in the peripheral nervous system and the central nervous system, and frequently expressed particularly in Schwann cells and satellite glial cells in the peripheral nervous system (see NPL 12 and 13). It has been shown that in various pain model animals such as partial sciatic nerve injury models, LPA1 receptor deficiency and the administration of antisense oligonucleotides or LPA1 receptor antagonists inhibits allodynia and hyperalgesia, and LPA and LPA1 receptors are involved in acute and chronic pain (see NPL 13 to 17). In addition, there have been reports that the intrathecal administration of LPA in mice induces allodynia and demyelination of spinal nerves, and LPA1 receptor deficiency inhibits these effects (see NPL 14). In addition, it has been reported that the inhibition of LPA and the administration of LPA1 receptor antagonists in animal models of spinal cord injury and spinal canal stenosis ameliorate pain symptoms or demyelinating disease states (see NPL 18 to 21). Furthermore, LPA levels are elevated in the cerebrospinal fluids of patients suffering from pain associated with various diseases and correlate with pain severity (see NPL 22 and 23).

In addition, LPA is also known to be involved in immune and inflammatory diseases. It has been reported that LPA enhances the migration of human monocytic cells and is involved in the proliferation and infiltration of T cells. Synovial cells in rheumatoid arthritis patients express LPA receptors and are caused to migrate or produce IL-6 and IL-8 by LPA stimulation. In addition, macrophages in patients with multiple sclerosis increase the expression of LPA1 receptors and are

transformed into M1 macrophages that produce inflammatory cytokines by LPA stimulation. It has been reported that these effects are inhibited by LPA receptor antagonists (see NPL 24 to 27).

Additionally, there have been reports that LPA contracts excised urethral specimens and prostate specimens and increases urethral pressure, thereby being involved in urological diseases (see PTL 1), LPA promotes cancer cell invasion, promotes the proliferation of ovarian cancer cells, or promotes the proliferation of prostate cancer cells, thereby being involved in cancer-related diseases (see NPL 28 to 30).

[0004] Based on what has been described above, it is considered that LPA receptors, in particular, LPA1 receptor antagonists are useful for the prevention and/or treatment of fibrotic diseases, central and peripheral nervous system diseases, immune and inflammatory diseases, urological diseases, cancer-related diseases, and the like.

Carboxamide compounds have been thus far disclosed in PTL 2 to 5 and NPL 31 and 32 as compounds having LPA receptor antagonism but all have different structures from a compound of the present invention.

Citation List

Patent Literature

[0005]

PTL 1: WO 2002-062389

PTL 2: WO 2019-234115

PTL 3: WO 2020-254408

PTL 4: WO 2021-110805

PTL 5: WO 2023-014907

Non Patent Literature

[0006]

NPL 1: Nature Medicine, 14 (2008) 45 to 54.

NPL 2: British Journal of Pharmacology, 160 (2010) 1699 to 1713.

NPL 3: Chest, 154 (2018) 1061 to 1069.

NPL 4: International Journal of Medical Sciences, 6 (2009) 168 to 76.

NPL 5: Arthritis & Rheumatism, 63 (2011) 1405 to 1415.

NPL 6: Experimental Dermatology, 24 (2015) 698 to 702.

NPL 7: Biochemical and Biophysical Research Communications, 248 (1998) 436 to 440.

NPL 8: Journal of Biomedical Science, 10 (2003) 352 to 358.

NPL 9: Journal of Clinical Gastroenterology, 41 (2007) 616 to 623.

NPL 10: Journal of the American Society of Nephrology, 18 (2007) 3110 to 3118.

NPL 11: The Journal of Pharmacology and Experimental Therapeutics, 336 (2011) 693 to 700.

NPL 12: Glia, 61 (2013) 2009 to 2022.

NPL 13: FASEB Journal, 36 (2022) e22236.

NPL 14: Nature Medicine, 10 (2004) 712 to 718.

NPL 15: Molecular Pain, 10 (2014) 71.

NPL 16: Neurobiology of Pain, 1 (2017) 16 to 25.

NPL 17: Cells, 9 (2020) 1906.

NPL 18: The American Journal of Pathology, 181 (2012) 978 to 992.

NPL 19: The Journal of Neuroscience, 35 (2015) 10224 to 10235.

NPL 20: Scientific Reports, 9 (2019) 16578.

NPL 21: Scientific Reports, 11 (2021) 3984.

NPL 22: PLoS ONE, 13 (2018) e0207310.

NPL 23: Scientific Reports, 9 (2019) 9144.

NPL 24: Journal of Biological Chemistry, 270 (1995) 25549 to 25556.

NPL 25: Biochimica et Biophysica Acta, 1582 (2002) 168 to 174.

NPL 26: Molecular Pharmacology, 73 (2008) 587 to 600.

NPL 27: Molecular Neurobiology, 58 (2021) 470 to 482.

NPL 28: Biochemical and Biophysical Research Communications, 193 (1993) 497 to 503.

NPL 29: Biochemical Journal, 309 (1995) 933 to 940.

NPL 30: The Journal of Urology, 163 (2000) 1027.

NPL 31: Journal of Medicinal Chemistry, 67 (2024) 2379.

NPL 32: Journal of Medicinal Chemistry, 67 (2024) 2397.

Disclosure of Invention

Technical Problem

[0007] The present invention provides a novel compound useful for the prevention, amelioration, and/or treatment of diseases by which symptoms are ameliorated by antagonizing an LPA receptor and a pharmaceutical composition containing the same.

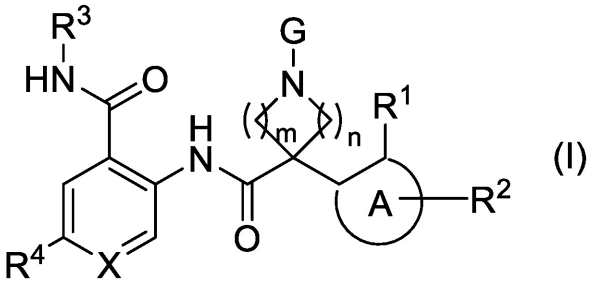
Solution to Problem

[0008] As a result of repeating intensive studies on compounds having LPA receptor antagonism, the present inventors found that the compound of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof has excellent LPA receptor antagonism and is useful for the prevention, amelioration, and/or treatment of diseases of which symptoms are ameliorated by antagonizing an LPA receptor and completed the present invention.

[0009] The present invention provides the following [1] to [13].

[1] A compound represented by the following general formula (I):

[C1]



(I)

[wherein

a ring A is a benzene ring or a 5- or 6-membered aromatic heterocycle,

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

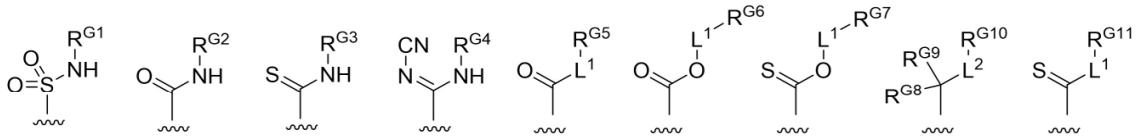
R^4 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, or a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from a group Q1, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from a group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C2]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group

optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with the carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of a halogen atom, a hydroxy group, an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group optionally substituted with one to five substituents independently selected from the group Q3, a cyano group, $NR^{N7}R^{N8}$, and a 3- to 12-membered non-aromatic heterocyclyl group,

R^{N7} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, a $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q4, a C_2-C_{10} acyl group optionally substituted with one to five substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_1-C_6 alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5}, R^{G6}, R^{G7}, and R^{G11} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl

groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms, and a C_2-C_6 acyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group,

the C_1-C_6 alkyl group may be substituted with one to five substituents independently selected from a halogen atom, a hydroxy group, and a C_1-C_6 alkoxy group,

R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_2-C_6 alkenyl group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

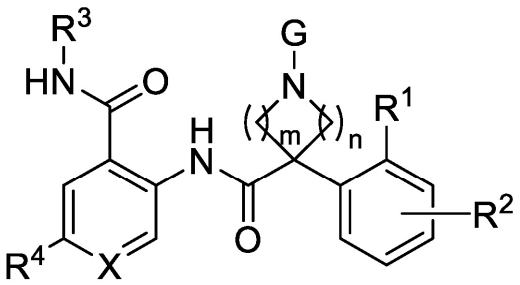
R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group,

m and n are each independently an integer of any of 1 or 2 (hereinafter also referred to as the compound of the present invention)],

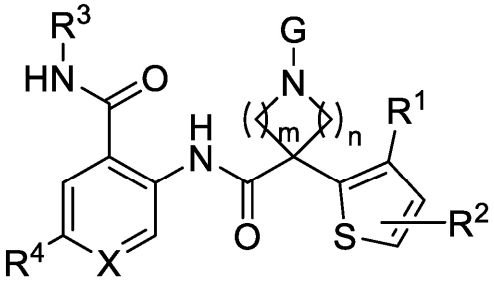
a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[2] The compound according to [1], which is represented by the following general formula (I-a) or (I-b):

[C3]



(I-a)



(I-b)

[wherein

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

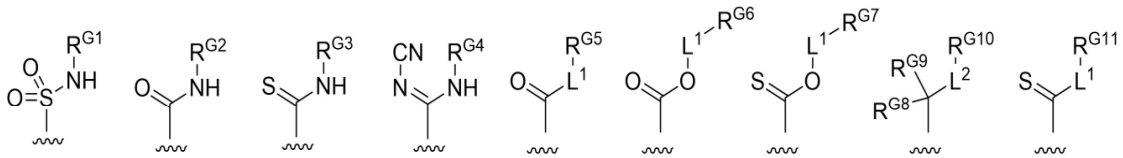
R^4 is a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 4- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C4]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, and a cyano group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, and a $NR^{N9}R^{N10}$,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl

group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_1-C_6 alkoxy-carbonyl group,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 akylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkyl group substituted with one hydroxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, a carboxy group, or a C_1-C_6 alkoxy-carbonyl group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered

non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group, and a C_2-C_6 acyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom, or a C_1-C_6 alkyl group,

the C_1-C_6 alkyl group may be substituted with one to five substituents independently selected from a hydroxy group, and a C_1-C_6 alkoxy group,

R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group,

m and n are each independently an integer of any of 1 or 2],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[3] The compound according to [2], wherein R^{N1} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N2} is a hydrogen atom,

R^{N5} and R^{N6} are hydrogen atoms,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, and a C_2-C_6 acyl group,

R^{N9} and R^{N10} are hydrogen atoms,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group, a C_1-C_6 alkoxy group, and an amino group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group may be substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_2-C_6 acyloxy group,

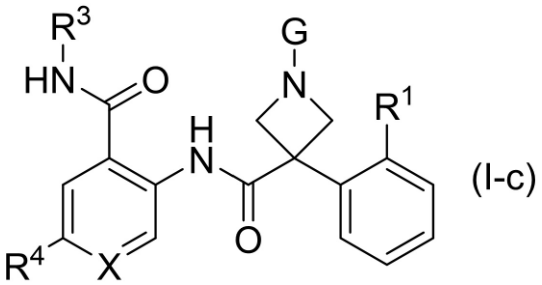
wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, and

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[4] The compound according to [1], which is represented by the following general formula (I-c):

[C5]



(I-c)

[wherein

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

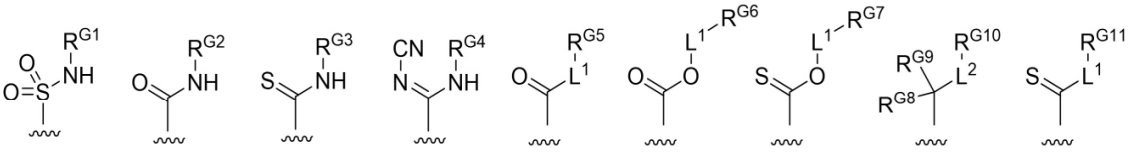
R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C6]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_4 alkoxy-carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-

membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, and a carboxy group,

R^{Q3} is a hydrogen atom, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_4 alkoxy-carbonyl group,

R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally

substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, or a C_1-C_4 alkyl-SO_2 group,

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_4 alkoxy-carbonyl group, or a C_1-C_4 alkyl-SO_2 group,

R^{N14} is a hydrogen atom or a C_1-C_4 alkyl group],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[5] The compound according to [4], wherein in the formula (I-c),

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

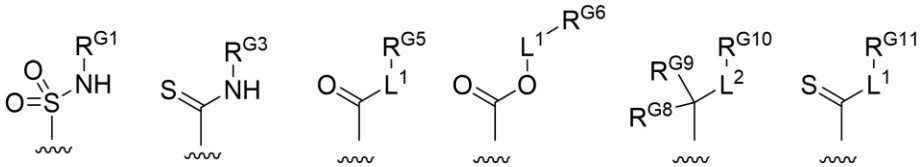
R^4 is a halogen atom or a methoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9);

[C7]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$;

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

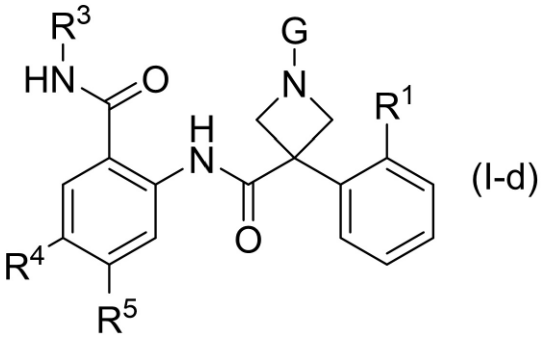
R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group, and

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group,

or a pharmaceutically acceptable salt thereof.

[6] The compound according to [5], which is represented by the following general formula (I-d):

[C8]



(I-d)

[wherein symbols are as defined in [5]] or

a pharmaceutically acceptable salt thereof.

[7] The compound according to [6], wherein in the formula (I-d),

R^1 is a C_1-C_4 alkyl group,

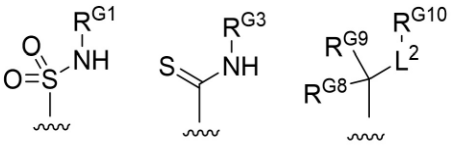
R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), or (II-8),

[C9]



(II-1) (II-3) (II-8)

the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group and a carboxy group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one substituent independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

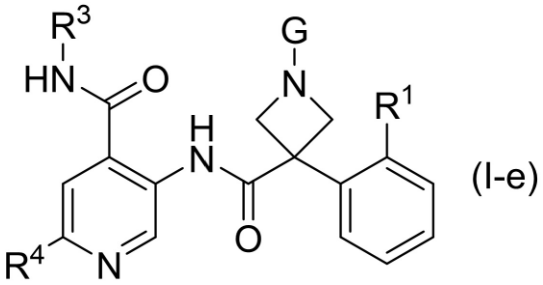
R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group, and

R^{G10} is a hydroxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group, or

a pharmaceutically acceptable salt thereof.

[8] The compound according to [5], which is represented by the following general formula (I-e):

[C10]



(I-e)

[wherein symbols are as defined in [5]] or

a pharmaceutically acceptable salt thereof.

[9] The compound according to [8], wherein in the formula (I-e),

R^1 is a C_1-C_4 alkyl group,

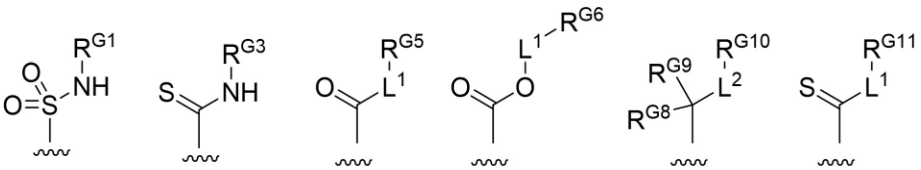
R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom or a methoxy group,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the

following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9);

[C11]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$;

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are hydrogen atoms, and

R^{G10} is a hydroxy group or a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, or

a pharmaceutically acceptable salt thereof.

[10] The compound according to [1], which is selected from the group consisting of N-(2-carbamoyl-4-chlorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-carbamoyl-4-chloro-5-fluorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-chloro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-bromo-2-carbamoylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-bromo-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-carbamoyl-5-fluoro-4-methylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(5-fluoro-4-methyl-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N^3-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide;

1-carbamothioyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

N-(4-chloro-5-fluoro-2-((methyl-d3)carbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4,5-difluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4,5-difluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4,5-difluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-bromo-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-bromo-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-fluoro-6-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-fluoro-6-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-fluoro-6-isopropylphenyl)-1-

sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-ethylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-ethylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-ethylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-propylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-propylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-propylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isobutylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isobutylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isobutylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-cyclopentylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-cyclopentylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-cyclopentylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(3-isopropylthiophen-2-yl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)-1-sulfamoylazetidine-3-carboxamide;

3-(5-chloro-3-isopropylthiophen-2-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-hydroxypropanoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N^3-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide;

2-chloro-5-(1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

2-chloro-5-(1-(3-hydroxy-3-methylbutanoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-carbamothioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-2-chloro-N-methylisonicotinamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)acetate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)acetic acid;

ethyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)butanoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)butanoic acid;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoate

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pentanoate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pentanoic acid;

methyl 1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclobutane-1-carboxylate;

1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclobutane-1-carboxylic acid;

methyl 2-(1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclopropyl)acetate;

2-(1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclopropyl)acetic acid;

methyl 4-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

4-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)nicotinate;

6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)nicotinic acid;

methyl 5-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)picolinate;

5-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)picolinic acid;

methyl 6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)pyridazine-3-carboxylate;

6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)pyridazine-3-carboxylic acid;

tert-butyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-methylazetidine-

3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydropyran-4-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-fluoro-3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoro-3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

3-hydroxypropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxypropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxyethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,4-dihydroxybutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

ethyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-5-carboxylic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-5-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)isonicotinate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)isonicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylnicotinic acid;

methyl 2-amino-6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

2-amino-6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-methylnicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methoxynicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-2-methoxynicotinic acid;

methyl 2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(thiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylic acid;

ethyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylic acid;

ethyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylic acid;

ethyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid;

ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylic acid;

ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-cyanopyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(6-acetylpyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-(methylsulfonyl)pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-sulfamoylpyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-chloro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methyl-1,2,4-thiadiazol-5-yl)azetidine-3-

carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(5-amino-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-methyl-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluoropicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluoropicolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylpicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylpicolinic acid;

methyl 6-chloro-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

6-chloro-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-6-methylpicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-methylpicolinic acid;

methyl 3-amino-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

3-amino-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-2-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-2-carboxylic acid;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

tert-butyl (6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazin-3-yl)carbamate;

1-(6-aminopyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-N-methylpyridazine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N,N-dimethylpyridazine-3-carboxamide;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxamide;

2-chloro-5-(1-(5-cyano-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(1-hydroxyethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(4-(hydroxymethyl)oxazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(hydroxymethyl)-1,2,4-thiadiazol-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

ethyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylate;

2-chloro-5-(1-(4-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-

carboxamido)-N-methylisonicotinamide;

methyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate;

2-chloro-5-(1-(5-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

1-(6-(aminomethyl)pyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-(2-hydroxypropan-2-yl)-1,2,4-thiadiazol-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(2-hydroxypropan-2-yl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cyanomethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyanoethyl)-3-(2-

isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((1-cyanocyclopropyl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-methoxyethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-methoxypropyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(prop-2-yn-1-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-2-ylmethyl)azetidine-3-carboxamide;

1-((1,3-dioxolan-2-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyano-2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(2-(1H-tetrazol-5-yl)ethyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-((1H-tetrazol-5-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methoxypropyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(1-(2-cyanoethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate;

3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid;

2-chloro-5-(1-(2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-benzyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(pyridin-4-ylmethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(pyridin-3-ylmethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyano-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxirane-2-ylmethyl)azetidine-3-carboxamide;

1-(3-amino-2-hydroxypropyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-

isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2,2,2-trifluoroethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoroethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3,3-difluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,1-dioxidothietan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-dioxido-2-thiaspiro[3.3]heptan-6-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(trans-3-(methylsulfonyl)cyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(cis-3-

(methylsulfonyl)cyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-(methylsulfonyl)butyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-(methylsulfonyl)propyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-fluoroethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(cyanomethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxan-5-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-hydroxy-2-(hydroxymethyl)propyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

3-fluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-ylmethyl)azetidine-3-carboxamide;

oxetan-3-ylmethyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2,2-difluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-chloro-5-(1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

3-cyanopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3,3-difluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-2-methylpropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-

N-methylisonicotinamide;

methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoic acid;

ethyl 2-(1-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutyl)acetate;

2-(1-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutyl)acetic acid;

ethyl 2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxetan-3-yl)acetate;

2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxetan-3-yl)acetic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-(cyanomethyl)oxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)-3,3,3-trifluoropropanoic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-(methylsulfonyl)ethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-(2-hydroxyethyl)oxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methoxypropan-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-cyclobutyl-3-(2-

isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(trans-3-methoxycyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(cis-3-methoxycyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydrofuran-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydropyran-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,1-dioxidotetrahydrothiopyran-4-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-oxaspiro[3.3]heptan-6-yl)azetidine-3-carboxamide;

1'-acetyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-[1,3'-biazetidine]-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,3-dihydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanooxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-cyclobutyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(1-(trans-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-oxaspiro[3.3]heptan-6-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl ((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2-hydroxyethyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2,3-dihydroxypropyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

tert-butyl ((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-methylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamide;

1-(N-acetylsulfamoyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(N-butyrylsulfamoyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-isobutyrylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-

pentanoylsulfamoyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-hexanoylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-octanoylsulfamoyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-(2-methoxyacetyl)sulfamoyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-pentanoylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(N-heptanoylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl (2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine)-1-sulfonamido)-2-oxoethyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-glycylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,3-

dihydroxypropyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-propionylazetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-acetyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

5-(1-butyryl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-formyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-ethanethioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(methylsulfonyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

ethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

propyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxy-2,2-dimethyl-3-oxopropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid;

(2,2-dimethyl-1,3-dioxan-5-yl)methyl 3-((4-chloro-5-fluoro-2-

(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxy-2-(hydroxymethyl)propyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-cyanoethyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxy-2,2-dimethyl-3-oxopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid;

3-hydroxy-3-methylbutyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-methoxyethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxypropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-hydroxy-2-methylpropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

O-methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbothioate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,4,5,6-

tetrahydropyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(3-hydroxypropyl)-6-oxo-1,6-dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(1-(2-aminoethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-(2-methoxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-oxopyridazin-1(6H)-yl)acetate;

2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-oxopyridazin-1(6H)-yl)acetic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrothiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-

dihydrothiazol-2-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-methyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(2-hydroxyethyl)-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(1-(4-ethyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-oxo-4-(2-oxopropyl)-4,5-dihydro-1,3,4-thiadiazol-2-

yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

ethyl (3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonothioyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-2,5-dihydro-1,2,4-oxadiazol-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)pyrrolidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)pyrrolidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylpyrrolidine-3-carboxamide;

tert-butyl 4-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-4-(2-isopropylphenyl)piperidine-4-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-4-(2-isopropylphenyl)-1-sulfamoylpiperidine-4-carboxamide;

tert-butyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-

isopropylphenyl)piperidine-1-carboxylate;

2-chloro-5-(4-(2-isopropylphenyl)piperidine-4-carboxamido)-N-methylisonicotinamide;

methyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

methyl 4-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

4-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylamino)nicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylamino)nicotinic acid;

methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(6-(methylsulfonyl)pyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-(methylsulfonyl)pyridin-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-sulfamoylpyridin-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylbenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylbenzoic acid;

methyl 3-chloro-4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

3-chloro-4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluorobenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluorobenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methoxybenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methoxybenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(trifluoromethyl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(trifluoromethyl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylsulfonyl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylsulfonyl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(difluoromethoxy)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(difluoromethoxy)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3,5-difluorobenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3,5-difluorobenzoic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-oxo-1,3-dihydroisobenzofuran-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(hydroxymethyl)benzoic acid;

ethyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

5-(1-(4-carbamoyl-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-cyanophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide;

5-(1-(4-carbamoylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinic acid;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(4-(1H-tetrazol-5-yl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

2-chloro-5-(1-(6-(hydroxymethyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylic acid;

methyl 4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-(2-isopropylphenyl)-3-((6-methoxy-2-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoate;

4-(3-(2-isopropylphenyl)-3-((6-methoxy-2-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoic acid;

methyl 6-(4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidin-1-yl)nicotinate;

6-(4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidin-1-yl)nicotinic acid;

2-chloro-5-(1-(3-ethoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-(trifluoromethoxy)propyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(difluoromethoxy)propyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3,3-difluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(trans-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-((3-(methoxymethyl)oxetan-3-yl)methyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(S)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-2-(1-hydroxycyclobutyl)ethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(2,5-dioxopyrrolidin-1-yl)-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-ethoxy-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-((3-hydroxytetrahydrofuran-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-4-methoxybutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(1,3-dimethoxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methoxybutan-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(methylamino)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylacetamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylmethylsulfonamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)ethyl)(methyl)carbamate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-((methylsulfonyl)carbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-((ethylsulfonyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(sulfamoylcarbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-((N,N-dimethylsulfamoyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl acetate;

(5-(3-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl propionate;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl methyl carbonate;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl L-valinate;

2-chloro-5-(1-(2-(hydroxymethyl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyrimidin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-methyl-1,1-dioxido-1,2,5-thiadiazolidine-2-carbonyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(6-methyl-1,1-dioxido-1,2,6-thiadiazinane-2-carbonyl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(N-methylsulfamoylcarbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(N,N-dimethylsulfamoyl)(methyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

6-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)nicotinamide;

5-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)picolinamide;

6-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)pyridazine-3-carboxamide;

2-chloro-5-(1-(3-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(diethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(dimethylphosphoryl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-hydroxypropylacetate;

(R)-1-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-hydroxypropan-2-yl acetate;

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propane-1,2-diyl diacetate;

2-chloro-5-(1-(5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-2-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-chloro-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-2-methylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-methylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-(dimethylphosphoryl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-(dimethylphosphoryl)pyridin-4-yl)carbamate;

5-(1-(4-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-(5-(dimethylphosphoryl)-4-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(3-amino-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

5-(1-(6-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoronicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxylate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxylic acid;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-(methylamino)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide; and

2-chloro-5-(1-(5-(dimethylphosphoryl)-6-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[11] A pharmaceutical composition comprising the compound according to any one of [1] to [10], a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[12] The pharmaceutical composition according to [11] for preventing, ameliorating, and/or treating a disease, the symptom of which is ameliorated by antagonizing a lysophosphatidic acid receptor.

[13] The pharmaceutical composition according to [12], wherein the disease in which symptoms are ameliorated by antagonizing a lysophosphatidic acid receptor is pain or fibrosis.

Advantageous Effects of Invention

[0010] The compound represented by the general formula (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof has LPA receptor antagonism. Therefore, the compound represented by the general formula (I) of the present invention, the deuterated compound thereof, or the pharmaceutically acceptable salt thereof are useful as preventive agents, palliative agents, and/or therapeutic agents of diseases of which symptoms are ameliorated by antagonizing LPA receptors, for example, pain or fibrosis.

Best Mode for Carrying Out the Invention

[0011] Embodiments of the present invention will be described below. In the present specification, “a

compound represented by the general formula (I)" or the like will be also referred to as "compound (I)" or the like for convenience. Various substituents defined or exemplified below can be optionally selected and combined. In addition, embodiments obtained by optionally selecting and combining individual embodiments to be defined below will be also included in the present invention.

[0012] Each term to be used in the present specification is defined as follows.

[0013] "Halogen atom" as described in the present specification means a fluorine atom, a chlorine atom, a bromine atom, or an iodine atom.

[0014] In a case where a substituent has been substituted with two or more halogen atoms or substituents, those halogen atoms or substituents may be the same as or different from each other.

[0015] "C_X-C_Y" as described in the present specification means that the number of carbon atoms is X to Y. For example, "C_1-C_6" means that the number of carbon atoms is one to six

[0016] "Alkyl group" as described in the present specification means a linear or branched saturated hydrocarbon group having one to six carbon atoms (C_1-C_6), for example, one to four carbon atoms (C_1-C_4), and examples thereof include a methyl group, an ethyl group, a propyl group, an isopropyl group, a n-butyl group, a tert-butyl group, an isobutyl group, a n-pentyl group, a n-hexyl group, and various branched-chain isomers thereof.

[0017] "Alkenyl group" as described in the present specification means a linear or branched unsaturated hydrocarbon group having two to six carbon atoms having one carbon-carbon double bond (C_2-C_6), for example, two to four carbon atoms (C_2-C_4), and examples thereof include a vinyl group, a propenyl group, an isopropenyl group, a butenyl group, and various branched-chain isomers thereof.

[0018] "Alkynyl group" as described in the present specification means a linear or branched unsaturated hydrocarbon group having two to six carbon atoms having one carbon-carbon triple bond (C_2-C_6), for example, two to four carbon atoms (C_2-C_4), and examples thereof include an ethynyl group, a 1-propynyl group, a 2-butynyl group, a 4-pentynyl group, a 5-hexynyl group, and various branched-chain isomers thereof.

[0019] "Acyl group" (which may also be referred to as "alkanoyl group") as described in the present

specification means a group having a carbonyl group binding to the linear or branched alkyl group, and examples thereof include an ethanoyl group (acetyl group), a propanoyl group, an isopropanoyl group, a n-butanoyl group, a tert-butanoyl group, an isobutanoyl group, a n-pentanoyl group, and various branched-chain isomers thereof.

[0020] "Alkyl-SO_2 group" as described in the present specification means a group having a sulfonyl group binding to the linear or branched alkyl group, and examples thereof include a methyl-SO_2 group, an ethyl-SO_2 group, a propyl-SO_2 group, an isopropyl-SO_2 group, a n-butyl-SO_2 group, a tert-butyl-SO_2 group, an isobutyl-SO_2 group, a n-pentyl-SO_2 group, a n-hexyl-SO_2 group, and various branched-chain isomers thereof.

[0021] "Alkoxy group" as described in the present specification means a group having an oxygen atom binding to the linear or branched alkyl group, and examples thereof include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, a tert-butoxy group, an isobutoxy group, a n-pentoxy group, a n-hexoxy group, and various branched-chain isomers thereof.

[0022] "Alkoxy-carbonyl group" as described in the present specification means a group having a carbonyl group binding to the linear or branched alkoxy group, and examples thereof include a methoxycarbonyl group, an ethoxycarbonyl group, a propoxycarbonyl group, an isopropoxycarbonyl group, a butoxycarbonyl group, a tert-butoxycarbonyl group, an isobutoxycarbonyl group, a n-pentoxycarbonyl group, a n-hexoxycarbonyl group, and various branched-chain isomers thereof.

[0023] "Alkylamino-carbonyl group" as described in the present specification means a group having an amino group and a carbonyl group binding to the linear or branched alkyl group, and examples thereof include a methylamino-carbonyl group, an ethylamino-carbonyl group, a propylamino-carbonyl group, an isopropylamino-carbonyl group, a n-butylamino-carbonyl group, a tert-butylamino-carbonyl group, an isobutylamino-carbonyl group, a n-pentylamino-carbonyl group, a n-hexylamino-carbonyl group, and various branched-chain isomers thereof.

[0024] "Acyloxy group" as described in the present specification means a group having an oxygen atom binding to the linear or branched acyl group, and examples thereof include an ethanoyloxy group

(acetyloxy group), a propanoyloxy group, an isopropanoyloxy group, a n-butanoyloxy group, a tert-butanoyloxy group, an isobutanoyloxy group, a n-pentanoyloxy group, and various branched-chain isomers thereof.

[0025] "Alkylene group" as described in the present specification means a divalent group obtained by removing one of the optional hydrogen atoms of the "alkyl group." Examples of the alkylene group include a C_1-C_6 alkylene group, a C_2-C_4 alkylene group, a C_2-C_3 alkylene group, and a C_1-C_2 alkylene group, and the like, and specific examples thereof include a methylene group, an ethylene group, a methylmethylene group, a trimethylene group, an ethylmethylene group, a dimethylmethylene group, a tetramethylene group, a pentamethylene group, a hexamethylene group, and the like.

[0026] "Cycloalkyl group" as described in the present specification means a monocyclic alicyclic saturated hydrocarbon group having three to six ring-forming carbon atoms (C_3-C_6), and examples thereof include a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, and a cyclohexyl group.

[0027] "Cycloalkane ring" as described in the present specification means a saturated hydrocarbon ring having three to six carbon atoms (C_3-C_6), and examples thereof include cyclopropane, cyclobutane, cyclopentane, and cyclohexane.

[0028] "Non-aromatic heterocyclyl group" as described in the present specification means a 3- to 8-membered monocyclic non-aromatic heterocyclic group or 6- to 12-membered bicyclic non-aromatic heterocyclic group having one to four heteroatoms selected from an oxygen atom, a sulfur atom, and a nitrogen atom other than a carbon atom, and examples thereof include an oxiranyl group, an azetidinyl group, an oxetanyl group, a thietanyl group, a pyrrolidinyl group, a piperidinyl group, a piperidino group, a tetrahydrofuryl group, a dioxolanyl group, a tetrahydropyranyl group, a dioxanyl group, a tetrahydrothienyl group (that is, a thiolanyl group), a tetrahydrothiopyranyl group, a piperazinyl group, a morpholinyl group, a morpholino group, a perhydroazepinyl group, a perhydroazocinyl group, a 6- to 12-membered azabicycloalkyl group (for example, an azabicyclohexyl group, an azabicycloheptyl group, an azabicyclooctyl group, an azabicyclononyl group, an azabicyclodecyl group, an azabicycloundecyl group, or an azabicyclododecyl group), a 6- to 12-membered azabicycloalkenyl

group (for example, an azabicyclohexenyl group, an azabicycloheptenyl group, an azabicyclooctenyl group, an azabicyclononenyl group, an azabicyclodecenyl group, an azabicycloundecenyl group, or an azabicyclododecenyl group), a 6- to 12-membered azaspiroalkyl group (for example, an azaspirohexyl group, an azaspiroheptyl group, an azaspirooctyl group, an azaspirononyl group, an azaspirodecyl group, an azaspiroundecyl group, or an azaspirododecyl group), a 6- to 12-membered oxaspiro-alkyl group (for example, an oxaspiroheptyl group, an oxaspirooctyl group, an oxaspirononyl group, or an oxaspirodecyl group), a 6- to 12-membered thiaspiroalkyl group (for example, a thiaspiroheptyl group, a thiaspirooctyl group, a thiaspirononyl group, or a thiaspirodecyl group), a dihydrooxazolyl group, a dihydrothiazolyl group, a dihydroimidazolyl group, a dihydropyridazinyl group, a tetrahydropyridazinyl group, and a dihydrothiadiazolyl group.

[0029] "Aryl group" as described in the present specification means a monocyclic or bicyclic aromatic hydrocarbon group having six to 10 (C_6-C_{10}) ring-forming carbon atoms, and examples thereof include a monocyclic aryl group such as a phenyl group; bicyclic aryl groups having nine to 10 ring-forming carbon atoms (C_9-C_{10}, that is, 9- or 10-membered) that may be partially saturated such as a naphthyl group, a tetrahydronaphthyl group, an indenyl group, and an indanyl group.

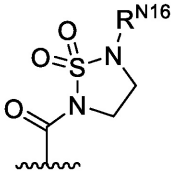
[0030] "Heteroaryl group" as described in the present specification means a 5- to 10-membered monocyclic or bicyclic aromatic heterocyclic group having one to four heteroatoms selected from an oxygen atom, a sulfur atom, and a nitrogen atom other than a carbon atom, and examples thereof include 5- or 6-membered monocyclic heteroaryl groups having one to four heteroatoms selected from an oxygen atom, a sulfur atom, and a nitrogen atom other than a carbon atom such as a pyrrolyl group, a furyl group, a thienyl group, a pyrazolyl group, an imidazolyl group, a tetrazolyl group, an oxazolyl group, an isoxazolyl group, an oxadiazolyl group, a thiazolyl group, an isothiazolyl group, a thiadiazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, and a triazinyl group; 8- to 10-membered bicyclic heteroaryl groups having one to four heteroatoms selected from an oxygen atom, a sulfur atom, and a nitrogen atom other than a carbon atom such as an indolyl group, an indolinyl group, an isoindolinyl group, an indazolyl group, a tetrahydroindazolyl group, a benzofuranyl

group, a dihydrobenzofuranyl group, a dihydroisobenzofuranyl group, a benzothiophenyl group, a dihydrobenzothiophenyl group, a dihydroisobenzothiophenyl group, a benzoxazolyl group, a dihydrobenzoxazolyl group, a benzothiazolyl group, a dihydrobenzothiazolyl group, a quinolyl group, a tetrahydroquinolyl group, an isoquinolyl group, a tetrahydroisoquinolyl group, a naphthyridinyl group, a tetrahydronaphthyridinyl group, a quinoxalinyl group, a tetrahydroquinoxalinyl group, a quinazolinyl group, and a benzotriazinyl group.

[0031] "5- or 6-membered aromatic heterocyclic ring" as described in the present specification means a 5- or 6-membered monocyclic aromatic heterocyclic ring having one to four heteroatoms selected from an oxygen atom, a sulfur atom, and a nitrogen atom other than a carbon atom, and examples thereof include aromatic heterocycles such as pyrrole, furan, thiophene, pyrazole, imidazole, tetrazole, oxazole, isoxazole, thiazole, isothiazole, oxadiazole, thiadiazole, pyridine, pyrazine, pyrimidine, pyridazine, and triazine.

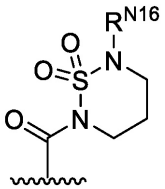
[0032] "When R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together" as described in the present specification means that $CONR^{N3}R^{N4}$ may form a structure represented by

[C12]



(a case where R^{N4} and R^{N15} form a C_2 alkylene group together) or

[C13]

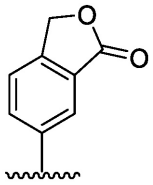


(a case where R^{N4} and R^{N15} form a C_3 alkylene group together).

[0033] "G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five

substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind" as described in the present specification means that, for example, in a case where G is a phenyl group in which adjacent two carbon atoms have been substituted with a carboxy group and a hydroxymethyl group, G may form a structure represented below.

[C14]



[0034] Hereinafter, embodiments of the compound (I) will be described. Embodiments obtained by optionally selecting and combining individual embodiments below will be also included in the present invention.

[0035] (Embodiment 1)

A compound of the present invention wherein a ring A is a benzene ring or a 5- or 6-membered aromatic heterocycle, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 2)

The compound of the present invention wherein the ring A is a benzene ring, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 3)

The compound of the present invention wherein the ring A is a 5- or 6-membered aromatic heterocycle, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 4)

The compound of the present invention wherein the ring A is a benzene ring or thiophene, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 5)

The compound of the present invention wherein the ring A is thiophene, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0036] (Embodiment 6)

The compound of the present invention according to any one of Embodiments 1 to 5 wherein R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 7)

The compound of the present invention according to any one of Embodiments 1 to 5 wherein R^1 is a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 8)

The compound of the present invention according to any one of Embodiments 1 to 5 wherein R^1 is a C_3-C_6 cycloalkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 9)

The compound of the present invention according to any one of Embodiments 1 to 5 wherein R^1 is a C_1-C_4 alkyl group or a C_3-C_4 cycloalkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 10)

The compound of the present invention according to any one of Embodiments 1 to 5 wherein R^1 is a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 11)

The compound of the present invention according to any one of Embodiments 1 to 5, wherein R^1 is a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 12)

The compound of the present invention according to any one of Embodiments 1 to 5, wherein R^1 is an isopropyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0037] (Embodiment 13)

The compound of the present invention according to any one of Embodiments 1 to 12, wherein R^2 is a hydrogen atom or a halogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 14)

The compound of the present invention according to any one of Embodiments 1 to 12, wherein R^2 is a hydrogen atom, a fluorine atom, or a chlorine atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 15)

The compound of the present invention according to any one of Embodiments 1 to 12, wherein R^2 is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0038] (Embodiment 16)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 17)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 18)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a hydrogen atom or a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 19)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 20)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a hydrogen atom, a methyl group, or a CD_3 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 21)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a hydrogen atom or a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 22)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 23)

The compound of the present invention according to any one of Embodiments 1 to 15, wherein R^3 is a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0039] (Embodiment 24)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, or a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 25)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 26)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 27)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 28)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 29)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 30)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 31)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom, a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 32)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein

R^4 is a halogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 33)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 34)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom or a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 35)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a chlorine atom, a bromine atom, or a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 36)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a chlorine atom or a bromine atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 37)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 38)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a halogen atom or a methoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 39)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a chlorine atom, a bromine atom, or a methoxy group, a deuterated compound thereof, or a

pharmaceutically acceptable salt thereof.

(Embodiment 40)

The compound of the present invention according to any one of Embodiments 1 to 23, wherein R^4 is a methoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0040] (Embodiment 41)

The compound of the present invention according to any one of Embodiments 1 to 40, wherein X is CR^5 or a nitrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 42)

The compound of the present invention according to any one of Embodiments 1 to 40, wherein X is CR^5, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 43)

The compound of the present invention according to any one of Embodiments 1 to 42, wherein R^5 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 44)

The compound of the present invention according to any one of Embodiments 1 to 42, wherein R^5 is a hydrogen atom, a halogen atom, a C_1-C_3 alkyl group, or a C_1-C_3 alkoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 45)

The compound of the present invention according to any one of Embodiments 1 to 42, wherein R^5 is a hydrogen atom or a halogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 46)

The compound of the present invention according to any one of Embodiments 1 to 42, wherein R^5 is a hydrogen atom or a fluorine atom, a deuterated compound thereof, or a pharmaceutically

acceptable salt thereof.

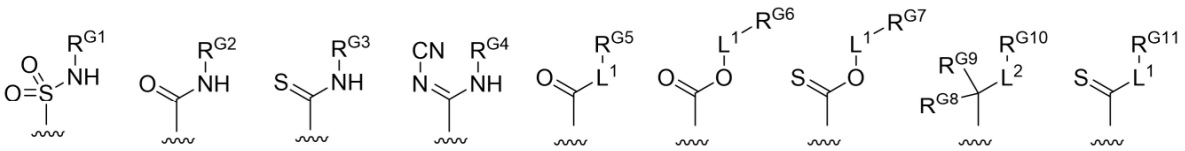
(Embodiment 47)

The compound of the present invention according to any one of Embodiments 1 to 40, wherein X is a nitrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0041] (Embodiment 48)

The compound of the present invention according to any one of Embodiments 1 to 47, wherein G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from a group Q1, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from a group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C15]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five

substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with the carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of a halogen atom, a hydroxy group, an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group optionally substituted with one to five substituents independently selected from the group Q3, a cyano group, $NR^{N7}R^{N8}$, and a 3- to 12-membered non-aromatic heterocyclyl group,

R^{N7} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a C_2-C_6 acyl group, a carboxy

group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, a $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 49)

The compound of the present invention according to Embodiment 48, wherein G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the formulae (II-1) to (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 50)

The compound of the present invention according to Embodiment 48, wherein G is a hydrogen atom, a formyl group, a C_1-C_3 alkyl-SO_2 group, a C_1-C_3 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_4 cycloalkyl group optionally substituted with one to three substituents independently selected from the group Q1, a phenyl optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one to three substituents independently selected from the group Q1, a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one to three substituents independently selected from the group Q2, or a group indicated by any of the formulae (II-1) to (II-9), a deuterated compound

thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 51)

The compound of the present invention according to any one of Embodiments 48 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 52)

The compound of the present invention according to any one of Embodiments 48 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, and $POR^{P1}R^{P2}$, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 53)

The compound of the present invention according to any one of Embodiments 48 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy group a carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 54)

The compound of the present invention according to any one of Embodiments 48 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_4 alkoxy-carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 55)

The compound of the present invention according to Embodiment 48, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, and $POR^{P1}R^{P2}$,

R^{N3}, R^{N4}, R^{N5}, and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

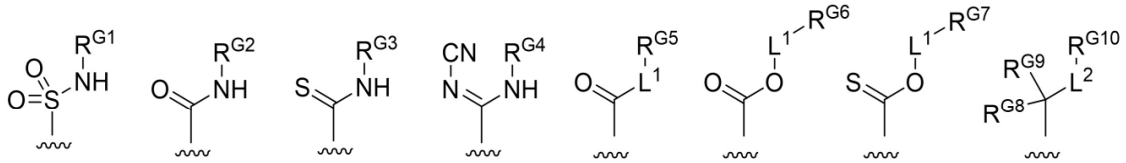
the group Q3 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 56)

The compound of the present invention according to any one of Embodiments 1 to 47, wherein G is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2, or a group

indicated by any of the following formulae (II-1) to (II-8),

[C16]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with the carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

the group Q2 is a group consisting of a halogen atom, a hydroxy group, an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy-carbonyl group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_2-C_6 acyl group, a cyano group, $NR^{N7}R^{N8}$, and a 3- to 12-membered non-aromatic heterocyclyl group,

R^{N7} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, a $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 57)

The compound of the present invention according to Embodiment 56, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$,

$CONR^{N3}R^{N4}$, and $SO_2NR^{N5}R^{N6}$,

R^{N3}, R^{N4}, R^{N5}, and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

the group Q3 is a group consisting of a halogen atom, a hydroxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 58)

The compound of the present invention according to any one of Embodiments 1 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with the carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 59)

The compound of the present invention according to Embodiment 58, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3}, R^{N4}, R^{N5}, and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 60)

The compound of the present invention according to any one of Embodiments 56 to 59, wherein G is a hydrogen atom, a C_1-C_3 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_4 cycloalkyl group optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one to three substituents independently selected from the group Q1, a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one to three substituents independently selected from the group Q2, or a

group indicated by any of the formulae (II-1) to (II-8), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 61)

The compound of the present invention according to any one of Embodiments 1 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with the carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 62)

The compound of the present invention according to Embodiment 61, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3}, R^{N4}, R^{N5}, and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 63)

The compound of the present invention according to any one of Embodiments 1 to 50, wherein the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_1-C_4 alkyl-SO_2 group, a cyano group, and $NR^{N1}R^{N2}$,

R^{N1} is a hydrogen atom, and

R^{N2} is a hydrogen atom,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 64)

The compound of the present invention according to any one of Embodiments 1 to 50, wherein the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} form a C_2-C_3 alkylene group together,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 65)

The compound of the present invention according to any one of Embodiments 1 to 50, wherein the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, and $POR^{P1}R^{P2}$, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 66)

The compound of the present invention according to any one of Embodiments 1 to 50, wherein the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 67)

The compound of the present invention according to any one of Embodiments 48 to 66, wherein R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 68)

The compound of the present invention according to any one of Embodiments 48 to 66, wherein

R^{P1} and R^{P2} are each independently a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 69)

The compound of the present invention according to any one of Embodiments 48 to 66, wherein R^{P1} and R^{P2} are each independently a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 70)

The compound of the present invention according to any one of Embodiments 1 to 69, wherein the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, and an amino group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 71)

The compound of the present invention according to any one of Embodiments 1 to 69, wherein the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group and a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 72)

The compound of the present invention according to any one of Embodiments 1 to 71, wherein the group Q2 is a group consisting of a halogen atom, a hydroxy group, an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group optionally substituted with one to five substituents independently selected from the group Q3, a cyano group, $NR^{N7}R^{N8}$, and a 3- to 12-membered non-aromatic heterocyclyl group,

R^{N7} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 73)

The compound of the present invention according to any one of Embodiments 1 to 71, wherein the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, and a cyano group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 74)

The compound of the present invention according to any one of Embodiments 1 to 71, wherein the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, and a C_2-C_6 acyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 75)

The compound of the present invention according to any one of Embodiments 1 to 71, wherein the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 76)

The compound of the present invention according to any one of Embodiments 1 to 71, wherein the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 77)

The compound of the present invention according to any one of Embodiments 1 to 71, wherein the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 78)

The compound of the present invention according to any one of Embodiments 1 to 77, wherein the group Q3 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 79)

The compound of the present invention according to any one of Embodiments 1 to 77, wherein the group Q3 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, and $NR^{N9}R^{N10}$,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 80)

The compound of the present invention according to any one of Embodiments 1 to 77, wherein the group Q3 is a group consisting of a halogen atom, OR^{Q3}, and a carboxy group, and

R^{Q3} is a hydrogen group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_4 alkoxy-carbonyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 81)

The compound of the present invention according to any one of Embodiments 1 to 77, wherein the group Q3 is a group consisting of a halogen atom, a hydroxy group, and a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 82)

The compound of the present invention according to any one of Embodiments 1 to 77, wherein the group Q3 is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 83)

The compound of the present invention according to any one of Embodiments 48 to 82, wherein R^{N1} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 84)

The compound of the present invention according to any one of Embodiments 48 to 82, wherein R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 85)

The compound of the present invention according to any one of Embodiments 48 to 84, wherein R^{N2} is a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 86)

The compound of the present invention according to any one of Embodiments 48 to 84, wherein R^{N2} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 87)

The compound of the present invention according to any one of Embodiments 48 to 86, wherein R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 88)

The compound of the present invention according to any one of Embodiments 48 to 87, wherein R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound

thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 89)

The compound of the present invention according to any one of Embodiments 48 to 88, wherein R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 90)

The compound of the present invention according to any one of Embodiments 48 to 89, wherein when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} form a C_2-C_3 alkylene group together, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 91)

The compound of the present invention according to any one of Embodiments 48 to 90, wherein when R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 92)

The compound of the present invention according to any one of Embodiments 48 to 90, wherein when R^{N5} and R^{N6} are hydrogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 93)

The compound of the present invention according to any one of Embodiments 48 to 92, wherein when R^{N9} and R^{N10} are hydrogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 94)

The compound of the present invention according to any one of Embodiments 48 to 82, wherein R^{N1} is a hydrogen atom or a C_1-C_3 alkyl group,

R^{N2} is a hydrogen atom or a C_1-C_3 alkyl group,

R^{N3} is a hydrogen atom or a C_1-C_3 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_3 alkyl group,

R^{N5} is a hydrogen atom or a C_1-C_3 alkyl group,

R^{N6} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N7} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N9} is a hydrogen atom or a C_1-C_6 alkyl group, and

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 95)

The compound of the present invention according to any one of Embodiments 48 to 82, wherein R^{N1} is a hydrogen atom or a methyl group,

R^{N2} is a hydrogen atom or a methyl group,

R^{N3} is a hydrogen atom or a methyl group,

R^{N4} is a hydrogen atom or a methyl group,

R^{N5} is a hydrogen atom or a methyl group,

R^{N6} is a hydrogen atom or a methyl group,

R^{N7} is a hydrogen atom or a methyl group,

R^{N8} is a hydrogen atom or a methyl group,

R^{N9} is a hydrogen atom or a methyl group, and

R^{N10} is a hydrogen atom or a methyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0042] (Embodiment 96)

The compound of the present invention according to any one of Embodiments 1 to 95, wherein R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q4, a C_2-C_{10} acyl group optionally substituted with one to five substituents independently selected from the group Q4, a C_1-C_6

alkoxy-carbonyl group, or a C_1-C_6 alkylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 97)

The compound of the present invention according to Embodiment 96, wherein R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one to three substituents independently selected from the group Q4, a C_2-C_6 acyl group optionally substituted with one to three substituents independently selected from the group Q4, a C_1-C_3 alkoxy-carbonyl group, or a C_1-C_3 alkylamino-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 98)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_1-C_6 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 99)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically

acceptable salt thereof.

(Embodiment 100)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 101)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 102)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 103)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a C_2-C_{10} acyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 104)

The compound of the present invention according to Embodiment 96 or 97, wherein R^{G1} is a C_2-C_3 acyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 105)

The compound of the present invention according to any one of Embodiments 96 to 104, wherein R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 akylamino-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 106)

The compound of the present invention according to any one of Embodiments 96 to 104, wherein R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 107)

The compound of the present invention according to any one of Embodiments 96 to 104, wherein R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 108)

The compound of the present invention according to any one of Embodiments 96 to 107, wherein R^{G2} is a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 109)

The compound of the present invention according to any one of Embodiments 96 to 107, wherein R^{G2} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 110)

The compound of the present invention according to any one of Embodiments 96 to 109, wherein R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 111)

The compound of the present invention according to any one of Embodiments 96 to 109,

wherein R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 112)

The compound of the present invention according to any one of Embodiments 96 to 109, wherein R^{G3} is a hydrogen atom or a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 113)

The compound of the present invention according to any one of Embodiments 96 to 109, wherein R^{G3} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 114)

The compound of the present invention according to any one of Embodiments 96 to 113, wherein R^{G4} is a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 115)

The compound of the present invention according to any one of Embodiments 96 to 113, wherein R^{G4} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 116)

The compound of the present invention according to any one of Embodiments 96 to 115, wherein the group Q4 is a hydroxy group, a C_1-C_6 alkoxy group, and an amino group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 117)

The compound of the present invention according to any one of Embodiments 96 to 115, wherein the group Q4 is a hydroxy group or a C_1-C_4 alkoxy group, a deuterated compound thereof, or a

pharmaceutically acceptable salt thereof.

(Embodiment 118)

The compound of the present invention according to any one of Embodiments 96 to 117, wherein R^{N11} is a hydrogen atom, a C_1-C_3 alkyl group, a C_2-C_3 acyl group, or a C_1-C_3 alkoxy-carbonyl group, and

R^{N12} is a hydrogen atom or a C_1-C_3 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 119)

The compound of the present invention according to any one of Embodiments 1 to 95, wherein R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

wherein the C_1-C_6 alkyl group is optionally substituted with one to five substituents independently selected from a halogen atom, a hydroxy group, a carboxy group, and a cyano group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 120)

The compound of the present invention according to any one of Embodiments 1 to 95, wherein R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_3 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 121)

The compound of the present invention according to any one of Embodiments 1 to 95, wherein R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0043] (Embodiment 122)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl

group optionally substituted with one to five halogen atoms, a C_1-C_6 alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

a deuterated compound thereof, or

a pharmaceutically acceptable salt thereof.

(Embodiment 123)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_2 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkyl group substituted with one hydroxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

a deuterated compound thereof, or

a pharmaceutically acceptable salt thereof.

(Embodiment 124)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 125)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_4 alkylene group, a deuterated compound thereof, or a pharmaceutically acceptable

salt thereof.

(Embodiment 126)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_2 alkylene group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 127)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 128)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_2 alkylene group,

wherein the linear C_1-C_2 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_3 alkyl group, and a C_1-C_3 alkoxy group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 129)

The compound of the present invention according to any one of Embodiments 1 to 121, wherein L^1 is a linear C_1-C_2 alkylene group,

wherein the linear C_1-C_2 alkylene group is optionally substituted with one or two C_1-C_3 alkyl groups,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0044] (Embodiment 130)

The compound of the present invention according to any one of Embodiments 1 to 129, wherein R^{G5}, R^{G6}, R^{G7}, and R^{G11} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 131)

The compound of the present invention according to any one of Embodiments 1 to 129, wherein R^{G5}, R^{G6}, R^{G7}, and R^{G11} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_3 alkoxy group, a carboxy group, a C_1-C_3 alkoxy-carbonyl group, a cyano group, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_3 alkyl groups, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 132)

The compound of the present invention according to any one of Embodiments 1 to 129, wherein R^{G5}, R^{G6}, R^{G7}, and R^{G11} are each independently a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 133)

The compound of the present invention according to any one of Embodiments 1 to 132, wherein R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, a carboxy group, or a C_1-C_6 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 134)

The compound of the present invention according to any one of Embodiments 1 to 132, wherein R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated

compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 135)

The compound of the present invention according to any one of Embodiments 1 to 132, wherein R^{G5} and R^{G11} are each a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 136)

The compound of the present invention according to any one of Embodiments 1 to 135, wherein R^{G5} is a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 137)

The compound of the present invention according to any one of Embodiments 1 to 135, wherein R^{G5} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 138)

The compound of the present invention according to any one of Embodiments 1 to 137, wherein R^{G11} is a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 139)

The compound of the present invention according to any one of Embodiments 1 to 138, wherein R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 140)

The compound of the present invention according to any one of Embodiments 1 to 138, wherein R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-

aromatic heterocyclyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 141)

The compound of the present invention according to any one of Embodiments 1 to 138, wherein R^{G6} and R^{G7} are each independently a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 142)

The compound of the present invention according to any one of Embodiments 1 to 138, wherein R^{G6} and R^{G7} are each a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 143)

The compound of the present invention according to any one of Embodiments 1 to 142, wherein R^{G6} is a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 144)

The compound of the present invention according to any one of Embodiments 1 to 143, wherein R^{G7} is a hydrogen atom, a hydroxy group, or a carboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 145)

The compound of the present invention according to any one of Embodiments 1 to 129, wherein R^{G5}, R^{G6}, and R^{G7} are each independently a hydrogen atom, a hydroxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, or a cyano group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 146)

The compound of the present invention according to any one of Embodiments 1 to 129, wherein R^{G5}, R^{G6}, and R^{G7} are each independently a hydrogen atom, a hydroxy group, a carboxy group, a C_1-C_3

alkoxy-carbonyl group, or a cyano group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 147)

The compound of the present invention according to any one of Embodiments 1 to 146, wherein R^{G5} is a hydroxy group, a carboxy group, or a C_1-C_3 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 148)

The compound of the present invention according to any one of Embodiments 1 to 146, wherein R^{G5} is a hydroxy group, a carboxy group, or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 149)

The compound of the present invention according to any one of Embodiments 1 to 148, wherein R^{G6} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 150)

The compound of the present invention according to any one of Embodiments 1 to 149, wherein R^{G7} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 151)

The compound of the present invention according to any one of Embodiments 1 to 150, wherein R^{G11} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0045] (Embodiment 152)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms, and a C_2-C_6 acyloxy

group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 153)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 154)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group, and a C_2-C_6 alkyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, a deuterated compound

thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 155)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 156)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_2-C_6 acyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 157)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 158)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_2 alkylene group,

wherein the linear C_1-C_2 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_2 alkyl group optionally substituted with one to three fluorine atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 159)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms, and

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 160)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a single bond or a linear C_1-C_2 alkylene group,

wherein the linear C_1-C_2 alkylene group is optionally substituted with one to three substituents

independently selected from the group consisting of, a halogen atom, a hydroxy group, a C_1-C_3 alkyl group, and a C_1-C_3 alkoxy group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 161)

The compound of the present invention according to any one of Embodiments 1 to 151, wherein L^2 is a methylene group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0046] (Embodiment 162)

The compound of the present invention according to any one of Embodiments 1 to 161, wherein R^{G8} and R^{G9} are each independently a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group, and

the C_1-C_6 alkyl group is optionally substituted with one to five substituents independently selected from a halogen atom, a hydroxy group, and a C_1-C_6 alkoxy group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 163)

The compound of the present invention according to any one of Embodiments 1 to 161, wherein R^{G8} and R^{G9} are each independently a hydrogen atom, a halogen atom, or a C_1-C_3 alkyl group,

the C_1-C_3 alkyl group is optionally substituted with one to three substituents independently selected from a halogen atom, a hydroxy group, and a C_1-C_6 alkoxy group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 164)

The compound of the present invention according to any one of Embodiments 1 to 161, wherein R^{G8} and R^{G9} are each independently a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 165)

The compound of the present invention according to any one of Embodiments 1 to 161, wherein R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_6 alkyl group optionally substituted with one hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 166)

The compound of the present invention according to any one of Embodiments 1 to 161, wherein R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_6 alkyl group, and

the C_1-C_6 alkyl group is optionally substituted with one to five substituents independently selected from a hydroxy group and a C_1-C_6 alkoxy group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0047] (Embodiment 167)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_2-C_6 alkenyl group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group, and

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 168)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_2-C_6 alkenyl group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, or a 3- to 12-membered non-aromatic heterocyclyl group optionally

substituted with one to five substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 169)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group, and

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 170)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group, and

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 171)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group, and

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 172)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a cyano group, $NR^{N13}R^{N14}$, or a C_1-C_4 alkyl-SO_2 group,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group, and

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 173)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, or a C_1-C_4 alkyl-SO_2 group,

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_4 alkoxy-carbonyl group, or a C_1-C_4 alkyl-SO_2 group, and

R^{N14} is a hydrogen atom or a C_1-C_4 alkyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 174)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 175)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 176)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 177)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group or a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 178)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group or a C_1-C_4 alkoxy group, a deuterated compound thereof, or a pharmaceutically

acceptable salt thereof.

(Embodiment 179)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, a C_1-C_6 alkyl-SO_2 group, a 5- to 10-membered heteroaryl group, or a 3- to 12-membered non-aromatic heterocyclyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 180)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a hydroxy group, a carboxy group, a C_1-C_3 alkoxy-carbonyl group, a cyano group, a C_1-C_3 alkyl-SO_2 group, a 5- or 6-membered heteroaryl group, or a 3- to 6-membered non-aromatic heterocyclyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 181)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a carboxy group or a C_1-C_3 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 182)

The compound of the present invention according to any one of Embodiments 1 to 166, wherein R^{G10} is a carboxy group or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0048] (Embodiment 183)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a

3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-2), a group indicated by the formula (II-3), a group indicated by the formula (II-4), a group indicated by the formula (II-5), a group indicated by the formula (II-6), a group indicated by the formula (II-7), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 184)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 4- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-2), a group indicated by the formula (II-3), a group indicated by the formula (II-4), a group indicated by the formula (II-5), a group indicated by the formula (II-6), a group indicated by the formula (II-7), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 185)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered

non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-2), a group indicated by the formula (II-3), a group indicated by the formula (II-4), a group indicated by the formula (II-5), a group indicated by the formula (II-6), a group indicated by the formula (II-7), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 186)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-2), a group indicated by the formula (II-3), a group indicated by the formula (II-4), a group indicated by the formula (II-5), a group indicated by the formula (II-6), a group indicated by the formula (II-7), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 187)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-3), a group indicated by the formula (II-5), a group indicated by

the formula (II-6), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 188)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-3), a group indicated by the formula (II-5), a group indicated by the formula (II-6), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 189)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-3), or a group indicated by the formula (II-8), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 190)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-3), a group indicated by the formula (II-5), a group indicated by the formula (II-6), a group indicated by the formula (II-8), or a group indicated by the formula (II-9), a

deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 191)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-2), a group indicated by the formula (II-3), a group indicated by the formula (II-4), a group indicated by the formula (II-5), a group indicated by the formula (II-6), or a group indicated by the formula (II-8), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 192)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a C_3-C_4 cycloalkyl group optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one to three substituents independently selected from the group Q1, a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one to three substituents independently selected from the group Q2, a group indicated by the formula (II-1), a group indicated by the formula (II-2), a group indicated by the formula (II-3), a group indicated by the formula (II-4), a group indicated by the formula (II-5), a group indicated by the formula (II-6), or a group indicated by the formula (II-8), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 193)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 194)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a formyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 195)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_6 alkyl-SO_2 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 196)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_4 alkyl-SO_2 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 197)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 198)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 199)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_3 alkyl group optionally substituted with one to three halogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 200)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms, a deuterated

compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 201)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a propyl group substituted with a fluorine atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 202)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 203)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 204)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a C_3-C_4 cycloalkyl group optionally substituted with one to three substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 205)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a hydroxycyclobutyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 206)

The compound of the present invention according to any one of Embodiments 48 to 182,

wherein G is a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 207)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 208)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a carboxy group or a phenyl group substituted with a C_1-C_6 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 209)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a phenyl group substituted with a carboxy group and a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 210)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a phenyl group substituted with a carboxy group and a halogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 211)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a phenyl group substituted with $POR^{P1}R^{P2}$, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 212)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a phenyl group substituted with (N,N-dimethylsufamoyl)carbomoyl, a deuterated

compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 213)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 214)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 5- or 6-membered heteroaryl group optionally substituted with one to three substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 215)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 216)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a carboxy group or a 5- or 6-membered heteroacryl group optionally substituted with a C_1-C_6 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 217)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a carboxy group or a 5- or 6-membered heteroacryl group optionally substituted with a C_1-C_3 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 218)

The compound of the present invention according to any one of Embodiments 48 to 182,

wherein G is a pyridyl group substituted with a carboxy group or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 219)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a pyridyl group substituted with a carboxy group and a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 220)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a pyridyl group substituted with a carboxy group and an amino group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 221)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a pyridazinyl group substituted with a carboxy group or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 222)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is an oxazolyl group substituted with a carboxy group or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 223)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is an oxazolyl group substituted with a hydroxymethyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 224)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a thiadiazolyl group substituted with a 2-hydroxypropan-2-yl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 225)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 5- or 6-membered heteroaryl group optionally substituted with a hydroxymethyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 226)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a pyrazyl group substituted with a hydroxymethyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 227)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a pyrimidyl group substituted with a hydroxymethyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 228)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 229)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one to three substituents independently selected from the group Q2, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 230)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, a deuterated compound thereof, or a

pharmaceutically acceptable salt thereof.

(Embodiment 231)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a 3- to 6-membered non-aromatic heterocyclyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 232)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is an oxetanyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 233)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a dihydropyridazinyl group substituted with an oxo group and a 2-hydroxyethyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 234)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a dihydrooxazolyl group substituted with an oxo group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 235)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a dihydrothiazolyl group substituted with an oxo group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 236)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a dihydrothiadiazolyl group substituted with an oxo group and methyl, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 237)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-1), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 238)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-1), and R^{G1} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 239)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-1), and R^{G1} is a C_2-C_3 acyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 240)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-1), and R^{G1} is a hydrogen atom or a C_2-C_3 acyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 241)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-2), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 242)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-2), and R^{G2} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 243)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-3), a deuterated compound thereof, or a

pharmaceutically acceptable salt thereof.

(Embodiment 244)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-3), and R^{G3} is a methyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 245)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-3), and R^{G3} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 246)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-4), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 247)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-4), and R^{G4} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 248)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-5), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 249)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-5), L^1 is a linear C_1-C_2 alkylene group optionally substituted with one or two C_1-C_3 alkyl groups, and R^{G5} is a hydroxy group, a carboxy group, or a C_1-C_3 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 250)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-5), L^1 is a methylene group or an ethylene group substituted with two methyl groups, and R^{G5} is a hydroxy group, a carboxy group, or a methoxycarboxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 251)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-5), L^1 is an ethylene group, and R^{G5} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 252)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-6), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 253)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-6), L^1 is a linear C_1-C_2 alkylene group optionally substituted with one or two C_1-C_3 alkyl groups, and R^{G6} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 254)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-6), L^1 is an ethylene group substituted with two methyl groups, and R^{G6} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 255)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-6), L^1 is a methylene group, and R^{G6} is a hydrogen

atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 256)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-7), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 257)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-7), L^1 is a linear C_1-C_2 alkylene group optionally substituted with one or two C_1-C_3 alkyl groups, and R^{G7} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 258)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-7), L^1 is a methylene group, and R^{G7} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 259)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 260)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is a linear C_1-C_2 alkylene group optionally substituted with one or two C_1-C_3 alkyl groups, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a carboxy group or a C_1-C_3 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 261)

The compound of the present invention according to any one of Embodiments 48 to 182,

wherein G is a group indicated by the formula (II-8), L^2 is a methylene group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a carboxy group or a C_1-C_3 alkoxy-carbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 262)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is a methylene group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a carboxy group or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 263)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is a methylene group, R^{G8} is a hydroxymethyl group, R^{G9} is a hydrogen atom, and R^{G10} is a cyano group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 264)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is a methylene group substituted with a trifluoromethyl group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 265)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is a methylene group, R^{G8} and R^{G9} are each a methyl group, and R^{G10} is a carboxy group or a methoxycarbonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 266)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is an ethylene group optionally substituted with

one hydroxy group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a hydroxy group, a methoxy group, a cyano group, or a methylsulfonyl group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 267)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is an ethylene group substituted with one hydroxy group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 268)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is an ethylene group substituted with one hydroxy group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a methoxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 269)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is an ethylene group substituted with one hydroxy group and two methyl groups, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 270)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-8), L^2 is an ethylene group, R^{G8} and R^{G9} are each a hydrogen atom, and R^{G10} is a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 271)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-9), a deuterated compound thereof, or a

pharmaceutically acceptable salt thereof.

A hydogenated compound thereof or a pharmaceutically acceptable salt thereof.

(Embodiment 272)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-9), L^1 is a linear C_1-C_2 alkylene group optionally substituted with one or two C_1-C_3 alkyl groups, and R^{G11} is a hydroxy group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 273)

The compound of the present invention according to any one of Embodiments 48 to 182, wherein G is a group indicated by the formula (II-9), L^1 is a methylene group, and R^{G11} is a hydrogen atom, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0049] (Embodiment 274)

The compound of the present invention according to any one of Embodiments 1 to 273, wherein m and n are each independently an integer of any of 1 or 2, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 275)

The compound of the present invention according to any one of Embodiments 1 to 273, wherein m is 1 and n is 1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 276)

The compound of the present invention according to any one of Embodiments 1 to 273, wherein m is 1 and n is 2, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 277)

The compound of the present invention according to any one of Embodiments 1 to 273, wherein m is 2 and n is 1, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 278)

The compound of the present invention according to any one of Embodiments 1 to 273, wherein

m is 2 and n is 2, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0050] (Embodiment 279)

A compound, wherein in a formula (I),

a ring A is a benzene ring or a 5- or 6-membered aromatic heterocycle,

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

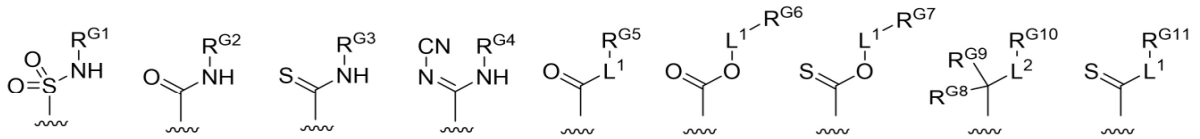
R^4 is a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from a group Q1, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from a group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C17]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group

Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3}, R^{N4}, R^{N5}, and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of a halogen atom, a hydroxy group, an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group optionally substituted with one to five substituents independently selected from the group Q3, a cyano group, $NR^{N7}R^{N8}$, and a 3- to 12-membered non-aromatic heterocyclyl group,

R^{N7} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

the group Q3 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q4, a C_2-C_{10} acyl group optionally substituted with one to five substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_1-C_6 alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5}, R^{G6}, R^{G7}, and R^{G11} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group,

the C_1-C_6 alkyl group is optionally substituted with one to five substituents independently selected from a halogen atom, a hydroxy group, and a C_1-C_6 alkoxy group,

R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_2-C_6 alkenyl group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, and

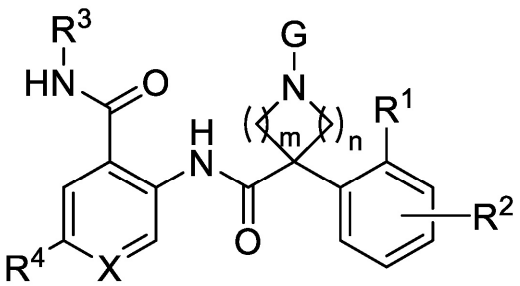
m and n are each independently an integer of any of 1 or 2,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

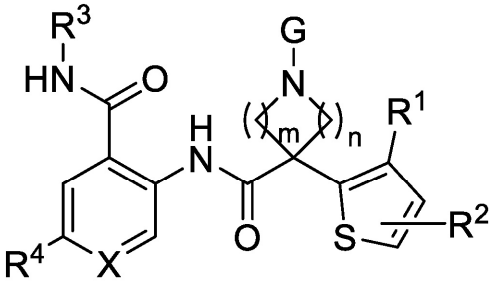
[0051] (Embodiment 280)

The compound of the present invention according to any one of Embodiments 1 to 278 that is represented by the following general formula (I-a) or (I-b):

[C18]



(I-a)



(I-b)

[wherein,

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

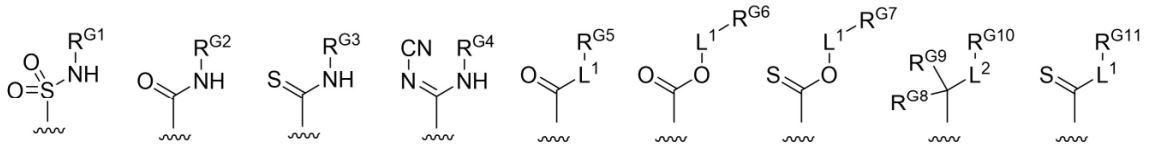
R^4 is a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from a group Q1, a phenyl group optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 4- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from a group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C19]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, and a cyano group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, and $NR^{N9}R^{N10}$,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from a group Q4, a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_1-C_6 alkoxy-carbonyl group,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 akylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl

group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkyl group substituted with one hydroxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, a carboxy group, or a C_1-C_6 alkoxy-carbonyl group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group, and a C_2-C_6 acyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom, or a C_1-C_6 alkyl group,

The C_1-C_6 alkyl group is optionally substituted with one to five substituents independently selected from a hydroxy group, and a C_1-C_6 alkoxy group,

R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, and

m and n are each independently an integer of any of 1 or 2],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 281)

The compound of the present invention according to Embodiment 280, wherein in the formula (I-a) or (I-b),

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

R^4 is a halogen atom or a C_1-C_6 alkyl group,

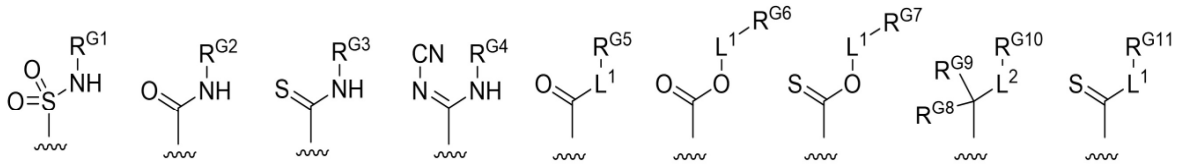
X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from a group Q1, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 4- to

12-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from a group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C20]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3}, R^{N4}, R^{N5}, and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, and a cyano group,

the group Q3 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, and $NR^{N9}R^{N10}$,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents

independently selected from a group Q4, a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_1-C_6 alkoxy-carbonyl group,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 akylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkyl group substituted with one hydroxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, a carboxy group, or a C_1-C_6 alkoxy-carbonyl group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents

independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom, or a C_1-C_6 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group, and

m and n are each independently an integer of any of 1 to 2],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 282)

The compound of the present invention according to Embodiment 280, wherein in the formula (I-a) or (I-b),

R^{N1} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N2} is a hydrogen atom,

R^{N5} and R^{N6} are hydrogen atoms,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted

with one to five substituents independently selected from the group Q3, and a C_2-C_6 acyl group,

R^{N9} and R^{N10} are hydrogen atoms,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from a group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group, a C_1-C_6 alkoxy group, and an amino group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_2-C_6 acyloxy group,

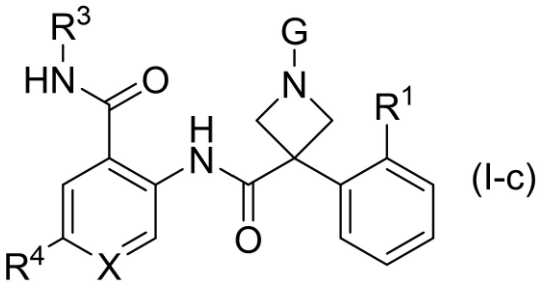
wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, and

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 283)

The compound of the present invention according to any one of Embodiments 1 to 278 that is represented by the following general formula (I-c):

[C21]



(I-c)

[wherein each symbol is as defined in any of Embodiments 1 to 278],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 284)

The compound of the present invention according to Embodiment 283, wherein in the formula (I-c),

R^1 is a C_1-C_6 alkyl group,

R^4 is a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom, and

other symbols are as defined in any of Embodiments 1 to 278,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 285)

The compound of the present invention according to Embodiment 283, wherein in the formula (I-c),

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

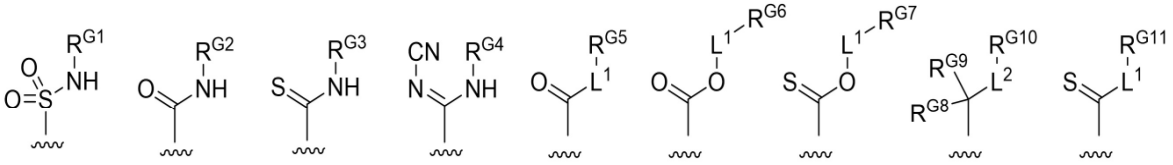
X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one or two

substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C22]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_4 alkoxy-carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, and a carboxy group,

R^{Q3} is a hydrogen atom, a C_2-C_6 acyl group optionally substituted with one amino group, or a

C_1-C_4 alkoxy-carbonyl group,

R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from a group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, or a C_1-C_4 alkyl-SO_2 group,

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_4 alkoxy-carbonyl group, or a C_1-C_4 alkyl-SO_2 group, and

R^{N14} is a hydrogen atom or a C_1-C_4 alkyl group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 286)

The compound of the present invention according to Embodiment 283, wherein in the formula (I-c),

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

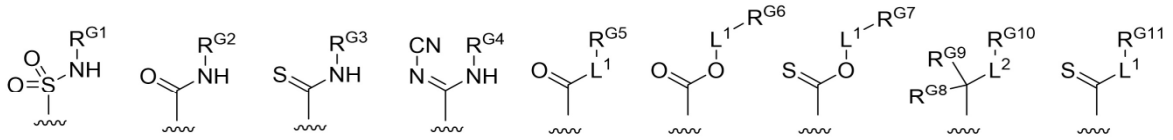
R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C23]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_1-C_4 alkyl-SO_2 group, a cyano group, and $NR^{N1}R^{N2}$,

R^{N1} is a hydrogen atom,

R^{N2} is a hydrogen atom,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3,

the group Q3 is a group consisting of a halogen atom, a hydroxy group, and a carboxy group,

R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, or a C_1-C_4 alkyl group optionally

substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from a group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 287)

The compound of the present invention according to Embodiment 283, wherein in the formula (I-c),

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom or a methoxy group,

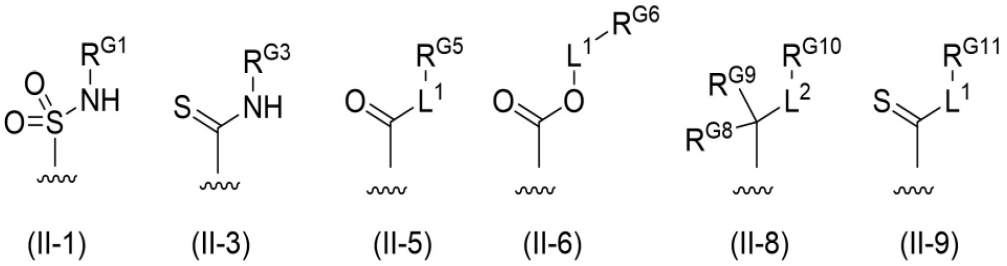
X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with

one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9),

[C24]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally

substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group,

a pharmaceutically acceptable salt thereof.

(Embodiment 288)

The compound of the present invention according to Embodiment 283, wherein in the formula (I-c),

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

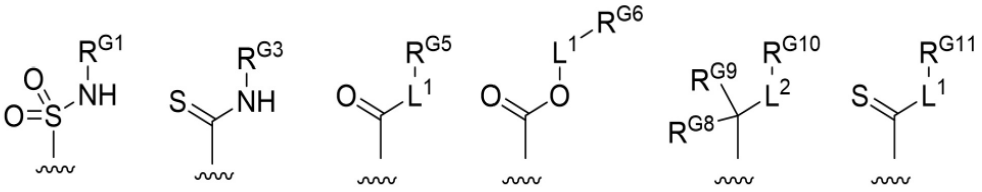
R^4 is a halogen atom,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9),

[C25]



the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, and an amino group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

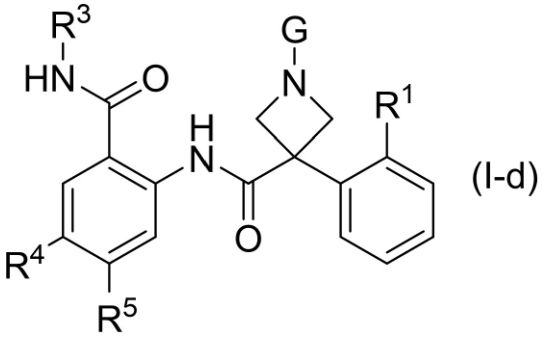
R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group,

a pharmaceutically acceptable salt thereof.

(Embodiment 289)

The compound of the present invention according to any one of Embodiments 1 to 278 that is represented by the following general formula (I-d):

[C26]



(I-d)

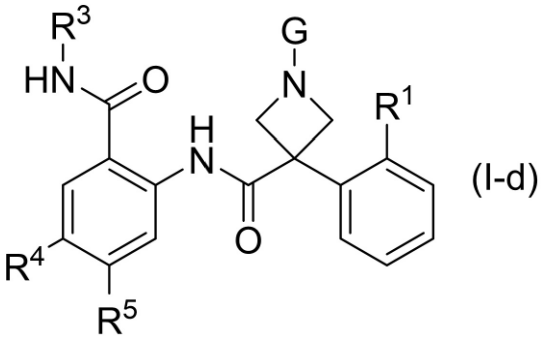
[wherein each symbol is as defined in any of Embodiments 1 to 278],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 290)

The compound of the present invention according to Embodiment 287 or 288 that is represented by the following general formula (I-d):

[C27]



(I-d)

[wherein each symbol is as defined in Embodiment 287 or 288] or

a pharmaceutically acceptable salt thereof.

(Embodiment 291)

The compound according to Embodiment 290, wherein in the formula (I-d),

R^1 is a C_1-C_4 alkyl group,

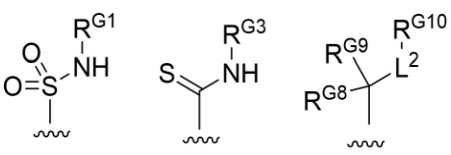
R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), or (II-8),

[C28]



(II-1) (II-3) (II-8)

the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group and a carboxy group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one substituent selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group, and

R^{G10} is a hydroxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group or

a pharmaceutically acceptable salt thereof.

(Embodiment 292)

The compound according to Embodiment 290, wherein in the formula (I-d),

R^1 is a C_1-C_6 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom or a methyl group,

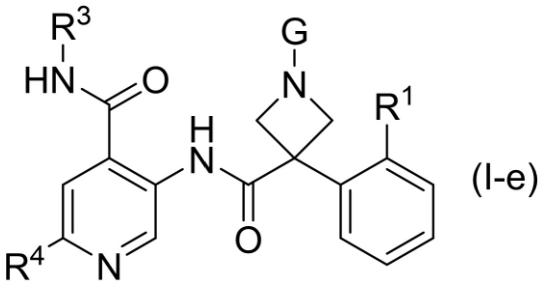
R^5 is a hydrogen atom or a fluorine atom or

a pharmaceutically acceptable salt thereof.

(Embodiment 293)

The compound of the present invention according to Embodiment 287 or 288 that is represented by the following general formula (I-e):

[C29]



(I-e)

[wherein each symbol is as defined in Embodiment 287 or 288] or

a pharmaceutically acceptable salt thereof.

(Embodiment 294)

The compound of the present invention according to Embodiment 293, wherein in the formula (I-e),

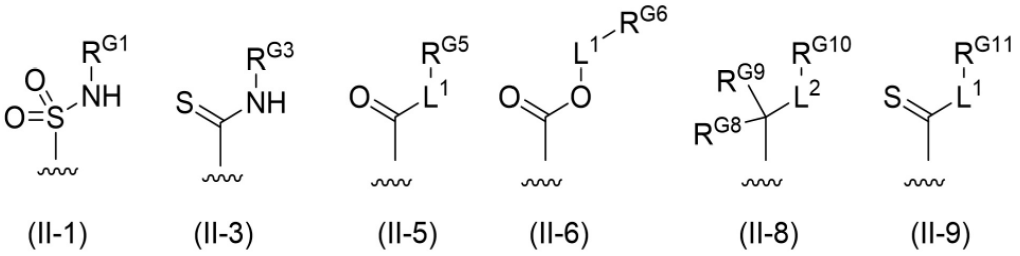
R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom or a methoxy group,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9),

[C30]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are hydrogen atoms,

R^{G10} is a hydroxy group or a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms or

a pharmaceutically acceptable salt thereof.

(Embodiment 295)

The compound of the present invention according to Embodiment 293, wherein in the formula (I-e),

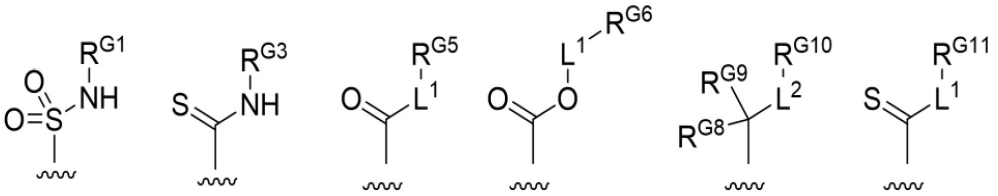
R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9),

[C31]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, and an amino group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one substituent selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are hydrogen atoms,

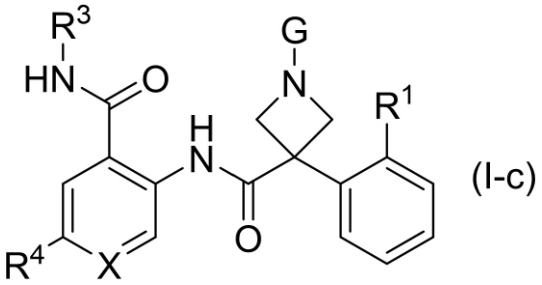
R^{G10} is a hydroxy group or a C_1-C_4 alkoxy group or

a pharmaceutically acceptable salt thereof.

(Embodiment 296)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c):

[C32]



(I-c)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

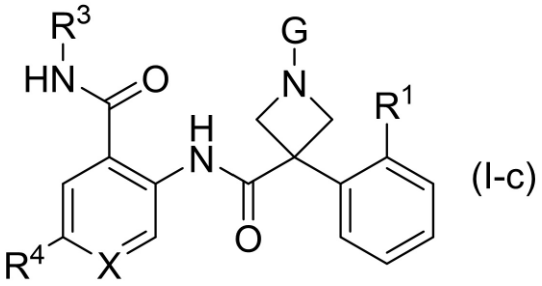
G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms] or

a pharmaceutically acceptable salt thereof.

(Embodiment 297)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c):

[C33]



(I-c)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a C_3-C_6 cycloalkyl group optionally substituted with one or two substituent independently selected from the group Q1,

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_1-C_4 alkyl- SO_2 group, a cyano group, and $NR^{N1}R^{N2}$,

R^{N1} is a hydrogen atom,

R^{N2} is a hydrogen atom, and

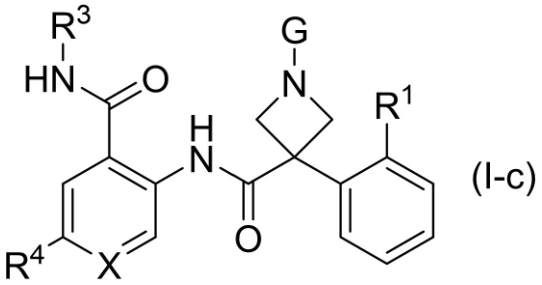
the group Q3 is a group consisting of a halogen atom, a hydroxy group, and a carboxy group]

or a pharmaceutically acceptable salt thereof.

(Embodiment 298)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c):

[C34]



(I-c)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a phenyl group optionally substituted with one or two substituents independently selected from the group Q1,

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_4 alkoxy-carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, and a carboxy group, and

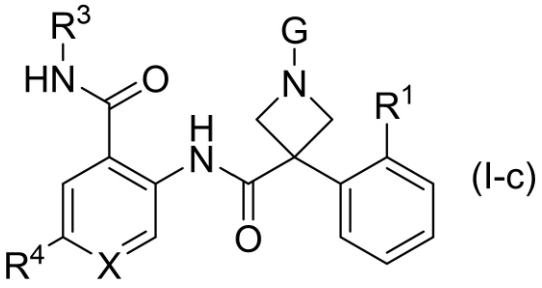
R^{Q3} is a hydrogen atom, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_4 alkoxy-carbonyl group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 299)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c):

[C35]



(I-c)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1,

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_4 alkoxy-carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, and a carboxy group, and

R^{Q3} is a hydrogen atom, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_4 alkoxy-carbonyl group] or

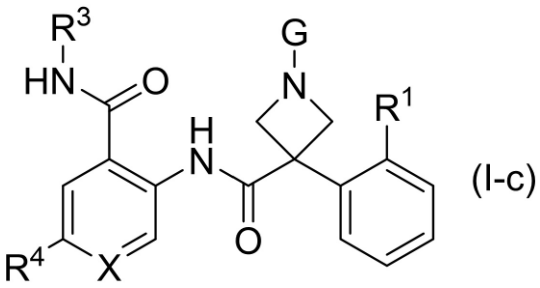
a pharmaceutically acceptable salt thereof.

(Embodiment 300)

The compound of the present invention according to Embodiment 286, wherein in the following

formula (I-c):

[C36]



(I-c)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituent independently selected from the group Q1,

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a carboxy group, a C_1-C_4 alkyl- SO_2 group, a cyano group, and $NR^{N1}R^{N2}$,

R^{N1} is a hydrogen atom,

R^{N2} is a hydrogen atom, and

the group Q3 is a group consisting of a halogen atom, a hydroxy group, and a carboxy group]

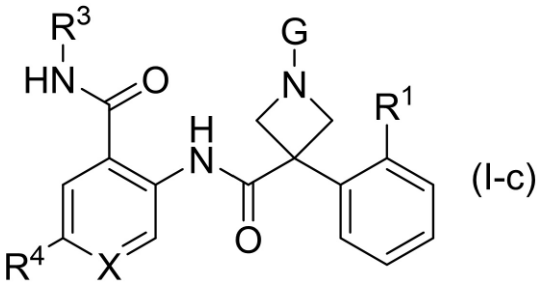
or

a pharmaceutically acceptable salt thereof.

(Embodiment 301)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c):

[C37]



(I-c)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituent independently selected from the group Q2,

the group Q2 is an oxo group or a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, and

the group Q3 is a group consisting of a halogen atom, a hydroxy group, and a carboxy group]

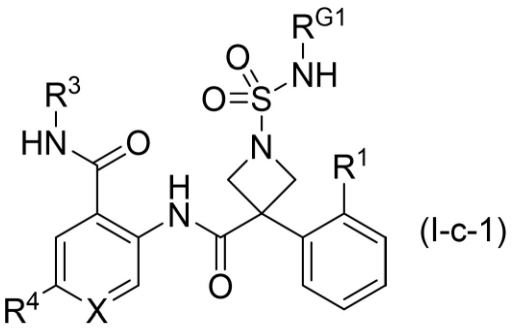
or

a pharmaceutically acceptable salt thereof.

(Embodiment 302)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-1):

[C38]



(I-c-1)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituent independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituent independently selected from the group Q4, and

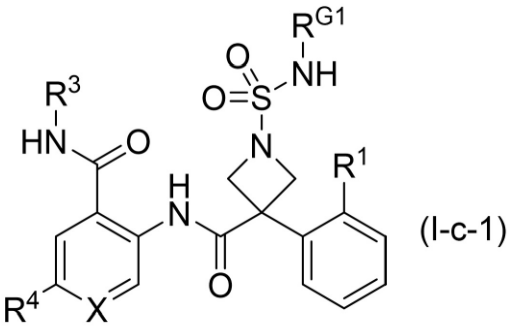
the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 303)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-1):

[C39]



(I-c-1)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituent independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituent independently selected from the group Q4, and

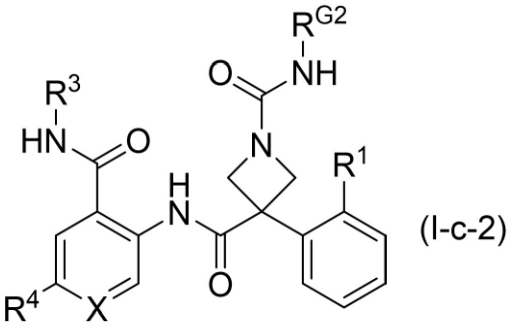
the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 304)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-2):

[C40]



(I-c-2)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

R^{G2} is a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituent independently selected from the group Q4, and

the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group] or

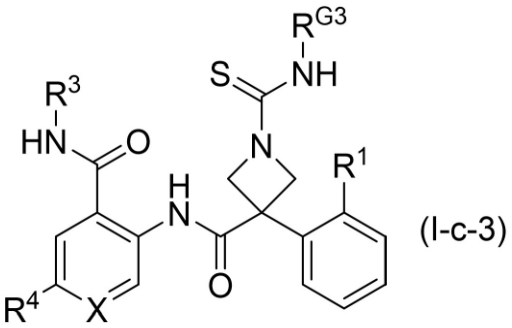
a pharmaceutically acceptable salt thereof.

(Embodiment 305)

The compound of the present invention according to Embodiment 286, wherein in the following

formula (I-c-3):

[C41]



(I-c-3)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituent independently selected from the group Q4, and

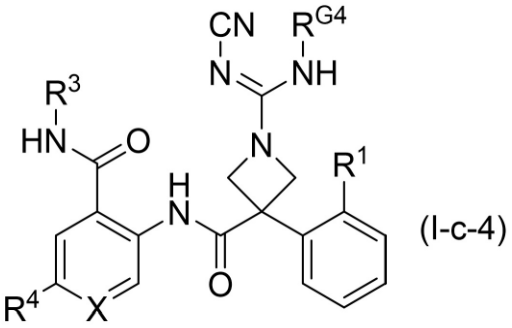
the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 306)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-4):

[C42]



(I-c-4)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

R^{G4} is a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituent independently selected from the group Q4, and

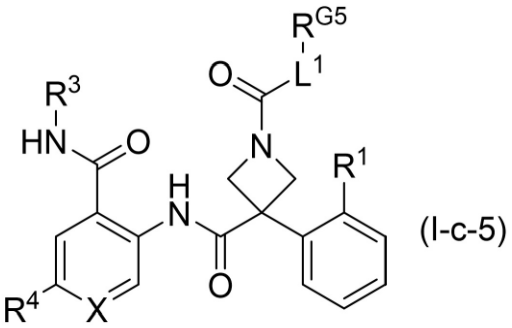
the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 307)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-5):

[C43]



(I-c-5)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups,

and

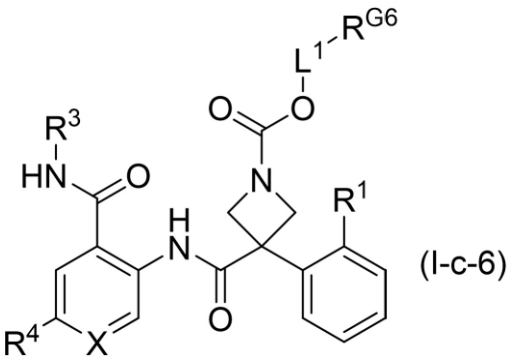
R^{G5} is a hydrogen atom, a hydroxy group, or a carboxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 308)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-6):

[C44]



[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups, and

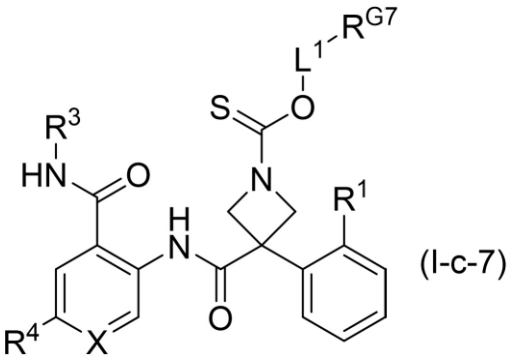
R^{G6} is a hydrogen atom, a hydroxy group, or a carboxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 309)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-7):

[C45]



(I-c-7)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups, and

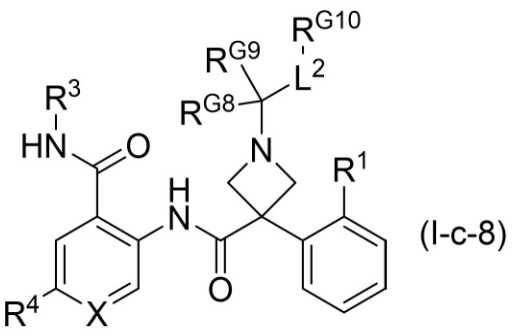
R^{G7} is a hydrogen atom, a hydroxy group, or a carboxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 310)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-8):

[C46]



(I-c-8)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from a group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, or a C_1-C_4 alkyl-SO_2 group,

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_4 alkoxy-carbonyl group, or a C_1-C_4 alkyl-SO_2 group,

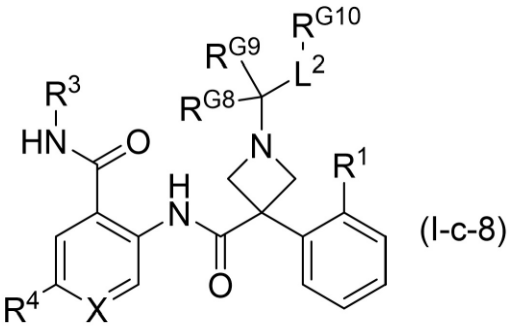
R^{N14} is a hydrogen atom or a C_1-C_4 alkyl group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 311)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-8):

[C47]



(I-c-8)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from a group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

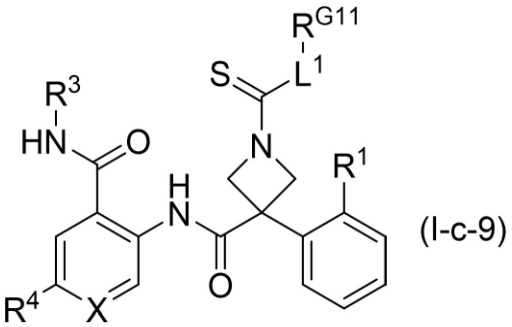
R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 312)

The compound of the present invention according to Embodiment 286, wherein in the following formula (I-c-9):

[C48]



(I-c-9)

[wherein,

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom or a C_1-C_4 alkyl group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups, and

R^{G11} is a hydrogen atom, a hydroxy group, or a carboxy group] or

a pharmaceutically acceptable salt thereof.

(Embodiment 313)

Compounds described in Examples, deuterated compounds thereof, or pharmaceutically acceptable salts thereof.

(Embodiment 314)

A compound selected from the group consisting of N-(2-carbamoyl-4-chlorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-carbamoyl-4-chloro-5-fluorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-chloro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-

sulfamoylazetidine-3-carboxamide;

N-(4-bromo-2-carbamoylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-bromo-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-carbamoyl-5-fluoro-4-methylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(5-fluoro-4-methyl-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N^3-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide;

1-carbamothioyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

N-(4-chloro-5-fluoro-2-((methyl-d3)carbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4,5-difluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4,5-difluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4,5-difluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-

carboxamide;

tert-butyl 3-((4-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-bromo-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-bromo-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-fluoro-6-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-fluoro-6-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-fluoro-6-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-ethylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-ethylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-ethylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-propylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-propylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-propylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isobutylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isobutylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isobutylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-cyclopentylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-cyclopentylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-cyclopentylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(3-isopropylthiophen-2-yl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)-1-sulfamoylazetidine-3-carboxamide;

3-(5-chloro-3-isopropylthiophen-2-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(1-(3-hydroxypropanoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N^3-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide;

2-chloro-5-(1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

2-chloro-5-(1-(3-hydroxy-3-methylbutanoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-carbamothioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-2-chloro-N-methylisonicotinamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)acetate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)acetic acid;

ethyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)butanoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)butanoic acid;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoate

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pentanoate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pentanoic acid;

methyl 1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclobutane-1-carboxylate;

1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclobutane-1-carboxylic acid;

methyl 2-(1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclopropyl)acetate;

2-(1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclopropyl)acetic acid;

methyl 4-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

4-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)methyl)nicotinate;

6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)nicotinic acid;

methyl 5-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)picolinate;

5-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)picolinic acid;

methyl 6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)pyridazine-3-carboxylate;

6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)pyridazine-3-carboxylic acid;

tert-butyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-methylazetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydropyran-4-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-fluoro-3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoro-3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

3-hydroxypropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxypropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidine-1-carboxylate;

3-hydroxyethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,4-dihydroxybutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

ethyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-5-carboxylic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)isonicotinate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)isonicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-2-fluoronicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylnicotinic acid;

methyl 2-amino-6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

2-amino-6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-methylnicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methoxynicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methoxynicotinic acid;

methyl 2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(thiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylic acid;

ethyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylic acid;

ethyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylic acid;

ethyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid;

ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylic acid;

ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-cyanopyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(6-acetylpyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-(methylsulfonyl)pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-sulfamoylpyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-chloro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methyl-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(5-amino-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-methyl-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)picolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluoropicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluoropicolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylpicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylpicolinic acid;

methyl 6-chloro-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

6-chloro-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-methylpicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-methylpicolinic acid;

methyl 3-amino-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

3-amino-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-2-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)pyrimidine-2-carboxylic acid;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

tert-butyl (6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazin-3-yl)carbamate;

1-(6-aminopyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-methylpyridazine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N,N-dimethylpyridazine-3-carboxamide;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxamide;

2-chloro-5-(1-(5-cyano-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(hydroxymethyl)pyridazin-3-yl)-3-(2-

isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(1-hydroxyethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(4-(hydroxymethyl)oxazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(hydroxymethyl)-1,2,4-thiadiazol-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

ethyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylate;

2-chloro-5-(1-(4-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate;

2-chloro-5-(1-(5-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

1-(6-(aminomethyl)pyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-(2-hydroxypropan-2-yl)-1,2,4-thiadiazol-5-yl)-3-(2-

isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(2-hydroxypropan-2-yl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cyanomethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyanoethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((1-cyanocyclopropyl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-methoxyethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-

methoxypropyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(prop-2-yn-1-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-2-ylmethyl)azetidine-3-carboxamide;

1-((1,3-dioxolan-2-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyano-2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(2-(1H-tetrazol-5-yl)ethyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-((1H-tetrazol-5-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methoxypropyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-cyanoethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate;

3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid;

2-chloro-5-(1-(2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

5-(1-benzyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(pyridin-4-ylmethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(pyridin-3-ylmethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyano-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxirane-2-ylmethyl)azetidine-3-carboxamide;

1-(3-amino-2-hydroxypropyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2,2,2-

trifluoroethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoroethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3,3-difluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,1-dioxidothietan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-dioxido-2-thiaspiro[3.3]heptan-6-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(trans-3-(methylsulfonyl)cyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(cis-3-(methylsulfonyl)cyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-(methylsulfonyl)butyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-

(methylsulfonyl)propyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-fluoroethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(cyanomethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxan-5-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-hydroxy-2-(hydroxymethyl)propyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

3-fluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-ylmethyl)azetidine-3-carboxamide;

oxetan-3-ylmethyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2,2-difluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-chloro-5-(1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

3-cyanopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-

hydroxypropyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3,3-difluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-2-methylpropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoic acid;

ethyl 2-(1-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutyl)acetate;

2-(1-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutyl)acetic acid;

ethyl 2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)oxetan-3-yl)acetate;

2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxetan-3-yl)acetic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-(cyanomethyl)oxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)-3,3,3-trifluoropropanoic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-(methylsulfonyl)ethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-(2-hydroxyethyl)oxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methoxypropan-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-cyclobutyl-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(trans-3-methoxycyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(cis-3-methoxycyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydrofuran-

3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydropyran-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,1-dioxidotetrahydrothiopyran-4-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-oxaspiro[3.3]heptan-6-yl)azetidine-3-carboxamide;

1'-acetyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-[1,3'-biazetidine]-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,3-dihydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanooxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-cyclobutyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(trans-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-oxaspiro[3.3]heptan-6-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl ((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2-hydroxyethyl)sulfamoyl)-3-(2-

isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2,3-dihydroxypropyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

tert-butyl ((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-methylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamide;

1-(N-acetylsulfamoyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(N-butyrylsulfamoyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-isobutyrylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-pentanoylsulfamoyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-hexanoylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-octanoylsulfamoyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-(2-methoxyacetyl)sulfamoyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-pentanoylsulfamoyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(1-(N-heptanoylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl (2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine)-1-sulfonamido)-2-oxoethyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-glycylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,3-dihydroxypropyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-propionylazetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-acetyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

5-(1-butyryl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-formyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(1-ethanethioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(methylsulfonyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

ethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

propyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxy-2,2-dimethyl-3-oxopropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid;

(2,2-dimethyl-1,3-dioxan-5-yl)methyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxy-2-(hydroxymethyl)propyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-cyanoethyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxy-2,2-dimethyl-3-oxopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid;

3-hydroxy-3-methylbutyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidine-1-carboxylate;

2-methoxyethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxypropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-hydroxy-2-methylpropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

O-methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbothioate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(3-hydroxypropyl)-6-oxo-1,6-

dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(1-(2-aminoethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-(2-methoxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-oxopyridazin-1(6H)-yl)acetate;

2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-oxopyridazin-1(6H)-yl)acetic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrothiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrothiazol-2-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-

carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-methyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(2-hydroxyethyl)-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(1-(4-ethyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-oxo-4-(2-oxopropyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

ethyl (3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonothioyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-2,5-dihydro-1,2,4-oxadiazol-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-

((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)pyrrolidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)pyrrolidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylpyrrolidine-3-carboxamide;

tert-butyl 4-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-4-(2-isopropylphenyl)piperidine-4-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-4-(2-isopropylphenyl)-1-sulfamoylpiperidine-4-carboxamide;

tert-butyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

2-chloro-5-(4-(2-isopropylphenyl)piperidine-4-carboxamido)-N-methylisonicotinamide; and

methyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

(Embodiment 315)

A compound selected from the group consisting of methyl 4-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

4-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylamino)nicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylamino)nicotinic acid;

methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(6-(methylsulfonyl)pyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-(methylsulfonyl)pyridin-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-sulfamoylpyridin-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylbenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylbenzoic acid;

methyl 3-chloro-4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

3-chloro-4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluorobenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluorobenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methoxybenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methoxybenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(trifluoromethyl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(trifluoromethyl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylsulfonyl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylsulfonyl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(difluoromethoxy)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(difluoromethoxy)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3,5-difluorobenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3,5-difluorobenzoic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-oxo-1,3-dihydroisobenzofuran-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(hydroxymethyl)benzoic acid;

ethyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

5-(1-(4-carbamoyl-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-cyanophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide;

5-(1-(4-carbamoylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinic acid;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(4-(1H-tetrazol-5-yl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

2-chloro-5-(1-(6-(hydroxymethyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylic acid;

methyl 4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-(2-isopropylphenyl)-3-((6-methoxy-2-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoate;

4-(3-(2-isopropylphenyl)-3-((6-methoxy-2-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoic acid;

methyl 6-(4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidin-1-yl)nicotinate;

6-(4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidin-1-yl)nicotinic acid;

2-chloro-5-(1-(3-ethoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-(trifluoromethoxy)propyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(difluoromethoxy)propyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3,3-difluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(trans-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-((3-(methoxymethyl)oxetan-3-yl)methyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(S)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-2-(1-hydroxycyclobutyl)ethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(2,5-dioxopyrrolidin-1-yl)-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-ethoxy-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-((3-hydroxytetrahydrofuran-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-4-methoxybutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(1,3-dimethoxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methoxybutan-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(methylamino)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylacetamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylmethylsulfonamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)ethyl)(methyl)carbamate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-((methylsulfonyl)carbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-((ethylsulfonyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(sulfamoylcarbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-((N,N-dimethylsulfamoyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl acetate;

(5-(3-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl propionate;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl methyl carbonate;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl L-valinate;

2-chloro-5-(1-(2-(hydroxymethyl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyrimidin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-methyl-1,1-dioxido-1,2,5-thiadiazolidine-2-carbonyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(6-methyl-1,1-dioxido-1,2,6-thiadiazinane-2-carbonyl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(N-methylsulfamoylcarbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(N,N-dimethylsulfamoyl)(methyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

6-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)nicotinamide;

5-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)picolinamide;

6-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)pyridazine-3-carboxamide;

2-chloro-5-(1-(3-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(diethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(dimethylphosphoryl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-hydroxypropylacetate;

(R)-1-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-hydroxypropan-2-yl acetate;

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propane-1,2-diyl diacetate;

2-chloro-5-(1-(5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-2-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-chloro-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-2-methylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-methylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-(dimethylphosphoryl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-(dimethylphosphoryl)pyridin-4-yl)carbamate;

5-(1-(4-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-(5-(dimethylphosphoryl)-4-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(3-amino-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

5-(1-(6-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoronicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxylate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxylic acid;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-(methylamino)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide; and

2-chloro-5-(1-(5-(dimethylphosphoryl)-6-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0052] Production method of compound (I)

One embodiment of the present invention provides a production method of the compound (I).

In one embodiment, the compound (I) can be produced according to a method including steps 1 to 6 as described in Production method 1 below.

In another embodiment, the compound (I) can be produced according to a method including steps 1 to 4 as described in Production method 2 below.

In still another embodiment, the compound (I) can be produced according to a method including steps 1 and 2 as described in Production method 3 below.

[0053] The compound (I) of the present invention or a synthetic intermediate thereof can be present in a form of a tautomer or a mixture thereof. The compound (I) of the present invention can be present in a form of a stereoisomer such as an enantiomer or a diastereomer or a mixture thereof. The compound (I) of the present invention includes a mixture of a tautomer or a stereoisomer or a pure or substantially pure isomer thereof.

[0054] In a case where the compound (I) of the present invention or a synthetic intermediate thereof is obtained in the form of a diastereomer or an enantiomer, this can be separated by a conventional method well known in the art, for example, chromatography or a fractional crystallization method.

[0055] The compound (I) of the present invention or a synthetic intermediate thereof includes a compound and a deuterated compound labeled with an isotope (for example, ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}F, ^{32}P, ^{35}S, ^{125}I, or the like).

[0056] Examples of a pharmaceutically acceptable salt of the compound (I) include alkali metal salts such as lithium, sodium, and potassium; group 2 metal salts such as magnesium and calcium; salts with aluminum or zinc; and salts with an amine such as ammonia, choline, diethanolamine, lysine, ethylenediamine, tert-butylamine, tert-octylamine, tris(hydroxymethyl)aminomethane, N-methyl-

glucosamine, triethanolamine, and dehydroabiethylamine; salts with an inorganic acid such as hydrogen chloride, hydrogen bromide, hydrogen iodide, sulfuric acid, nitric acid, and phosphoric acid; salts with an organic acid such as formic acid, acetic acid, trifluoroacetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, tartaric acid, citric acid, methanesulfonic acid, ethanesulfonic acid, and benzene sulfonic acid; or salts with an acidic amino acid such as aspartic acid and glutamic acid.

[0057] The synthetic intermediate of the compound (I) may be in a free form or a salt form. Examples of a salt of the synthetic intermediate of the compound (I) include the same salts as ones exemplified in the "pharmaceutically acceptable salt of the compound (I)" and pharmaceutically unacceptable salts.

[0058] Furthermore, the compound (I) or a pharmaceutically acceptable salt thereof, and the synthetic intermediate of the compound (I) or a salt thereof include intramolecular salts, hydrates, and solvates thereof.

[0059] In the present specification, "being pharmaceutically acceptable" generally means being harmless to recipients, means that ingredients are compatible with each other in the preparation of a pharmaceutical composition, and includes those useful not only for use as human medicines but also for veterinary use.

[0060] (Applications)

The compound (I) of the present invention as defined by each of the above-described embodiments and combinations thereof, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof are all useful as an active ingredient of a pharmaceutical composition, and even a compound as defined by any of the embodiments and a combination thereof or a pharmaceutically acceptable salt thereof can be administered to a subject (preferably a human).

[0061] The compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof can be administered alone or as a pharmaceutical composition containing the compound (I) or the like and a pharmaceutically acceptable carrier orally or parenterally. Preferably, a pharmaceutical composition of the present invention contains the compound (I) of the

present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. The pharmaceutically acceptable carrier may be a conventional carrier in the art, and examples thereof include diluents, binders (syrup, gum Arabic, gelatin, sorbitol, tragacanth, polyvinylpyrrolidone, and the like), excipients (lactose, sucrose, corn starch, potassium phosphate, sorbitol, glycine, and the like.), lubricants (magnesium stearate, talc, polyethylene glycol, silica, and the like), disintegrating agents (potato starch and the like), wetting agents (sodium lauryl sulfate and the like), and the like. In addition, the dosage form of the pharmaceutical composition is not particularly limited, but the pharmaceutical composition can be used as conventional pharmaceutical preparations such as tablets, granules, capsules, powders, injections, inhalations, or suppositories.

[0062] The dosage (that is, the effective amount) of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof may differ depending on the administration method and the age, body weight, and conditions of patients, but is, commonly, preferably set to 0.001 to 500 mg/kg, particularly, 0.01 to 10 mg/kg per day, and the compound (I) or the like is administered once or twice to four times per day.

[0063] The compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof has LPA receptor antagonism and is effective for the prevention, amelioration, and/or treatment of diseases of which symptoms are ameliorated by antagonizing LPA receptors. Examples of such diseases include pain (for example, chronic pain such as neuropathic pain (for example, diabetic neuropathy, chemotherapeutic peripheral neuropathy, postherpetic neuralgia, or the like), nociceptive pain (for example, rheumatoid arthritis or the like), and central dysfunction pain (for example, fibromyalgia, spinal cord injury, and the like); and acute pain such as nociceptive pain (for example, traumatic pain, postoperative pain, and the like)); fibrosis (for example, pulmonary fibrosis (for example, idiopathic pulmonary fibrosis or the like), liver fibrosis (for example, nonalcoholic steatohepatic liver disease or the like), renal fibrosis, heart fibrosis, vascular fibrosis, skin fibrosis, pancreatic fibrosis, myelofibrosis, skeletal muscle fibrosis, and the like), autoimmune diseases (for example, rheumatoid arthritis, multiple sclerosis, Guillain-Barre syndrome, and the like), and the like.

In addition, the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof may exhibit LPA receptor antagonism by being metabolized in a living organism and converted to a different form of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof. That is, the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof may be a therapeutic prodrug of preventive, palliative, and/or therapeutic agents of diseases of which symptoms are ameliorated by antagonizing LPA receptors.

[0064] One embodiment of the present invention relates to a pharmaceutical composition containing the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. In one embodiment, the pharmaceutical composition is used in the prevention, amelioration, and/or treatment of diseases of which symptoms are ameliorated by antagonizing LPA receptors. In another embodiment, the pharmaceutical composition is used for the prevention, amelioration, and/or treatment of pain (for example, chronic pain such as neuropathic pain (for example, diabetic neuropathy, chemotherapeutic peripheral neuropathy, postherpetic neuralgia, or the like), nociceptive pain (for example, rheumatoid arthritis or the like), and central dysfunction pain (for example, fibromyalgia, spinal cord injury, and the like); and acute pain such as nociceptive pain (for example, traumatic pain, postoperative pain, and the like)). In another embodiment, the pharmaceutical composition is used for the prevention, amelioration, and/or treatment of fibrosis (for example, pulmonary fibrosis (for example, idiopathic pulmonary fibrosis or the like), liver fibrosis (for example, nonalcoholic steatohepatic liver disease or the like), renal fibrosis, heart fibrosis, vascular fibrosis, skin fibrosis, pancreatic fibrosis, myelofibrosis, skeletal muscle fibrosis, and the like). In still another embodiment, the pharmaceutical composition is used for the prevention, amelioration, and/or treatment of autoimmune diseases (for example, rheumatoid arthritis, multiple sclerosis, Guillain-Barre syndrome, and the like).

[0065] One embodiment of the present invention relates to the use of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof in the

manufacture of a medicine. In one embodiment, the medicine is used for the prevention, amelioration and/or treatment of diseases of which symptoms are ameliorated by antagonizing LPA receptors. In another embodiment, the medicine is used for the prevention, amelioration, and/or treatment of pain (for example, chronic pain such as neuropathic pain (for example, diabetic neuropathy, chemotherapeutic peripheral neuropathy, postherpetic neuralgia, or the like), nociceptive pain (for example, rheumatoid arthritis or the like), and central dysfunction pain (for example, fibromyalgia, spinal cord injury, and the like); and acute pain such as nociceptive pain (for example, traumatic pain, postoperative pain, and the like)). In another embodiment, embodiment, the medicine is used for the prevention, amelioration, and/or treatment of fibrosis (for example, pulmonary fibrosis (for example, idiopathic pulmonary fibrosis or the like), liver fibrosis (for example, nonalcoholic steatohepatic liver disease or the like), renal fibrosis, heart fibrosis, vascular fibrosis, skin fibrosis, pancreatic fibrosis, myelofibrosis, skeletal muscle fibrosis, and the like). In still another embodiment, the medicine is used for the prevention, amelioration, and/or treatment of autoimmune diseases (for example, rheumatoid arthritis, multiple sclerosis, Guillain-Barre syndrome, and the like).

[0066] One embodiment of the present invention relates to the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof for the prevention, amelioration and/or treatment of diseases. One embodiment of the present invention relates to the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof for the prevention, amelioration and/or treatment of diseases of which symptoms are ameliorated by antagonizing LPA receptors. Another embodiment of the present invention relates to the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof for the prevention, amelioration, and/or treatment of pain (for example, chronic pain such as neuropathic pain (for example, diabetic neuropathy, chemotherapeutic peripheral neuropathy, postherpetic neuralgia, or the like), nociceptive pain (for example, rheumatoid arthritis or the like), and central dysfunction pain (for example, fibromyalgia, spinal cord injury, and the like); and acute pain such as nociceptive pain (for example, traumatic pain, postoperative pain, and the like)).

Another embodiment of the present invention relates to the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof for the prevention, amelioration, and/or treatment of fibrosis (for example, pulmonary fibrosis (for example, idiopathic pulmonary fibrosis or the like), liver fibrosis (for example, nonalcoholic steatohepatic liver disease or the like), renal fibrosis, heart fibrosis, vascular fibrosis, skin fibrosis, pancreatic fibrosis, myelofibrosis, skeletal muscle fibrosis, and the like). Still another embodiment of the present invention relates to the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof for the prevention, amelioration, and/or treatment of autoimmune diseases (for example, rheumatoid arthritis, multiple sclerosis, Guillain-Barre syndrome, and the like).

[0067] One embodiment of the present invention relates to a method for the prevention, amelioration and/or treatment of diseases of which symptoms are ameliorated by antagonizing LPA receptors, the method including administration of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof. Another embodiment of the present invention relates to a method for the prevention, amelioration and/or treatment of pain (for example, chronic pain such as neuropathic pain (for example, diabetic neuropathy, chemotherapeutic peripheral neuropathy, postherpetic neuralgia, or the like), nociceptive pain (for example, rheumatoid arthritis or the like), and central dysfunction pain (for example, fibromyalgia, spinal cord injury, and the like); and acute pain such as nociceptive pain (for example, traumatic pain, postoperative pain, and the like)), the method including administration of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof. Another embodiment of the present invention relates to a method for the prevention, amelioration and/or treatment of fibrosis (for example, pulmonary fibrosis (for example, idiopathic pulmonary fibrosis or the like), liver fibrosis (for example, nonalcoholic steatohepatic liver disease or the like), renal fibrosis, heart fibrosis, vascular fibrosis, skin fibrosis, pancreatic fibrosis, myelofibrosis, skeletal muscle fibrosis, and the like), the method including administration of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof. Still another embodiment of the present invention relates to a

method for the prevention, amelioration and/or treatment of autoimmune diseases (for example, rheumatoid arthritis, multiple sclerosis, Guillain-Barre syndrome, and the like), the method including administration of the compound (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

[0068] The compound (I), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof can be produced by the following method, but the method is not limited thereto. In addition, each step in the following production method may be carried out in an appropriate combination.

[0069] The compound (I), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof can be produced by the following method, but the method is not limited thereto. In addition, each step in the following production method may be carried out in an appropriate combination.

[0070] In a case where protection of a functional group contained in the compound is required in each production step of the compound (I) to be described below, the compound (I) can be appropriately protected by a method to be specifically described below or a conventional method. Regarding a general description of a protective group and the use thereof, "Protective Groups in Organic Synthesis", John Wiley & Sons, New York, Fifth Edition by T.W. Greene, et al., is referred to. The protective group can be removed in a subsequent step using a method to be specifically described below or a conventional method. In addition, a carboxylic acid compound or a salt thereof and an amine compound or a salt thereof can be each converted into each other by a method to be specifically described below or a conventional salt formation treatment or desalination treatment.

[0071] The compound (I), a deuterated compound thereof, or a pharmaceutically acceptable salt thereof can be produced by the following method, but the method is not limited thereto. In addition, each step in the following production method may be carried out in an appropriate combination.

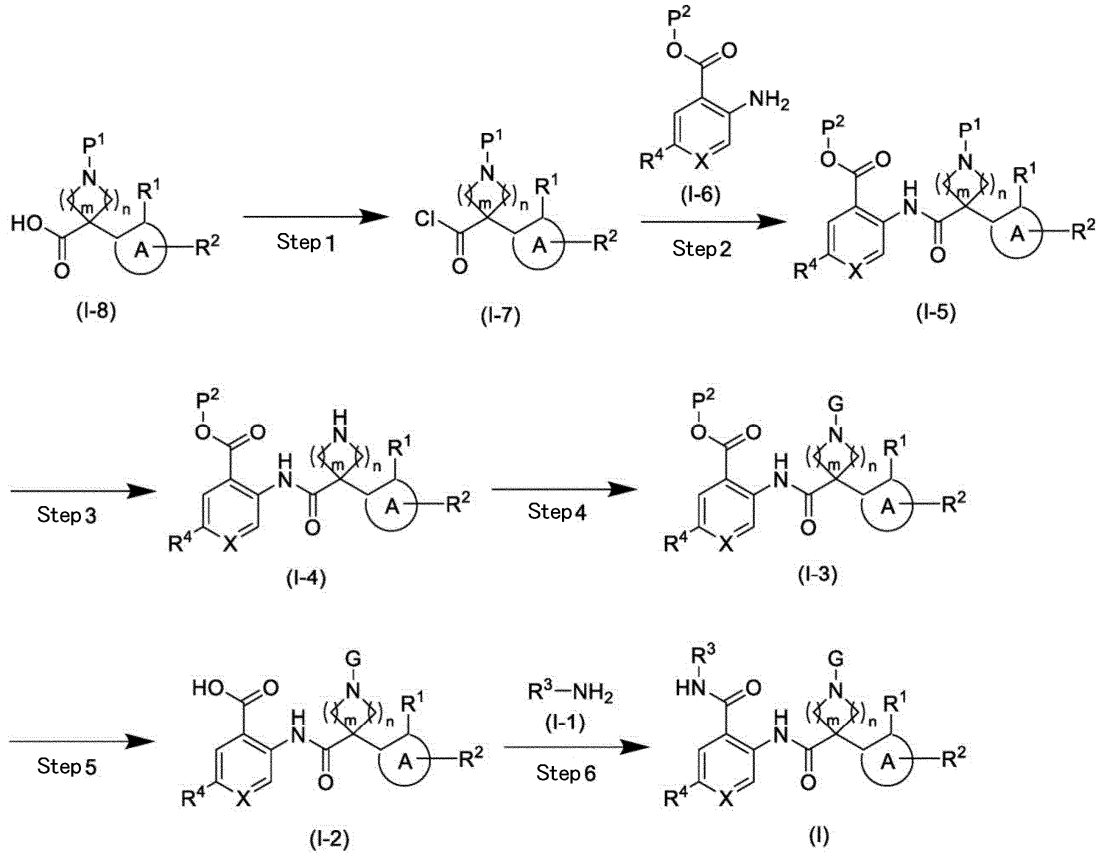
[0072] In a case where protection of a functional group contained in the compound is required in each production step of the compound (I) to be described below, the compound (I) can be appropriately protected by a method to be specifically described below or a conventional method. Regarding a general description of a protective group and the use thereof, "Protective Groups in Organic Synthesis", John

Wiley & Sons, New York, Fifth Edition by T.W. Greene, et al., is referred to. The protective group can be removed in a subsequent step using a method to be specifically described below or a conventional method. In addition, a carboxylic acid compound or a salt thereof and an amine compound or a salt thereof can be each converted into each other by a method to be specifically described below or a conventional salt formation treatment or desalination treatment.

[0073] Production method 1

The compound (I) can be produced according to, for example, the following scheme.

[C49]



[Wherein P^1 means a protective group such as a tert-butoxycarbonyl group; P^2 means an alkyl group such as a methyl group; and other symbols have the same meanings as described above.]

[0074] Step 1

A compound (I-8) is reacted with an acid chlorination agent in the presence of N,N-dimethylformamide in a solvent in the presence or absence of a base, whereby a compound (I-7) can be

produced.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran and 1,4-dioxane; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; aromatic hydrocarbons such as toluene; mixtures of two or more thereof, and the like.

Examples of the base include pyridines such as pyridine; alkyl amines such as triethylamine and N,N-diisopropylethylamine; and the like.

Examples of the acid chlorination agent include oxalyl chloride, thionyl chloride, phosphorus oxychloride, phosphorus trichloride, and the like.

[0075] The amount of N,N-dimethylformamide used can be set to 0.01 to 1.0 equivalents, preferably 0.05 to 0.2 equivalents, of the compound (I-8) in terms of molar ratio.

The amount of the base used can be 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8) in terms of molar ratio.

The amount of acid chlorination agent used may be from 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice bath to at 100°C, preferably in an ice bath to at room temperature.

[0076] Step 2

The compound (I-7) is reacted with a compound (I-6) in the presence of a base in a solvent, whereby a compound (I-5) can be produced. As the compound (I-6), a commercially available material may be used, or the compound (I-6) may be produced from a commercially available material by a known method.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran and 1,4-dioxane; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; aromatic hydrocarbons such as toluene; mixtures of two or more thereof, and the like.

Examples of the base include pyridines such as pyridine; alkyl amines such as triethylamine and N,N-diisopropylethylamine; and the like.

[0077] The amount of the compound (I-7) used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-6) in terms of molar ratio.

The amount of the base used can set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-6) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice bath to at 100°C, preferably at room temperature to 80°C.

[0078] Step 3

A compound (I-4) can be produced by reacting the compound (I-5) in the presence of an acid in a solvent. The compound (I-4) may be a free body or in a salt form such as a hydrochloride salt.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran, 1,4-dioxane, and cyclopentyl methyl ether; alcohols such as methanol, ethanol and isopropanol; halogenated aliphatic hydrocarbons such as chloroform and dichloromethane; aromatic hydrocarbons such as toluene; esters such as ethyl acetate; nitriles such as acetonitrile; mixtures of two or more thereof, and the like.

Examples of the acid include hydrogen chloride and the like.

[0079] The amount of the acid used can be set to 1.0 to 100.0 equivalents, preferably 1.0 to 50.0 equivalents, of the compound (I-5) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice bath to at 100°C, preferably at room temperature.

[0080] Step 4

A compound (I-3) can be produced from the compound (I-4) by combining known reactions.

[0081] Step 5

A compound (I-2) can be produced by reacting the compound (I-3) in the presence of a base in a solvent.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; alcohols such as methanol, ethanol and isopropanol; aromatic hydrocarbons such as toluene; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; nitriles such as acetonitrile; dimethyl sulfoxide; water; mixtures of two or more thereof, and the like.

Examples of the base include alkali metal hydroxides such as sodium hydroxide and lithium hydroxide.

[0082] The amount of the base used can be set to 1.0 to 10.0 equivalents, preferably 1.0 to 5.0 equivalents, of the compound (I-3) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice bath to at 100°C, preferably at room temperature to 50°C.

[0083] Step 6

A compound (I) can be produced by reacting the compound (I-2) in the presence of a base and a condensing agent in a solvent with the compound (I-1). As the compound (I-1), a commercially available material may be used, or the compound (I-1) may be produced from a commercially available material by a known method. The compound (I-1) may be a free body or in a salt form such as a hydrochloride salt.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; aromatic hydrocarbons such as toluene; nitriles such as acetonitrile; mixtures of two or more thereof, and the like.

Examples of the base include alkali metal carbonates such as cesium carbonate, potassium carbonate, sodium carbonate, and sodium bicarbonate; alkali metal phosphates such as tripotassium phosphate, sodium phosphate, and sodium hydrogenphosphate; alkali metal fluorides such as cesium fluoride and potassium fluoride; alkyl amines such as triethylamine and N,N-diisopropylethylamine; pyridines such as pyridine and 4-dimethylaminopyridine; 1,8-diazabicyclo[5.4.0]-7-undecene, and the

like.

Examples of the condensing agent include 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC·HCl), O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU), 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM), and the like.

[0084] The amount of the compound (I-1) used can be set to 1.0 to 10.0 equivalents, preferably 1.0 to 5.0 equivalents, of the compound (I-2) in terms of molar ratio.

The amount of the base used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-2) in terms of molar ratio.

The amount of the condensing agent used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-2) in terms of molar ratio.

The present reaction can be carried out at room temperature to under heating, for example, at room temperature to 100°C, preferably at room temperature.

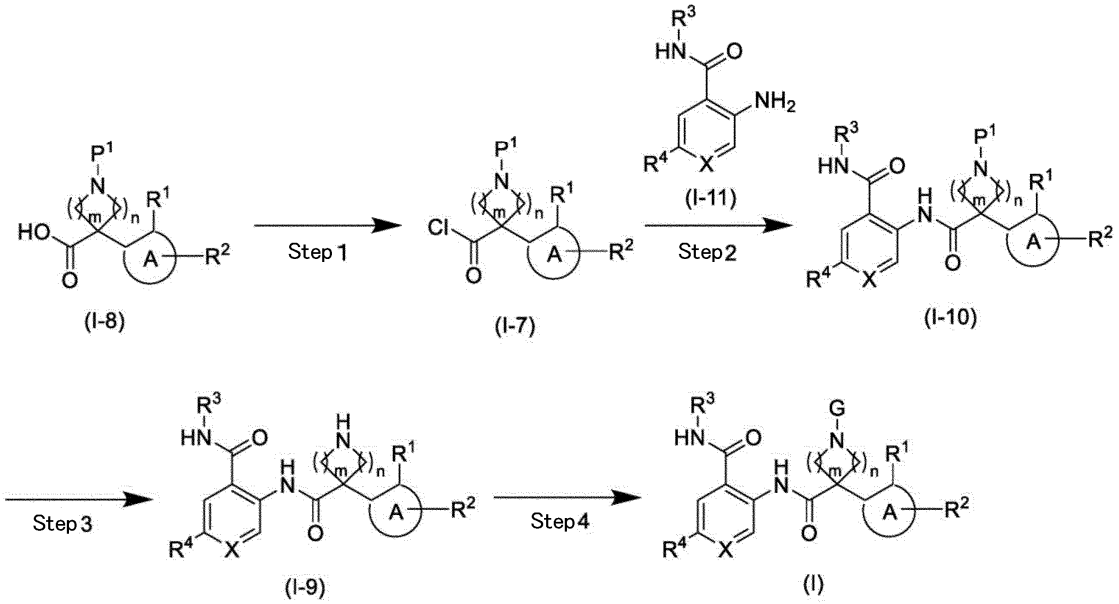
In a case where a protective group is present in the compound (I), the compound (I) can be subjected to a deprotection step if necessary.

A compound that is contained in a different form of the compound (I) can be produced from a compound that is contained in the compound (I) using a known method.

[0085] Production method 2

The compound (I) can also be produced according to, for example, the following scheme.

[C50]



[Wherein symbols have the same meanings as described above.]

[0086] A step 1 can be carried out by the same method for the step 1 of the production method 1.

[0087] A step 2 can be carried out by the same method for the step 2 of the production method 1 using a compound (I-11) instead of the compound (I-6).

[0088] A step 3 can be carried out by the same method for the step 3 of the production method 1 using a compound (I-10) instead of the compound (I-5).

[0089] A step 4 can be carried out by the same method for the step 4 of the production method 1 using a compound (I-9) instead of the compound (I-4).

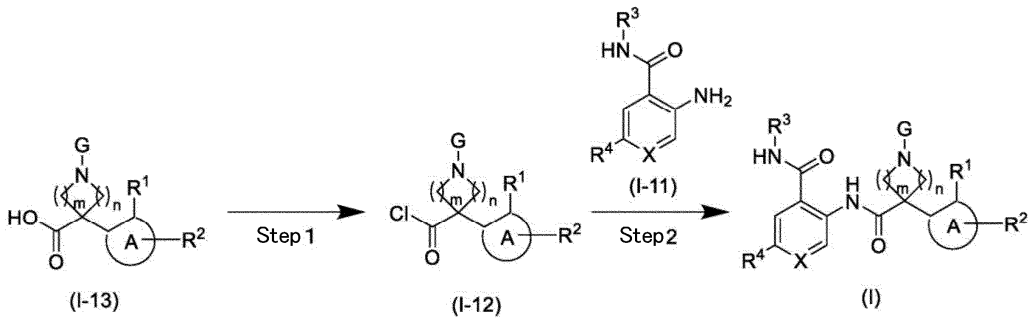
In a case where a protective group is present in the compound (I), the compound (I) can be subjected to a deprotection step if necessary.

A compound that is contained in a different form of the compound (I) can be produced from a compound that is contained in the compound (I) using a known method known.

[0090] Production method 3

The compound (I) can also be produced according to, for example, the following scheme.

[C51]



[Wherein symbols have the same meanings as described above.]

[0091] A step 1 can be carried out by the same method for the step 1 of the production method 1 using a compound (I-13) instead of the compound (I-8).

[0092] A step 2 can be carried out by the same method for the step 2 of the production method 2 using a compound (I-12) instead of the compound (I-7).

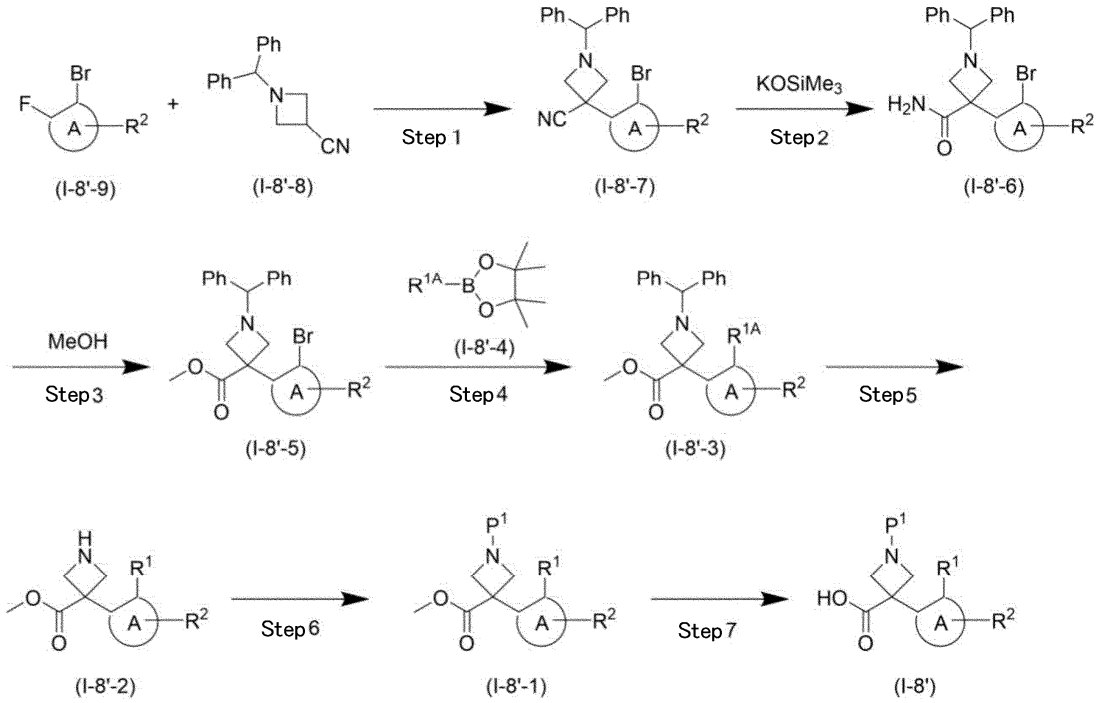
In a case where a protective group is present in the compound (I), the compound (I) can be subjected to a deprotection step if necessary.

A compound that is contained in a different form of the compound (I) can be produced from a compound that is contained in the compound (I) using a known method known.

[0093] Reference production method 1

As the compound (I-8), a compound (I-8') in which m is 1 and n is 1 can be produced according to, for example, the following scheme.

[C52]



[Wherein R^{1A} means a C_1-C_6 alkyl group, a C_3-C_6 cycloalkyl group, a C_2-C_6 alkenyl group, or a C_5-C_6 cycloalkenyl group, Ph means a phenyl group; and other symbols have the same meanings as described above.]

[0094] Step 1

A compound (I-8'-8) and a compound (I-8'-9) are reacted with a metal amide in a solvent, whereby a compound (I-8'-7) can be produced.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; aromatic hydrocarbons such as toluene; mixtures of two or more thereof, and the like.

Examples of the metal amide include potassium bis(trimethylsilyl) amide and the like.

[0095] The amount of the compound (I-8'-9) used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8’-8) in terms of molar ratio.

The amount of the metal amide used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8’-8) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice

bath to at 100°C, preferably in an ice bath to at room temperature.

[0096] Step 2

A compound (I-8'-7) is reacted with potassium trimethylsilanolate in a solvent, whereby a compound (I-8'-6) can be produced.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; aromatic hydrocarbons such as toluene; mixtures of two or more thereof, and the like.

[0097] The amount of potassium trimethylsilanolate used can be set to 1.0 to 10.0 equivalents, preferably 1.0 to 5.0 equivalents, of the compound (I-8'-7) in terms of molar ratio.

The reaction can be carried out at room temperature to under heating, for example, at room temperature to 200°C, preferably at room temperature to 150°C.

[0098] Step 3

A compound (I-8'-6) is reacted with methanol in a methanol solvent in the presence of an acid, whereby a compound (I-8'-5) can be produced.

Examples of the acid include sulfuric acid and the like.

[0099] The amount of the acid used can be set to 1.0 to 20.0 equivalents, preferably 1.0 to 10.0 equivalents, of the compound (I-8'-6) in terms of molar ratio.

The reaction can be carried out at room temperature to under heating, for example, at room temperature to 100°C, preferably at room temperature to 75°C.

[0100] Step 4

A step 4 is a so-called Suzuki reaction, and a compound (I-8'-5) is reacted with a compound (I-8'-4) in the presence of a base and a catalyst in a solvent, whereby a compound (I-8'-3) can be produced. As the compounds (I-8'-4), a commercially available material may be used, or the compound (I-8'-4) may be produced from a commercially available material by a known method.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-

dioxane; alcohols such as methanol, ethanol and isopropanol; aromatic hydrocarbons such as toluene; nitriles such as acetonitrile; dimethyl sulfoxide; water; mixtures of two or more thereof, and the like.

Examples of the base include, for example, alkali metal carbonates such as cesium carbonate, potassium carbonate, sodium carbonate, and sodium bicarbonate; alkali metal phosphates such as tripotassium phosphate, sodium phosphate, and sodium hydrogenphosphate; alkali metal fluorides such as cesium fluoride and potassium fluoride; alkyl amines such as triethylamine, N,N-diisopropylethylamine, and N,N-dicyclohexylmethylamine; pyridines such as pyridine and 4-dimethylaminopyridine; 1,8-diazabicyclo[5.4.0]-7-undecene, and the like.

Examples of the catalyst include palladium catalysts such as bis(di-tert-butyl(4-dimethylaminophenyl)phosphine) dichloropalladium (II).

[0101] The amount of (I-8'-4) used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8'-5) in terms of molar ratio.

The amount of the base used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8'-5) in terms of molar ratio.

The amount of the catalyst used can be set to 0.001 to 1.0 equivalents, preferably 0.01 to 0.2 equivalents, of the compound (I-8'-5) in terms of molar ratio.

The reaction can be carried out at room temperature to under heating, for example, at room temperature to 200°C, preferably at room temperature to 150°C.

[0102] Step 5

A compound (I-8'-2) can be produced by reacting the compound (I-8'-3) in the presence of hydrogen gas and a metal catalyst in a solvent.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran and 1,4-dioxane; alcohols such as methanol, ethanol and isopropanol; aromatic hydrocarbons such as toluene; carboxylic acids such as formic acid and acetic acid; water; mixtures of two or more thereof, and the like.

Examples of the metal catalyst include palladium on carbon and the like.

[0103] The amount of the metal catalyst used can be set to 0.01 to 5.0 equivalents, preferably 0.05 to 1.0 equivalents, of the compound (I-8'-3) in terms of weight ratio.

The present reaction can be carried out at room temperature to under heating, for example, at room temperature to 100°C, preferably at room temperature.

[0104] Step 6

A compound (I-8'-1) can be produced by introducing a protective group P^1 into the compound (I-8'-2).

Regarding conditions for introducing the protective group, the protective group can be introduced as appropriate in accordance with the prior art, for example, the above-description of "Protective Groups in Organic Synthesis", John Wiley & Sons, New York, Fifth Edition by T.W. Greene, et al., or reference examples in the present specification.

[0105] Step 7

A compound (I-8') can be produced by reacting the compound (I-8'-1) in the presence of a base in a solvent.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; alcohols such as methanol, ethanol and isopropanol; aromatic hydrocarbons such as toluene; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; nitriles such as acetonitrile; dimethyl sulfoxide; water; mixtures of two or more thereof, and the like.

Examples of the base include alkali metal hydroxides such as sodium hydroxide and lithium hydroxide.

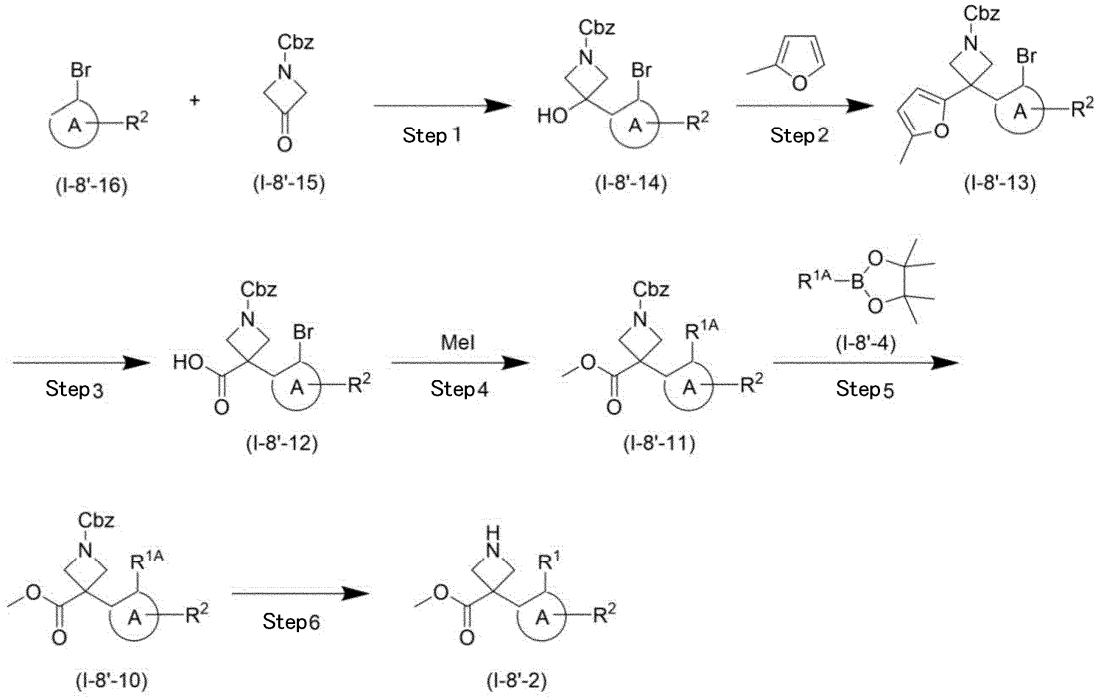
[0106] The amount of the base used can be set to 1.0 to 10.0 equivalents, preferably 1.0 to 5.0 equivalents, of the compound (I-8’-1) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice bath to at 100°C, preferably at room temperature to 50°C.

[0107] Reference production method 2

The compound (I-8’-2) can also be produced according to, for example, the following scheme.

[C53]



[Wherein Cbz means a benzyloxycarbonyl group; and other symbols have the same meanings as described above.]

[0108] Step 1

A compound (I-8'-15) and a compound (I-8'-16) are reacted with a metal amide in a solvent, whereby a compound (I-8'-14) can be produced.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran and 1,4-dioxane; aromatic hydrocarbons such as toluene; mixtures of two or more thereof, and the like.

Examples of the metal amide include lithium diisopropylamide and the like.

[0109] The amount of the compound (I-8'-16) used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8’-15) in terms of molar ratio.

The amount of the metal amide used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8’-16) in terms of molar ratio.

The reaction can be carried out at -100°C to room temperature, preferably -80°C to 0°C.

[0110] Step 2

In a step 2, the compound (I-8'-14) is reacted with 2-methylfuran in the presence of a catalyst and an additive in a solvent, whereby a compound (I-8'-13) can be produced.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran and 1,4-dioxane; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; aromatic hydrocarbons such as toluene; mixtures of two or more thereof, and the like.

Examples of the catalyst include bis(trifluoromethanesulfonyl)imide calcium (II) and the like.

Examples of the additive include tetrabutylammonium hexafluorophosphate and the like.

[0111] The amount of 2-methylfuran used can be set to 1.0 to 10.0 equivalents, preferably 1.0 to 5.0 equivalents, of the compound (I-8'-14) in terms of molar ratio.

The amount of the catalyst used can be set to 0.001 to 1.0 equivalents, preferably 0.01 to 0.2 equivalents, of the compound (I-8'-14) in terms of molar ratio.

The amount of the additive used can be set to 0.001 to 1.0 equivalents, preferably 0.01 to 0.2 equivalents, of the compound (I-8'-14) in terms of molar ratio.

The reaction can be carried out at room temperature to under heating, for example, at room temperature to 100°C, preferably at room temperature to 60°C.

[0112] Step 3

A compound (I-8'-12) can be produced by reacting the compound (I-8'-13) in the presence of a catalyst and an oxidant.

The solvent needs to not affect the present reaction, and examples thereof include ethers such as tetrahydrofuran and 1,4-dioxane; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; aromatic hydrocarbons such as toluene; esters such as ethyl acetate; aliphatic hydrocarbons such as hexane and heptane; water; mixtures of two or more thereof, and the like.

Examples of the catalyst include ruthenium (III) chloride and the like.

Examples of the oxidant include sodium periodate.

[0113] The amount of the catalyst used can be set to 0.001 to 1.0 equivalents, preferably 0.01 to 0.2 equivalents, of the compound (I-8'-13) in terms of molar ratio.

The amount of the oxidant used can be set to 1.0 and 20.0 equivalents, preferably 1.0 and 10.0 equivalents, of the compound (I-8'-13) in terms of molar ratio.

The present reaction can be carried out in an ice bath to under heating, for example, in an ice bath to at 100°C, preferably in an ice bath to at room temperature.

[0114] Step 4

In a step 4, the compound (I-8'-12) is reacted with iodomethane in the presence of a base in a solvent, whereby a compounds (I-8'-11) can be produced.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; nitriles such as acetonitrile, mixtures of two or more thereof, and the like.

Examples of the base include alkali metal carbonates such as cesium carbonate, potassium carbonate, sodium carbonate, and sodium bicarbonate.

[0115] The amount of iodomethane used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8'-12) in terms of molar ratio.

The amount of the base used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8'-12) in terms of molar ratio.

The reaction can be carried out in an ice bath to under heating, for example at room temperature to 100°C, preferably at room temperature to 50°C.

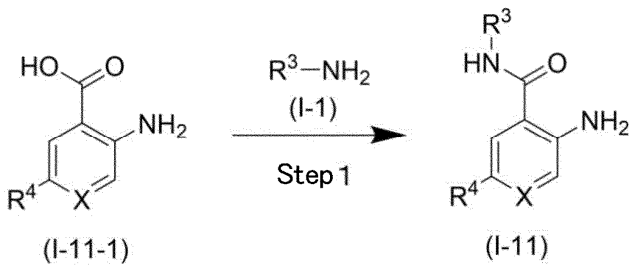
[0116] A step 5 can be carried out by the same method as for the step 4 of the reference production method 1 using the compound (I-8'-11) instead of the compound (I-8'-5).

[0117] A step 6 can be carried out by the same method as for the step 5 of the reference production method 1 using the compound (I-8'-10) instead of the compound (I-8'-3).

[0118] Reference production method 3

A compound (I-11) can be produced according to, for example, the following scheme.

[C54]



[Wherein symbols have the same meanings as described above.]

[0119] Step 1

A compound (I-11-1) is reacted with a compound (I-1) in the presence of a base and a condensing agent in a solvent, whereby a compound (I-11) can be produced. As the compounds (I-1), a commercially available material may be used, or the compound (I-1) may be produced from a commercially available material by a known method. The compound (I-1) may be a free body or in a salt form such as a hydrochloride salt.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; halogenated aliphatic hydrocarbons such as chloroform, dichloromethane, and dichloroethane; aromatic hydrocarbons such as toluene; nitriles such as acetonitrile; mixtures of two or more thereof, and the like.

Examples of the base include alkali metal carbonates such as cesium carbonate, potassium carbonate, sodium carbonate, and sodium bicarbonate; alkali metal phosphates such as tripotassium phosphate, sodium phosphate, and sodium hydrogenphosphate; alkali metal fluorides such as cesium fluoride and potassium fluoride; alkyl amines such as triethylamine and N,N-diisopropylethylamine; pyridines such as pyridine and 4-dimethylaminopyridine; 1,8-diazabicyclo[5.4.0]-7-undecene, and the like.

Examples of the condensing agent include 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide

hydrochloride (EDC·HCl), O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU), 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM), and the like.

[0120] The amount of the compound (I-1) used can be set to 1.0 to 10.0 equivalents, preferably 1.0 to 5.0 equivalents, of the compound (I-11-1) in terms of molar ratio.

The amount of the base used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-11-1) in terms of molar ratio.

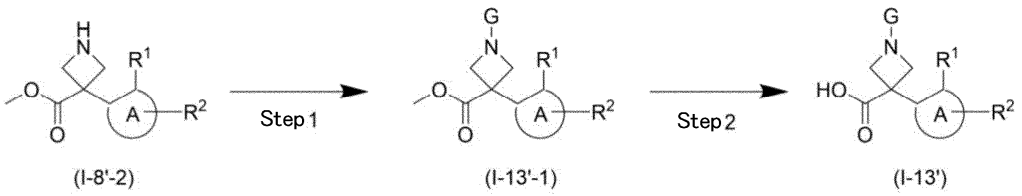
The amount of the condensing agent used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-11-1) in terms of molar ratio.

The present reaction can be carried out at room temperature to under heating, for example, at room temperature to 100°C, preferably at room temperature.

[0121] Reference synthesis method 4

As the compound (I-13), a compound (I-13') in which m is 1 and n is 1 can be produced according to, for example, the following scheme.

[C55]



(I-8'-2) (I-13'-1) (I-13')

[Wherein symbols have the same meanings as described above.]

[0122] Step 1

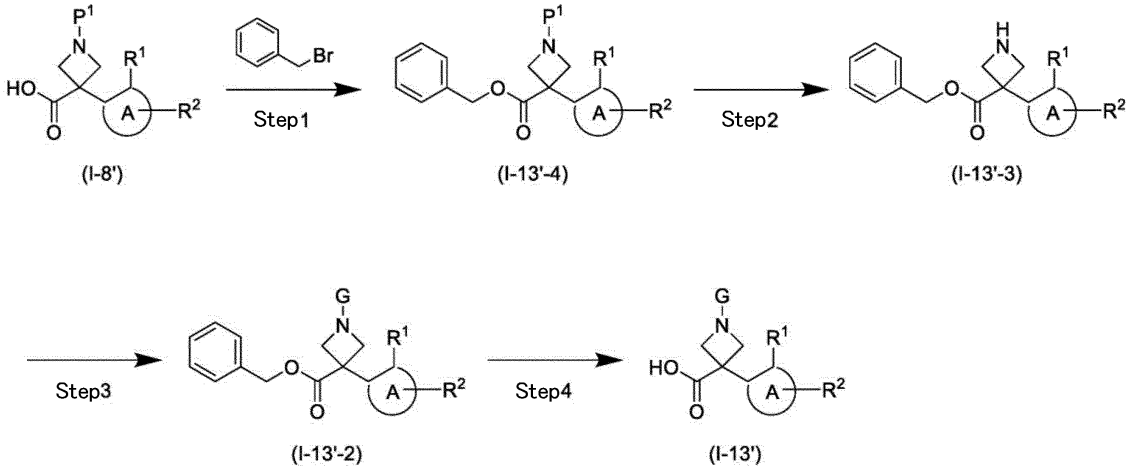
A compound (I-13'-1) can be produced from the compound (I-8'-2) by combining known reactions.

[0123] A step 2 can be carried out by the same method as for the step 7 of the reference production method 1 using the compound (I-13'-1) instead of the compound (I-8'-1).

[0124] Reference synthesis method 5

The compound (I-13') can also be produced according to, for example, the following scheme.

[C56]



[Wherein symbols have the same meanings as described above.]

[0125] Step 1

A compound (I-8') is reacted with benzyl bromide in the presence of a base in a solvent, whereby a compound (I-13'-4) can be produced.

The solvent needs to not affect the present reaction, and examples thereof include amides such as N-methyl-2-pyrrolidinone and N,N-dimethylformamide; ethers such as tetrahydrofuran and 1,4-dioxane; nitriles such as acetonitrile, mixtures of two or more thereof, and the like.

Examples of the base include alkali metal carbonates such as cesium carbonate, potassium carbonate, sodium carbonate, and sodium bicarbonate.

[0126] The amount of benzyl bromide used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8') in terms of molar ratio.

The amount of the base used can be set to 1.0 to 5.0 equivalents, preferably 1.0 to 3.0 equivalents, of the compound (I-8') in terms of molar ratio.

The reaction can be carried out in an ice bath to under heating, for example, at room temperature to 100°C, preferably at room temperature to 50°C.

[0127] A step 2 can be carried out by the same method as for the step 3 of the production method 1 using the compound (I-13'-4) instead of the compound (I-5).

[0128] Step 3

A compounds (I-13'-2) can be produced from a compound (I-13'-3) by combining known reactions.

[0129] A step 4 can be carried out by the same method as for the step 5 of the reference production method 1 using the compound (I-13'-2) instead of the compound (I-8'-3).

[0130] Examples of the known reactions include the following reactions.

(1) Conversion of amino group to sulfamide group

A compound having an amino group is reacted with sulfamide in the presence of a base (for example, triethylamine or the like) in a solvent (for example, 1,4-dioxane), whereby a compound having a corresponding sulfamide group can be produced.

(2) Conversion of amino group to amido group

A compound having an amino group is reacted with a carboxylic acid (for example, hydroxyacetic acid or the like) in the presence of a base (for example, N,N-diisopropylethylamine or the like) and a condensing agent (for example, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU), or the like) in a solvent (for example, N,N-dimethylformamide or the like), whereby a compound having a corresponding amide group can be produced.

Alternatively, a compound having an amino group is reacted with a carboxylic anhydride (for example propionic anhydride or the like) in the presence or absence of a base (for example, N,N-diisopropylethylamine, triethylamine, and the like) and 4-dimethylaminopyridine in a solvent (for example, acetonitrile, dichloromethane, and the like), whereby a compound having a corresponding amide group can be produced.

(3) Conversion of amino group to urea group

A compound having an amino group is reacted with an isocyanate (for example, trimethylsilyl isocyanate or the like) in the presence of a base (for example, N,N-diisopropylethylamine or the like) in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding urea group can be produced.

(4) Conversion of amino group to thiourea group

A compound having an amino group is reacted with thioisocyanate (for example, methyl isothiocyanate or the like) in a solvent (for example, acetonitrile, dichloromethane, and the like), whereby a compound having a corresponding thiourea group can be produced.

Alternatively, a compound having an amino group is reacted with 1,1'-thiocarbonyldiimidazole in a solvent (for example, tetrahydrofuran or the like) and then reacted with an alkylamine (for example, 2-hydroxyethylamine or the like) in a solvent (for example, tetrahydrofuran or the like), whereby a compound having a corresponding thiourea group can be produced.

(5) Conversion of amino group to cyanoguanidine group

A compound having an amino group is reacted with diphenyl N-cyanocarbonimidate in the presence of a base (for example, N,N-diisopropylethylamine or the like) in a solvent (for example, dichloromethane or the like) and then reacted with an amine (for example, ammonia or the like) in a solvent (for example, methanol or the like), whereby a compound having a corresponding cyanoguanidine group can be produced.

(6) Alkylation to amino group

A compound having an amino group is reacted with an alkyl halide (for example, methyl 3-bromopropionate or the like), an alkyl triflate (fluoropropyl triflate or the like), or an alkyl tosylate (3-(methylsulfonyl)propyl tosylate or the like) in the presence of a base (for example, potassium carbonate, N,N-diisopropylethylamine, and the like) in a solvent (for example, N,N-dimethylformamide, acetonitrile, and the like), whereby a corresponding compound having an alkylated amino group can be produced.

Alternatively, a compound having an amino group is reacted with a ketone (for example, 3-oxetanone or the like) or an aldehyde (for example, formaldehyde or the like) in the presence of a reducing agent (for example, sodium triacetoxyborohydride or the like) in a solvent (for example, dichloromethane, acetic acid, or the like), whereby a corresponding compound having an alkylated amino group can be produced.

Alternatively, a compound having an amino group is reacted with an alkyloxirane (for example, 2-(trifluoromethyl)oxirane) in the presence of a base (for example, triethylamine or the like) in a solvent (for example, ethanol, N,N-dimethylformamide, a mixture thereof, and the like), whereby a corresponding compound having an alkylated amino group can be produced.

Alternatively, a compound having an amino group is reacted with an electron-withdrawing group substituted alkene (for example, methyl 3,3-dimethylacrylate) in the presence of a base (for example, 1,8-diazabicyclo[5.4.0]-7-undecene or the like) in a solvent (for example, acetonitrile or the like), whereby a corresponding compound having an alkylated amino group can be produced.

(7) Conversion of amino group to aminoheteroaryl group

A compound having an amino group is reacted with a heteroaryl halide (for example, methyl 6-chloronicotinate or the like) in the presence of a base (for example, N,N-diisopropylethylamine, potassium carbonate, and the like) in a solvent (for example, N,N-dimethylformamide, N-methyl-2-pyrrolidinone, 1,4-dioxane, dimethylsulfoxide, and the like), whereby a compound having a corresponding amino heteroaryl group can be produced.

Alternatively, a compound having an amino group is reacted with a heteroaryl halide ((5-bromopyrimidin-2-yl)methanol or the like) in the presence of a catalyst ([(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) and (2-dicyclohexylphosphino-2',6'-diisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: RuPhos Pd G3), and the like) and a base (tripotassium phosphate, cesium carbonate, and the like) in a solvent (1,4-dioxane, water, a mixture thereof, and the like), whereby a compound having a corresponding amino heteroaryl group can be produced.

(8) Conversion of alkoxycarbonyl group to carboxy group

A compound having an alkoxycarbonyl group is reacted in the presence of a base (for example, potassium hydroxide, lithium hydroxide, and the like) or an acid (for example, sulfuric acid or the like) in a solvent (for example, tetrahydrofuran, methanol, ethanol, water, a mixture thereof, and the like),

whereby a compound having a corresponding carboxy group can be produced.

(9) Deprotection of hydroxy group protected with tert-butyldimethylsilyl group or tert-butyldiphenylsilyl group

A compound having a hydroxy group protected with a tert-butyldimethylsilyl group or a tert-butyldiphenylsilyl group is reacted in the presence of a base (for example, tetra-n-butylammonium fluoride or the like) or in the presence of an acid (for example, hydrogen chloride or the like) in a solvent (for example, tetrahydrofuran or the like), whereby a protective group can be deprotected.

(10) Conversion of amino group to carbamate group

An alcohol (for example, methyl hydroxypivalate or the like) is reacted with 1,1'-carbonyldiimidazole in a solvent (for example, dichloromethane or the like) and then reacted with a compound having an amino group in a solvent (for example, 1,4-dioxane or the like), whereby a compound having a corresponding carbamate group can be produced.

Alternatively, a compound having an amino group is reacted with an alkyl chloroformate (for example, methyl chloroformate or the like) in the presence of a base (for example, triethylamine or the like) in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding carbamate group can be produced.

(11) Conversion of amino group to thiocarbamate group

An alcohol (for example, methyl hydroxypivalate or the like) is reacted with O,O'-di-2-pyridyl thiocarbonate in the presence of 4-dimethylaminopyridine in a solvent (for example, tetrahydrofuran or the like) and then reacted with a compound having an amino group in a solvent (for example, 1,4-dioxane or the like), whereby a compound having a corresponding thiocarbamate group can be produced.

Alternatively, a compound having an amino group is reacted with thiophosgene in a solvent (for example, dichloromethane or the like) and then reacted with a metal alkoxide (for example, sodium methoxide or the like) in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding thiocarbamate group can be produced.

(12) Conversion of nitro group to amino group

A compound having a nitro group is reacted in the presence of hydrogen gas and a catalyst (for example, sulfur-modified platinum carbon or the like) in a solvent (for example, ethyl acetate or the like), whereby a compound having a corresponding amino group can be produced.

(13) Conversion of amino group to aminoaryl group

A compound having an amino group is reacted with aryl boronic acid (4-(methoxycarbonyl)phenyl boronic acid or the like) in the presence of a catalyst (copper sulfate or the like), a base (pyridine or the like), and a dehydrating agent (a molecular sieve or the like) in a solvent (dichloromethane or the like), whereby a compound having a corresponding aminoaryl group can be produced.

Alternatively, a compound having an amino group was reacted with an aryl halide (methyl 4-bromobenzoate or the like) in the presence of a catalyst ([(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) or the like) and a base (tripotassium phosphate, potassium carbonate, cesium carbonate, and the like) in a solvent (1,4-dioxane or the like), whereby a compound having a corresponding aminoaryl group can be produced.

(14) Conversion of carboxy groups to alkoxycarbonylamino groups

A compound having a carboxy group is reacted with diphenylphosphoryl azide and an alcohol (for example, tert-butanol or the like) in the presence of a base (triethylamine or the like) in a solvent (for example, tert-butanol or the like), whereby a compound having a corresponding alkoxycarbonylamino group can be produced.

(15) Deprotection of amino group protected with tert-butoxycarbonyl group

A compound having an amino group protected with a tert-butoxycarbonyl group is reacted in the presence of an acid (for example, hydrogen chloride, trifluoroacetic acid, or the like) in a solvent (for example, 1,4-dioxane, dichloromethane, and the like), whereby a protective group can be deprotected.

(16) Conversion of carboxy group to amide group

A compound having a carboxy group is reacted with an amine (for example, methylamine or the like) in the presence of a base (for example, N,N-diisopropylethylamine or the like) and a condensing agent (for example, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) or the like) in a solvent (for example, N,N-dimethylformamide or the like), whereby a compound having a corresponding amide group can be produced.

(17) Conversion of alkoxycarbonyl group to amide group

A compound having an alkoxycarbonyl group is reacted with an amine (for example, ammonia or the like) in a solvent (for example, tetrahydrofuran or the like), whereby a compound having a corresponding amide group can be produced.

(18) Conversion of amide group to cyano group

A compound having an amide group is reacted with trifluoroacetic anhydride in the presence of a base (for example, triethylamine) in a solvent (for example, tetrahydrofuran or the like), whereby a compound having a corresponding cyano group can be produced.

(19) Conversion of alkoxycarbonyl group to hydroxymethyl group

A compound having an alkoxycarbonyl group is reacted in the presence of a reducing agent (for example, sodium borohydride, lithium borohydride, and the like) in a solvent (for example, tetrahydrofuran, ethanol, methanol, a mixture thereof, and the like), whereby a compound having a corresponding hydroxymethyl group can be produced.

(20) Conversion of alkoxycarbonyl group to dialkylhydroxymethyl group

A compound having an alkoxycarbonyl group is reacted with an organometallic reagent (for example, methylmagnesium bromide or the like) in a solvent (for example, tetrahydrofuran or the like), whereby a compound having a corresponding dialkylhydroxymethyl group can be produced.

(21) Conversion of ketone to alcohol

A compound having a ketone group is reacted with a reducing agent (for example, sodium borohydride or the like) in a solvent (for example, tetrahydrofuran, ethanol, a mixture thereof, and the like), whereby a compound having a corresponding alcohol group can be produced.

(22) Conversion of hydroxy group to amino group

A compound having a hydroxy group is reacted with phthalimide in the presence of an azodicarboxamide (for example, 1,1'-azobis(N,N-dimethylformamide) or the like) and tri-n-butylphosphine in a solvent (for example, tetrahydrofuran or the like) and then reacted with hydrazine monohydrate in a solvent (ethanol or the like), whereby a compound having a corresponding amino group can be produced.

(23) Conversion of cyano group to tetrazole group

A compound having a cyano group is reacted with azidotrimethyltin (IV) in a solvent (for example, toluene or the like), whereby a compound having a corresponding tetrazole group can be produced.

(24) Conversion of epoxy group to cyanohydroxyethyl group

A compound having an epoxy group is reacted with trimethylsilylcyanide in the presence of tetrabutylammonium fluoride in a solvent (for example, tetrahydrofuran or the like), whereby a compound having a corresponding cyanohydroxyethyl group can be produced.

(25) Conversion of epoxy group to aminohydroxyethyl group

A compound having an epoxy group is reacted with an amine (for example, ammonia or the like) in a solvent (for example, methanol or the like), whereby a compound having a corresponding aminohydroxyethyl group can be produced.

(26) Deprotection of diol group protected with acetonide group

A compound having a diol group protected with an acetonide group is reacted in the presence of an acid (for example, hydrogen chloride or the like) in a solvent (for example, methanol or the like), whereby the protective group can be deprotected.

(27) Conversion of amino group to N-tert-butoxycarbonylsulfamide group

Chlorosulfonyl isocyanate is reacted with tert-butanol in a solvent (for example, dichloromethane or the like) and then reacted with a compound having an amino group in the presence of a base (for example, triethylamine or the like) in a solvent (for example, dichloromethane or the like),

whereby a compound having a corresponding N-tert-butoxycarbonylsulfamide group can be produced.

(28) Conversion of N-tert-butoxycarbonylsulfamide group to N-alkylsulfamide group

A compound having N-tert-butoxycarbonylsulfamide group is reacted with an alcohol (for example, 2-((tetrahydropyran-2-yl)oxy)ethan-1-ol) in the presence of an azodicarboxylic acid diester (for example, diisopropyl azodicarboxylate or the like) and triphenylphosphine in a solvent (for example, tetrahydrofuran or the like) then reacted in the presence of an acid (for example, hydrogen chloride, trifluoroacetic acid, and the like) in a solvent (for example, 1,4-dioxane, dichloromethane, and the like), and a tert-butoxycarbonyl group is deprotected, whereby a compound having a N-alkylsulfamide group can be thereby produced.

Alternatively, a compound having N-tert-butoxycarbonylsulfamide group is reacted with an alkyl halide (for example, iodomethane) in the presence of a base (for example, cesium carbonate or the like) in a solvent (N,N-dimethylformamide or the like) and then reacted in the presence of an acid (for example, hydrogen chloride or the like) in a solvent (for example, 1,4-dioxane or the like), and a tert-butoxycarbonyl group is deprotected, whereby a compound having a N-alkylsulfamide group can be produced.

(29) Conversion of sulfamide group to N-acylsulfamide group

A compound having a sulfamide group is reacted with a carboxylic acid anhydride (for example, propionic anhydride or the like) in the presence of 4-dimethylaminopyridine in a solvent (for example, acetonitrile or the like), whereby a compound having a corresponding N-acylsulfamide group can be produced.

Alternatively, a compound having a sulfamide group is reacted with N-succinimidyl ester (for example, 2,5-dioxopyrrolidin-1-yl (tert-butoxycarbonyl) glycinate or the like) in the presence of a base (for example, N,N-diisopropylethylamine or the like) in a solvent (for example, acetonitrile or the like), whereby a compound having a corresponding a N-acylsulfamide group can be produced.

(30) Conversion of amino group to formamide group

A compound having an amino group is reacted with 2,2,2-trifluoroethyl formate in the presence

of a base (for example, N,N-diisopropylethylamine or the like) in a solvent (for example, N,N-dimethylformamide or the like), whereby a compound having a corresponding formamide group can be produced.

(31) Conversion of amide group to thioamide group

A compound having an amide group is reacted with a Lawson's reagent in a solvent (for example, tetrahydrofuran or the like), whereby a compound having a corresponding thioamide group can be produced.

(32) Conversion of amino group to sulfonamido group

A compound having an amino group is reacted with an alkylsulfonyl halide (for example, methanesulfonyl chloride or the like) in the presence of a base (for example, triethylamine) in a solvent (dichloromethane or the like), whereby a compound having a corresponding sulfonamide group can be produced.

(33) Conversion of chloropyridazine ring to pyridazinone ring

A compound having a chloropyridazine ring is reacted in the presence of acetic acid, whereby a compound having a corresponding pyridazinone ring can be produced.

(34) Conversion of pyridazinone ring to dihydropyridazinone ring

A compound having a pyridazinone ring is reacted in the presence of zinc in a solvent (for example, acetic acid or the like), whereby a compound having a corresponding dihydropyridazinone ring can be produced.

(35) Alkylation of nitrogen atom of nitrogen-containing ring

A compound having a nitrogen-containing ring is reacted with an alkyl halide (for example, iodomethane or the like) in the presence of a base (for example, cesium carbonate, N,N-diisopropylethylamine, and the like) in a solvent (for example, N,N-dimethylformamide or the like), whereby a corresponding compound in which a nitrogen atom of a nitrogen-containing ring has been alkylated can be produced.

(36) Conversion of amino group to (4-oxo-4,5-dihydrooxazol-2-yl)amino group

A compound having an amino group is reacted with chloroacetylisocyanate in a solvent (dichloromethane or the like) and then reacted in the presence of a base (such as 1,8-diazabicyclo[5.4.0]-7-undecene) in a solvent (tetrahydrofuran or the like), whereby a compound having a corresponding (4-oxo-4,5-dihydrooxazol-2-yl)amino group can be produced.

(37) Conversion of amino group to (4-oxo-4,5-dihydrothiazol-2-yl)amino group

A compound having an amino group is reacted with 2-(methylthio)thiazol-4(5H)-one in a solvent (methanol or the like), whereby a compound having a corresponding (4-oxo-4,5-dihydrothiazol-2-yl)amino group can be produced.

(38) Conversion of amino group to (4-oxo-4,5-dihydro-1H-imidazol-2-yl)amino group

A compound having an amino group is reacted with tert-butyl 2-(methylthio)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate (CAS Reg. No. 1638890-07-9) in a solvent (for example, ethanol or the like) and then reacted in the presence of an acid (for example, hydrochloric acid or the like) in a solvent (for example, 1,4-dioxane or the like), and a tert-butoxycarbonyl group is deprotected, whereby a compound having a corresponding (4-oxo-4,5-dihydro-1H-imidazol-2-yl)amino group can be produced.

(39) Conversion of amino group to (5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)amino group

A compound having an amino group is reacted with 1,1'-thiocarbonyldiimidazole in the presence of a base (triethylamine or the like) in a solvent (tetrahydrofuran or the like), then, reacted with hydrazine monohydrate, and then reacted with 1,1'-carbonyldiimidazole in the presence of a base (triethylamine or the like) in a solvent (dichloromethane or the like), whereby a compound having a corresponding (5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)amino group can be produced.

(40) Conversion of amino group to (5-oxo-2,5-dihydro-1,2,4-oxadiazol-3-yl)amino group

A compound having an amino group is reacted with ethoxycarbonyl isothiocyanate in a solvent (dichloromethane or the like), then, reacted with iodomethane in a solvent (N,N-dimethylformamide or the like), and then reacted with hydroxylamine hydrochloride in a solvent (pyridine or the like), whereby a compound having a corresponding (5-oxo-2,5-dihydro-1,2,4-oxadiazol-3-yl)amino group can be

produced.

(41) Conversion of amino group to (2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)amino group

4-chlorophenyl chloroformate and potassium thiocyanate are reacted in a solvent (acetone or the like), then, reacted with a compound having an amino group in a solvent (dichloromethane or the like), then, reacted with methylamine in a solvent (dichloromethane, N,N-dimethylformamide, and the like), and then reacted with bromine in a solvent (dichloromethane or the like), whereby a compound having a corresponding (2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)amino group can be produced.

(42) Conversion of cyano group to 5-oxo-4,5-dihydro-1,2,4-oxadiazole ring

A compound having a cyano group is reacted with hydroxylamine in a solvent (for example, dimethyl sulfoxide or the like) and then reacted with 1,1'-carbonyldiimidazole in the presence of a base (for example, 1,8-diazabicyclo[5.4.0]-7-undecene or the like) in a solvent (for example, dimethyl sulfoxide or the like), whereby a compound having a corresponding 5-oxo-4,5-dihydro-1,2,4-oxadiazole ring can be produced.

(43) Conversion of carboxy group to hydroxymethyl group

A compound having a carboxy group is reacted with alkyl chloroformate (for example, isobutyl chloroformate or the like) in the presence of a base (for example, triethylamine or the like) in a solvent (for example tetrahydrofuran or the like) and then reacted in the presence of a reducing agent (for example, sodium borohydride or the like) in a solvent (for example, tetrahydrofuran, water, a mixture thereof, and the like), whereby a compound having a corresponding hydroxymethyl group can be produced.

(44) Deprotection of nitrogen atom on nitrogen-containing ring protected with 2-(trimethylsilyl)ethoxymethyl group

A compound having a nitrogen atom of a nitrogen-containing ring protected with a 2-(trimethylsilyl)ethoxymethyl group is reacted in the presence of an acid (for example, hydrogen chloride or the like) in a solvent (for example, ethyl acetate or the like), whereby the protective group can be

deprotected.

(45) Conversion of carboxy group to alkylsulfonylcarbamoyl group

A compound having a carboxy group is reacted with an alkylsulfonamide (for example, methanesulfonamide or the like) in the presence of a condensing agent (for example, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl), or the like) and 4-dimethylaminopyridine in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding alkylsulfonylcarbamoyl group can be produced.

(46) Conversion of carboxy group to sulfamoylcarbamoyl group

A compound having a carboxy group is reacted with sulfamide (for example, sulfamide, dimethylsulfamide, and the like) in the presence of a condensing agent (for example, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl) or the like) and 4-dimethylaminopyridine in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding sulfamide-carbamoyl group can be produced.

(47) Conversion of hydroxy group to acyloxy group

A compound having a hydroxy group is reacted with a carboxylic anhydride (for example, acetic anhydride or the like) in the presence or absence of a base (for example, pyridine or the like) and 4-dimethylaminopyridine in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding acyloxy group can be produced.

(48) Conversion of hydroxy group to alkyl carbonate group

A compound having a hydroxy group is reacted with an alkyl chloroformate (for example, methyl chloroformate or the like) in the presence of a base (for example, pyridine or the like) in a solvent (for example, dichloromethane or the like), whereby a compound having a corresponding alkyl carbonate group can be produced.

(49) Conversion of hydroxy group to amino acid ester

A compound having a hydroxy group is reacted with a tert-butoxycarbonyl group-protected amino acid (for example, N-(tert-butoxycarbonyl)-L-valine) in the presence of a condensing agent (for

example, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl) or the like) and 4-dimethylaminopyridine in a solvent (for example, dichloromethane or the like), and the tert-butoxycarbonyl group is then deprotected, whereby a compound having an amino acid ester can be produced.

[0131] The obtained target compound can be separated and purified as necessary by appropriately combining common methods, for example, recrystallization, reprecipitation, filtration, concentration, drying, or a method that is conventionally used commonly for the separation and purification of an organic compound (for example, column chromatography).

[0132] The compound (I) of the present invention and the intermediate can be produced not only by the above-described production methods but also by methods to be described in the examples or reference examples to be described below. Furthermore, the compound (I) of the present invention and the intermediate can be converted to a different target compound or intermediate by the above-described production methods, the methods to be described in the examples or reference examples to be described below, and/or known methods or combinations thereof.

[0133] Furthermore, a different form of the compound (I) of the present invention and the intermediate can be produced using a starting material different from the starting materials described in the above-described production methods and the examples or reference examples to be described below and the above-described production methods and the methods to be described in the examples or reference examples to be described below, and/or known methods or combinations thereof.

Examples

[0134] Hereinafter, the present invention will be described more specifically reference to reference examples, examples, test examples, and the like, but the present invention is not limited thereto.

[0135] Conditions used in LCMS analysis will be described below.

LCMS conditions 1

LC: LCMS-8030 System, Shimadzu Corporation

Columns: Waters Acquity UPLC BEH C18 (2.1 mm × 50 mm, 1.7 μm)

Column temperature: 40°C

Flow rate: 0.6 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.5 min; A/B= 75/25 → 5/95, 1.5 min to 3 min; A/B = 5/95

Ionization: DUIS

[0136] LCMS conditions 2

LC: LCMS-2020 System Shimadzu Corporation

Columns: Waters Acquity UPLC BEH C18 (2.1 mm × 50 mm, 1.7 μm)

Column temperature: 40°C

Flow rate: 0.6 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.5 min; A/B= 75/25 → 5/95, 1.5 min to 3 min; A/B = 5/95

Ionization: ESI

[0137] LCMS conditions 3

LC: LCMS-2020 System Shimadzu Corporation

Columns: Waters Acquity UPLC CSH C18 (2.1 mm × 50 mm, 1.7 μm)

Column temperature: 40°C

Flow rate: 0.6 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.5 min; A/B= 75/25 → 5/95, 1.5 min to 3 min; A/B = 5/95

Ionization: ESI

[0138] LCMS conditions 4

LC: LCMS-8030 System, Shimadzu Corporation

Columns: Waters Acquity UPLC CSH C18 (2.1 mm × 50 mm, 1.7 μm)

Column temperature: 40°C

Flow rate: 0.6 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.5 min; A/B= 75/25 → 5/95, 1.5 min to 3 min; A/B = 5/95

Ionization: DUIS

[0139] LCMS conditions 5

LC: LCMS-8030 System, Shimadzu Corporation

Columns: Waters Acquity UPLC HSS T3 (2.1 mm × 50 mm, 1.8 μm)

Column temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.0 min; A/B= 95/5 → 70/30, 1.0 min to 2.0 min; A/B= 70/30 → 5/95, 2.0 min to 3.0 min; A/B = 5/95

Ionization: DUIS

[0140] LCMS conditions 6

LC: LCMS-8030 System, Shimadzu Corporation

Columns: Waters Acquity UPLC BEH C18 (2.1 mm × 50 mm, 1.7 μm)

Flow rate: 0.8 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 0.75 min; A/B= 75/25 → 5/95, 0.75 min to 1.5 min; A/B = 5/95

Ionization: DUIS

[0141] LCMS conditions 7

LC: LCMS-2050 System Shimadzu Corporation

Columns: Waters Acquity UPLC BEH C18 (2.1 mm × 50 mm, 1.7 μm)

Flow rate: 0.8 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 0.75 min; A/B= 75/25 → 5/95, 0.75 min to 1.5 min; A/B = 5/95

Ionization: DUIS

[0142] LCMS conditions 8

LC: LCMS-2050 System Shimadzu Corporation

Columns: Waters Acquity UPLC BEH C18 (2.1 mm × 50 mm, 1.7 μm)

Flow rate: 0.6 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.5 min; A/B= 75/25 → 5/95, 1.5 min to 3 min; A/B = 5/95

Ionization: DUIS

[0143] LCMS conditions 9

LC: LCMS-2050 System Shimadzu Corporation

Columns: Waters Acquity UPLC CSH C18 (2.1 mm × 50 mm, 1.7 μm)

Flow rate: 0.6 ml/min.

Temperature: 40°C

Mobile phase A: 0.1% formic acid aqueous solution

Mobile phase B: 0.1% formic acid-acetonitrile solution

Gradient: 0 to 1.5 min; A/B= 75/25 → 5/95, 1.5 min to 3 min; A/B = 5/95

Ionization: DUIS

[0144] "DNH silica gel" indicates CHROMATOREX (trade name) DNH manufactured by Fuji Silysia Chemical Ltd., "DIOL silica gel" indicates CHROMATOREX (trade name) DIOL manufactured by Fuji Silysia Chemical Ltd., and "ODS column" indicates Universal column ODS manufactured by Yamazen Corporation.

[0145] An ionization mode "DUIS" of mass spectrum is a mixed mode of ESI and APCI.

[0146] ^{1}H-NMR is expressed by a chemical shift (δ) with tetramethylsilane as an internal standard (0 ppm), and a coupling constant (J value) is expressed by the Hz unit unless particularly otherwise described. In addition, the abbreviations of the splitting patterns of individual peaks refer to the following meanings. s: Singlet, d: Doublet, t: Triplet, q: Quartet, quin: Quintet, spt: Septet, br: Broad, m: Multiplet.

[0147] An Rf value is a value measured using thin layer chromatography (Merck, TLC glass plate silica gel 60 F_{254}).

[0148] Abbreviations that are described in the reference examples, the examples, and chemical structure formulae are commonly used as meanings that are generally used in the field of organic chemistry or pharmacy. Each abbreviation is specifically as understood by those skilled in the art as follows.

Boc: tert-Butoxycarbonyl group

DMSO: Dimethyl sulfoxide

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

N: Normality

M: Molar concentration

Ph: Phenyl group

TBS: tert-Butyldimethylsilyl group

Cbz: Benzyloxycarbonyl group

TBDPS: tert-Butyldiphenylsilyl group

Tf: Trifluoromethylsulfonyl group

Bn: Benzyl group APCI: Atmospheric pressure ionization

EI: Electron Ionization

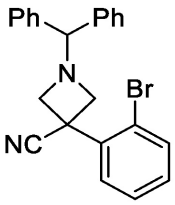
ESI: Electrospray ionization

[0149] (Reference Example)

Reference Example 1-(a)

Production of 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carbonitrile

[C57]



41 ml of a 1M potassium bis(trimethylsilyl)amide/tetrahydrofuran solution was added dropwise to a tetrahydrofuran (100 ml) solution of 10.0 g of 1-benzhydrylazetidine-3-carbonitrile and 6.6 ml of 2-bromofluorobenzene at room temperature under an argon flow and stirred at room temperature for 4.5 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 12.94 g of a title compound as a slightly yellow foamy substance.

Mass spectrum (ESI, m/z): 403, 405 $[M+H]^+$

Retention time (LCMS conditions 2): 1.741 min.

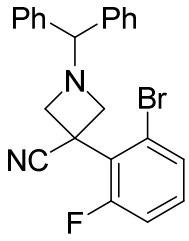
[0150] Reference Example 26-(a)

A compound shown in Table 1 below was obtained by treating a corresponding raw material

compound in the same manner as in Reference Example 1-(a).

[Table 1]

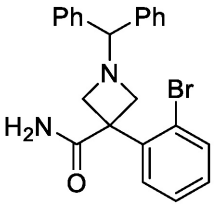
Table 1

Reference Example	Structural formula	Analysis data
26-(a)		Mass spectrum (DUIS, m/z): 421, 423 $[M+H]^+$ Retention time (LCMS conditions 1): 1.758 min

[0151] Reference Example 1-(b)

Production of 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carboxamide

[C58]



17.4 g of potassium trimethylsilanolate was added to a toluene (130 ml) solution of 12.27 g of 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carbonitrile produced in Reference Example 1-(a) under an argon gas flow at room temperature and stirred at 100°C for one hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate twice. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 12.49 g of a title compound as a slightly yellow foamy substance.

Mass spectrum (ESI, m/z): 421, 423 $[M+H]^+$

Retention time (LCMS conditions 2): 0.932 min.

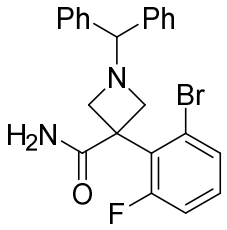
[0152] Reference Example 26-(b)

A compound shown in Table 2 below was obtained by treating a corresponding raw material

compound in the same manner as in Reference Example 1-(b).

[Table 2]

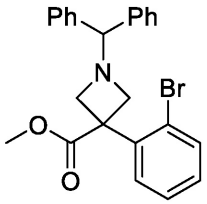
Table 2

Reference Example	Structural formula	Analysis data
26-(b)		Mass spectrum (DUIS, m/z): 439, 441 $[M+H]^+$ Retention time (LCMS conditions 1): 1.096 min

[0153] Reference Example 1-(c)

Production of methyl 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carboxylate

[C59]



12.6 ml of sulfuric acid was added to a methanol (130 ml) solution of 12.4 g of 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carboxamide produced in Reference Example 1-(b) at room temperature under an argon flow and stirred at 75°C for 50 hours. A mixture was concentrated by approximately half, and ethyl acetate was added thereto. This solution was neutralized by adding a saturated sodium bicarbonate solution and sodium bicarbonate and separated. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 10.12 g of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 436, 438 $[M+H]^+$

Retention time (LCMS conditions 2): 1.433 min.

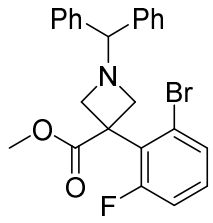
[0154] Reference Example 26-(c)

A compound shown in Table 3 below was obtained by treating a corresponding raw material

compound in the same manner as in Reference Example 1-(c).

[Table 3]

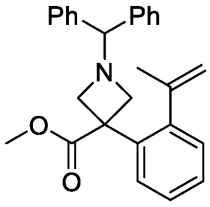
Table 3

Reference Example	Structural formula	Analysis data
26-(c)		Mass spectrum (DUIS, m/z): 454, 456 $[M+H]^+$ Retention time (LCMS conditions 1): 1.415 min

[0155] Reference Example 1-(d)

Production of methyl 1-benzhydryl-3-(2-(prop-1-en-2-yl)phenyl)azetidine-3-carboxylate

[C60]



Reaction 1

A 1,4-dioxane (16 ml)-water (4 ml) solution of 1.00 g of methyl 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carboxylate produced in Reference Example 1-(c) was degassed and substituted with nitrogen. 0.65 ml of 2-isopropenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 633 mg of potassium carbonate and 162 mg of bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium (II) were added at room temperature under an argon gas flow and stirred at 100°C for two hours.

[0156] Reaction 2

A 1,4-dioxane (120 ml)-water (30 ml) solution of 7.80 g of methyl 1-benzhydryl-3-(2-bromophenyl)azetidine-3-carboxylate produced in Reference Example 1-(c) was degassed and substituted with nitrogen. 5.1 ml of 2-isopropenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 4.94 g of potassium carbonate and 1.27 g of bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium (II) were added at room temperature under an

argon gas flow and stirred at 100°C for 2.5 hours.

[0157] A mixture obtained by combining reaction mixtures of the reaction 1 and the reaction 2 was separated by adding water and ethyl acetate thereto. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 6.41 g of a title compound as a slightly yellow foamy substance.

Mass spectrum (ESI, m/z): 398 $[M+H]^+$

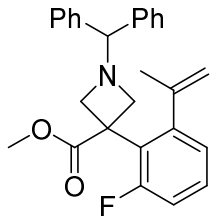
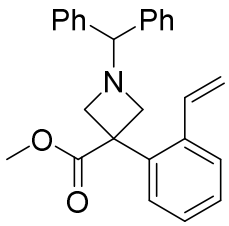
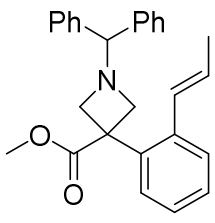
Retention time (LCMS conditions 2): 1.431 min.

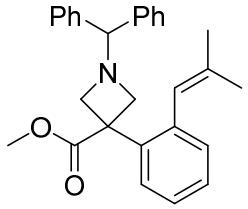
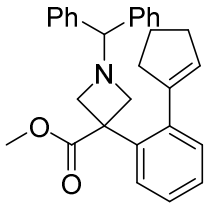
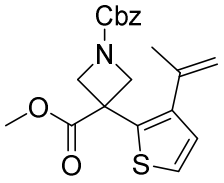
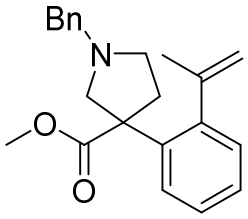
[0158] Reference Example 26-(d) and the like

Compounds shown in Table 4 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(d).

[Table 4]

Table 4

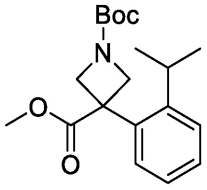
Reference Example	Structural formula	Analysis data
26-(d)		Mass spectrum (DUIS, m/z): 416 $[M+H]^+$ Retention time (LCMS conditions 1): 1.287 min
27-(a)		
28-(a)		

29-(a)		
30-(a)		
31-(e)		Mass spectrum (ESI, m/z): 372 $[M+H]^+$ Retention time (LCMS conditions 2): 1.537 min
290-(b)		Mass spectrum (DUIS, m/z): 336 $[M+H]^+$ Retention time (LCMS conditions 1): 0.901 min

[0159] Reference Example 1-(e)

Production of 1-(tert-butyl) 3-methyl 3-(2-isopropylphenyl)azetidine-1,3-dicarboxylate

[C61]



2.5 g of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) was added to a methanol (100 ml) solution of 6.41 g of methyl 1-benzhydryl-3-(2-(prop-1-en-2-yl)phenyl)azetidine-3-carboxylate produced in Reference Example 1-(d) at room temperature and stirred at room temperature under a hydrogen atmosphere for five hours. Celite and ethyl acetate were added to a reaction mixture, the reaction mixture was filtered through celite and washed with ethyl acetate, and

a filtrate was concentrated under reduced pressure. 8.3 ml of N,N-diisopropylethylamine and 5.6 ml of di-tert-butyl dicarbonate were added to a dichloromethane (50 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow, and a mixture was stirred at room temperature for 3.5 hours. A reaction mixture was separated by adding a saturated ammonium chloride aqueous solution thereto. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 4.60 g of a title compound as a white solid.

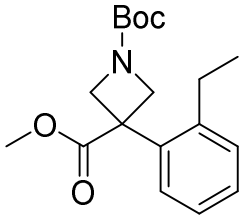
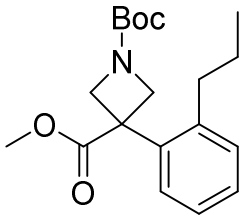
Retention time (LCMS conditions 2): 1.664 min.

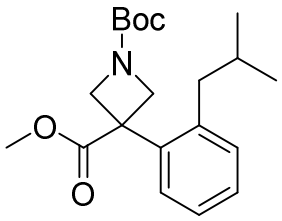
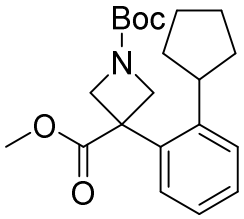
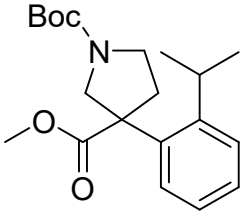
[0160] Reference Example 27-(b) and the like

Compounds shown in Table 5 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(e). The syntheses of Reference Example 27-(b), Reference Example 28-(b), Reference Example 29-(b), and Reference Example 30-(b) were performed using a mixed solvent of methanol and tetrahydrofuran instead of methanol.

[Table 5]

Table 5

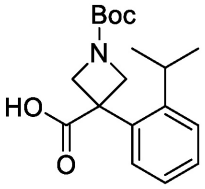
Reference Example	Structural formula	Analysis data
27-(b)		
28-(b)		

29-(b)		
30-(b)		
290-(c)		Retention time (LCMS conditions 1): 1.625 min

[0161] Reference Example 1-(f)

Production of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)azetidine-3-carboxylic acid

[C62]



1.65 g of lithium hydroxide was added to a tetrahydrofuran (35 ml)/methanol (35 ml)/water (35 ml) solution of 4.60 g of 1-(tert-butyl) 3-methyl 3-(2-isopropylphenyl)azetidine-1,3-dicarboxylate produced in Reference Example 1-(e) at room temperature under an argon gas flow and stirred at 50°C for 3.5 hours. The pH was adjusted to three by adding 6N hydrochloric acid to a reaction mixture, and the reaction mixture was separated by adding water and ethyl acetate thereto. An aqueous layer was extracted with ethyl acetate, and a combined organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Dichloromethane was added to a concentrated residue, insoluble matter was removed by filtration, and a filtrate was concentrated under reduced pressure to obtain 4.38 g of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 318 $[M-H]^-$

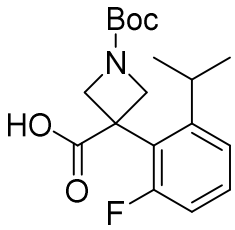
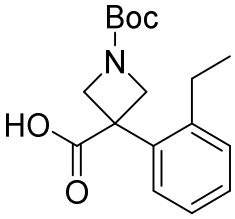
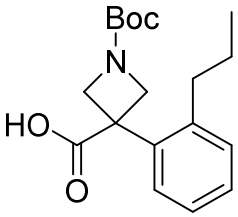
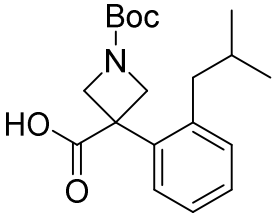
Retention time (LCMS conditions 2): 1.420 min.

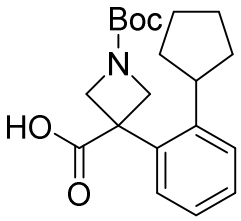
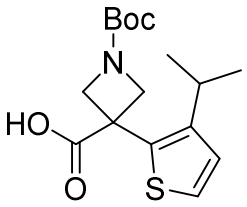
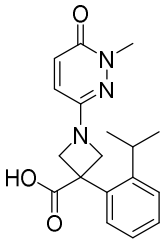
[0162] Reference Example 26-(f) and the like

Compounds shown in Table 6 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(f). The syntheses of Reference Example 26-(f) and Reference Example 265-(e) were performed at room temperature as the reaction temperature.

[Table 6]

Table 6

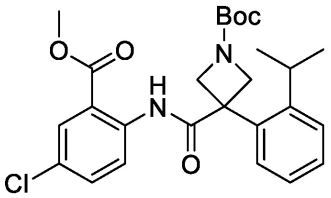
Reference Example	Structural formula	Analysis data
26-(f)		Mass spectrum (DUIS, m/z): 336 $[M-H]^-$ Retention time (LCMS conditions 1): 1.390 min
27-(c)		Mass spectrum (ESI, m/z): 304 $[M-H]^-$ Retention time (LCMS conditions 2): 1.309 min
28-(c)		Mass spectrum (ESI, m/z): 318 $[M-H]^-$ Retention time (LCMS conditions 2): 1.402 min
29-(c)		Mass spectrum (ESI, m/z): 332 $[M-H]^-$ Retention time (LCMS conditions 2): 1.476 min

30-(c)		Mass spectrum (ESI, m/z): 344 $[M-H]^-$ Retention time (LCMS conditions 2): 1.496 min
31-(g)		Mass spectrum (ESI, m/z): 324 $[M-H]^-$ Retention time (LCMS conditions 2): 1.373 min
265-(e)		Mass spectrum (ESI, m/z): 328 $[M+H]^+$ Retention time (LCMS conditions 2): 0.960 min

[0163] Reference Example 1-(g)

Production of tert-butyl 3-((4-chloro-2-(methoxycarbonyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C63]



0.143 ml of oxalyl chloride and 0.01 ml of N,N-dimethylformamide were added to a dichloromethane (5 ml) solution of 407 mg of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)azetidine-3-carboxylic acid produced in the same manner as in Reference Example 1-(f) at 0°C under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure. 0.437 ml of N,N-diisopropylethylamine and 234 mg of methyl 2-amino-5-chlorobenzoate were added to a dichloromethane (5 ml) solution of the obtained concentrated residue at 0°C under an argon gas flow and stirred at room temperature for two hours. A saturated sodium bicarbonate aqueous solution was added to the reaction mixture, and the reaction mixture was extracted

with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 341 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 485 $[M-H]^-$

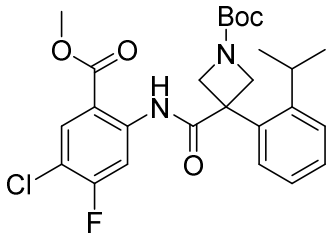
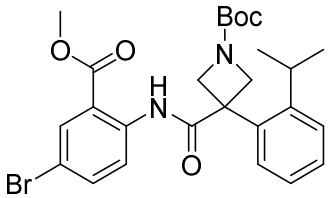
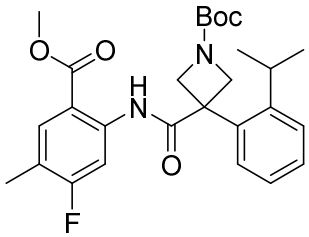
Retention time (LCMS conditions 2): 1.963 min.

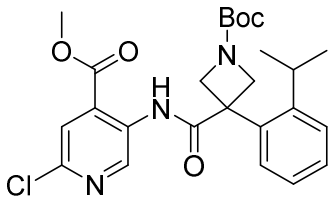
[0164] Reference Example 2-(c) and the like

Compounds shown in Table 7 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(g).

[Table 7]

Table 7

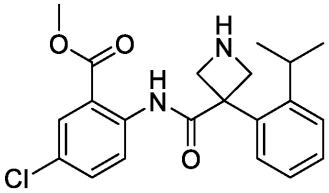
Reference Example	Structural formula	Analysis data
2-(c)		Mass spectrum (DUIS, m/z): 503 $[M-H]^-$ Retention time (LCMS conditions 1): 2.018 min
5-(a)		Mass spectrum (DUIS, m/z): 529, 531 $[M-H]^-$ Retention time (LCMS conditions 1): 2.005 min
8-(a)		Mass spectrum (ESI, m/z): 483 $[M-H]^-$ Retention time (LCMS conditions 2): 1.970 min

10-(a)		Mass spectrum (DUIS, m/z): 486 $[M-H]^-$ Retention time (LCMS conditions 1): 1.783 min

[0165] Reference Example 1-(h)

Production of methyl 5-chloro-2-(3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate

[C64]



8.73 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (1 ml) solution of 340 mg of tert-butyl 3-((4-chloro-2-(methoxycarbonyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in Reference Example 1-(g) at room temperature under an argon gas flow and stirred at room temperature for three hours. After a reaction mixture was concentrated under reduced pressure, a saturated sodium bicarbonate aqueous solution was added thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 305 mg of a title compound as a yellow oily substance.

Mass spectrum (ESI, m/z): 387 $[M+H]^+$

Retention time (LCMS conditions 2): 1.008 min.

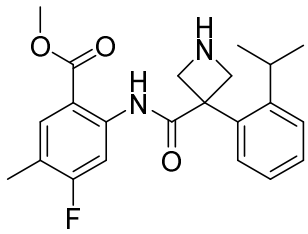
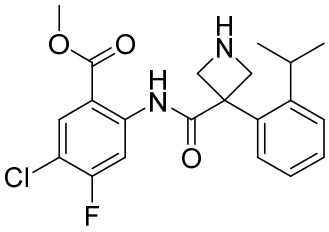
[0166] Reference Example 8-(b) and the like

Compounds shown in Table 8 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(h).

[Table 8]

Table 8

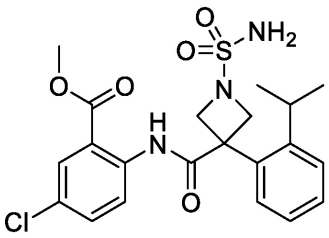
Reference Example	Structural formula	Analysis data

8-(b)		Mass spectrum (ESI, m/z): 385 $[M+H]^+$ Retention time (LCMS conditions 2): 1.037 min
18-(a)		Mass spectrum (ESI, m/z): 405 $[M+H]^+$ Retention time (LCMS conditions 2): 1.075 min

[0167] Reference Example 1-(i)

Production of methyl 5-chloro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoate

[C65]



0.769 ml of triethylamine and 455 mg of sulfamide were added to a 1,4-dioxane (5 ml) solution of 305 mg of methyl 5-chloro-2-(3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate produced in Reference Example 1-(h) at room temperature under an argon gas flow and stirred at 100°C for eight hours. Water was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 263 mg of a title compound as a slightly yellow solid.

Mass spectrum (ESI, m/z): 466 $[M+H]^+$

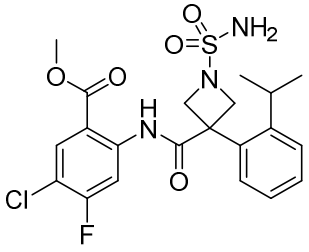
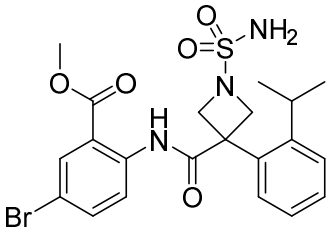
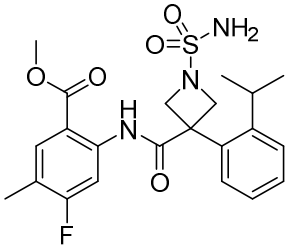
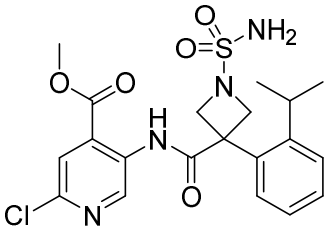
Retention time (LCMS conditions 2): 1.525 min.

[0168] Reference Example 2-(e) and the like

Compounds shown in Table 9 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(i).

[Table 9]

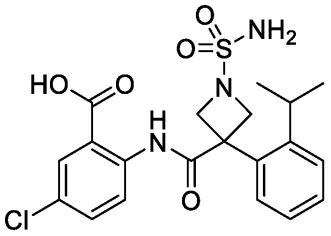
Table 9

Reference Example	Structural formula	Analysis data
2-(e)		Mass spectrum (DUIS, m/z): 484 $[M+H]^+$ Retention time (LCMS conditions 1): 1.580 min
5-(c)		Mass spectrum (DUIS, m/z): 510, 512 $[M+H]^+$ Retention time (LCMS conditions 1): 1.550 min
8-(c)		Mass spectrum (ESI, m/z): 464 $[M+H]^+$ Retention time (LCMS conditions 2): 1.515 min
10-(c)		Mass spectrum (DUIS, m/z): 467 $[M+H]^+$ Retention time (LCMS conditions 1): 1.331 min

[0169] Reference Example 1-(j)

Production of 5-chloro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid

[C66]



72 mg of lithium hydroxide monohydrate was added to a tetrahydrofuran (2 ml)/methanol (0.5 ml)/water (0.5 ml) solution of methyl 5-chloro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoate 263 mg produced in Reference Example 1-(i) at room temperature under an argon gas flow and stirred at room temperature for three hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 269 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 452 $[M+H]^+$

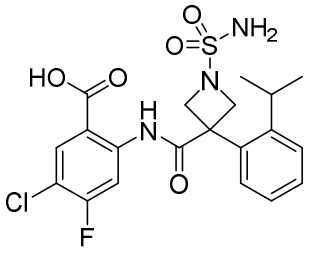
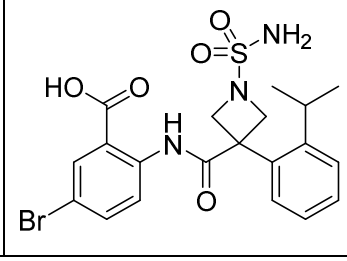
Retention time (LCMS conditions 2): 1.276 min.

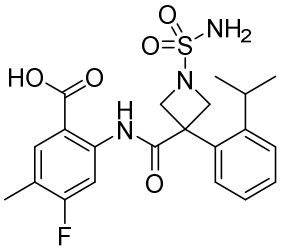
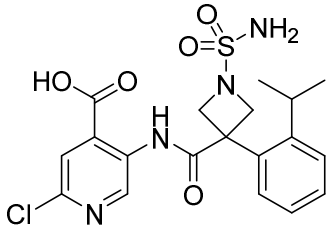
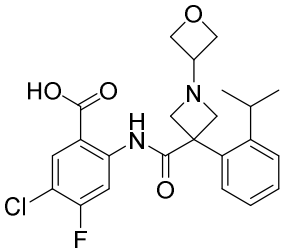
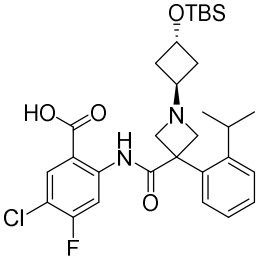
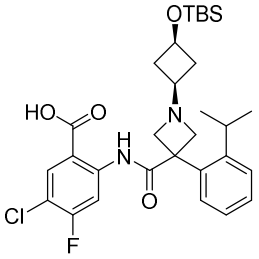
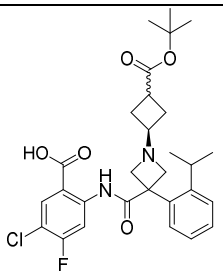
[0170] Reference Example 2-(f) and the like

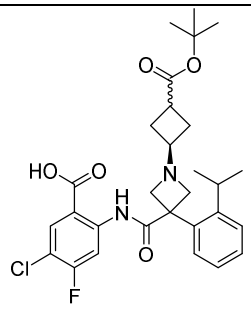
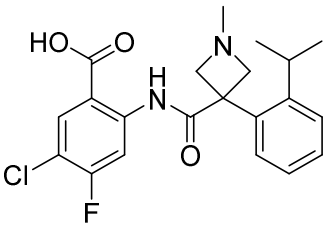
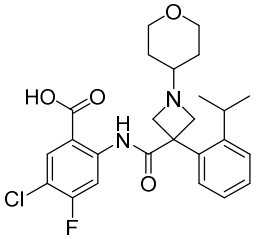
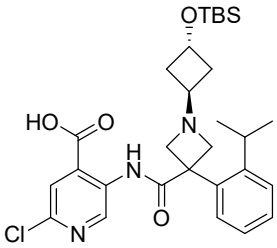
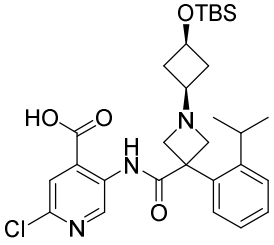
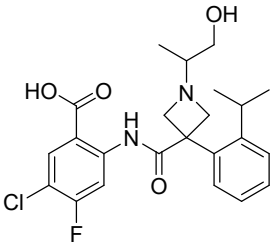
Compounds shown in Table 10 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 1-(j).

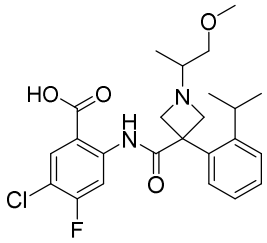
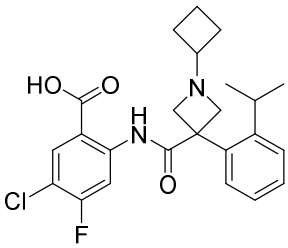
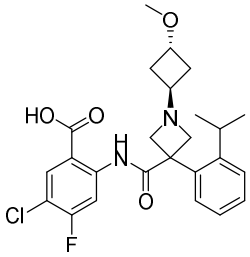
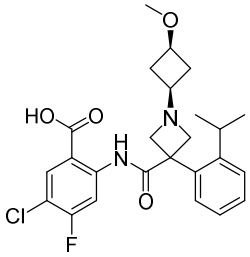
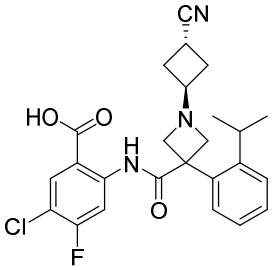
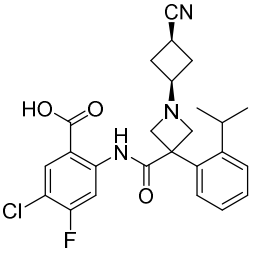
[Table 10]

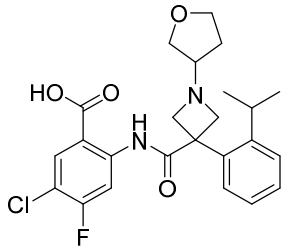
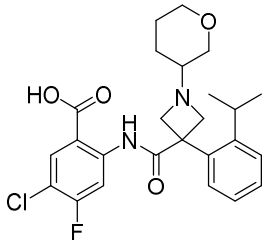
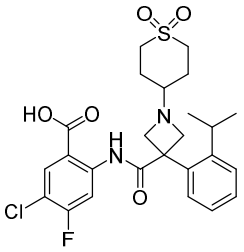
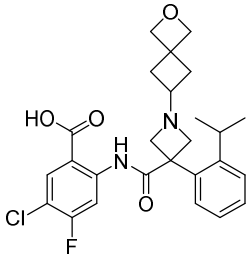
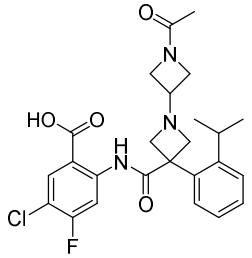
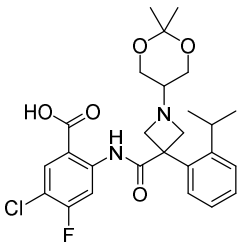
Table 10

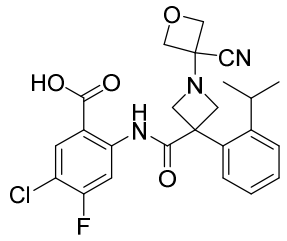
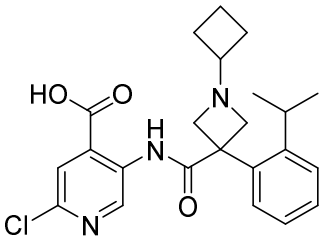
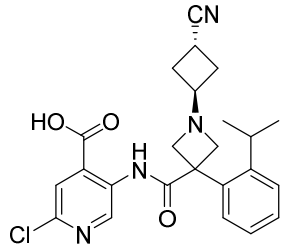
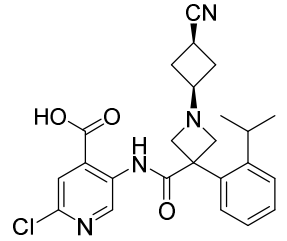
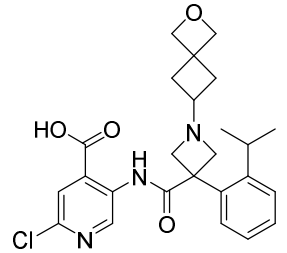
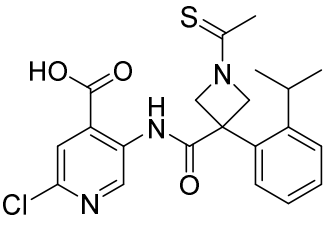
Reference Example	Structural formula	Analysis data
2-(f)		Mass spectrum (DUIS, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 1): 1.338 min
5-(d)		Mass spectrum (ESI, m/z): 496, 498 $[M+H]^+$ Retention time (LCMS conditions 2): 1.311 min

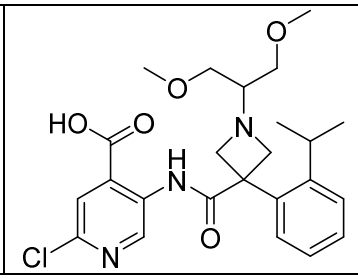
8-(d)		Mass spectrum (ESI, m/z): 450 $[M+H]^+$ Retention time (LCMS conditions 2): 1.295 min
10-(d)		Mass spectrum (DUIS, m/z): 453 $[M+H]^+$ Retention time (LCMS conditions 1): 1.018 min
18-(c)		Mass spectrum (ESI, m/z): 447 $[M+H]^+$ Retention time (LCMS conditions 2): 0.962 min
19-(b)		Mass spectrum (ESI, m/z): 575 $[M+H]^+$ Retention time (LCMS conditions 2): 1.472 min
20-(b)		Mass spectrum (ESI, m/z): 575 $[M+H]^+$ Retention time (LCMS conditions 2): 1.419 min
52-(b)	 Diastereomer 1	Mass spectrum (DUIS, m/z): 545 $[M+H]^+$ Retention time (LCMS conditions 4): 1.213 min

53-(b)	 Diastereomer 2	Mass spectrum (DUIS, m/z): 545 $[M+H]^+$ Retention time (LCMS conditions 4): 1.209 min
54-(b)		Mass spectrum (ESI, m/z): 405 $[M+H]^+$ Retention time (LCMS conditions 2): 0.937 min
55-(b)		Mass spectrum (ESI, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 2): 0.983 min
62-(b)		Mass spectrum (ESI, m/z): 558 $[M+H]^+$ Retention time (LCMS conditions 2): 1.368 min
63-(b)		Mass spectrum (ESI, m/z): 558 $[M+H]^+$ Retention time (LCMS conditions 2): 1.330 min
206-(b)		Mass spectrum (ESI, m/z): 449 $[M+H]^+$ Retention time (LCMS conditions 2): 0.954 min

207-(b)		Mass spectrum (ESI, m/z): 463 $[M+H]^+$ Retention time (LCMS conditions 2): 1.047 min
208-(b)		Mass spectrum (DUIS, m/z): 445 $[M+H]^+$ Retention time (LCMS conditions 1): 1.086 min
209-(b)		Mass spectrum (ESI, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 2): 1.032 min
210-(b)		Mass spectrum (ESI, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 2): 1.030 min
211-(b)		Mass spectrum (ESI, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 3): 1.039 min
212-(b)		Mass spectrum (ESI, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 3): 1.007 min

213-(b)		Mass spectrum (ESI, m/z): 461 $[M+H]^+$ Retention time (LCMS conditions 2): 0.981 min
214-(b)		Mass spectrum (ESI, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 2): 1.020 min
215-(b)		Mass spectrum (ESI, m/z): 523 $[M+H]^+$ Retention time (LCMS conditions 2): 1.009 min
216-(b)		Mass spectrum (ESI, m/z): 487 $[M+H]^+$ Retention time (LCMS conditions 2): 0.974 min
217-(b)		Mass spectrum (ESI, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 2): 0.963 min
218-(b)		Mass spectrum (ESI, m/z): 505 $[M+H]^+$ Retention time (LCMS conditions 2): 1.065 min

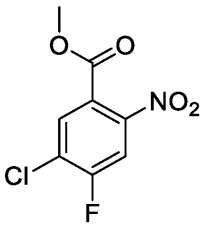
219-(b)		Mass spectrum (ESI, m/z): 472 $[M+H]^+$ Retention time (LCMS conditions 2): 1.529 min
220-(b)		Mass spectrum (ESI, m/z): 428 $[M+H]^+$ Retention time (LCMS conditions 2): 0.840 min
221-(b)		Mass spectrum (DUIS, m/z): 453 $[M+H]^+$ Retention time (LCMS conditions 1): 0.829 min
222-(b)		Mass spectrum (DUIS, m/z): 453 $[M+H]^+$ Retention time (LCMS conditions 1): 0.782 min
223-(b)		Mass spectrum (ESI, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 2): 0.755 min
248-(c)		Mass spectrum (ESI, m/z): 432 $[M+H]^+$ Retention time (LCMS conditions 2): 1.186 min

343-(b)		Mass spectrum (DUIS, m/z): 476 $[M+H]^+$ Retention time (LCMS conditions 7): 0.611 min

[0171] Reference Example 2-(a)

Production of methyl 5-chloro-4-fluoro-2-nitrobenzoate

[C67]



0.284 ml of nitric acid was added dropwise to a sulfuric acid (0.848 ml) solution of 1.00 g of methyl 3-chloro-4-fluorobenzoate at room temperature under an argon gas flow and stirred at room temperature for 7.5 hours. A reaction mixture was diluted with dichloromethane, poured into ice water, and extracted with dichloromethane. An organic layer was successively washed with a saturated sodium bicarbonate aqueous solution and saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 1.00 g of a title compound as a white solid.

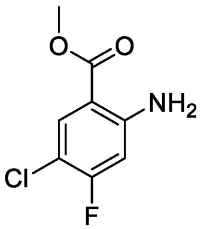
Mass spectrum (EI, m/z) 233 $[M]^+$

Retention time (LCMS conditions 1): 1.237 min.

[0172] Reference Example 2-(b)

Production of methyl 2-amino-5-chloro-4-fluorobenzoate

[C68]



202 mg of sulfur-modified 3% platinum carbon (from Kawaken Fine Chemicals Co., Ltd., 57.5% water-wet) was added to an ethyl acetate (10 ml) solution of 1.00 g of methyl 5-chloro-4-fluoro-2-nitrobenzoate produced in Reference Example 2-(a) at room temperature and stirred at room temperature for 18.5 hours under a hydrogen atmosphere. A reaction mixture was filtered through celite and washed with ethyl acetate, and a filtrate was concentrated under reduced pressure to obtain 852 mg of a title compound as a light brown solid.

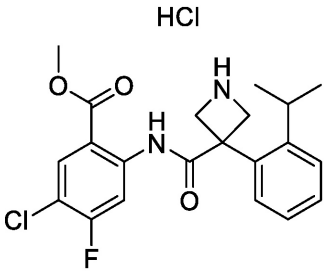
Mass spectrum (DUIS, m/z): 204 $[M+H]^+$

Retention time (LCMS conditions 1): 1.290 min.

[0173] Reference Example 2-(d)

Production of methyl 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate hydrochloride

[C69]



5 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (4 ml) solution of 205 mg of tert-butyl 3-((4-chloro-5-fluoro-2-(methoxycarbonyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in Reference Example 2-(c) under an argon gas flow and stirred at room temperature for 3.5 hours. A reaction mixture was concentrated under reduced pressure to obtain 183 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 405 $[M+H]^+$

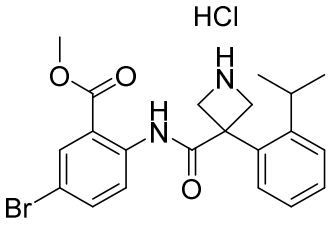
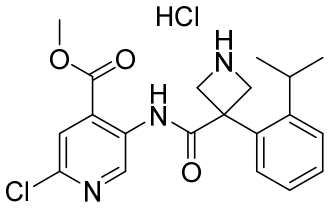
Retention time (LCMS conditions 1): 1.061 min.

[0174] Reference Example 5-(b) and the like

Compounds shown in Table 11 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 2-(d).

[Table 11]

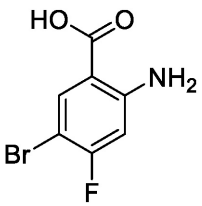
Table 11

Reference Example	Structural formula	Analysis data
5-(b)		Mass spectrum (ESI, m/z): 431, 433 $[M+H]^+$ Retention time (LCMS conditions 2): 1.086 min
10-(b)		Mass spectrum (DUIS, m/z): 388 $[M+H]^+$ Retention time (LCMS conditions 1): 0.898 min

[0175] Reference Example 7-(a)

Production of 2-amino-5-bromo-4-fluorobenzoic acid

[C70]



58 mg of lithium hydroxide was added to a tetrahydrofuran (3 ml)/methanol (1 ml)/water (1 ml) solution of 200 mg of methyl 2-amino-5-bromo-4-fluorobenzoate at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. The pH was adjusted to two by adding 1N hydrochloric acid to a reaction mixture, saturated saline was added to the reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure to obtain 178 mg of a title

compound as an orange solid.

Mass spectrum (DUIS, m/z): 234, 236 $[M+H]^+$

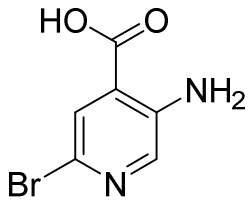
Retention time (LCMS conditions 1): 0.991 min.

[0176] Reference Example 25-(a)

A compound shown in Table 12 below was obtained by treating a corresponding raw material compound in the same manner as in Reference Example 7-(a).

[Table 12]

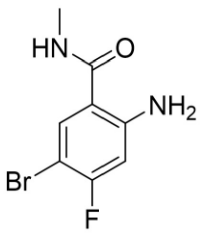
Table 12

Reference Example	Structural formula	Analysis data
25-(a)		Mass spectrum (DUIS, m/z): 217, 219 $[M+H]^+$ Retention time (LCMS conditions 1): 0.558 min

[0177] Reference Example 7-(b)

Production of 2-amino-5-bromo-4-fluoro-N-methylbenzamide

[C71]



0.40 ml of N,N-diisopropylethylamine, 434 mg of HATU, and 1.2 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (2 ml) solution of 178 mg of 2-amino-5-bromo-4-fluorobenzoic acid produced in Reference Example 7-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 173 mg of a title compound as a slightly yellow solid.

Mass spectrum (DUIS, m/z): 247, 249 $[M+H]^+$

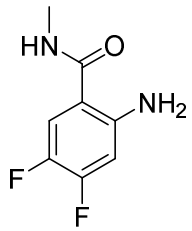
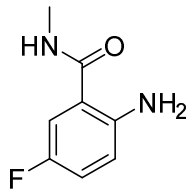
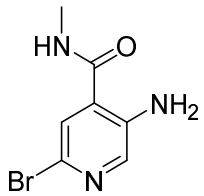
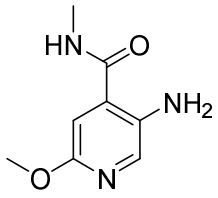
Retention Time (LCMS condition 1): 0.879 min.

[0178] Reference Example 23-(a) and the like

Compounds shown in Table 13 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 7-(b).

[Table 13]

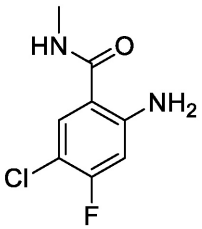
Table 13

Reference Example	Structural formula	Analysis data
23-(a)		Mass spectrum (DUIS, m/z): 187 $[M+H]^+$ Retention time (LCMS conditions 5): 1.566 min
24-(a)		Mass spectrum (DUIS, m/z): 169 $[M+H]^+$ Retention time (LCMS conditions 1): 0.422 min
25-(b)		Mass spectrum (DUIS, m/z): 230, 232 $[M+H]^+$ Retention time (LCMS conditions 1): 0.454 min
326-(a)		Mass spectrum (DUIS, m/z): 182 $[M+H]^+$ Retention time (LCMS conditions 7): 0.214 min

[0179] Reference Example 11-(a)

Production of 2-amino-5-chloro-4-fluoro-N-methylbenzamide

[C72]



655 mg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 523 mg of 1-hydroxybenzotriazole, 0.597 ml of N,N-diisopropylethylamine, and 2.6 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (7 ml) solution of 540 mg of 2-amino-5-chloro-4-fluorobenzoic acid at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 14 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with tert-butyl methyl ether three times. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 439 mg of a title compound as a white solid.

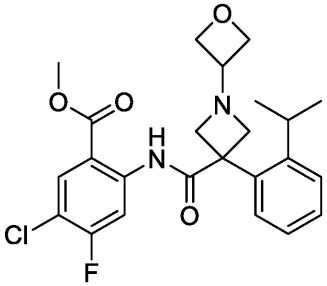
Mass spectrum (ESI, m/z): 203 $[M+H]^+$

Retention time (LCMS conditions 2): 0.846 min.

[0180] Reference Example 18-(b)

Production of methyl 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)-1-(oxetan-3-yl)azetidine-3-carboxamide)benzoate

[C73]



80 mg of sodium triacetoxyborohydride was added to a dichloromethane (1 ml) solution of 100

mg of methyl 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate and 0.020 ml of 3-oxetanone produced in Reference Example 18-(a) at room temperature under an argon gas flow, stirred at room temperature for two hours, and left to stand at room temperature for 15 hours. 0.020 ml of 3-oxetanone and 78 mg of sodium triacetoxyborohydride were added thereto at room temperature and stirred at room temperature for 1.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 86 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 461 $[M+H]^+$

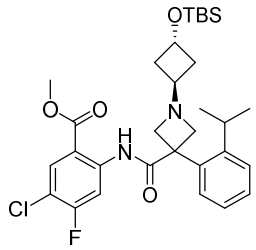
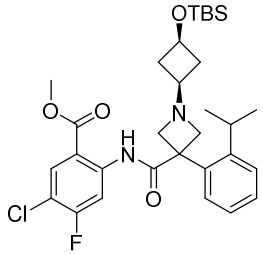
Retention time (LCMS conditions 2): 1.163 min.

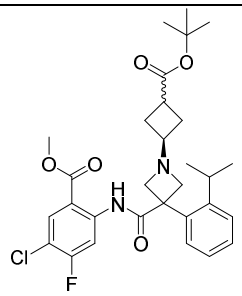
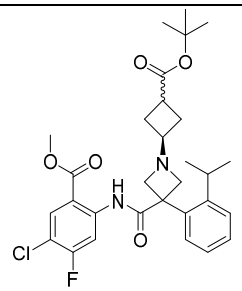
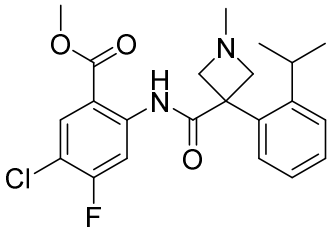
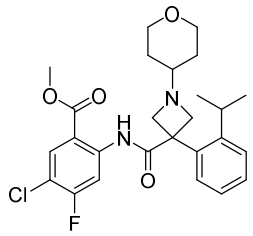
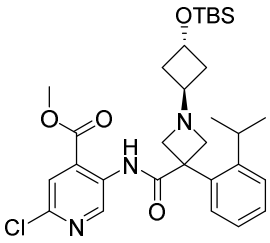
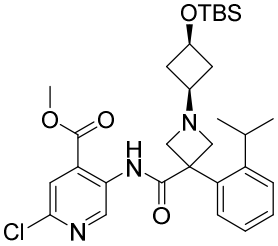
[0181] Reference Example 19-(a) and the like

Compounds shown in Table 14 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 18-(b). In the syntheses of Reference Example 62-(a) and Reference Example 63-(a), the compound of Reference Example 10-(b) was used instead of the compound of Reference Example 18-(a), and triethylamine was added.

[Table 14]

Table 14

Reference Example	Structural formula	Analysis data
19-(a)		Mass spectrum (ESI, m/z): 589 $[M+H]^+$ Retention time (LCMS conditions 3): 1.424 min
20-(a)		Mass spectrum (ESI, m/z): 589 $[M+H]^+$ Retention time (LCMS conditions 3): 1.380 min

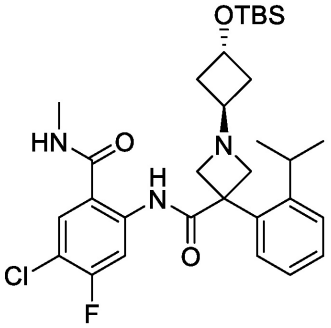
52-(a)	 Diastereomer 1	Mass spectrum (DUIS, m/z): 559 $[M+H]^+$ Retention time (LCMS conditions 4): 1.216 min
53-(a)	 Diastereomer 2	Mass spectrum (DUIS, m/z): 559 $[M+H]^+$ Retention time (LCMS conditions 4): 1.205 min
54-(a)		Mass spectrum (ESI, m/z): 419 $[M+H]^+$ Retention time (LCMS conditions 2): 1.100 min
55-(a)		Mass spectrum (ESI, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 2): 1.132 min
62-(a)		Mass spectrum (ESI, m/z): 572 $[M+H]^+$ Retention time (LCMS conditions 3): 1.282 min
63-(a)		Mass spectrum (ESI, m/z): 572 $[M+H]^+$ Retention time (LCMS conditions 3): 1.245 min

[0182] Reference Example 19-(c)

Production of 1-(trans-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-N-(4-chloro-5-fluoro-2-

(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C74]



0.043 ml of N,N-diisopropylethylamine, 47 mg of HATU, and 0.124 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (1 ml) solution of 48 mg of 2-(1-(trans-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-5-chloro-4-fluorobenzoic acid produced in Reference Example 19-(b) at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 14 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 40 mg of a title compound as a colorless oily substance.

Mass spectrum (ESI, m/z): 588 $[M+H]^+$

Retention time (LCMS conditions 2): 1.404 min.

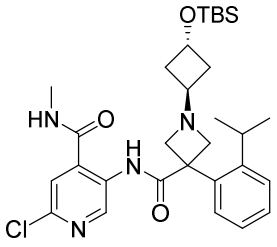
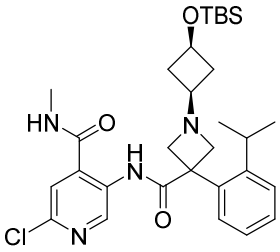
[0183] Reference Example 62-(c) and the like

Compounds shown in Table 15 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 19-(c). The syntheses of Reference Example 62-(c) and Reference Example 63-(c) were performed using methylamine hydrochloride instead of the 2M methylamine/tetrahydrofuran solution.

[Table 15]

Table 15

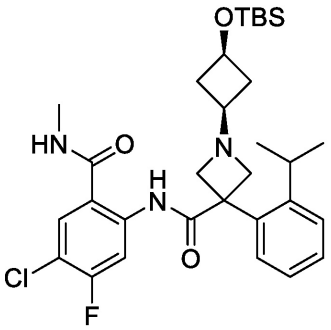
Reference Example	Structural formula	Analysis data

62-(c)		Mass spectrum (ESI, m/z): 571 $[M+H]^+$ Retention time (LCMS conditions 2): 1.268 min
63-(c)		Mass spectrum (ESI, m/z): 571 $[M+H]^+$ Retention time (LCMS conditions 2): 1.252 min

[0184] Reference Example 20-(c)

Production of 1-(cis-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C75]



0.053 ml of N,N-diisopropylethylamine, 58 mg of HATU, and 0.153 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (1 ml) solution of 59 mg of 2-(1-(cis-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-5-chloro-4-fluorobenzoic acid produced in Reference Example 20-(b) at room temperature under an argon gas flow and stirred at room temperature for 0.5 hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 51 mg of a title compound as a colorless oily substance.

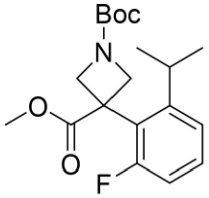
Mass spectrum (ESI, m/z): 588 $[M+H]^+$

Retention time (LCMS conditions 2): 1.370 min.

[0185] Reference Example 26-(e)

Production of 1-(tert-butyl) 3-methyl 3-(2-fluoro-6-isopropylphenyl)azetidine-1,3-dicarboxylate

[C76]



0.79 ml of di-tert-butyl dicarbonate and 275 mg of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) were added to a tetrahydrofuran (17 ml) solution of 715 mg of methyl 1-benzhydryl-3-(2-fluoro-6-(prop-1-en-2-yl)phenyl)azetidine-3-carboxylate produced in Reference Example 26-(d) at room temperature and stirred at room temperature under a hydrogen atmosphere for two hours. 275 mg of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) was added thereto at room temperature and stirred at room temperature under a hydrogen atmosphere for one hour. 275 mg of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) was added thereto at room temperature and stirred at room temperature under a hydrogen atmosphere for two hours. Celite and ethyl acetate were added to a reaction mixture, the reaction mixture was filtered through celite and washed with ethyl acetate, and a filtrate was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 185 mg of a title compound as a colorless oily substance.

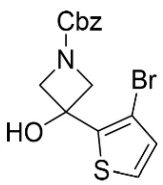
Mass spectrum (DUIS, m/z): 352 $[M+H]^+$

Retention time (LCMS conditions 1): 1.629 min.

[0186] Reference Example 31-(a)

Production of benzyl 3-(3-bromothiophen-2-yl)-3-hydroxyazetidine-1-carboxylate

[C77]



30 ml of a 2M lithium diisopropylamide/tetrahydrofuran solution was added dropwise to a tetrahydrofuran (100 ml) solution of 8.15 g of 3-bromothiophene at -78°C under an argon gas flow and stirred at -78°C for one hour. Next, a tetrahydrofuran (50 ml) solution of 13.3 g of benzyl 3-oxoazetidine-1-carboxylate was added dropwise thereto at -78°C and stirred at -78°C for one hour. A reaction mixture was returned to room temperature by adding a saturated ammonium chloride aqueous solution thereto and was separated. An aqueous layer was extracted with ethyl acetate, a combined organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 17.9 g of a title compound as a yellow oily substance.

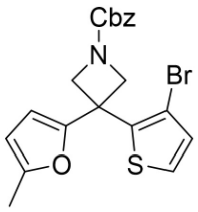
Mass spectrum (ESI, m/z): 368, 370 $[M+H]^+$

Retention time (LCMS conditions 2): 1.222 min.

[0187] Reference Example 31-(b)

Production of benzyl 3-(3-bromothiophen-2-yl)-3-(5-methylfuran-2-yl)azetidine-1-carboxylate

[C78]



2.90 g of bis(trifluoromethanesulfonyl)imide calcium (II), 1.87 g of tetrabutylammonium hexafluorophosphate, and 13.0 ml of 2-methylfuran were added to a dichloromethane (200 ml) solution of 17.8 g of benzyl 3-(3-bromothiophen-2-yl)-3-hydroxyazetidine-1-carboxylate produced in Reference Example 31-(a) at room temperature under an argon gas flow and stirred at 45°C for eight hours. 3.0 ml of 2-methylfuran was added thereto and stirred at 45°C for nine hours. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was filtered through celite and separated. An organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure

preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 10.6 g of a title compound as a yellow oily substance.

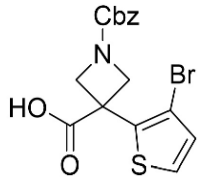
Mass spectrum (ESI, m/z): 432, 434 $[M+H]^+$

Retention time (LCMS conditions 2): 1.721 min.

[0188] Reference Example 31-(c)

Production of 1-((benzyloxy)carbonyl)-3-(3-bromothiophen-2-yl)azetidine-3-carboxylic acid

[C79]



50 ml of heptane was added to a water (100 ml) solution of 12.9 g of sodium periodate under an argon gas flow and stirred for 10 minutes. An ethyl acetate (50 ml) solution of 3.46 g of benzyl 3-(3-bromothiophen-2-yl)-3-(5-methylfuran-2-yl)azetidine-1-carboxylate produced in Reference Example 31-(b) was added thereto. Next, 90 mg of ruthenium (III) chloride n-hydrate was added thereto at 0°C and stirred at 0°C for five hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate three times. An organic layer was washed with 5% sodium bisulfite and saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). 30 ml of a 1N sodium hydroxide aqueous solution was added to the obtained purified product, and the purified product was washed with tert-butyl methyl ether twice. The pH was adjusted to two by adding 6N hydrochloric acid to an aqueous layer, and the aqueous layer was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure to obtain 1.38 g of a title compound as a yellow foamy substance.

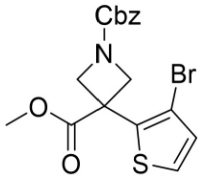
Mass spectrum (ESI, m/z): 394, 396 $[M-H]^-$

Retention time (LCMS conditions 2): 1.241 min.

[0189] Reference Example 31-(d)

Production of 1-benzyl 3-methyl 3-(3-bromothiophen-2-yl)azetidine-1,3-dicarboxylic acid

[C80]



722 mg of potassium carbonate and 0.26 ml of iodomethane were added to a N,N-dimethylformamide (15 ml) solution of 1.38 g of 1-((benzyloxy)carbonyl)-3-(3-bromothiophen-2-yl)azetidine-3-carboxylic acid produced in Reference Example 31-(c) at room temperature under an argon gas flow and stirred at room temperature for three hours. Water was added to a reaction mixture, and the reaction mixture was extracted with tert-butyl methyl ether three times. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 1.23 g of a title compound as a colorless oily substance.

Mass spectrum (ESI, m/z): 410, 412 $[M+H]^+$

Retention time (LCMS conditions 2): 1.473 min.

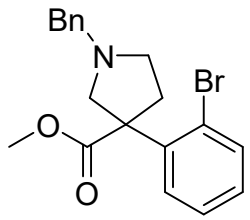
[0190] Reference Example 290-(a)

A compound shown in Table 16 below was obtained by treating a corresponding raw material compound in the same manner as in Reference Example 31-(d).

[Table 16]

Table 16

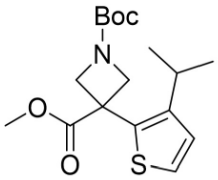
Reference Example	Structural formula	Analysis data

290-(a)		Mass spectrum (DUIS, m/z): 374, 376 $[M+H]^+$ Retention time (LCMS conditions 1): 0.806 min

[0191] Reference Example 31-(f)

Production of 1-(tert-butyl) 3-methyl 3-(3-isopropylthiophen-2-yl)azetidine-1,3-dicarboxylic acid

[C81]



0.42 g of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) and 1.4 ml of di-tert-butyl dicarbonate were added to a tetrahydrofuran (20 ml) solution of 1.08 g of 1-benzyl 3-methyl 3-(3-isopropylthiophen-2-yl)azetidine-1,3-dicarboxylate produced in Reference Example 31-(e) at room temperature and stirred at room temperature under a hydrogen atmosphere for four hours. 0.42 g of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) was added thereto and stirred at room temperature under a hydrogen atmosphere for two hours. 0.42 g of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) was added thereto at room temperature and stirred at room temperature under a hydrogen atmosphere for 5.5 hours. Celite and ethyl acetate were added to a reaction mixture, the reaction mixture was filtered through celite and washed with ethyl acetate, and a filtrate was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 0.74 g of a title compound as a white solid.

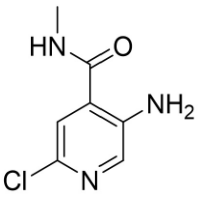
Mass spectrum (ESI, m/z): 338 $[M-H]^-$

Retention time (LCMS conditions 2): 1.625 min.

[0192] Reference Example 33-(a)

Production of 5-amino-2-chloro-N-methylisonicotinamide

[C82]



237 mg of methylamine hydrochloride, 665 mg of HATU, and 1.22 ml of N,N-diisopropylethylamine were added to a N,N-dimethylformamide (4 ml) solution of 201 mg of 5-amino-2-chloro-4-isonicotinic acid at room temperature under an argon gas flow and stirred at room temperature for 15 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 164 mg of a title compound as a slightly yellow solid.

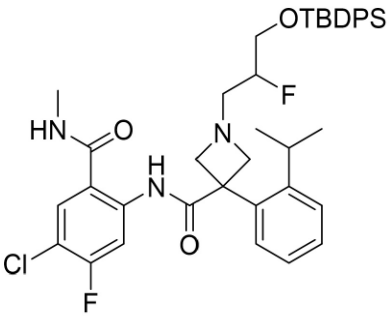
Mass spectrum (DUIS, m/z): 186 $[M+H]^+$

Retention time (LCMS conditions 1): 0.408 min.

[0193] Reference Example 56-(a)

Production of 1-(3-((tert-butyldiphenylsilyl)oxy)-2-fluoropropyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C83]



41 mg of 3-((tert-butyldiphenylsilyl)oxy)-2-fluoropropyltrifluoromethanesulfonate, and 0.026 ml of N,N-diisopropylethylamine were added to an acetonitrile (0.6 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced

in the same manner as in Example 11-(b) under an argon gas flow at 0°C and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 48 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 718 $[M+H]^+$

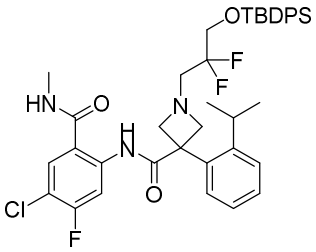
Retention time (LCMS conditions 2): 1.581 min.

[0194] Reference Example 57-(a)

A compound shown in Table 17 below was obtained by treating a corresponding raw material compound in the same manner as in Reference Example 56-(a).

[Table 17]

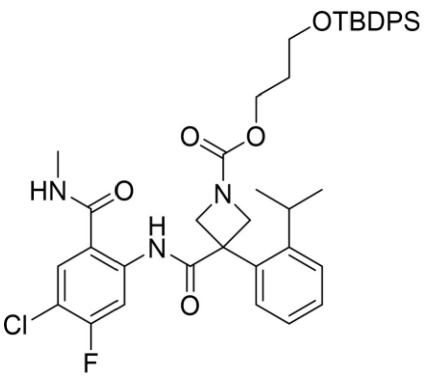
Table 17

Reference Example	Structural formula	Analysis data
57-(a)		Mass spectrum (ESI, m/z): 736 $[M+H]^+$ Retention time (LCMS conditions 2): 2.315 min

[0195] Reference Example 58-(a)

Production of 3-((tert-butyldiphenylsilyl)oxy)propyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C84]



48 mg of 1,1'-carbonyldiimidazole was added to a dichloromethane (0.5 ml) solution of 94 mg

of 3-((tert-butyldiphenylsilyl)oxy)propan-1-ol at room temperature under an argon gas flow and stirred at room temperature for two hours. 0.25 ml of the obtained solution was added to a 1,4-dioxane (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow, stirred at room temperature for one hour, and then stirred at 90°C for two hours. A reaction mixture was left to stand at room temperature for 14 hours and then stirred at 90°C for two hours. Water was added to the reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 39 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 744 $[M+H]^+$

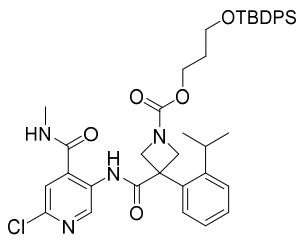
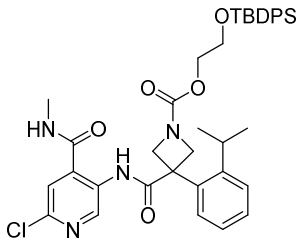
Retention time (LCMS conditions 1): 2.303 min.

[0196] Reference Example 59-(a) and the like

Compounds shown in Table 18 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 58-(a).

[Table 18]

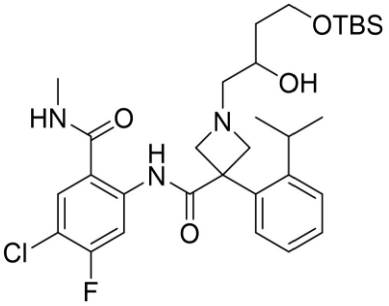
Table 18

Reference Example	Structural formula	Analysis data
59-(a)		Mass spectrum (ESI, m/z): 727 $[M+H]^+$ Retention time (LCMS conditions 2): 2.137 min
60-(a)		Mass spectrum (ESI, m/z): 713 $[M+H]^+$ Retention time (LCMS conditions 2): 2.055 min

[0197] Reference Example 61-(a)

Production of 1-(4-((tert-butyldimethylsilyl)oxy)-2-hydroxybutyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C85]



40 mg of tert-butyldimethyl(2-(oxiran-2-yl)ethoxy)silane and 0.031 ml of triethylamine were added to an ethanol (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for 161 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 35 mg of a title compound as a colorless oily substance.

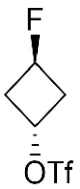
Mass spectrum (ESI, m/z): 606 $[M+H]^+$

Retention time (LCMS conditions 2): 1.350 min.

[0198] Reference Example 166-(a)

Production of trans-3-fluorocyclobutyl trifluoromethanesulfonate

[C86]



0.097 ml of 2,6-lutidine was added to a dichloromethane (1 ml) solution of 50 mg of trans-3-fluorocyclobutan-1-ol at room temperature under an argon gas flow. Next, 0.131 ml of trifluromethanesulfonic anhydride was added dropwise thereto under an ice bath and stirred under an

ice bath for 15 minutes. Water was added to a reaction mixture under an ice bath, and the reaction mixture was extracted with dichloromethane. An organic layer was washed successively with 1N hydrochloric acid and a saturated sodium bicarbonate aqueous solution, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 70 mg of a title compound as a brown oily substance.

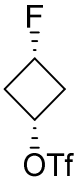
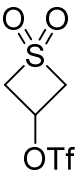
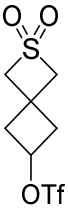
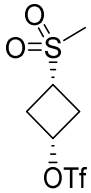
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ: 5.58 - 5.50 (m, 1H), 5.42 - 5.21 (m, 1H), 2.91 - 2.66 (m, 4H)

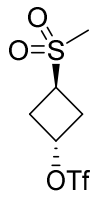
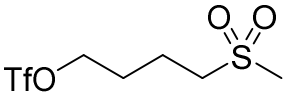
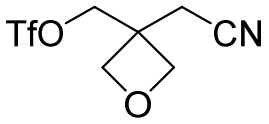
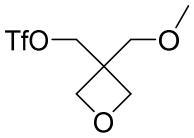
[0199] Reference Example 167-(a) and the like

Compounds shown in Table 19 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 166-(a).

[Table 19]

Table 19

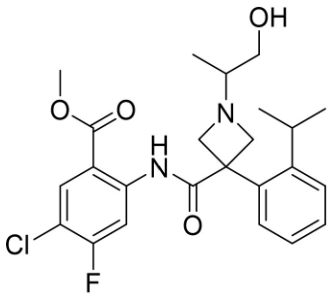
Reference Example	Structural formula	Analysis data
167-(a)		^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ: 4.92 - 4.62 (m, 2H), 3.13 - 3.01 (m, 2H), 2.84 - 2.64 (m, 2H)
169-(a)		
170-(a)		
171-(a)		

172-(a)		
173-(a)		
178-(a)		
334-(a)		

[0200] Reference Example 206-(a)

Production of methyl 5-chloro-4-fluoro-2-(1-(1-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate

[C87]



0.024 ml of N,N-diisopropylethylamine was added to a tetrahydrofuran (1.3 ml) solution of 60 mg of methyl 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate hydrochloride produced in the same manner as in Example 2-(d) at room temperature under an argon gas flow and stirred at room temperature for 10 minutes. Next, 0.012 ml of hydroxyacetone was added

thereto at room temperature and stirred at room temperature for 30 minutes. Next, 43 mg of sodium triacetoxyborohydride was added thereto and stirred at room temperature for two hours. A saturated sodium bicarbonate aqueous solution was added to the reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) to obtain 42 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 463 $[M+H]^+$

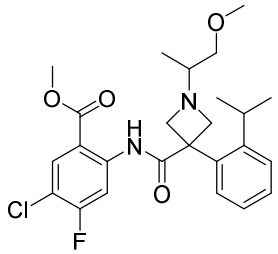
Retention time (LCMS conditions 2): 1.089 min.

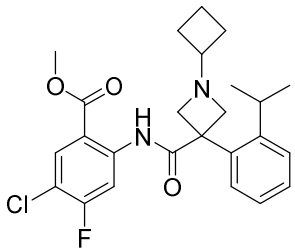
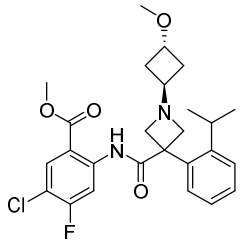
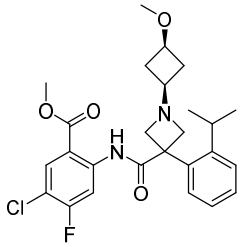
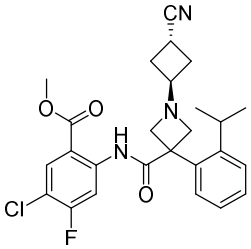
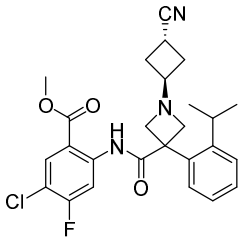
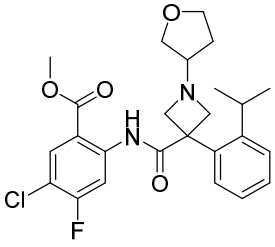
[0201] Reference Example 207-(a) and the like

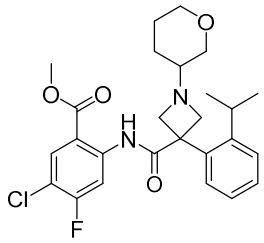
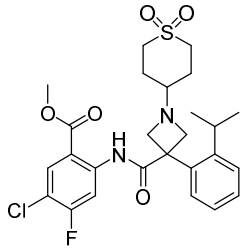
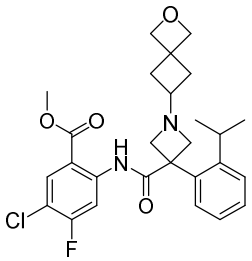
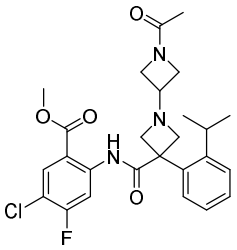
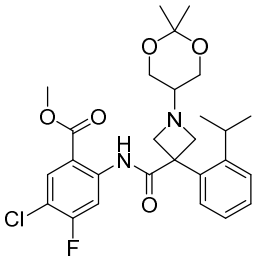
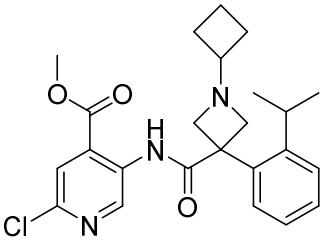
Corresponding raw material compounds were treated in the same manner as in Reference Example 206-(a) to obtain compounds shown in Table 20 below. The syntheses of Reference Example 211-(a), Reference Example 212-(a), Reference Example 218-(a), Reference Example 221-(a), and Reference Example 222-(a) were performed using dichloromethane instead of tetrahydrofuran and triethylamine instead of N,N-diisopropylethylamine. The syntheses of Reference Example 213-(a), Reference Example 214-(a), Reference Example 216-(a), Reference Example 217-(a), Reference Example 220-(a), Reference Example 223-(a), and Reference Example 343-(a) were performed using dichloromethane instead of tetrahydrofuran.

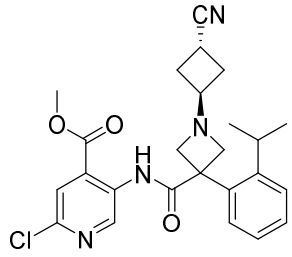
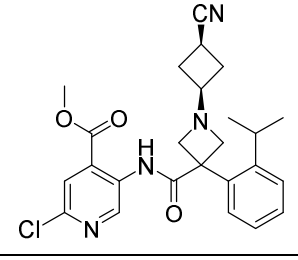
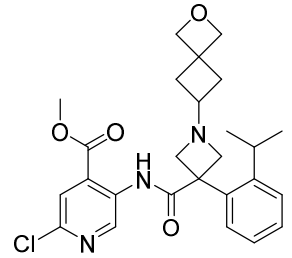
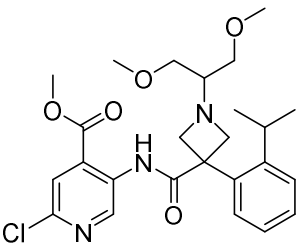
[Table 20]

Table 20

Reference Example	Structural formula	Analysis data
207-(a)		Mass spectrum (ESI, m/z): 477 $[M+H]^+$ Retention time (LCMS conditions 2): 1.190 min

208-(a)		Mass spectrum (DUIS, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 1): 1.278 min
209-(a)		Mass spectrum (ESI, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 2): 1.185 min
210-(a)		Mass spectrum (ESI, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 2): 1.187 min
211-(a)		Mass spectrum (DUIS, m/z): 484 $[M+H]^+$ Retention time (LCMS conditions 4): 1.109 min
212-(a)		Mass spectrum (DUIS, m/z): 484 $[M+H]^+$ Retention time (LCMS conditions 4): 1.084 min
213-(a)		Mass spectrum (ESI, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 2): 1.089 min

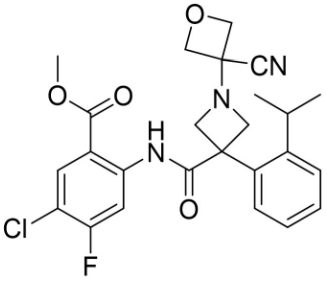
214-(a)		Mass spectrum (ESI, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 2): 1.158 min
215-(a)		Mass spectrum (ESI, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 2): 1.231 min
216-(a)		Mass spectrum (ESI, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 2): 0.929 min
217-(a)		Mass spectrum (ESI, m/z): 502 $[M+H]^+$ Retention time (LCMS conditions 2): 1.187 min
218-(a)		Mass spectrum (ESI, m/z): 519 $[M+H]^+$ Retention time (LCMS conditions 2): 1.212 min
220-(a)		Mass spectrum (ESI, m/z): 442 $[M+H]^+$ Retention time (LCMS conditions 2): 1.037 min

221-(a)		Mass spectrum (DUIS, m/z): 467 $[M+H]^+$ Retention time (LCMS conditions 1): 1.015 min
222-(a)		Mass spectrum (DUIS, m/z): 467 $[M+H]^+$ Retention time (LCMS conditions 1): 0.994 min
223-(a)		Mass spectrum (ESI, m/z): 484 $[M+H]^+$ Retention time (LCMS conditions 2): 0.965 min
343-(a)		Mass spectrum (DUIS, m/z): 490 $[M+H]^+$ Retention time (LCMS conditions 7): 0.703 min

[0202] Reference Example 219-(a)

Production of methyl 5-chloro-2-(1-(3-cyanooxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-4-fluorobenzoate

[C88]



0.021 ml of N,N-diisopropylethylamine was added to a 1,2-dichloroethane (1 ml) solution of 53 mg of methyl 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)azetidine-3-carboxamide)benzoate hydrochloride produced in the same manner as in Reference Example 2-(d) at room temperature under

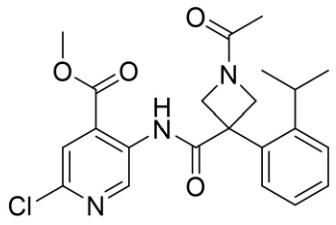
an argon gas flow and stirred at room temperature for 10 minutes. Next, 0.019 ml of 3-oxetanone was added thereto at room temperature and stirred at room temperature for 10 minutes. Next, 0.020 ml of trimethylsilylcyanide and 0.009 ml of acetic acid were added thereto at room temperature and stirred at 70°C for 4.5 hours. 0.019 ml of 3-oxetanone and 0.020 ml of trimethylsilylcyanide were added thereto at 70°C and stirred at 70°C for 1.5 hours. 0.038 ml of 3-oxetanone and 0.040 ml of trimethylsilylcyanide were added at 70°C and stirred at 70°C for one hour. 0.038 ml of 3-oxetanone and 0.040 ml of trimethylsilylcyanide were added thereto at 70°C and stirred at 70°C for one hour. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 49 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 486 $[M+H]^+$

Retention time (LCMS conditions 2): 1.764 min.

[0203] Reference Example 248-(a)

Production of methyl 5-(1-acetyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloroisonicotinate [C89]



0.049 ml of triethylamine and 0.012 ml of acetic anhydride were added to a dichloromethane (0.5 ml) suspension of 50 mg of methyl 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)isonicotinate hydrochloride produced in the same manner as in Reference Example 10-(b) at 0°C under an argon gas flow and stirred at room temperature for 45 minutes. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted

with dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 47 mg of a title compound as a white foamy substance.

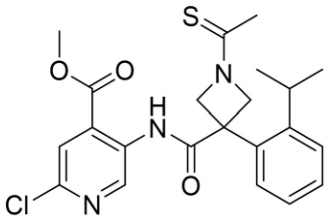
Mass spectrum (ESI, m/z): 430 $[M+H]^+$

Retention time (LCMS conditions 2): 1.330 min.

[0204] Reference Example 248-(b)

Production of methyl 2-chloro-5-(1-ethanethioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)isonicotinate

[C90]



28 mg of Lawson's reagent was added to a tetrahydrofuran (1 ml) solution of 47 mg of methyl 5-(1-acetyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloroisonicotinate produced in Reference Example 248-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 48 mg of a title compound as a white foamy substance.

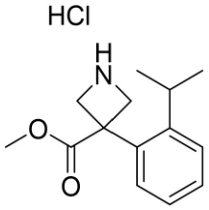
Mass spectrum (ESI, m/z): 446 $[M+H]^+$

Retention time (LCMS conditions 2): 1.540 min.

[0205] Reference Example 265-(a)

Production of methyl 3-(2-isopropylphenyl)azetidine-3-carboxylate hydrochloride

[C91]



1.5 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (0.5 ml) solution of 100 mg of 1-(tert-butyl) 3-methyl 3-(2-isopropylphenyl)azetidine-1,3-dicarboxylate produced in the same manner as in Reference Example 1-(e) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. A reaction mixture was concentrated under reduced pressure to obtain 82 mg of a title compound as a white foamy substance.

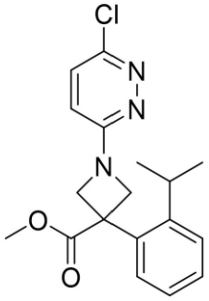
Mass spectrum (ESI, m/z): 234 $[M+H]^+$

Retention time (LCMS conditions 2): 0.581 min.

[0206] Reference Example 265-(b)

Production of methyl 1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxylate

[C92]



0.16 ml of N,N-diisopropylethylamine and 91 mg of 3,6-dichloropyridazine were added to a 1,4-dioxane (1 ml) suspension of 82 mg of methyl 3-(2-isopropylphenyl)azetidine-3-carboxylate hydrochloride produced in Reference Example 265-(a) at room temperature under an argon gas flow and stirred at 100°C for six hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 86 mg of a title compound as a white solid.

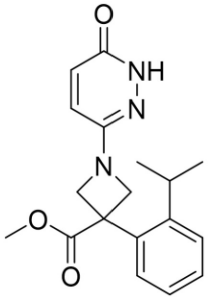
Mass spectrum (ESI, m/z): 346 $[M+H]^+$

Retention time (LCMS conditions 2): 1.339 min.

[0207] Reference Example 265-(c)

Production of methyl 3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxylate

[C93]



An acetic acid (1 ml) solution of 46 mg of methyl 1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxylate produced in Reference Example 265-(b) was stirred at 140°C for nine hours. A reaction mixture was concentrated under reduced pressure to obtain 47 mg of a title compound as a slightly yellow foamy substance.

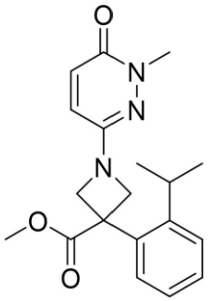
Mass spectrum (ESI, m/z): 328 $[M+H]^+$

Retention time (LCMS conditions 2): 1.059 min.

[0208] Reference Example 265-(d)

Production of methyl 3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxylate

[C94]



0.013 ml of iodomethane and 94 mg of cesium carbonate were added to a N,N-dimethylformamide (1 ml) solution of 47 mg of methyl 3-(2-isopropylphenyl)-1-(6-oxo-1,6-

dihydropyridazin-3-yl)azetidine-3-carboxylate produced in Reference Example 265-(c) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 35 mg of a title compound as a yellow oily substance.

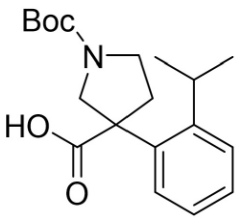
Mass spectrum (ESI, m/z): 342 $[M+H]^+$

Retention time (LCMS conditions 2): 1.192 min

[0209] Reference Example 290-(d)

Production of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)pyrrolidine-3-carboxylic acid

[C95]



0.138 ml of a 1M potassium hydroxide aqueous solution was added to a DMSO (0.73 ml) solution of 24 mg of 1-(tert-butyl) 3-methyl 3-(2-isopropylphenyl)pyrrolidine-1,3-dicarboxylate produced in Reference Example 290-(c) at room temperature under an argon gas flow and stirred at 40°C for three hours and at 60°C for 1.5 hours. The pH was adjusted to six by adding 1N hydrochloric acid to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. A 5% potassium hydrogen sulfate aqueous solution was added to an aqueous layer, the aqueous layer was extracted with a mixed solvent of dichloromethane: Methanol = 8: 1, and a combined organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 23 mg of a title compound as a yellow oily substance.

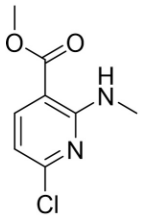
Mass spectrum (DUIS, m/z): 332 $[M-H]^-$

Retention time (LCMS conditions 1): 1.368 min.

[0210] Reference Example 294-(a)

Production of methyl 6-chloro-2-(methylamino)nicotinate

[C96]

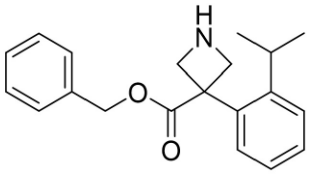


0.833 ml of a 2M methylamine/tetrahydrofuran solution was added to an ethanol (1.9 ml) suspension of 100 mg of 2,6-dichloronicotinic acid at room temperature under an argon gas flow, stirred at 100°C for 30 minutes, stirred at 120°C for 40 minutes, and stirred at 150°C for 30 minutes using a microwave reactor. A reaction mixture was concentrated under reduced pressure. 1N hydrochloric acid was added to a concentrated residue, and the concentrated residue was extracted with a mixed solvent of ethyl acetate:methanol = 4:1. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 0.052 ml of thionyl chloride was added to a methanol (2 ml) solution of the concentrated residue at room temperature under an argon gas flow and stirred at 70°C for three hours. A reaction mixture was concentrated under reduced pressure. A saturated sodium bicarbonate aqueous solution was added to the concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 12 mg of a title compound as a white solid.

[0211] Reference Example 325-(a)

Production of benzyl 3-(2-isopropylphenyl)azetidine-3-carboxylate

[C97]



0.447 ml of benzyl bromide and 650 mg of potassium carbonate were added to a N,N-

dimethylformamide (10 ml) solution of 1.00 g of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)azetidine-3-carboxylic acid produced in the same manner as in Reference Example 1-(f) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed successively with water and saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate).

16 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (6 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at room temperature for 17 hours. A reaction mixture was concentrated under reduced pressure. A saturated sodium bicarbonate aqueous solution was added to the concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 981 mg of a title compound as a slightly yellow oily substance.

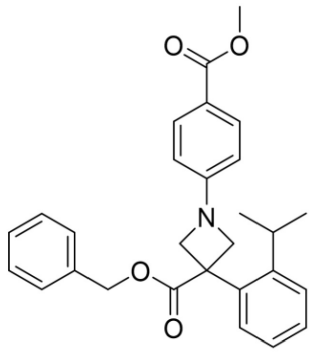
Mass spectrum (DUIS, m/z): 310 $[M+H]^+$

Retention time (LCMS conditions 7): 0.591 min.

[0212] Reference Example 325-(b)

Production of benzyl 3-(2-isopropylphenyl)-1-(4-(methoxycarbonyl)phenyl)azetidine-3-carboxylate

[C98]



1.02 g of methyl 4-bromobenzoate, 302 mg of [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (tradename: XantPhos

Pd G3) and 1.35 g of tripotassium phosphate were added to a 1,4-dioxane (15 ml) solution of 981 mg of benzyl 3-(2-isopropylphenyl)azetidine-3-carboxylate produced in Reference Example 325-(a) at room temperature under an argon gas flow and stirred at 110°C for five hours under an argon atmosphere. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 1.22 g of a title compound as a slightly yellow foamy substance.

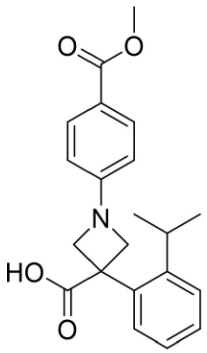
Mass spectrum (DUIS, m/z): 444 $[M+H]^+$

Retention time (LCMS conditions 7): 1.098 min.

[0213] Reference Example 325-(c)

Production of 3-(2-isopropylphenyl)-1-(4-(methoxycarbonyl)phenyl)azetidine-3-carboxylic acid

[C99]



123 mg of a 10% palladium on carbon (wetted with water, N.E. Chemcat Corporation-PE type) was added to an ethanol (12 ml) solution of 1.22 g of benzyl 3-(2-isopropylphenyl)-1-(4-(methoxycarbonyl)phenyl)azetidine-3-carboxylate produced in Reference Example 325-(b) at room temperature under an argon gas flow and stirred at room temperature for one hour under a hydrogen atmosphere. A reaction mixture was filtered through celite, and a filtrate was concentrated under reduced pressure. 15 ml of tert-butyl methyl ether was added to the obtained concentrated residue and stirred at 0°C for 30 minutes. A solid was collected by filtration, washed with tert-butyl methyl ether, and dried under reduced pressure to obtain 341 mg of a title compound as a white solid.

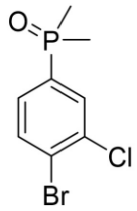
Mass spectrum (DUIS, m/z): 354 $[M+H]^+$

Retention time (LCMS conditions 7): 0.873 min.

[0214] Reference Example 377-(a)

Production of (4-bromo-3-chlorophenyl)dimethylphosphine oxide

[C100]



54 mg of dimethylphosphine oxide, 0.11 ml of triethylamine, 29 mg of tris(dibenzylideneacetone)dipalladium(0), and 37 mg of Xantphos were added to a 1,4-dioxane (1 ml) solution of 200 mg of 1-bromo-2-chloro-4-iodobenzene at room temperature, degassed, substituted with nitrogen, and then stirred at 90°C for one hour under an argon gas flow. Water was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol) to obtain 175 mg of a title compound as a yellow solid.

Mass spectrum (DUIS, m/z): 267, 269 $[M+H]^+$

Retention time (LCMS conditions 7): 0.569 min.

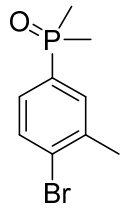
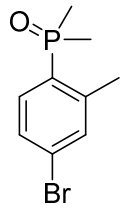
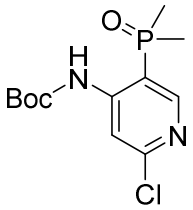
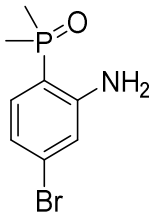
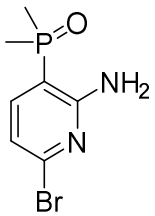
[0215] Reference Example 378-(a) and the like

Compounds shown in Table 21 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 377-(a). The synthesis of Reference Example 384-(a) was performed at room temperature as the reaction temperature.

[Table 21]

Table 21

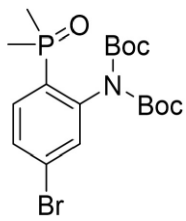
Reference Example	Structural formula	Analysis data

378-(a)		Mass spectrum (DUIS, m/z): 247, 249 $[M+H]^+$ Retention time (LCMS conditions 7): 0.563 min
379-(a)		Mass spectrum (DUIS, m/z): 247, 249 $[M+H]^+$ Retention time (LCMS conditions 7): 0.548 min
381-(a)		Mass spectrum (DUIS, m/z): 305 $[M+H]^+$ Retention time (LCMS conditions 7): 0.743 min
383-(a)		Mass spectrum (DUIS, m/z): 248, 250 $[M+H]^+$ Retention time (LCMS conditions 8): 0.700 min
384-(a)		Mass spectrum (DUIS, m/z): 249, 251 $[M+H]^+$ Retention time (LCMS conditions 8): 0.467 min

[0216] Reference Example 383-(b)

Production of tert-butyl (5-bromo-2-(dimethylphosphoryl)phenyl)(tert-butoxycarbonyl)carbamate

[C101]



3 mg of 4-dimethylaminopyridine was added to a di-tert-butyl dicarbonate (1 ml) suspension of 55 mg of (2-amino-4-bromophenyl)dimethylphosphine oxide produced in Reference Example 383-(a) at room temperature under an argon gas flow and stirred at 60°C for 30 minutes. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol) to obtain 81 mg of a title compound as a white solid.

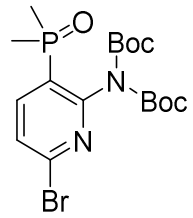
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 7.74 - 7.66 (m, 2H), 7.63 - 7.59 (m, 1H), 1.62 (d, J = 13.4 Hz, 6H), 1.36 (s, 18H)

[0217] Reference Example 384-(b)

A compound shown in Table 22 below was obtained by treating a corresponding raw material compound in the same manner as in Reference Example 383-(b).

[Table 22]

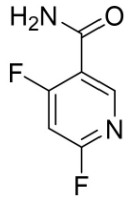
Table 22

Reference Example	Structural formula	Analysis data
384-(b)		Retention time (LCMS conditions 8): 1.144 min

[0218] Reference Example 385-(a)

Production of 4,6-difluoronicotinamide

[C102]



0.099 ml of N,N-diisopropylethylamine and 57 mg of HATU were added to a N,N-dimethylformamide (0.1 ml) solution of 20 mg of 4,6-difluoropyridine-3-carboxylic acid at room temperature under an argon gas flow and stirred at room temperature for five minutes. Next, 20 mg of ammonium chloride was added thereto at room temperature and stirred at room temperature for one

hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 20 mg of a title compound as an orange oily substance.

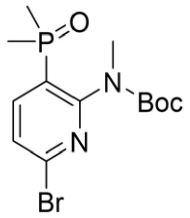
Mass spectrum (DUIS, m/z): 159 $[M+H]^+$

Retention time (LCMS conditions 7): 0.247 min.

[0219] Reference Example 388-(a)

Production of tert-butyl (6-bromo-3-(dimethylphosphoryl)pyridin-2-yl)(methyl)carbamate

[C103]



0.0039 ml of pyridine and 0.5 mg of 4-dimethylaminopyridine were added to a tetrahydrofuran (0.5 ml) solution of 10 mg of (2-amino-6-bromopyridin-3-yl)dimethylphosphine oxide produced in the same manner as in Reference Example 384-(a) at room temperature under an argon gas flow. Next, 0.0068 ml of trifluoroacetic anhydride was added thereto in an ice bath, stirred in the ice bath for 30 minutes, and stirred at room temperature for 30 minutes. 0.0078 ml of pyridine and 0.014 ml of trifluoroacetic anhydride were added thereto in the ice bath and stirred for 30 minutes in the ice bath. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 11 mg of potassium carbonate and 0.006 ml of iodomethane were added to a N,N-dimethylformamide (0.5 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow; stirred at room temperature for 30 minutes, stirred at 60°C for 30 minutes, and left to stand at room temperature for 14 hours. 16 mg of cesium carbonate was added at room temperature and stirred at 60°C for three hours. 32 mg of cesium carbonate was added thereto at 60°C, stirred at 60°C for five hours, and left to stand at room temperature for 14 hours. Next, 0.20 ml

of a 1M sodium hydroxide aqueous solution was added thereto at room temperature and stirred at room temperature for 15 minutes. Water was added to the reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 0.5 mg of 4-dimethylaminopyridine was added to a di-tert-butyl dicarbonate (0.5 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow, stirred at 60°C for 30 minutes, and stirred at 90°C for 1.5 hours. The reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol) to obtain 8.5 mg of a title compound as a yellow foamy substance.

Mass spectrum (DUIS, m/z): 363,365 $[M+H]^+$

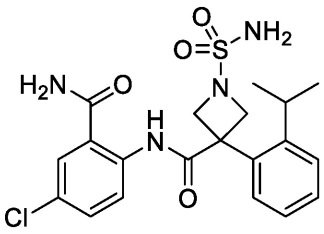
Retention time (LCMS conditions 8): 0.919 min.

[0220] (Examples)

Example 1-(a)

Production of N-(2-carbamoyl-4-chlorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C104]



0.045 ml of N,N-diisopropylethylamine, 34 mg of HATU, and 13 mg of ammonium chloride were added to a N,N-dimethylformamide (1 ml) solution of 25 mg of 5-chloro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in the same manner as in Reference Example 1-(j) at room temperature under an argon gas flow, stirred at room temperature for eight hours, and then left to stand at room temperature overnight. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica

gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 21 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 451 $[M+H]^+$

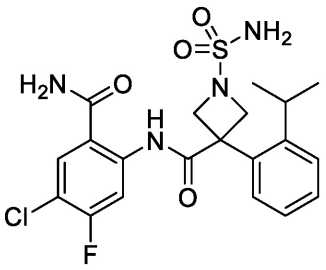
Retention time (LCMS conditions 2): 1.175 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.92 (s, 1H), 8.51 (d, J = 9.0 Hz, 1H), 8.35 (br s, 1H), 7.91 - 7.82 (m, 2H), 7.58 (dd, J = 2.4, 9.0 Hz, 1H), 7.38 - 7.25 (m, 4H), 7.02 (s, 2H), 4.35 (br d, J = 7.7 Hz, 2H), 4.15 (br d, J = 7.7 Hz, 2H), 2.70 - 2.61 (m, 1H), 1.08 (d, J = 6.8 Hz, 6H)

[0221] Example 2-(a)

Production of N-(2-carbamoyl-4-chloro-5-fluorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C105]



0.261 ml of N,N-diisopropylethylamine, 189 mg of HATU, and 54 mg of ammonium chloride were added to a N,N-dimethylformamide (3 ml) solution of 156 mg of 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in Reference Example 2-(f) at room temperature under an argon gas flow and stirred at room temperature for 16.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 94 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 469 $[M+H]^+$

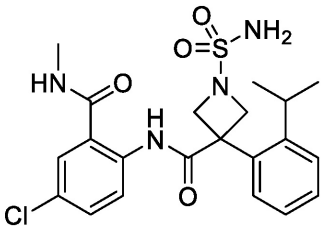
Retention time (LCMS conditions 1): 1.198 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.28 (s, 1H), 8.54 (d, J = 12.3 Hz, 1H), 8.34 (s, 1H), 8.08 (d, J = 8.2 Hz, 1H), 7.91 (s, 1H), 7.40 - 7.24 (m, 4H), 7.03 (s, 2H), 4.35 (br d, J = 7.7 Hz, 2H), 4.16 (br d, J = 7.7 Hz, 2H), 2.66 - 2.55 (m, 1H), 1.08 (d, J = 6.7 Hz, 6H)

[0222] Example 3-(a)

Production of N-(4-chloro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C106]



0.039 ml of N,N-diisopropylethylamine and 36 mg of HATU were added to a N,N-dimethylformamide (1 ml) solution of 27 mg of 5-chloro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in the same manner as in Reference Example 1-(j) and 0.115 ml of a 2M methylamine/tetrahydrofuran solution at room temperature under an argon gas flow, stirred at room temperature for four hours, and then left to stand at room temperature for 18.5 hours. After the components were further stirred at room temperature for one hour, 33 mg of HATU was added thereto at room temperature and stirred at room temperature for 4.5 hours. 35 mg of HATU was added at room temperature and stirred at room temperature for two hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 11 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 465 $[M+H]^+$

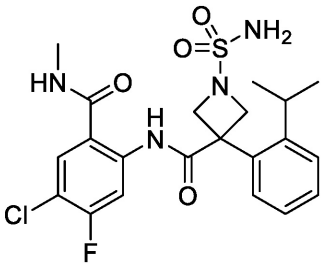
Retention time (LCMS conditions 2): 1.242 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.44 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 2.5 Hz, 1H), 7.67 - 7.60 (m, 1H), 7.48 - 7.33 (m, 4H), 4.42 (br d, J = 7.7 Hz, 2H), 4.24 (br d, J = 7.7 Hz, 2H), 2.75 (s, 3H), 2.72 - 2.63 (m, 1H), 1.13 (d, J = 6.8 Hz, 6H)

[0223] Example 4-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C107]



0.102 ml of N,N-diisopropylethylamine, 111 mg of HATU, and 0.30 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (1 ml) solution of 92 mg of 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in the same manner as in Reference Example 2-(f) at room temperature under an argon gas flow and stirred at room temperature for 18 hours. Water was added to the reaction mixture thus obtained, and the reaction mixture was extracted with ethyl acetate. The resulting organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 73 mg of the title compound as a white solid.

Mass spectrum (DUIS, m/z): 483 $[M+H]^+$

Retention time (LCMS conditions 1): 1.292 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.81 (s, 1H), 8.87 - 8.73 (m, 1H), 8.44 (d, J = 12.2

Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.42 - 7.26 (m, 4H), 7.04 (s, 2H), 4.36 (br d, J = 7.5 Hz, 2H), 4.18 (br d, J = 7.5 Hz, 2H), 2.73 - 2.57 (m, 4H), 1.07 (d, J = 6.7 Hz, 6H)

[0224] In addition, as an alternative method, the title compound was also synthesized as follows.

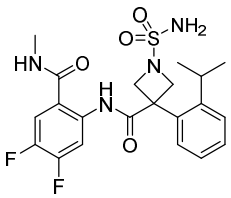
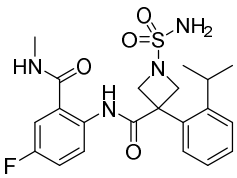
0.745 ml of triethylamine and 428 mg of sulfamide were added to a 1,4-dioxane (7.2 ml) solution of 360 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 100°C for seven hours. Water was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 365 mg of the title compound as a white solid.

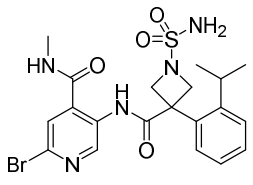
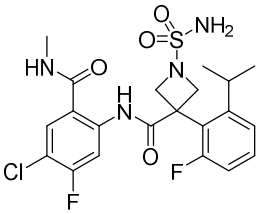
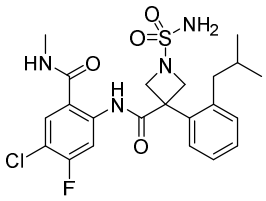
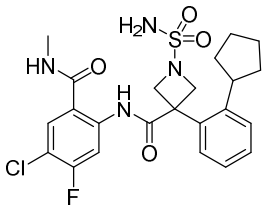
[0225] Example 23-(c) and the like

Compounds shown in Table 23 below were obtained by treating corresponding raw material compounds in the same manner as the alternative method in Example 4-(a).

[Table 23]

Table 23

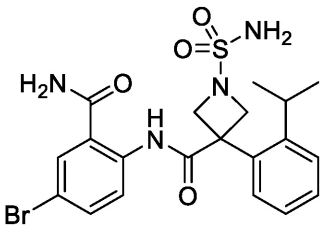
Example	Structural formula	Analysis data	Raw material
23-(c)		Mass spectrum (DUIS, m/z): 467 $[M+H]^+$ Retention time (LCMS conditions 1): 1.221 min	Example 23-(b)
24-(c)		Mass spectrum (DUIS, m/z): 449 $[M+H]^+$ Retention time (LCMS conditions 1): 1.129 min	Example 24-(b)

25-(c)		Mass spectrum (DUIS, m/z): 510, 512 $[M+H]^+$ Retention time (LCMS conditions 1): 1.123 min	Example 25-(b)
26-(c)		Mass spectrum (DUIS, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 1): 1.344 min	Example 11-(b)
29-(c)		Mass spectrum (DUIS, m/z): 497 $[M+H]^+$ Retention time (LCMS conditions 1): 1.386 min	Example 29-(b)
30-(c)		Mass spectrum (DUIS, m/z): 509 $[M+H]^+$ Retention time (LCMS conditions 1): 1.406 min	Example 30-(b)

[0226] Example 5-(a)

Production of N-(4-bromo-2-carbamoylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C108]



0.04 ml of N,N-diisopropylethylamine, 29 mg of HATU, and 8 mg of ammonium chloride were added to a N,N-dimethylformamide (1 ml) solution of 25 mg of 5-bromo-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in Reference Example 5-(d) at room

temperature under an argon gas flow and stirred at room temperature for 2.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 24 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 495, 497 $[M+H]^+$

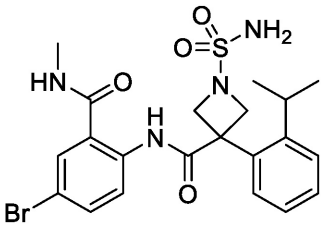
Retention time (LCMS conditions 2): 1.202 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.92 (s, 1H), 8.45 (d, J = 9.0 Hz, 1H), 8.35 (s, 1H), 7.98 (d, J = 2.4 Hz, 1H), 7.86 (s, 1H), 7.70 (dd, J = 2.4, 9.0 Hz, 1H), 7.38 - 7.23 (m, 4H), 7.02 (s, 2H), 4.35 (br d, J = 7.6 Hz, 2H), 4.15 (br d, J = 7.6 Hz, 2H), 2.64 (spt, J = 6.7 Hz, 1H), 1.08 (d, J = 6.7 Hz, 6H)

[0227] Example 6-(a)

Production of N-(4-bromo-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C109]



0.026 ml of N,N-diisopropylethylamine, 29 mg of HATU, and 0.08 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (1 ml) solution of 25 mg of 5-bromo-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in Reference Example 5-(d) at room temperature under an argon gas flow and stirred at room temperature for 2.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 25 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 509, 511 $[M+H]^+$

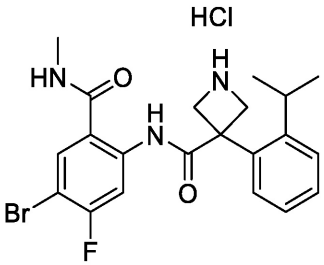
Retention time (LCMS conditions 2): 1.271 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.46 (br s, 1H), 8.86 (br s, 1H), 8.40 (d, J = 8.9 Hz, 1H), 7.91 (d, J = 2.3 Hz, 1H), 7.79 - 7.70 (m, 1H), 7.44 - 7.35 (m, 4H), 7.09 (br s, 2H), 4.41 (br d, J = 7.7 Hz, 2H), 4.23 (br d, J = 7.7 Hz, 2H), 2.76 - 2.65 (m, 4H), 1.13 (d, J = 6.7 Hz, 6H)

[0228] Example 7-(b)

Production of N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide hydrochloride

[C110]



0.4 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (0.2 ml) solution of 35 mg of tert-butyl 3-((4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in Example 7-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure to obtain 31 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 448, 450 $[M+H]^+$

Retention time (LCMS conditions 2): 0.900 min.

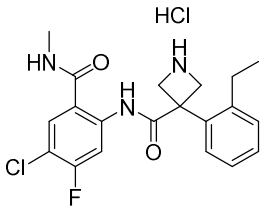
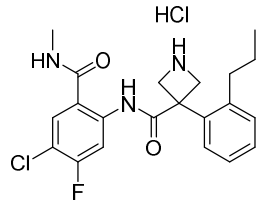
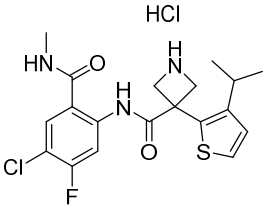
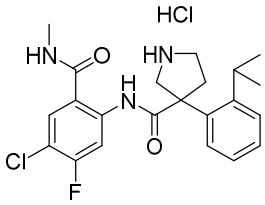
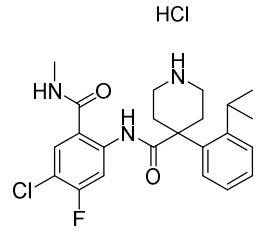
[0229] Example 27-(b) and the like

Compounds shown in Table 24 below were obtained by treating corresponding raw material compounds in the same manner as in Example 7-(b).

[Table 24]

Table 24

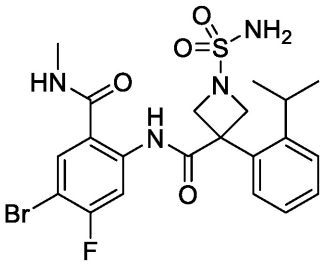
Example	Structural formula	Analysis data	Raw material

27-(b)		Mass spectrum (ESI, m/z): 390 $[M+H]^+$ Retention time (LCMS conditions 2): 0.839 min	Example 27-(a)
28-(b)		Mass spectrum (ESI, m/z): 404 $[M+H]^+$ Retention time (LCMS conditions 2): 0.900 min	Example 28-(a)
31-(b)		Mass spectrum (ESI, m/z): 410 $[M+H]^+$ Retention time (LCMS conditions 2): 0.858 min	Example 31-(a)
290-(b)		Mass spectrum (ESI, m/z): 418 $[M+H]^+$ Retention time (LCMS conditions 2): 0.907 min	Example 290-(a)
291-(b)		Mass spectrum (ESI, m/z): 432 $[M+H]^+$ Retention time (LCMS conditions 2): 0.968 min	Example 291-(a)

[0230] Example 7-(c)

Production of N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C111]



0.062 ml of triethylamine and 37 mg of sulfamide were added to a 1,4-dioxane (1 ml) solution of 31 mg of N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide hydrochloride produced in Example 7-(b) at room temperature under an argon gas flow and stirred at 100°C for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 29 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 527, 529 $[M+H]^+$

Retention time (LCMS conditions 2): 1.324 min.

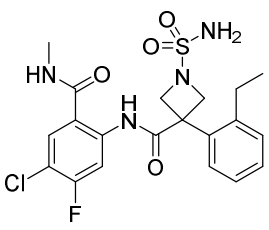
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.82 (s, 1H), 8.82 (br q, J = 4.5 Hz, 1H), 8.41 (d, J = 11.7 Hz, 1H), 8.06 (d, J = 7.5 Hz, 1H), 7.39 - 7.30 (m, 4H), 7.05 (s, 2H), 4.36 (br d, J = 7.7 Hz, 2H), 4.18 (br d, J = 7.7 Hz, 2H), 2.68 (d, J = 4.5 Hz, 3H), 2.61 (spt, J = 6.7 Hz, 1H), 1.07 (d, J = 6.7 Hz, 6H)

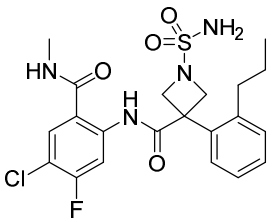
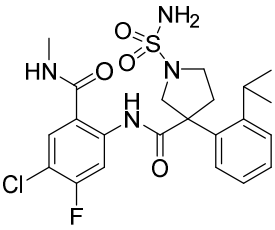
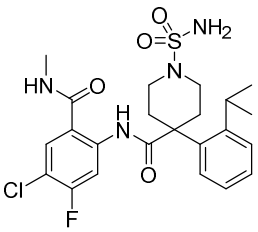
[0231] Example 27-(c) and the like

Compounds shown in Table 25 below were obtained by treating corresponding raw material compounds in the same manner as in Example 7-(c).

[Table 25]

Table 25

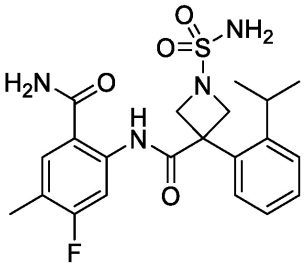
Example	Structural formula	Analysis data	Raw material
27-(c)		Mass spectrum (ESI, m/z): 469 $[M+H]^+$ Retention time (LCMS conditions 2): 1.251 min	Example 27-(b)

28-(c)		Mass spectrum (ESI, m/z): 483 $[M+H]^+$ Retention time (LCMS conditions 2): 1.330 min	Example 28-(b)
290-(c)		Mass spectrum (ESI, m/z): 497 $[M+H]^+$ Retention time (LCMS conditions 2): 1.321 min	Example 290-(b)
291-(c)		Mass spectrum (ESI, m/z): 511 $[M+H]^+$ Retention time (LCMS conditions 2): 1.360 min	Example 291-(b)

[0232] Example 8-(a)

Production of N-(2-carbamoyl-5-fluoro-4-methylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C112]



0.052 ml of N,N-diisopropylethylamine, 40 mg of HATU, and 14 mg of ammonium chloride were added to a N,N-dimethylformamide (1 ml) solution of 30 mg of 4-fluoro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)-5-methylbenzoic acid produced in Reference Example 8-(d) at room temperature under an argon gas flow, stirred at room temperature for 6.5 hours, and then left to stand at room temperature overnight. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel,

eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:acetonitrile). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 449 $[M+H]^+$

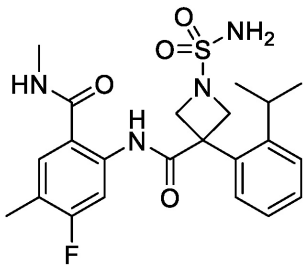
Retention time (LCMS conditions 1): 1.168 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.22 (br s, 1H), 8.31 (d, J = 12.8 Hz, 1H), 8.19 (br s, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.72 (br s, 1H), 7.38 - 7.25 (m, 4H), 7.03 (br s, 2H), 4.35 (br d, J = 7.7 Hz, 2H), 4.15 (br d, J = 7.7 Hz, 2H), 2.69 - 2.59 (m, 1H), 2.19 (s, 3H), 1.08 (d, J = 6.7 Hz, 6H)

[0233] Example 9-(a)

Production of N-(5-fluoro-4-methyl-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C113]



0.055 ml of N,N-diisopropylethylamine, 60 mg of HATU, and 0.16 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (1 ml) solution of 47 mg of 4-fluoro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)-5-methylbenzoic acid produced in Reference Example 8-(d) at room temperature under an argon gas flow and stirred at room temperature for 15.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1%

formic acid aqueous solution:acetonitrile). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 39 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 463 $[M+H]^+$

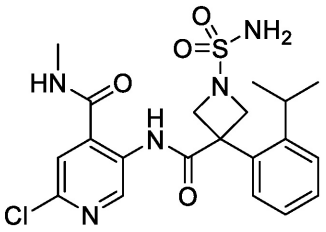
Retention time (LCMS conditions 1): 1.238 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.76 (br s, 1H), 8.74 - 8.59 (m, 1H), 8.20 (d, J = 12.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.41 - 7.25 (m, 4H), 7.05 (br s, 2H), 4.35 (br d, J = 7.7 Hz, 2H), 4.17 (br d, J = 7.7 Hz, 2H), 2.73 - 2.58 (m, 4H), 2.19 (s, 3H), 1.07 (d, J = 6.7 Hz, 6H)

[0234] Example 10-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide

[C114]



0.027 ml of N,N-diisopropylethylamine, 30 mg of HATU, and 0.08 ml of a 2M methylamine/tetrahydrofuran solution were added to a N,N-dimethylformamide (1 ml) solution of 23 mg of 2-chloro-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)isonicotinic acid produced in Reference Example 10-(d) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 466 $[M+H]^+$

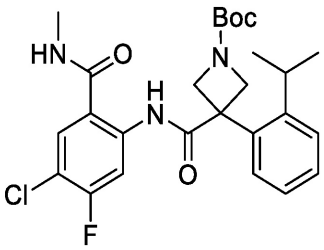
Retention time (LCMS conditions 1): 1.088 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.83 (s, 1H), 9.39 (s, 1H), 9.16 - 9.00 (m, 1H), 7.79 (s, 1H), 7.49 - 7.34 (m, 4H), 7.10 (s, 2H), 4.43 (br d, J = 7.2 Hz, 2H), 4.24 (br d, J = 7.2 Hz, 2H), 2.72 (d, J = 4.3 Hz, 3H), 2.67 - 2.59 (m, 1H), 1.13 (d, J = 6.7 Hz, 6H)

[0235] Example 11-(a)

Production of tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C115]



An operation of adding toluene to 600 mg of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)azetidine-3-carboxylic acid produced in the same manner as in Reference Example 1-(f) and concentrating a mixture under reduced pressure was performed twice. 0.211 ml of oxalyl chloride and 0.010 ml of N,N-dimethylformamide were added to a dichloromethane (12 ml) solution of a concentrated residue at room temperature under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure. 250 mg of 2-amino-5-chloro-4-fluoro-N-methylbenzamide produced in Reference Example 11-(a) and 0.703 ml of N,N-diisopropylethylamine were added to a dichloromethane (12 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 14 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 508 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 502 $[M-H]^-$

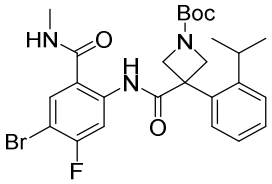
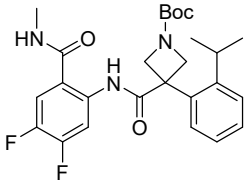
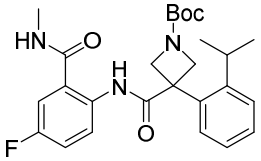
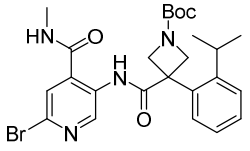
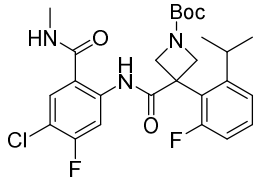
Retention time (LCMS conditions 2): 1.756 min.

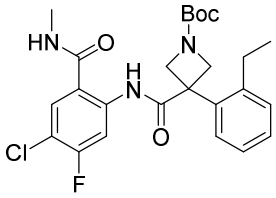
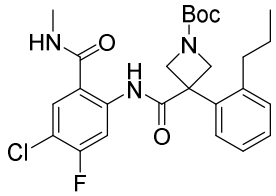
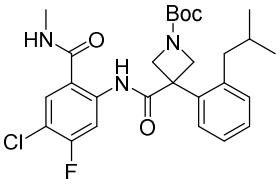
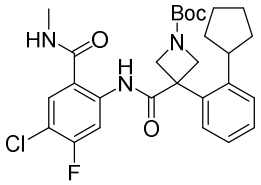
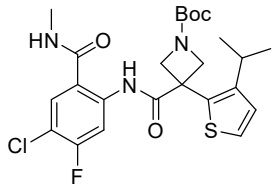
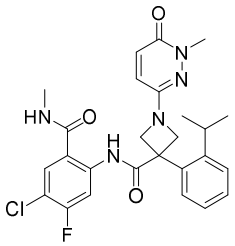
[0236] Example 7-(a) and the like

Compounds shown in Table 26 below were obtained by treating corresponding raw material compounds in the same manner as in Example 11-(a).

[Table 26]

Table 26

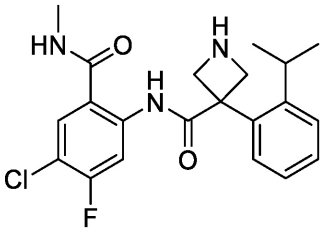
Example	Structural formula	Analysis data	Raw material
7-(a)		Mass spectrum (ESI, m/z): 546, 548 $[M-H]^-$ Retention time (LCMS conditions 2): 1.772 min	Reference Example 1-(f), Reference Example 7-(b)
23-(a)		Mass spectrum (DUIS, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 1): 1.687 min	Reference Example 1-(f), Reference Example 23-(a)
24-(a)		Mass spectrum (DUIS, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 1): 1.583 min	Reference Example 1-(f), Reference Example 24-(a)
25-(a)		Mass spectrum (DUIS, m/z): 529, 531 $[M-H]^-$ Retention time (LCMS conditions 1): 1.587 min	Reference Example 1-(f), Reference Example 25-(b)
26-(a)		Mass spectrum (DUIS, m/z): 520 $[M-H]^-$ Retention time (LCMS conditions 1): 1.775 min	Reference Example 26-(f), Reference Example 11-(a)

27-(a)		Mass spectrum (ESI, m/z): 490 $[M+H]^+$ Retention time (LCMS conditions 2): 1.707 min	Reference Example 27-(c), Reference Example 11-(a)
28-(a)		Mass spectrum (ESI, m/z): 502 $[M-H]^-$ Retention time (LCMS conditions 2): 1.784 min	Reference Example 28-(c), Reference Example 11-(a)
29-(a)		Mass spectrum (DUIS, m/z): 516 $[M-H]^-$ Retention time (LCMS conditions 1): 1.843 min	Reference Example 29-(c), Reference Example 11-(a)
30-(a)		Mass spectrum (DUIS, m/z): 528 $[M-H]^-$ Retention time (LCMS conditions 1): 1.857 min	Reference Example 30-(c), Reference Example 11-(a)
31-(a)		Mass spectrum (ESI, m/z): 508 $[M-H]^-$ Retention time (LCMS conditions 2): 1.746 min	Reference Example 31-(g), Reference Example 11-(a)
265-(a)		Mass spectrum (ESI, m/z): 512 $[M+H]^+$ Retention time (LCMS conditions 2): 1.376 min	Reference Example 265-(e), Reference Example 11-(a)

[0237] Example 11-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C116]



12.7 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to 1.35 g of tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in the same manner as in Example 11-(a) at room temperature under an argon gas flow and stirred at room temperature for 2.5 hours. A reaction mixture was concentrated under reduced pressure. Ethyl acetate and a 2M sodium carbonate aqueous solution were added to a concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 965 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 404 $[M+H]^+$

Retention time (LCMS conditions 2): 0.899 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.47 (d, J = 12.3 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.35 - 7.22 (m, 4H), 4.09 (d, J = 8.2 Hz, 2H), 4.00 (br d, J = 8.2 Hz, 2H), 2.70 (s, 3H), 2.66 - 2.56 (m, 1H), 1.04 (d, J = 6.8 Hz, 6H)

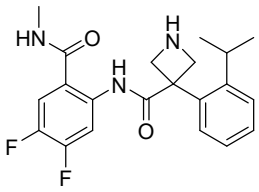
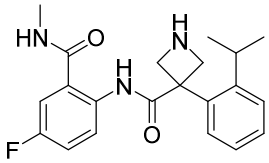
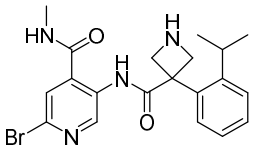
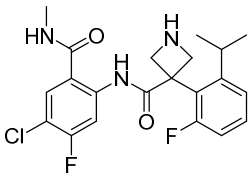
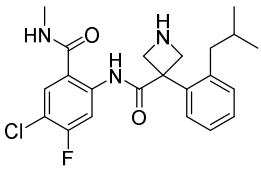
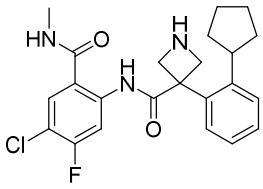
[0238] Example 23-(b) and the like

Compounds shown in Table 27 below were obtained by treating corresponding raw material compounds in the same manner as in Example 11-(b).

[Table 27]

Table 27

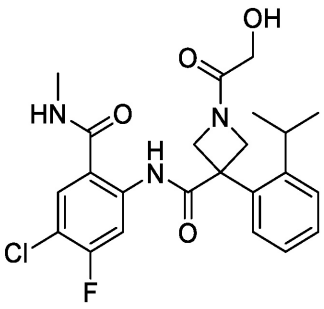
Example	Structural formula	Analysis data	Raw material

23-(b)		Mass spectrum (DUIS, m/z): 388 $[M+H]^+$ Retention time (LCMS conditions 1): 0.830 min	Example 23-(a)
24-(b)		Mass spectrum (DUIS, m/z): 370 $[M+H]^+$ Retention time (LCMS conditions 1): 0.751 min	Example 24-(a)
25-(b)		Mass spectrum (DUIS, m/z): 431, 433 $[M+H]^+$ Retention time (LCMS conditions 1): 0.741 min	Example 25-(a)
26-(b)		Mass spectrum (ESI, m/z): 422 $[M+H]^+$ Retention time (LCMS conditions 2): 0.896 min	Example 26-(a)
29-(b)		Mass spectrum (ESI, m/z): 418 $[M+H]^+$ Retention time (LCMS conditions 2): 0.967 min	Example 29-(a)
30-(b)		Mass spectrum (DUIS, m/z): 430 $[M+H]^+$ Retention time (LCMS conditions 1): 1.030 min	Example 30-(a)

[0239] Example 12-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C117]



0.051 ml of N,N-diisopropylethylamine and 43 mg of HATU were added to a N,N-dimethylformamide (0.5 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) and 10 mg of glycolic acid at room temperature under an argon gas flow and stirred at room temperature for four hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 27 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 462 $[M+H]^+$

Retention time (LCMS conditions 2): 1.183 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.38 (s, 1H), 8.78 - 8.66 (m, 1H), 8.46 (d, J = 12.3 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.51 - 7.30 (m, 4H), 5.05 (t, J = 6.1 Hz, 1H), 4.93 - 4.84 (m, 1H), 4.71 - 4.61 (m, 1H), 4.61 - 4.52 (m, 1H), 4.36 - 4.23 (m, 1H), 3.97 (d, J = 6.1 Hz, 2H), 2.61 (d, J = 4.4 Hz, 3H), 2.48 - 2.38 (m, 1H), 1.05 (d, J = 6.5 Hz, 6H)

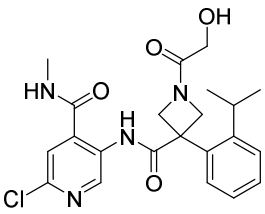
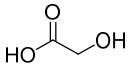
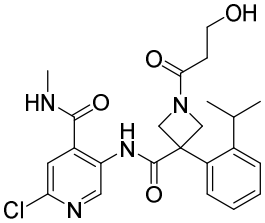
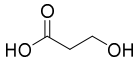
[0240] Example 33-(c) and the like

Compounds shown in Table 28 below were obtained by treating corresponding raw material compounds in the same manner as in Example 12-(a).

[Table 28]

Table 28

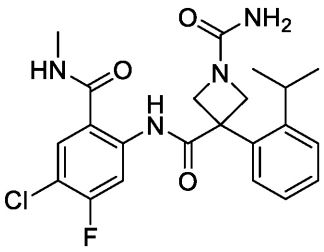
Example	Structural formula	Analysis data	Raw material

33-(c)		Mass spectrum (ESI, m/z): 445 $[M+H]^+$ Retention time (LCMS conditions 2): 0.970 min	Example 33-(b), 
34-(a)		Mass spectrum (ESI, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 2): 0.965 min	Example 33-(b), 

[0241] Example 13-(a)

Production of N^3-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide

[C118]



0.052 ml of triethylamine and 0.013 ml of trimethylsilyl isocyanate were added to a dichloromethane (1 ml) solution of 32 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. 0.005 ml of trimethylsilyl isocyanate was added thereto at room temperature and stirred at room temperature for two hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 34 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 447 $[M+H]^+$

Retention time (LCMS conditions 2): 1.161 min.

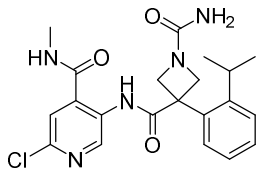
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.46 (s, 1H), 8.80 - 8.69 (m, 1H), 8.46 (d, J = 12.2 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.44 - 7.29 (m, 4H), 6.07 (s, 2H), 4.49 (br d, J = 8.2 Hz, 2H), 4.20 (br d, J = 8.2 Hz, 2H), 2.64 (d, J = 4.5 Hz, 3H), 2.50 - 2.43 (m, 1H), 1.05 (d, J = 6.8 Hz, 6H)

[0242] Example 35-(a)

A compound shown in Table 29 below was obtained by treating a corresponding raw material compound in the same manner as in Example 13-(a).

[Table 29]

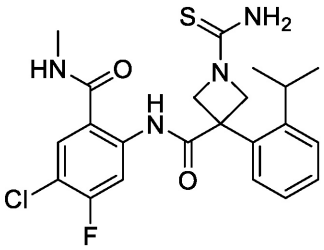
Table 29

Example	Structural formula	Analysis data	Raw material
35-(a)		Mass spectrum (ESI, m/z): 430 $[M+H]^+$ Retention time (LCMS conditions 2): 0.963 min	Example 33-(b)

[0243] Example 14-(a)

Production of 1-carbamothioyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C119]



23 mg of 9-fluorenylmethoxycarbonyl isothiocyanate was added to a dichloromethane (1 ml) solution of 29 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for two hours. A reaction mixture

was concentrated under reduced pressure. 0.029 ml of piperidine was added to a N,N-dimethylformamide (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for two hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 32 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 463 $[M+H]^+$

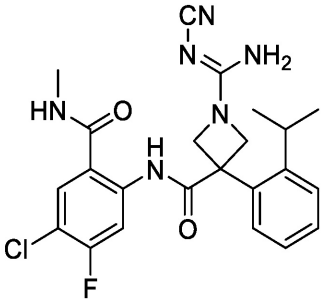
Retention time (LCMS conditions 2): 1.285 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.34 (s, 1H), 8.69 - 8.63 (m, 1H), 8.38 (d, J = 12.2 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.54 - 7.21 (m, 6H), 4.72 - 4.48 (m, 2H), 4.40 - 4.19 (m, 2H), 2.55 (d, J = 4.5 Hz, 3H), 2.41 - 2.34 (m, 1H), 0.99 (d, J = 6.4 Hz, 6H)

[0244] Example 15-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C120]



0.021 ml of triethylamine and 22 mg of diphenyl N-cyanocarbonimidate were added to a dichloromethane (1 ml) solution of 31 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at 0°C under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure. 0.211 ml of a 7M ammonia/methanol solution was added to a methanol (0.5 ml) suspension of the obtained concentrated residue at room temperature under an argon

gas flow and stirred at room temperature for six hours, and a reaction mixture was concentrated under reduced pressure. 0.211 ml of a 7M ammonia/methanol solution was added to an ethanol (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for three hours. The reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 26 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 471 $[M+H]^+$

Retention time (LCMS conditions 2): 1.247 min.

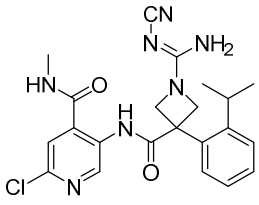
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.32 (s, 1H), 8.70 - 8.61 (m, 1H), 8.39 (d, J = 12.2 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.37 - 7.22 (m, 4H), 7.18 (s, 2H), 4.66 - 4.46 (m, 2H), 4.38 - 4.21 (m, 2H), 2.54 (d, J = 4.4 Hz, 3H), 2.37 - 2.28 (m, 1H), 0.97 (d, J = 6.7 Hz, 6H)

[0245] Example 36-(a)

A compound shown in Table 30 below was obtained by treating a corresponding raw material compound in the same manner as in Example 15-(a).

[Table 30]

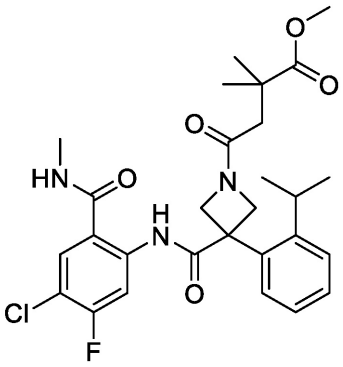
Table 30

Example	Structural formula	Analysis data	Raw material
36-(a)		Mass spectrum (ESI, m/z): 454 $[M+H]^+$ Retention time (LCMS conditions 2): 1.052 min	Example 33-(b)

[0246] Example 16-(a)

Production of methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate

[C121]



0.038 ml of N,N-diisopropylethylamine and 46 mg of HATU were added to a N,N-dimethylformamide (1 ml) solution of 31 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) and 21 mg of 1-methyl 2,2-dimethylsuccinate at room temperature under an argon gas flow and stirred at room temperature for 2.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 34 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 546 $[M+H]^+$

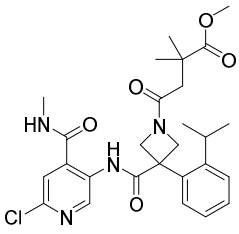
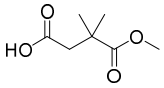
Retention time (LCMS conditions 2): 1.517 min.

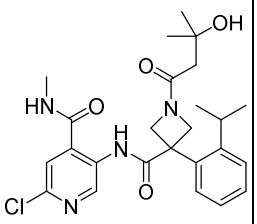
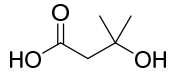
[0247] Example 37-(a) and the like

Compounds shown in Table 31 below were obtained by treating corresponding raw material compounds in the same manner as in Example 16-(a).

[Table 31]

Table 31

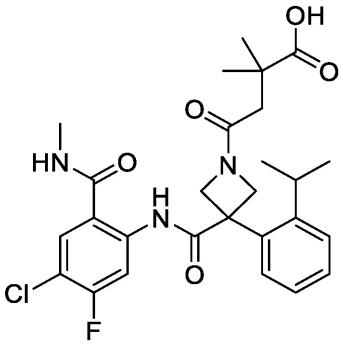
Example	Structural formula	Analysis data	Raw material
37-(a)		Mass spectrum (ESI, m/z): 529 $[M+H]^+$ Retention time (LCMS conditions 2): 1.319 min	Example 33-(b), 

38-(a)		Mass spectrum (ESI, m/z): 487 $[M+H]^+$ Retention time (LCMS conditions 2): 1.116 min	Example 33-(b), 

[0248] Example 16-(b)

Production of 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid

[C122]



13 mg of lithium hydroxide monohydrate was added to a tetrahydrofuran (0.5 ml)/methanol (0.5 ml)/water (0.25 ml) solution of 34 mg of methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate produced in Example 16-(a) at room temperature under an argon gas flow and stirred at 50°C for 5.5 hours. Water was added to a reaction mixture allowed to cool to room temperature, the pH was adjusted to four by adding 0.1N hydrochloric acid thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 15 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 532 $[M+H]^+$

Retention time (LCMS conditions 2): 1.358 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.43 (d, J = 12.2 Hz, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.46 (d, J = 7.5 Hz, 1H), 7.40 - 7.30 (m, 3H), 4.86 - 4.73 (m, 1H), 4.64 - 4.53 (m, 1H), 4.53 -

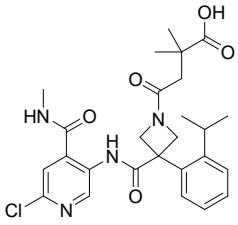
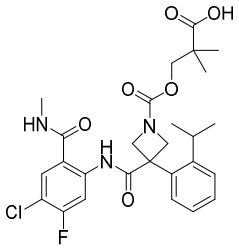
4.42 (m, 1H), 4.30 - 4.18 (m, 1H), 2.60 (s, 3H), 2.47 - 2.35 (m, 3H), 1.14 (d, J = 7.8 Hz, 6H), 1.09 - 0.98 (m, 6H)

[0249] Example 37-(b) and the like

Compounds shown in Table 32 below were obtained by treating corresponding raw material compounds in the same manner as in Example 16-(b). The synthesis of Example 253-(b) was performed without using methanol.

[Table 32]

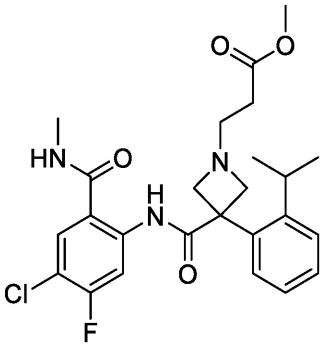
Table 32

Example	Structural formula	Analysis data	Raw material
37-(b)		Mass spectrum (ESI, m/z): 515 $[M+H]^+$ Retention time (LCMS conditions 2): 1.166 min	Example 37-(a)
253-(b)		Mass spectrum (DUIS, m/z): 548 $[M+H]^+$ Retention time (LCMS conditions 1): 1.414 min	Example 253-(a)

[0250] Example 17-(a)

Production of methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate

[C123]



21 mg of potassium carbonate and 0.009 ml of methyl 3-bromopropionate were added to a N,N-

dimethylformamide (0.5 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for 5.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate) to obtain 36 mg of a title compound as a white foamy substance.

Mass spectrum (DUIS, m/z): 490 $[M+H]^+$

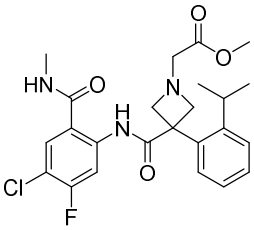
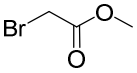
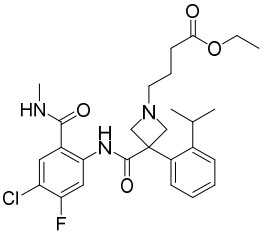
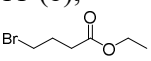
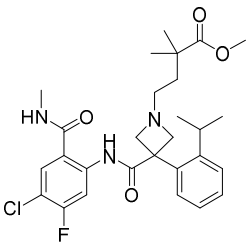
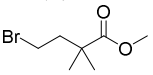
Retention time (LCMS conditions 1): 0.992 min.

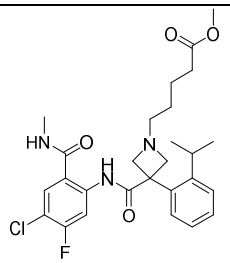
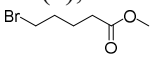
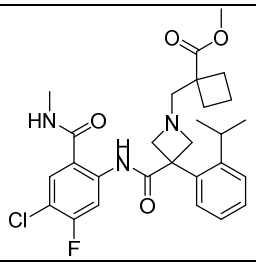
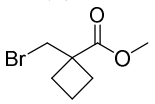
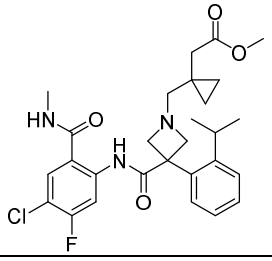
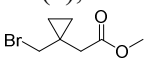
[0251] Example 40-(a) and the like

Compounds shown in Table 33 below were obtained by treating corresponding raw material compounds in the same manner as in Example 17-(a). The syntheses of Example 42-(a) and Example 43-(a) were performed at 40°C as the reaction temperature.

[Table 33]

Table 33

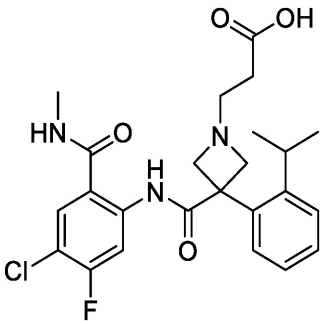
Example	Structural formula	Analysis data	Raw material
40-(a)		Mass spectrum (DUIS, m/z): 476 $[M+H]^+$ Retention time (LCMS conditions 1): 1.006 min	Example 11-(b), 
41-(a)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.032 min	Example 11-(b), 
42-(a)		Mass spectrum (DUIS, m/z): 532 $[M+H]^+$ Retention time (LCMS conditions 1): 1.091 min	Example 11-(b), 

43-(a)		Mass spectrum (DUIS, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 1): 1.052 min	Example 11-(b), 
44-(a)		Mass spectrum (DUIS, m/z): 530 $[M+H]^+$ Retention time (LCMS conditions 1): 1.099 min	Example 11-(b), 
45-(a)		Mass spectrum (ESI, m/z): 530 $[M+H]^+$ Retention time (LCMS conditions 2): 1.080 min	Example 11-(b), 

[0252] Example 17-(b)

Production of 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid

[C124]



A water (0.25 ml) solution of 10 mg of lithium hydroxide monohydrate was added dropwise to a tetrahydrofuran (1 ml)/methanol (0.25 ml) solution of 36 mg of methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate produced in Example 17-(a) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline,

dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The organic layer was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 33 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 476 $[M+H]^+$

Retention time (LCMS conditions 1): 0.915 min.

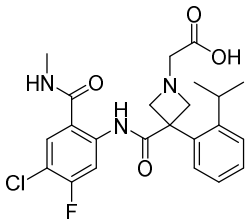
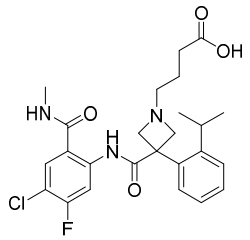
^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.44 (d, J = 12.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.35 - 7.19 (m, 4H), 4.13 (br d, J = 6.8 Hz, 2H), 3.46 (br d, J = 6.8 Hz, 2H), 2.76 - 2.63 (m, 6H), 2.29 (t, J = 6.9 Hz, 2H), 1.05 (d, J = 6.8 Hz, 6H)

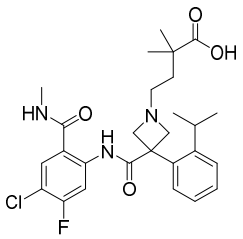
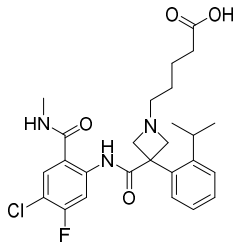
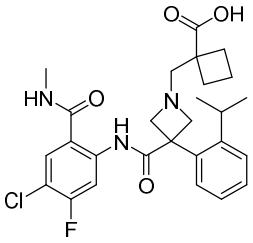
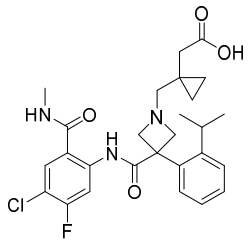
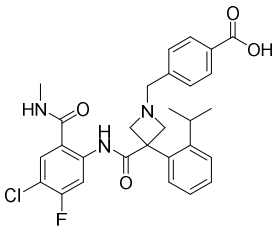
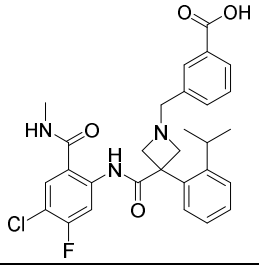
[0253] Example 40-(b) and the like

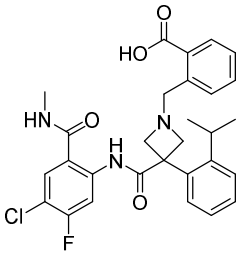
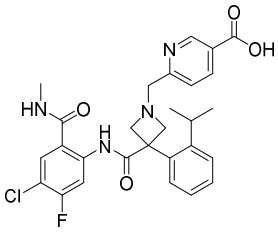
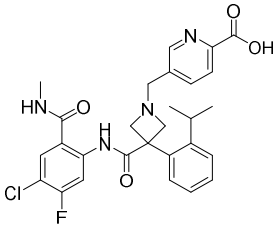
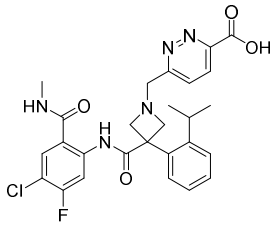
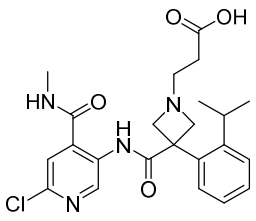
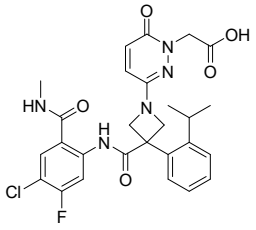
Compounds shown in Table 34 below were obtained by treating corresponding raw material compounds in the same manner as in Example 17-(b). The syntheses of Example 42-(b) and Example 44-(b) were performed at 60°C as the reaction temperature. The synthesis of Example 43-(b) was performed at 40°C as the reaction temperature.

[Table 34]

Table 34

Example	Structural formula	Analysis data	Raw material
40-(b)		Mass spectrum (DUIS, m/z): 462 $[M+H]^+$ Retention time (LCMS conditions 1): 0.922 min	Example 40-(a)
41-(b)		Mass spectrum (DUIS, m/z): 490 $[M+H]^+$ Retention time (LCMS conditions 1): 0.939 min	Example 41-(a)

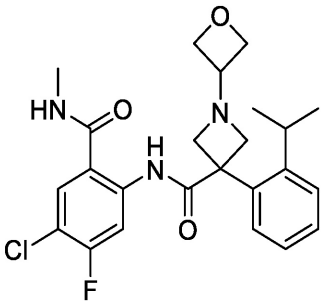
42-(b)		Mass spectrum (DUIS, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 1): 1.022 min	Example 42-(a)
43-(b)		Mass spectrum (DUIS, m/z): 504 $[M+H]^+$ Retention time (LCMS conditions 1): 0.952 min	Example 43-(a)
44-(b)		Mass spectrum (DUIS, m/z): 516 $[M+H]^+$ Retention time (LCMS conditions 1): 1.046 min	Example 44-(a)
45-(b)		Mass spectrum (ESI, m/z): 516 $[M+H]^+$ Retention time (LCMS conditions 2): 0.985 min	Example 45-(a)
46-(b)		Mass spectrum (ESI, m/z): 538 $[M+H]^+$ Retention time (LCMS conditions 2): 1.003 min	Example 46-(a)
47-(b)		Mass spectrum (ESI, m/z): 538 $[M+H]^+$ Retention time (LCMS conditions 2): 0.997 min	Example 47-(a)

48-(b)		Mass spectrum (ESI, m/z): 538 $[M+H]^+$ Retention time (LCMS conditions 2): 1.092 min	Example 48-(a)
49-(b)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 0.982 min	Example 49-(a)
50-(b)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 0.920 min	Example 50-(a)
51-(b)		Mass spectrum (ESI, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 2): 0.910 min	Example 51-(a)
151-(b)		Mass spectrum (DUIS, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 1): 0.743 min	Example 151-(a)
272-(b)		Mass spectrum (ESI, m/z): 556 $[M+H]^+$ Retention time (LCMS conditions 2): 1.271 min	Example 272-(a)

[0254] Example 18-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-yl)azetidine-3-carboxamide

[C125]



0.141 ml of N,N-diisopropylethylamine and 119 mg of HATU were added to a N,N-dimethylformamide (1 ml) solution of 90 mg of 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)-1-(oxetan-3-yl)azetidine-3-carboxamide)benzoic acid produced in Reference Example 18-(c) and 0.403 ml of a 2M methylamine/tetrahydrofuran solution at room temperature under an argon gas flow and stirred at room temperature for four hours. 114 mg of HATU was added thereto at room temperature and stirred at room temperature for two hours. 0.403 ml of a 2M methylamine/tetrahydrofuran solution was added thereto at room temperature and stirred at room temperature for one hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate) to obtain 44 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 460 $[M+H]^+$

Retention time (LCMS conditions 2): 0.929 min.

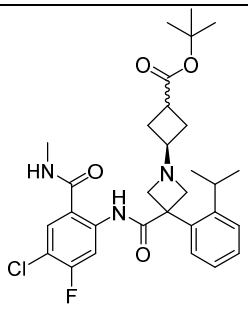
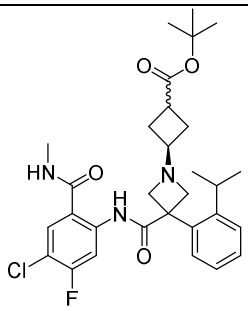
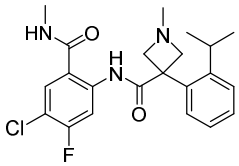
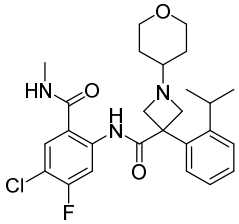
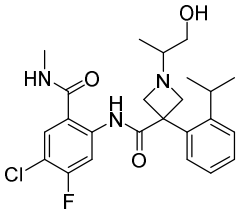
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.05 (s, 1H), 8.86 - 8.79 (m, 1H), 8.49 (d, J = 12.4 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.33 - 7.20 (m, 4H), 4.54 (t, J = 6.5 Hz, 2H), 4.37 (dd, J = 5.3, 6.5 Hz, 2H), 4.10 (br d, J = 7.0 Hz, 2H), 3.76 - 3.69 (m, 1H), 3.52 (br d, J = 7.0 Hz, 2H), 2.78 - 2.68 (m, 4H), 1.06 (d, J = 6.8 Hz, 6H)

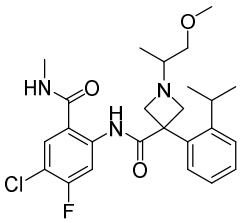
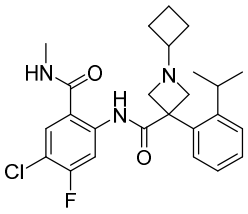
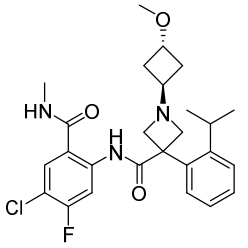
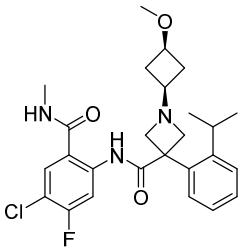
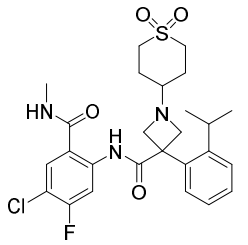
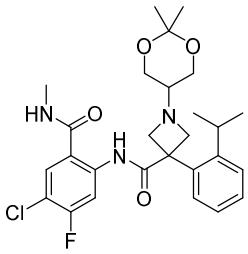
[0255] Example 52-(a) and the like

Compounds shown in Table 35 below were obtained by treating corresponding raw material compounds in the same manner as in Example 18-(a).

[Table 35]

Table 35

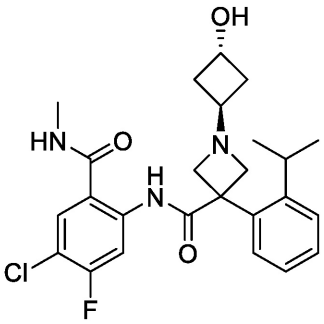
Example	Structural formula	Analysis data	Raw material
52-(a)	 Diastereomer 1	Mass spectrum (ESI, m/z): 558 $[M+H]^+$ Retention time (LCMS conditions 3): 1.036 min	Reference Example 52-(b)
53-(a)	 Diastereomer 2	Mass spectrum (ESI, m/z): 558 $[M+H]^+$ Retention time (LCMS conditions 3): 1.036 min	Reference Example 53-(b)
54-(a)		Mass spectrum (ESI, m/z): 418 $[M+H]^+$ Retention time (LCMS conditions 2): 0.905 min	Reference Example 54-(b)
55-(a)		Mass spectrum (ESI, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 2): 0.949 min	Reference Example 55-(b)
206-(a)		Mass spectrum (ESI, m/z): 462 $[M+H]^+$ Retention time (LCMS conditions 2): 0.931 min	Reference Example 206-(b)

207-(a)		Mass spectrum (ESI, m/z): 476 $[M+H]^+$ Retention time (LCMS conditions 2): 1.013 min	Reference Example 207-(b)
208-(a)		Mass spectrum (DUIS, m/z): 458 $[M+H]^+$ Retention time (LCMS conditions 1): 1.056 min	Reference Example 208-(b)
209-(a)		Mass spectrum (ESI, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 2): 0.999 min	Reference Example 209-(b)
210-(a)		Mass spectrum (DUIS, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 1): 1.017 min	Reference Example 210-(b)
215-(a)		Mass spectrum (ESI, m/z): 536 $[M+H]^+$ Retention time (LCMS conditions 2): 0.965 min	Reference Example 215-(b)
218-(a)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.046 min	Reference Example 218-(b)

[0256] Example 19-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C126]



Reaction 1

0.013 ml of a 1M tetrabutylammonium fluoride/tetrahydrofuran solution was added to a tetrahydrofuran (0.2 ml) solution of 5 mg of 1-(trans-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in Reference Example 19-(c) at room temperature under an argon gas flow, stirred at room temperature for five hours, and left to stand at room temperature for 40 hours.

[0257] Reaction 2

0.088 ml of a 1M tetrabutylammonium fluoride/tetrahydrofuran solution was added to a tetrahydrofuran (0.52 ml) solution of 35 mg of 1-(trans-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in Reference Example 19-(c) at room temperature under an argon gas flow, stirred at room temperature for two hours, and left to stand at room temperature for 40 hours.

[0258] A mixture obtained by combining reaction mixtures of the reaction 1 and the reaction 2 concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate:methanol) to obtain 18 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 474 $[M+H]^+$

Retention time (LCMS conditions 3): 0.761 min.

^{1}H-NMR spectrum (600 MHz, $CDCl_3$) δ: 11.31 (s, 1H), 8.59 (d, J = 12.0 Hz, 1H), 7.41 (d, J = 7.5 Hz, 1H), 7.33 - 7.22 (m, 4H), 6.05 - 5.95 (m, 1H), 4.59 - 4.54 (m, 1H), 4.24 - 4.16 (m, 2H), 3.44 -

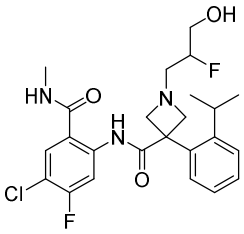
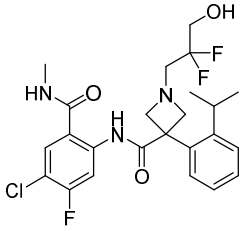
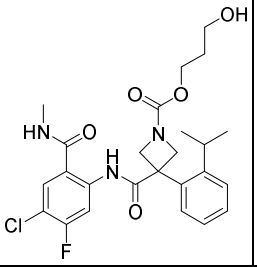
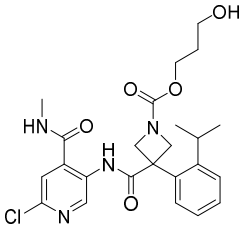
3.35 (m, 2H), 3.12 - 3.07 (m, 1H), 2.91 (d, J = 4.9 Hz, 3H), 2.80 - 2.71 (m, 1H), 2.29 - 2.20 (m, 2H), 1.97 - 1.91 (m, 2H), 1.76 - 1.62 (m, 1H), 1.12 (d, J = 6.8 Hz, 6H)

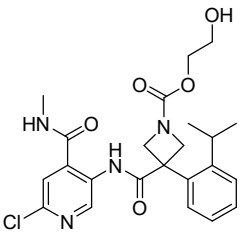
[0259] Example 56-(a) and the like

Compounds shown in Table 36 below were obtained by treating corresponding raw material compounds in the same manner as in Example 19-(a).

[Table 36]

Table 36

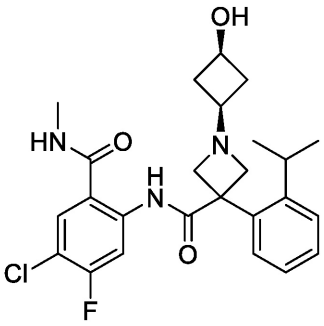
Example	Structural formula	Analysis data	Raw material
56-(a)		Mass spectrum (ESI, m/z): 480 $[M+H]^+$ Retention time (LCMS conditions 2): 0.912 min	Reference Example 56-(a)
57-(a)		Mass spectrum (ESI, m/z): 498 $[M+H]^+$ Retention time (LCMS conditions 2): 1.151 min	Reference Example 57-(a)
58-(a)		Mass spectrum (DUIS, m/z): 506 $[M+H]^+$ Retention time (LCMS conditions 1): 1.322 min	Reference Example 58-(a)
59-(a)		Mass spectrum (ESI, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 2): 1.129 min	Reference Example 59-(a)

60-(a)		Mass spectrum (ESI, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 2): 1.079 min	Reference Example 60-(a)

[0260] Example 20-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C127]



Reaction 1

0.013 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a dicyclomethane (0.052 ml) solution of 5 mg of 1-(cis-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in Reference Example 20-(c) at room temperature under an argon gas flow and stirred at room temperature for 0.5 hour.

[0261] Reaction 2

0.118 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a dichloromethane (0.472 ml) solution of 46 mg of 1-(cis-3-((tert-butyldimethylsilyl)oxy)cyclobutyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in Reference Example 20-(c) at room temperature under an argon gas flow and stirred at room temperature for 0.5 hour.

[0262] A mixture obtained by combining reaction mixtures of the reaction 1 and the reaction 2 was

concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate:methanol) to obtain 32 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 474 $[M+H]^+$

Retention time (LCMS conditions 3): 0.762 min.

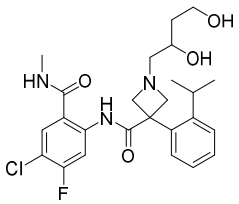
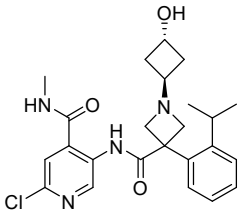
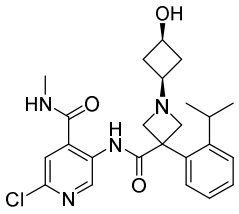
^{1}H-NMR spectrum (600 MHz, $CDCl_3$) δ: 11.77 (s, 1H), 8.57 (d, J = 12.1 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.31 - 7.20 (m, 3H), 7.15 - 7.12 (m, 1H), 6.11 - 6.02 (m, 1H), 4.20 - 4.04 (m, 3H), 3.50 - 3.38 (m, 2H), 2.95 (d, J = 4.9 Hz, 3H), 2.84 - 2.74 (m, 1H), 2.65 (spt, J = 6.7 Hz, 1H), 2.55 - 2.49 (m, 2H), 1.94 - 1.85 (m, 2H), 1.14 (d, J = 6.7 Hz, 6H)

[0263] Example 61-(a) and the like

Compounds shown in Table 37 below were obtained by treating corresponding raw material compounds in the same manner as in Example 20-(a).

[Table 37]

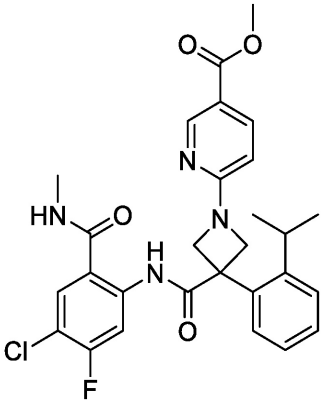
Table 37

Example	Structural formula	Analysis data	Raw material
61-(a)		Mass spectrum (ESI, m/z): 492 $[M+H]^+$ Retention time (LCMS conditions 2): 0.860 min	Reference Example 61-(a)
62-(a)		Mass spectrum (DUIS, m/z): 457 $[M+H]^+$ Retention time (LCMS conditions 1): 0.710 min	Reference Example 62-(c)
63-(a)		Mass spectrum (DUIS, m/z): 457 $[M+H]^+$ Retention time (LCMS conditions 1): 0.706 min	Reference Example 63-(c)

[0264] Example 21-(a)

Production of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate

[C128]



15 mg of methyl 6-chloronicotinate and 0.019 ml of N,N-diisopropylethylamine were added to a N,N-dimethylformamide (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 80°C for six hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 36 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 539 $[M+H]^+$

Retention time (LCMS conditions 1): 1.587 min.

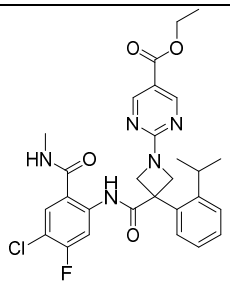
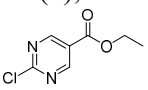
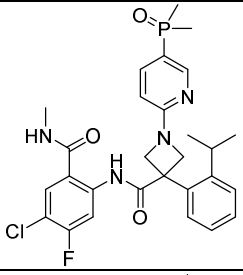
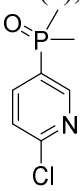
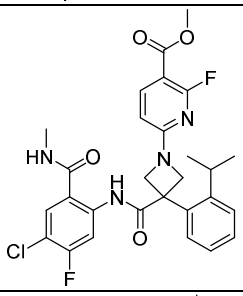
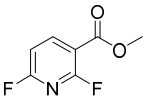
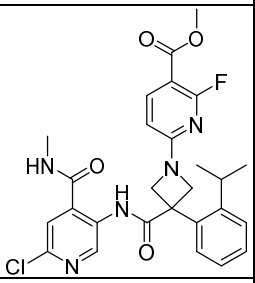
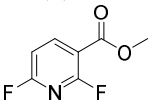
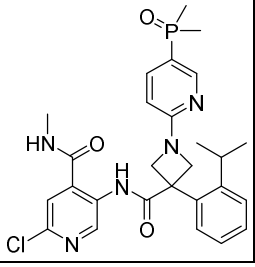
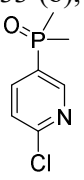
[0265] Example 64-(a) and the like

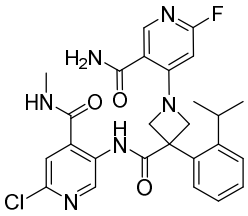
Compounds shown in Table 38 below were obtained by treating corresponding raw material compounds in the same manner as in Example 21-(a). The synthesis of Example 64-(a) was performed at room temperature as the reaction temperature. The syntheses of Example 68-(a), Example 316-(a), and Example 385-(a) were performed in an ice bath as the reaction temperature by adding triethylamine

instead of N,N-diisopropylethylamine.

[Table 38]

Table 38

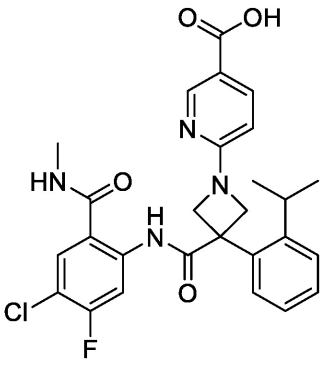
Example	Structural formula	Analysis data	Raw material
64-(a)		Mass spectrum (DUIS, m/z): 554 $[M+H]^+$ Retention time (LCMS conditions 1): 1.700 min	Example 11-(b), 
65-(a)		Mass spectrum (ESI, m/z): 557 $[M+H]^+$ Retention time (LCMS conditions 2): 1.163 min	Example 11-(b), 
68-(a)		Mass spectrum (ESI, m/z): 557 $[M+H]^+$ Retention time (LCMS conditions 2): 1.688 min	Example 11-(b), 
316-(a)		Mass spectrum (DUIS, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 7): 0.916 min	Example 33-(b), 
375-(a)		Mass spectrum (DUIS, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 8): 0.964 min	Example 33-(b), 

385-(a)		Mass spectrum (DUIS, m/z): 525 $[M+H]^+$ Retention time (LCMS conditions 8): 1.115 min	Example 39-(a), Reference Example 385-(a)

[0266] Example 21-(b)

Production of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid

[C129]



A water (0.25 ml) solution of 9 mg of lithium hydroxide monohydrate was added dropwise to a tetrahydrofuran (1 ml)/methanol (0.25 ml) solution of 36 mg of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate produced in Example 21-(a) at room temperature under an argon gas flow, stirred at room temperature for four hours, and stirred at 40°C for three hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The organic layer was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 34 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 525 $[M+H]^+$

Retention time (LCMS conditions 1): 1.314 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.63 (d, J = 2.1 Hz, 1H), 8.45 (d, J = 12.2

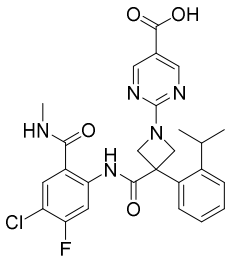
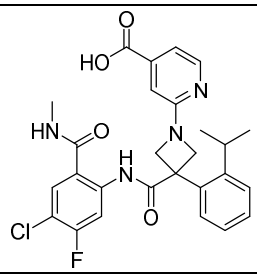
Hz, 1H), 7.98 (dd, J = 2.1, 8.8 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 7.4 Hz, 1H), 7.45 - 7.29 (m, 3H), 6.58 (d, J = 8.8 Hz, 1H), 4.78 (br d, J = 8.5 Hz, 2H), 4.48 (br d, J = 8.5 Hz, 2H), 2.63 (s, 3H), 2.59 - 2.48 (m, 1H), 1.08 (d, J = 6.7 Hz, 6H)

[0267] Example 64-(b) and the like

Compounds shown in Table 39 below were obtained by treating corresponding raw material compounds in the same manner as in Example 21-(b). The synthesis of Example 64-(b) was performed at room temperature as the reaction temperature.

[Table 39]

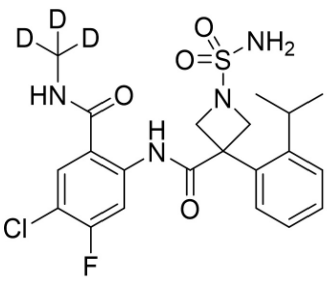
Table 39

Example	Structural formula	Analysis data	Raw material
64-(b)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 1): 1.362 min	Example 64-(a)
67-(b)		Mass spectrum (DUIS, m/z): 525 $[M+H]^+$ Retention time (LCMS conditions 1): 1.174 min	Example 67-(a)

[0268] Example 22-(a)

Production of N-(4-chloro-5-fluoro-2-((methyl-d3)carbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

[C130]



0.033 ml of N,N-diisopropylethylamine, 27 mg of HATU, and 7 mg of methyl-d3-amine

hydrochloride were added to a N,N-dimethylformamide (0.6 ml) solution of 30 mg of 5-chloro-4-fluoro-2-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide)benzoic acid produced in the same manner as in Reference Example 2-(f) at room temperature under an argon gas flow and stirred at room temperature for 18 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 22 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 486 $[M+H]^+$

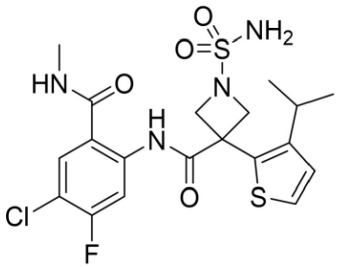
Retention time (LCMS conditions 2): 1.305 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.82 (s, 1H), 8.79 (s, 1H), 8.44 (d, J = 12.2 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.38 - 7.28 (m, 4H), 7.04 (s, 2H), 4.35 (br d, J = 7.8 Hz, 2H), 4.18 (br d, J = 7.8 Hz, 2H), 2.66 - 2.52 (m, 1H), 1.07 (d, J = 6.8 Hz, 6H)

[0269] Example 31-(c)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)-1-sulfamoylazetidine-3-carboxamide

[C131]



0.13 ml of triethylamine and 78 mg of sulfamide were added to a 1,4-dioxane (1 ml) solution of 60 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)azetidine-3-carboxamide hydrochloride produced in Example 31-(b) at room temperature under an argon gas flow and stirred at 100°C for 5.5 hours. A reaction mixture was purified by medium pressure preparative

chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 57 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 489 $[M+H]^+$

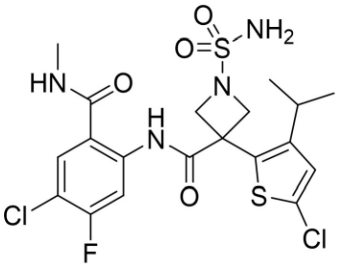
Retention time (LCMS conditions 2): 1.281 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.94 (s, 1H), 8.90 - 8.81 (m, 1H), 8.46 (d, J = 12.0 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.51 (d, J = 5.3 Hz, 1H), 7.15 (s, 2H), 7.08 (d, J = 5.3 Hz, 1H), 4.42 (d, J = 7.9 Hz, 2H), 4.04 (d, J = 7.9 Hz, 2H), 2.71 (d, J = 4.5 Hz, 3H), 2.69 - 2.60 (m, 1H), 1.03 (d, J = 6.7 Hz, 6H)

[0270] Example 32-(a)

Production of 3-(5-chloro-3-isopropylthiophen-2-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-sulfamoylazetidine-3-carboxamide

[C132]



10 mg of N-chlorosuccinimide was added to a N,N-dimethylformamide (0.5 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)-1-sulfamoylazetidine-3-carboxamide produced in Example 31-(c) at room temperature under an argon gas flow and stirred at 80°C for two hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 20 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 523 $[M+H]^+$

Retention time (LCMS conditions 2): 1.423 min.

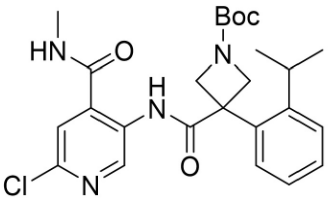
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.98 (s, 1H), 8.91 - 8.83 (m, 1H), 8.45 (d, J = 12.0 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.20 - 7.14(m, 3H), 4.39 (d, J = 8.1 Hz, 2H), 4.00 (d, J = 8.1 Hz, 2H),

2.72 (d, J = 4.5 Hz, 3H), 2.57 - 2.51 (m, 1H), 1.01 (d, J = 6.7 Hz, 6H)

[0271] Example 33-(a)

Production of tert-butyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C133]



An operation of adding toluene to 4.08 g of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)azetidine-3-carboxylic acid produced in the same manner as in Reference Example 1-(f) and concentrating the components under reduced pressure was performed twice. The obtained concentrated residue and a dichloromethane (20 ml) solution of 1.03 ml of pyridine were added dropwise to a solution of 1.12 ml of oxalyl chloride and 0.10 ml of N,N-dimethylformamide at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. Next, 2.16 g of 5-amino-2-chloro-N-methylisonicotinamide produced in Reference Example 33-(a) and 1.03 ml of pyridine were added thereto at room temperature under an argon gas flow and stirred at room temperature for 16 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with a saturated ammonium chloride aqueous solution, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 5.69 g of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 485 $[M-H]^-$

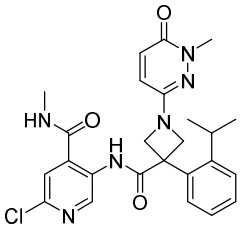
Retention time (LCMS conditions 2): 1.570 min.

[0272] Example 267-(a)

A compound shown in Table 40 below was obtained by treating a corresponding raw material compound in the same manner as in Example 33-(a).

[Table 40]

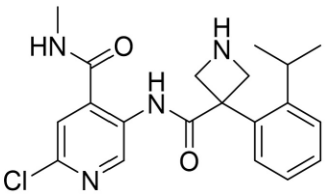
Table 40

Example	Structural formula	Analysis data	Raw material
267-(a)		Mass spectrum (ESI, m/z): 495 $[M+H]^+$ Retention time (LCMS conditions 2): 1.166 min	Reference Example 265-(e) Reference Example 33-(a)

[0273] Example 33-(b)

Production of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C134]



58 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (20 ml) solution of 5.69 g of tert-butyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in Example 33-(a) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. After the reaction mixture thus obtained was concentrated under reduced pressure, a saturated sodium bicarbonate solution was added thereto, and the reaction mixture was extracted with ethyl acetate. The resulting organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 4.19 g of the title compound as a white solid.

Mass spectrum (ESI, m/z): 387 $[M+H]^+$

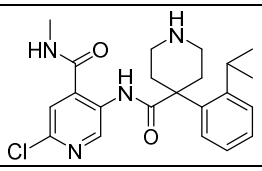
Retention time (LCMS conditions 2): 0.705 min.

[0274] Example 292-(b)

A compound shown in Table 41 below was obtained by treating a corresponding raw material compound in the same manner as in Example 33-(b).

[Table 41]

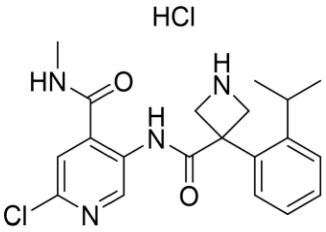
Table 41

Example	Structural formula	Analysis data	Raw material
292-(b)		Mass spectrum (ESI, m/z): 415 $[M+H]^+$ Retention time (LCMS conditions 2): 0.786 min	Example 292-(a)

[0275] Example 39-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride

[C135]



11 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (4 ml) solution of 412 mg of tert-butyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in the same manner as in Example 33-(a) at room temperature under an argon gas flow and stirred at room temperature for two hours. A reaction mixture was concentrated under reduced pressure to obtain 341 mg of a title compound as a white solid.

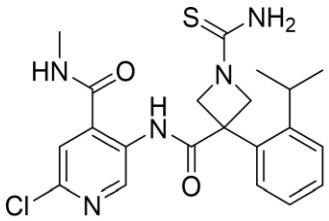
Mass spectrum (DUIS, m/z): 387 $[M+H]^+$

Retention time (LCMS conditions 1): 0.703 min.

[0276] Example 39-(b)

Production of 5-(1-carbamothioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-2-chloro-N-methylisonicotinamide

[C136]



0.012 ml of N,N-diisopropylethylamine and 20 mg of 9-fluorenylmethoxycarbonyl isothiocyanate were added to a dichloromethane (1 ml) suspension of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in Example 39-(a) at room temperature under an argon gas flow and stirred at room temperature for 15.5 hours. A reaction mixture was concentrated under reduced pressure. 0.028 ml of piperidine was added to a N,N-dimethylformamide (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for one hour. A saturated ammonium chloride aqueous solution was added to the reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 22 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 446 $[M+H]^+$

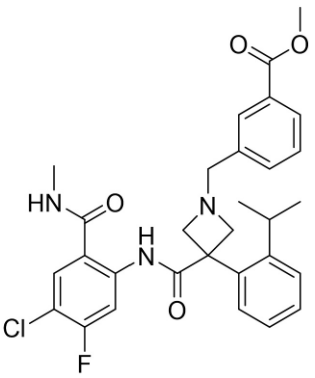
Retention time (LCMS conditions 1): 1.077 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.48 (s, 1H), 9.34 (s, 1H), 8.98 - 8.91 (m, 1H), 7.69 (s, 1H), 7.59 - 7.30 (m, 6H), 4.78 - 4.56 (m, 2H), 4.49 - 4.25 (m,2H), 2.62 (d, J = 4.5 Hz, 3H), 2.46 - 2.38 (m, 1H), 1.06 (d, J = 6.1 Hz, 6H)

[0277] Example 47-(a)

Production of methyl 3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate

[C137]



0.016 ml of N,N-diisopropylethylamine and 16 mg of methyl 3-(bromomethyl)benzoate were added to a N,N-dimethylformamide (0.5 ml) solution of 25 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 31 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 552 $[M+H]^+$

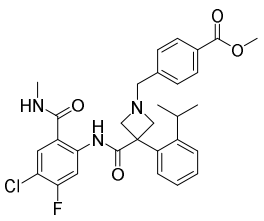
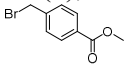
Retention time (LCMS conditions 2): 1.108 min.

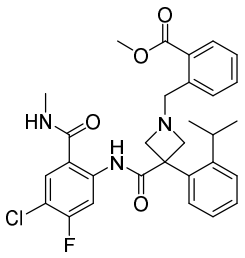
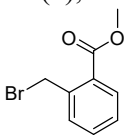
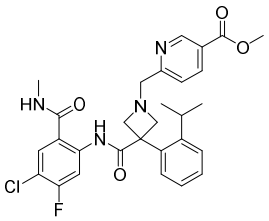
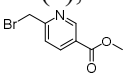
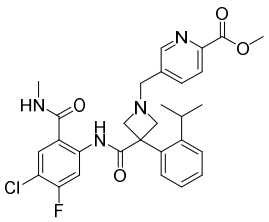
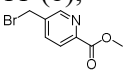
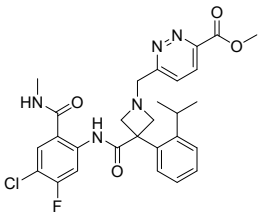
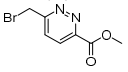
[0278] Example 46-(a) and the like

Compounds shown in Table 42 below were obtained by treating corresponding raw material compounds in the same manner as in Example 47-(a). The synthesis of Example 46-(a) was performed using a mixed solvent of N,N-dimethylformamide and acetonitrile instead of N,N-dimethylformamide.

[Table 42]

Table 42

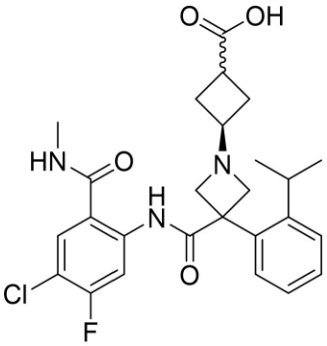
Example	Structural formula	Analysis data	Raw material
46-(a)		Mass spectrum (ESI, m/z): 552 $[M+H]^+$ Retention time (LCMS conditions 2): 1.106 min	Example 11-(b), 

48-(a)		Mass spectrum (ESI, m/z): 552 $[M+H]^+$ Retention time (LCMS conditions 2): 1.144 min	Example 11-(b), 
49-(a)		Mass spectrum (ESI, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 2): 1.084 min	Example 11-(b), 
50-(a)		Mass spectrum (ESI, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 2): 0.980 min	Example 11-(b), 
51-(a)		Mass spectrum (ESI, m/z): 554 $[M+H]^+$ Retention time (LCMS conditions 2): 0.971 min	Example 11-(b), 

[0279] Example 52-(b)

Production of 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylic acid (diastereomer 1)

[C138]



0.011 ml of formic acid was added to a dichloromethane (1 ml) solution of 32 mg of tert-butyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-

yl)cyclobutane-1-carboxylate produced in Example 52-(a) at room temperature under an argon gas flow, stirred at room temperature for 21.5 hours, and stirred at 40°C for two hours. A reaction mixture was concentrated under reduced pressure. The obtained concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 28 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 502 $[M+H]^+$

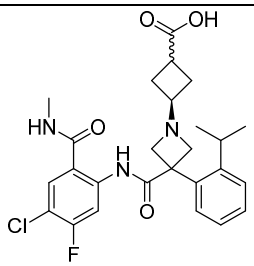
Retention time (LCMS conditions 2): 0.936 min.

[0280] Example 53-(b)

A compound shown in Table 43 below was obtained by treating a corresponding raw material compound in the same manner as in Example 52-(b).

[Table 43]

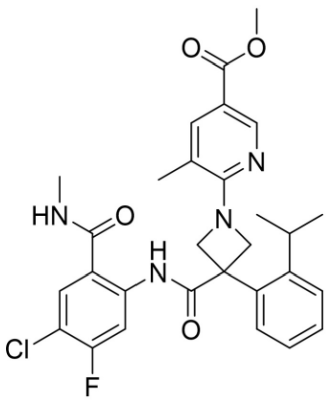
Table 43

Example	Structural formula	Analysis data	Raw material
53-(b)	 Diastereomer 2	Mass spectrum (ESI, m/z): 502 $[M+H]^+$ Retention time (LCMS conditions 2): 0.917 min	Example 53-(a)

[0281] Example 66-(a)

Production of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinate

[C139]



23 mg of methyl 6-chloro-5-methylnicotinate and 0.027 ml of N,N-diisopropylethylamine were added to a N-methyl-2-pyrrolidinone (0.5 ml) solution of 25 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 80°C for seven hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 21 mg of a title compound as a slightly yellow foamy substance.

Mass spectrum (DUIS, m/z): 553 $[M+H]^+$

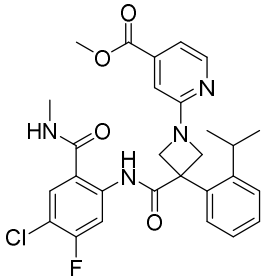
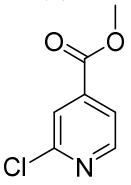
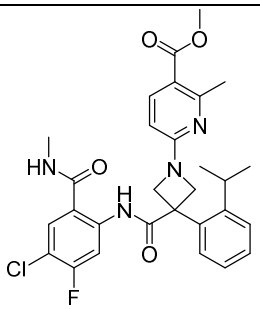
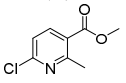
Retention time (LCMS conditions 1): 1.692 min.

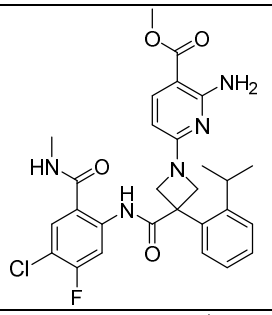
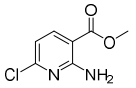
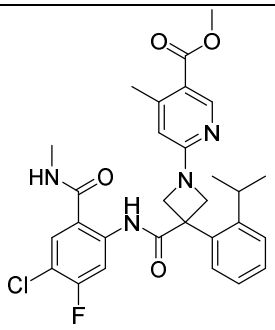
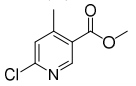
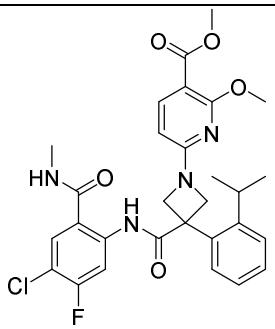
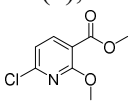
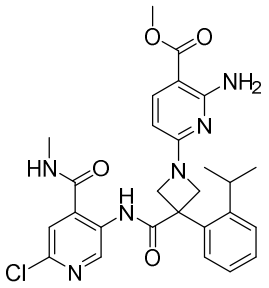
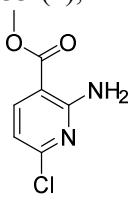
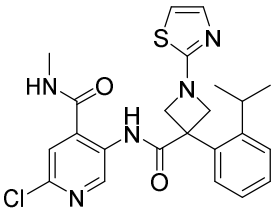
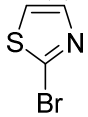
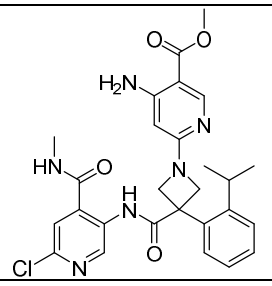
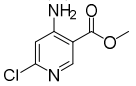
[0282] Example 67-(a) and the like

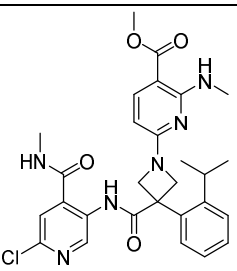
Compounds shown in Table 44 below were obtained by treating corresponding raw material compounds in the same manner as in Example 66-(a).

[Table 44]

Table 44

Example	Structural formula	Analysis data	Raw material
67-(a)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 1.544 min	Example 11-(b), 
69-(a)		Mass spectrum (ESI, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 2): 1.578 min	Example 11-(b), 

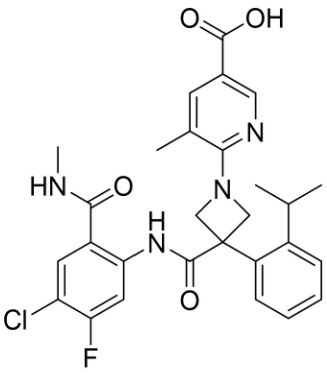
70-(a)		Mass spectrum (ESI, m/z): 554 $[M+H]^+$ Retention time (LCMS conditions 2): 1.508 min	Example 11-(b), 
71-(a)		Mass spectrum (ESI, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 2): 1.573 min	Example 11-(b), 
72-(a)		Mass spectrum (ESI, m/z): 569 $[M+H]^+$ Retention time (LCMS conditions 2): 1.749 min	Example 11-(b), 
73-(a)		Mass spectrum (ESI, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 2): 1.301 min	Example 33-(b), 
74-(a)		Mass spectrum (ESI, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 2): 1.212 min	Example 33-(b) 
293-(a)		Mass spectrum (DUIS, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 7): 0.666 min	Example 33-(b) 

294-(a)		Mass spectrum (DUIS, m/z): 551 $[M+H]^+$ Retention time (LCMS conditions 7): 1.037 min	Example 33-(b) Reference Example 294-(a)

[0283] Example 66-(b)

Production of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinic acid

[C140]



5 mg of lithium hydroxide was added to a tetrahydrofuran (0.6 ml)/2-propanol (0.2 ml)/water (0.2 ml) suspension of 21 mg of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinate produced in Example 66-(a) at room temperature under an argon gas flow and stirred at 50°C for six hours. A 1N sodium hydroxide aqueous solution and tert-butyl methyl ether were added to a reaction mixture, and the reaction mixture was separated. The pH was adjusted to four by adding 1N hydrochloric acid to an aqueous layer, and the aqueous layer was extracted with ethyl acetate. An organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The organic layer was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 19 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 539 $[M+H]^+$

Retention time (LCMS conditions 2): 1.376 min.

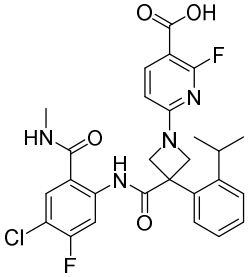
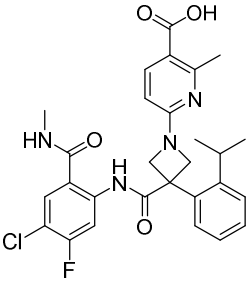
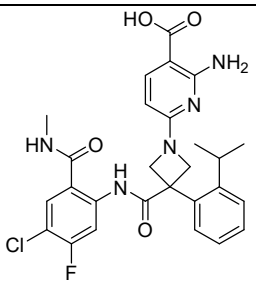
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.57 (br s, 1H), 11.64 (s, 1H), 8.80 - 8.72 (m, 1H), 8.52 - 8.46 (m, 2H), 7.92 (d, J = 8.2 Hz, 1H), 7.77 - 7.74 (m, 1H), 7.54 - 7.48 (m, 1H), 7.40 - 7.28 (m, 3H), 4.90 (br d, J = 8.4 Hz, 2H), 4.64 (br d, J = 8.4 Hz, 2H), 2.65 (d, J = 4.5 Hz, 3H), 2.63 - 2.55 (m, 1H), 2.29 (s, 3H), 1.08 (d, J = 6.7 Hz, 6H)

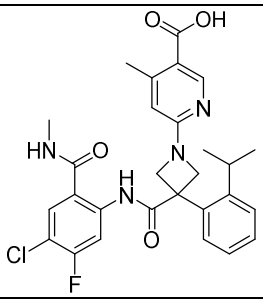
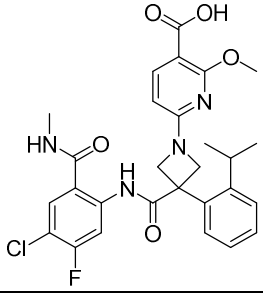
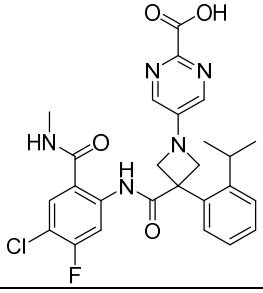
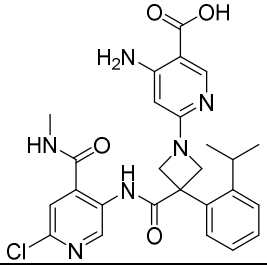
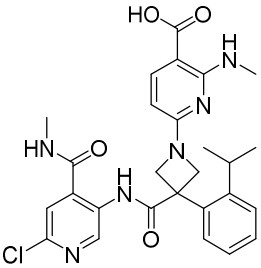
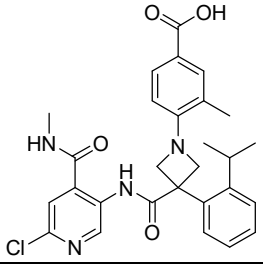
[0284] Example 68-(b) and the like

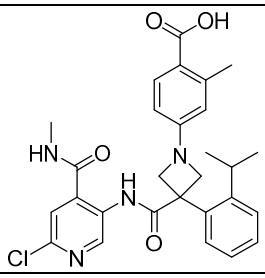
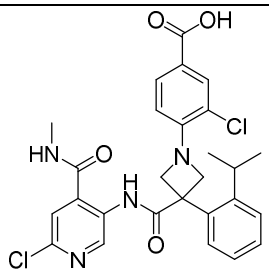
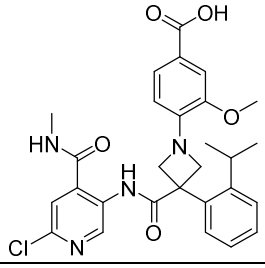
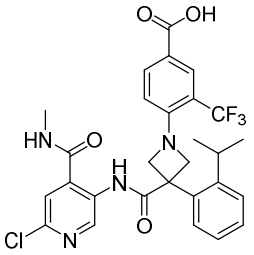
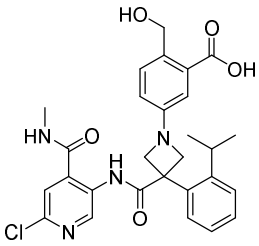
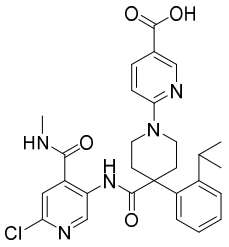
Compounds shown in Table 45 below were obtained by treating corresponding raw material compounds in the same manner as in Example 66-(b). The syntheses of Example 294-(b) and Example 300-(b) were performed at 75°C as the reaction temperature. The syntheses of Example 299-(b) and Example 303-(b) were performed at 60°C as the reaction temperature.

[Table 45]

Table 45

Example	Structural formula	Analysis data	Raw material
68-(b)		Mass spectrum (ESI, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 2): 1.456 min	Example 68-(a)
69-(b)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 1.245 min	Example 69-(a)
70-(b)		Mass spectrum (ESI, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 2): 1.223 min	Example 70-(a)

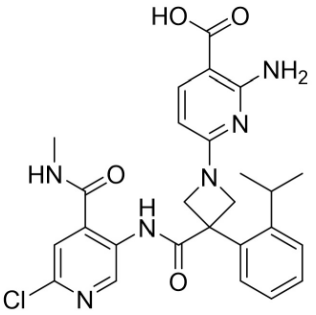
71-(b)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 1.287 min	Example 71-(a)
72-(b)		Mass spectrum (ESI, m/z): 555 $[M+H]^+$ Retention time (LCMS conditions 2): 1.560 min	Example 72-(a)
108-(b)		Mass spectrum (ESI, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 2): 1.266 min	Example 108-(a)
293-(b)		Mass spectrum (DUIS, m/z): 523 $[M+H]^+$ Retention time (LCMS conditions 8): 0.955 min	Example 293-(a)
294-(b)		Mass spectrum (DUIS, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 8): 1.407 min	Example 294-(a)
299-(b)		Mass spectrum (DUIS, m/z): 521 $[M+H]^+$ Retention time (LCMS conditions 8): 1.368 min	Example 299-(a)

300-(b)		Mass spectrum (DUIS, m/z): 521 $[M+H]^+$ Retention time (LCMS conditions 8): 1.400 min	Example 300-(a)
301-(b)		Mass spectrum (DUIS, m/z): 541 $[M+H]^+$ Retention time (LCMS conditions 8): 1.431 min	Example 301-(a)
303-(b)		Mass spectrum (DUIS, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 8): 1.355 min	Example 303-(a)
304-(b)		Mass spectrum (DUIS, m/z): 575 $[M+H]^+$ Retention time (LCMS conditions 8): 1.477 min	Example 304-(a)
308-(b)		Mass spectrum (DUIS, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 8): 1.209 min	Example 308-(a)
327-(b)		Mass spectrum (DUIS, m/z): 536 $[M+H]^+$ Retention time (LCMS conditions 8): 1.156 min	Example 327-(a)

[0285] Example 73-(b)

Production of 2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid

[C141]



6 mg of lithium hydroxide was added to a tetrahydrofuran (0.6 ml)/2-propanol (0.2 ml)/water (0.2 ml) suspension of 29 mg of methyl 2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate produced in Example 73-(a) at room temperature under an argon gas flow and stirred at 60°C for five hours. A mixture was left to stand at room temperature for 14 hours and then stirred at 75°C for nine hours. 1M hydrochloric acid was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) and then purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 523 $[M+H]^+$

Retention time (LCMS conditions 2): 1.023 min.

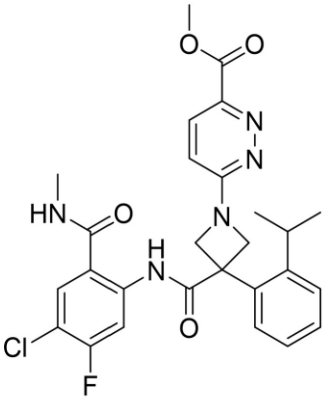
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.98 (br s, 1H), 10.57 (s, 1H), 9.35 (s, 1H), 8.99 - 8.92 (m, 1H), 7.78 (d, J = 8.6 Hz, 1H), 7.70 (s, 1H), 7.54 - 7.49 (m, 1H), 7.43 - 7.31 (m, 3H), 7.12 (br s, 2H), 5.75 (d, J = 8.6 Hz, 1H), 4.71 (br d, J = 8.5 Hz, 2H), 4.39 (br d, J = 8.5 Hz, 2H), 2.63 (d, J = 4.6 Hz, 3H), 2.56 - 2.43 (m, 1H), 1.07 (d, J = 6.7 Hz, 6H)

[0286] Example 75-(a)

Production of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate

[C142]



38 mg of methyl 6-chloropyridazine-3-carboxylate and 0.068 ml of N,N-diisopropylethylamine were added to a 1,4-dioxane (2 ml) suspension of 80 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 100°C for 3.5 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone) to obtain 108 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 540 $[M+H]^+$

Retention time (LCMS conditions 2): 1.393 min.

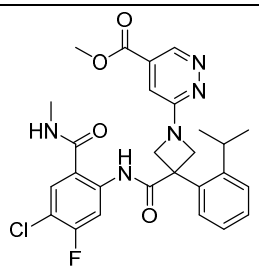
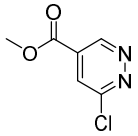
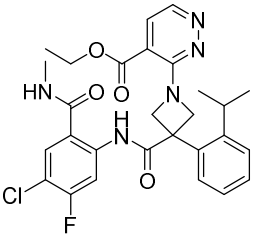
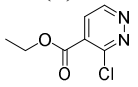
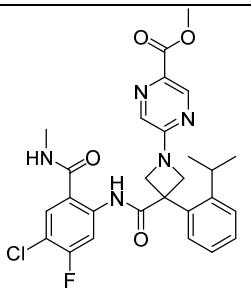
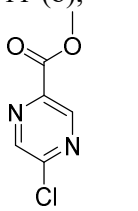
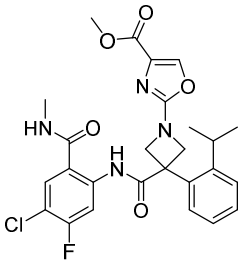
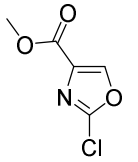
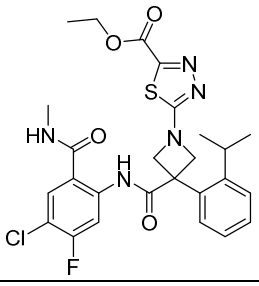
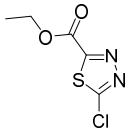
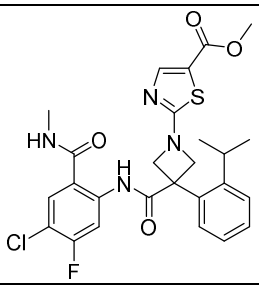
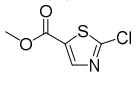
[0287] Example 77-(a) and the like

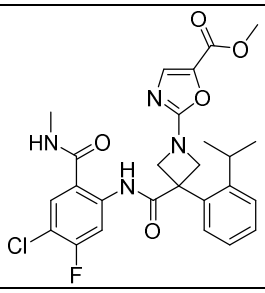
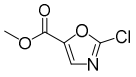
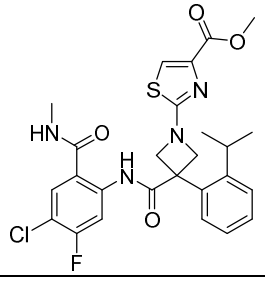
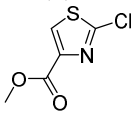
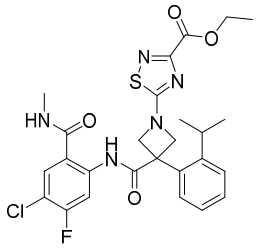
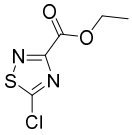
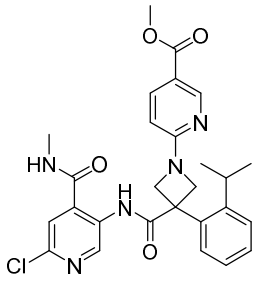
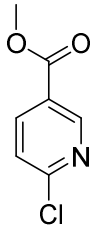
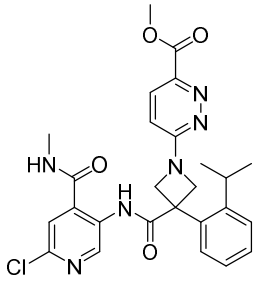
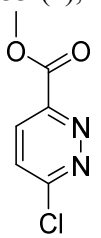
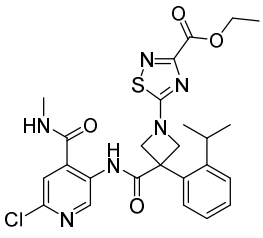
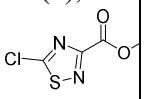
Compounds shown in Table 46 below were obtained by treating corresponding raw material compounds in the same manner as in Example 75-(a).

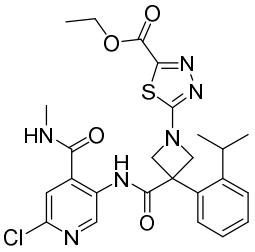
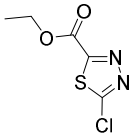
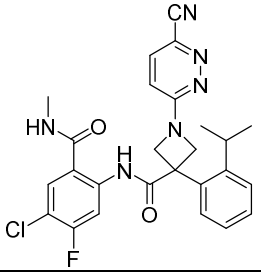
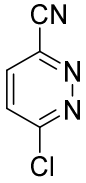
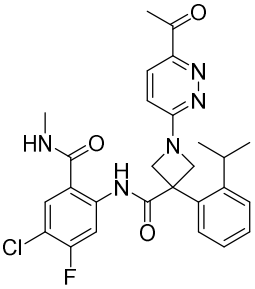
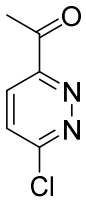
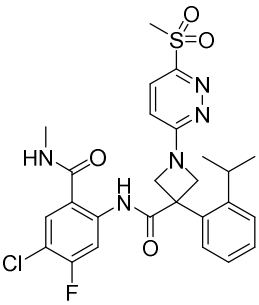
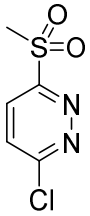
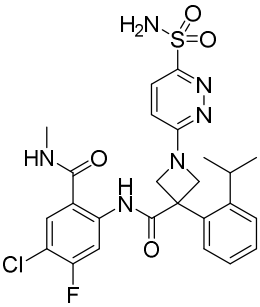
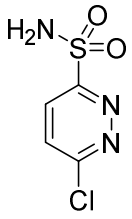
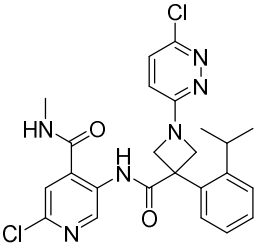
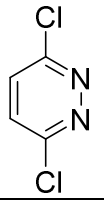
[Table 46]

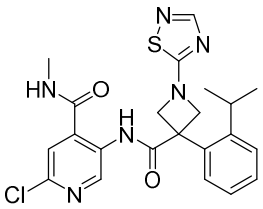
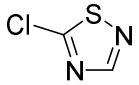
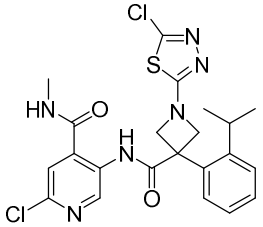
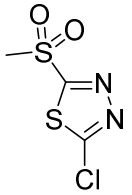
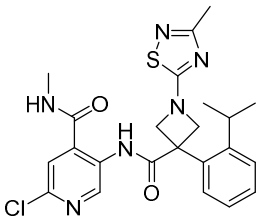
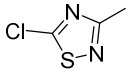
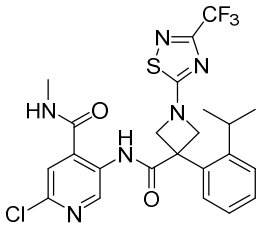
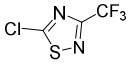
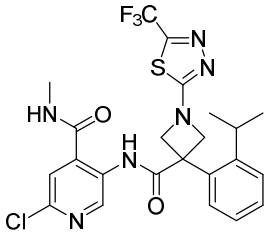
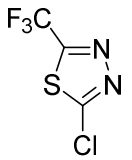
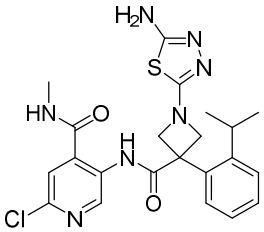
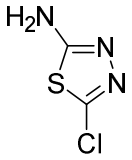
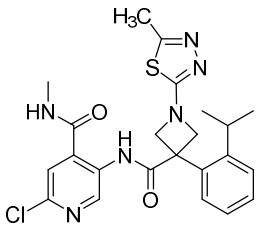
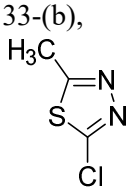
Table 46

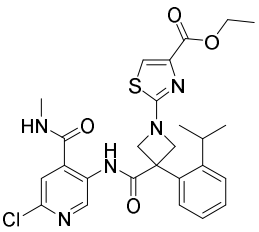
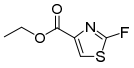
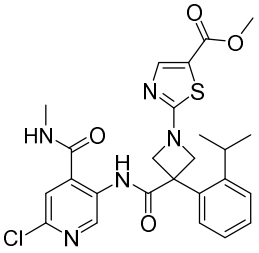
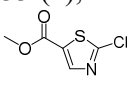
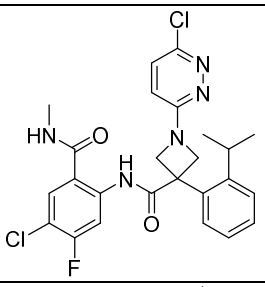
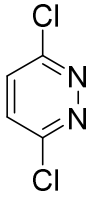
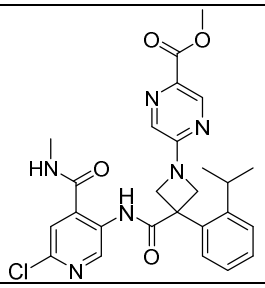
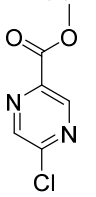
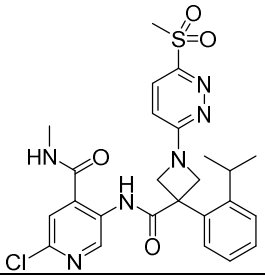
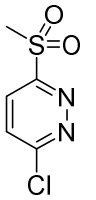
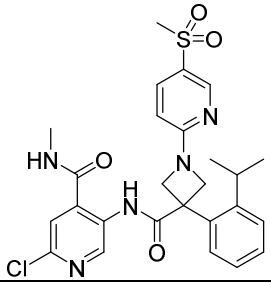
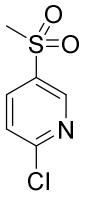
Example	Structural formula	Analysis data	Raw material

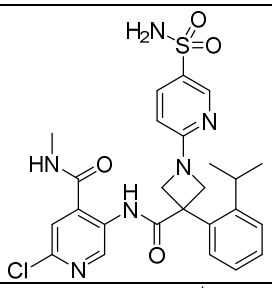
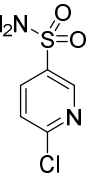
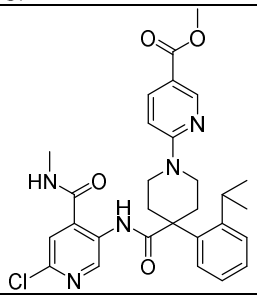
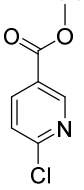
77-(a)		Mass spectrum (DUIS, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 1): 1.417 min	Example 11-(b), 
78-(a)		Mass spectrum (DUIS, m/z): 554 $[M+H]^+$ Retention time (LCMS conditions 1): 1.525 min	Example 11-(b), 
79-(a)		Mass spectrum (DUIS, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 1): 1.497 min	Example 11-(b), 
80-(a)		Mass spectrum (DUIS, m/z): 529 $[M+H]^+$ Retention time (LCMS conditions 1): 1.510 min	Example 11-(b), 
81-(a)		Mass spectrum (ESI, m/z): 560 $[M+H]^+$ Retention time (LCMS conditions 2): 1.600 min	Example 11-(b), 
82-(a)		Mass spectrum (DUIS, m/z): 545 $[M+H]^+$ Retention time (LCMS conditions 1): 1.630 min	Example 11-(b), 

83-(a)		Mass spectrum (ESI, m/z): 529 $[M+H]^+$ Retention time (LCMS conditions 2): 1.515 min	Example 11-(b), 
84-(a)		Mass spectrum (ESI, m/z): 545 $[M+H]^+$ Retention time (LCMS conditions 2): 1.589 min	Example 11-(b), 
85-(a)		Mass spectrum (DUIS, m/z): 560 $[M+H]^+$ Retention time (LCMS conditions 1): 1.593 min	Example 11-(b), 
86-(a)		Mass spectrum (DUIS, m/z): 522 $[M+H]^+$ Retention time (LCMS conditions 1): 1.384 min	Example 33-(b), 
87-(a)		Mass spectrum (DUIS, m/z): 523 $[M+H]^+$ Retention time (LCMS conditions 1): 1.200 min	Example 33-(b), 
88-(a)		Mass spectrum (ESI, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 2): 1.381 min	Example 33-(b), 

89-(a)		Mass spectrum (DUIS, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 1): 1.398 min	Example 33-(b), 
90-(a)		Mass spectrum (DUIS, m/z): 507 $[M+H]^+$ Retention time (LCMS conditions 1): 1.478 min	Example 11-(b), 
91-(a)		Mass spectrum (DUIS, m/z): 524 $[M+H]^+$ Retention time (LCMS conditions 1): 1.466 min	Example 11-(b), 
92-(a)		Mass spectrum (DUIS, m/z): 560 $[M+H]^+$ Retention time (LCMS conditions 1): 1.381 min	Example 11-(b), 
93-(a)		Mass spectrum (DUIS, m/z): 561 $[M+H]^+$ Retention time (LCMS conditions 1): 1.279 min	Example 11-(b), 
94-(a)		Mass spectrum (ESI, m/z): 499 $[M+H]^+$ Retention time (LCMS conditions 2): 1.303 min	Example 33-(b), 

95-(a)		Mass spectrum (DUIS, m/z): 471 $[M+H]^+$ Retention time (LCMS conditions 1): 1.285 min	Example 33-(b), 
96-(a)		Mass spectrum (DUIS, m/z): 505 $[M+H]^+$ Retention time (LCMS conditions 1): 1.518 min	Example 33-(b), 
97-(a)		Mass spectrum (ESI, m/z): 485 $[M+H]^+$ Retention time (LCMS conditions 2): 1.329 min	Example 33-(b), 
98-(a)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 1.620 min	Example 33-(b), 
99-(a)		Mass spectrum (ESI, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 2): 1.551 min	Example 33-(b), 
100-(a)		Mass spectrum (DUIS, m/z): 486 $[M+H]^+$ Retention time (LCMS conditions 1): 0.999 min	Example 33-(b), 
101-(a)		Mass spectrum (DUIS, m/z): 485 $[M+H]^+$ Retention time (LCMS conditions 1): 1.239 min	Example 33-(b), 

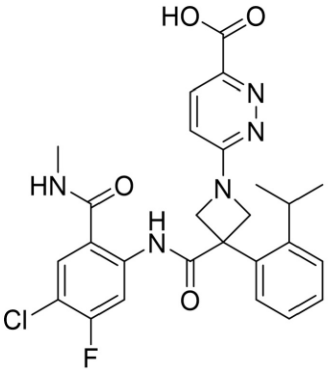
125-(a)		Mass spectrum (ESI, m/z): 542 $[M+H]^+$ Retention time (LCMS conditions 2): 1.472 min	Example 33-(b), 
126-(a)		Mass spectrum (ESI, m/z): 528 $[M+H]^+$ Retention time (LCMS conditions 2): 1.438 min	Example 33-(b), 
262-(a)		Mass spectrum (ESI, m/z): 516 $[M+H]^+$ Retention time (LCMS conditions 2): 1.504 min	Example 11-(b), 
295-(a)		Mass spectrum (DUIS, m/z): 523 $[M+H]^+$ Retention time (LCMS conditions 7): 0.813 min	Example 33-(b), 
296-(a)		Mass spectrum (DUIS, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 8): 1.180 min	Example 33-(b), 
297-(a)		Mass spectrum (DUIS, m/z): 542 $[M+H]^+$ Retention time (LCMS conditions 8): 1.245 min	Example 33-(b), 

298-(a)		Mass spectrum (DUIS, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 8): 1.146 min	Example 33-(b), 
327-(a)		Mass spectrum (DUIS, m/z): 550 $[M+H]^+$ Retention time (LCMS conditions 7): 0.917 min	Example 292-(b), 

[0288] Example 76-(a)

Production of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid

[C143]



A water (0.125 ml) solution of 6 mg of lithium hydroxide monohydrate was added dropwise to a tetrahydrofuran (0.5 ml)/methanol (0.125 ml) solution of 25 mg of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate produced in Example 75-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. The pH was adjusted to four by adding 1N hydrochloric acid to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain

26 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 526 $[M+H]^+$

Retention time (LCMS conditions 1): 1.234 min.

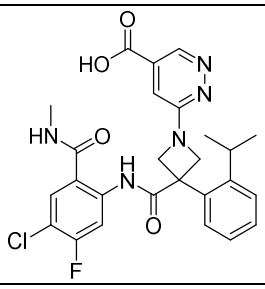
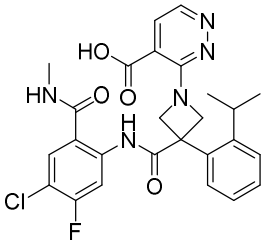
^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.42 (d, J =12.0 Hz, 1H), 7.90 - 7.80 (m, 2H), 7.55 - 7.48 (m, 1H), 7.41 - 7.30 (m, 3H), 6.99 (d, J = 9.4 Hz, 1H), 4.92 - 4.79 (m, 2H), 4.66 - 4.49 (m, 2H), 2.60 (s, 3H), 2.56 - 2.46 (m, 1H), 1.09 (d, J = 6.7 Hz, 6H)

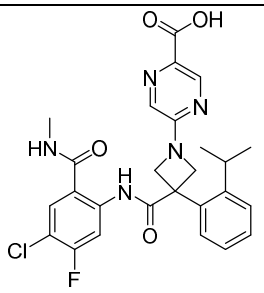
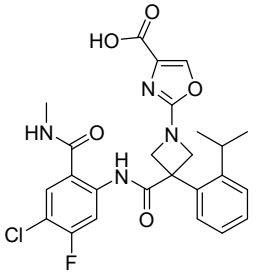
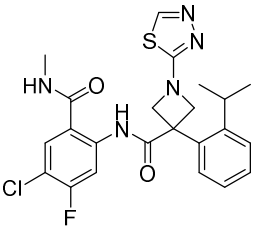
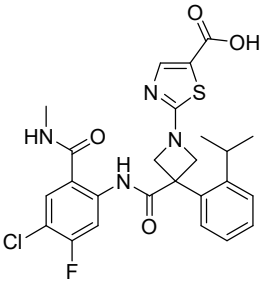
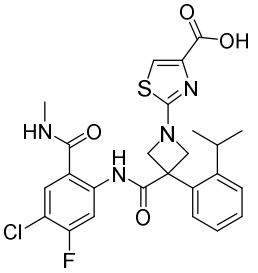
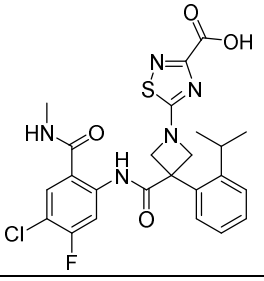
[0289] Example 77-(b) and the like

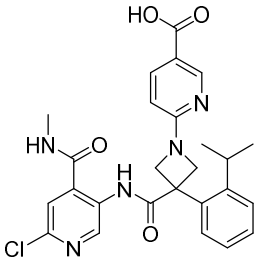
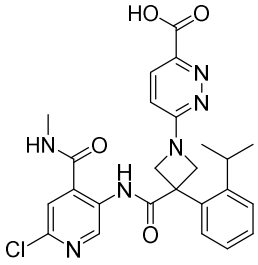
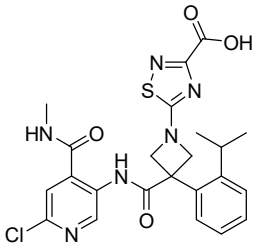
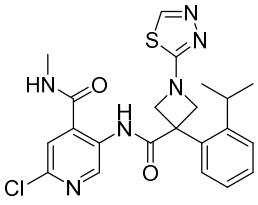
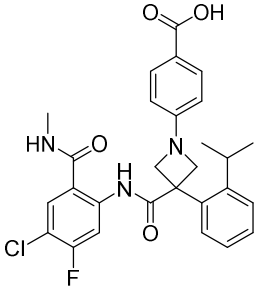
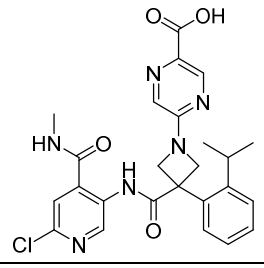
Compounds shown in Table 47 below were obtained by treating corresponding raw material compounds in the same manner as in Example 76-(a). The synthesis of Example 109-(b) was performed at 40°C as the reaction temperature. The synthesis of Example 322-(b) was performed at 60°C as the reaction temperature. The syntheses of Example 302-(b), Example 306-(b), Example 307-(a), and Example 316-(b) were performed at 50°C as the reaction temperature.

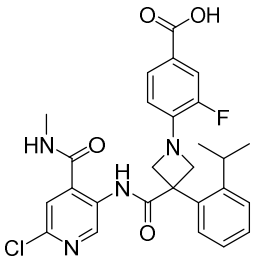
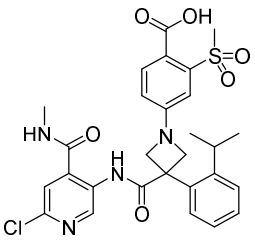
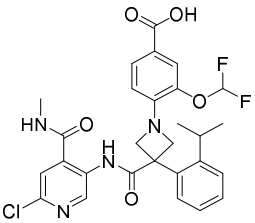
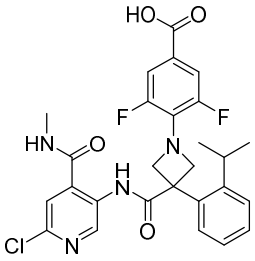
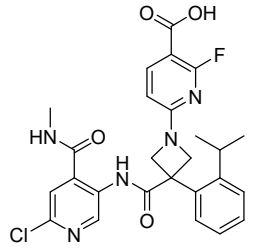
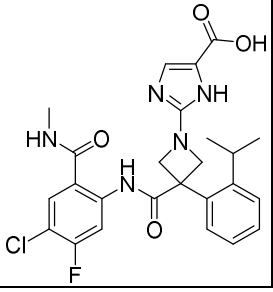
[Table 47]

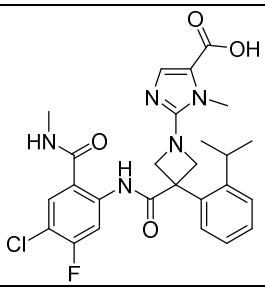
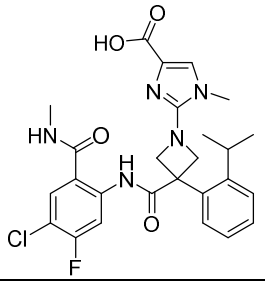
Table 47

Example	Structural formula	Analysis data	Raw material
77-(b)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 1): 1.124 min	Example 77-(a)
78-(b)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 1): 1.029 min	Example 78-(a)

79-(b)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 1): 1.328 min	Example 79-(a)
80-(b)		Mass spectrum (DUIS, m/z): 515 $[M+H]^+$ Retention time (LCMS conditions 1): 1.345 min	Example 80-(a)
81-(b)		Mass spectrum (ESI, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 2): 1.395 min	Example 81-(a)
82-(b)		Mass spectrum (ESI, m/z): 531 $[M+H]^+$ Retention time (LCMS conditions 2): 1.391 min	Example 82-(a)
84-(b)		Mass spectrum (ESI, m/z): 531 $[M+H]^+$ Retention time (LCMS conditions 2): 1.406 min	Example 84-(a)
85-(b)		Mass spectrum (DUIS, m/z): 532 $[M+H]^+$ Retention time (LCMS conditions 1): 1.336 min	Example 85-(a)

86-(b)		Mass spectrum (DUIS, m/z): 508 $[M+H]^+$ Retention time (LCMS conditions 1): 1.110 min	Example 86-(a)
87-(b)		Mass spectrum (DUIS, m/z): 509 $[M+H]^+$ Retention time (LCMS conditions 1): 1.023 min	Example 87-(a)
88-(b)		Mass spectrum (ESI, m/z): 515 $[M+H]^+$ Retention time (LCMS conditions 2): 1.127 min	Example 88-(a)
89-(b)		Mass spectrum (DUIS, m/z): 471 $[M+H]^+$ Retention time (LCMS conditions 1): 1.175 min	Example 89-(a)
109-(b)		Mass spectrum (DUIS, m/z): 524 $[M+H]^+$ Retention time (LCMS conditions 1): 1.544 min	Example 109-(a)
295-(b)		Mass spectrum (DUIS, m/z): 509 $[M+H]^+$ Retention time (LCMS conditions 8): 1.117 min	Example 295-(a)

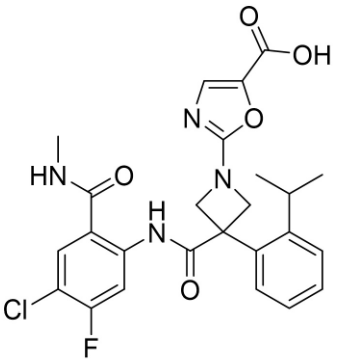
302-(b)		Mass spectrum (DUIS, m/z): 525 $[M+H]^+$ Retention time (LCMS conditions 8): 1.377 min	Example 302-(a)
305-(b)		Mass spectrum (DUIS, m/z): 585 $[M+H]^+$ Retention time (LCMS conditions 8): 1.244 min	Example 305-(a)
306-(b)		Mass spectrum (DUIS, m/z): 573 $[M+H]^+$ Retention time (LCMS conditions 8): 1.399 min	Example 306-(a)
307-(b)		Mass spectrum (DUIS, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 8): 1.429 min	Example 307-(a)
316-(b)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 7): 0.807 min	Example 316-(a)
322-(b)		Mass spectrum (DUIS, m/z): 514 $[M+H]^+$ Retention time (LCMS conditions 8): 0.987 min	Example 322-(a)

323-(b)		Mass spectrum (DUIS, m/z): 528 $[M+H]^+$ Retention time (LCMS conditions 8): 1.063 min	Example 323-(a)
324-(b)		Mass spectrum (DUIS, m/z): 528 $[M+H]^+$ Retention time (LCMS conditions 9): 1.035 min	Example 324-(a)

[0290] Example 83-(b)

Production of 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylic acid

[C144]



A water (0.25 ml) solution of 9 mg of lithium hydroxide monohydrate was added dropwise to a tetrahydrofuran (1 ml)/methanol (0.25 ml) solution of 34 mg of methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylate produced in Example 83-(a) at room temperature under argon gas and stirred at room temperature for five hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The concentrated residue was purified by high performance liquid chromatography (column; XBridge C18,

mobile phase; 0.1% formic acid aqueous solution:acetonitrile). Water was added to the purified product, and the purified product was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The obtained concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 25 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 515 $[M+H]^+$

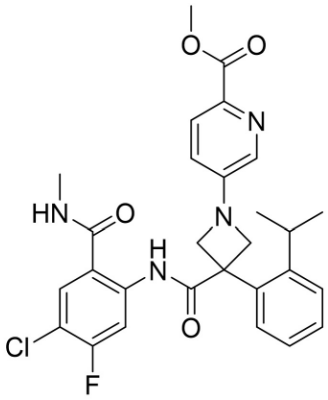
Retention time (LCMS conditions 2): 1.297 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.45 (s, 1H), 8.78 - 8.68 (m, 1H), 8.46 (d, J = 12.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.49 (br d, J = 7.5Hz, 1H), 7.43 - 7.28 (m, 3H), 4.89 - 4.75 (m, 2H), 4.69 - 4.54 (m, 2H), 2.62 (d, J = 4.5 Hz, 3H), 2.46 - 2.37 (m, 1H), 1.06 (br d, J = 6.7 Hz, 6H)

[0291] Example 102-(a)

Production of methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate

[C145]



9 mg of methyl 5-fluoropicolinate and 8 mg of potassium carbonate were added to a DMSO (0.5 ml) solution of 20 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 110°C for one hour. Water was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with

dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone) to obtain 26 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 539 $[M+H]^+$

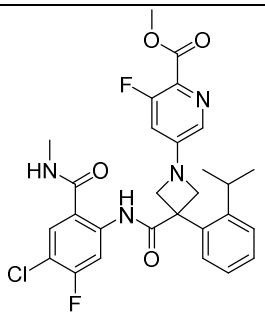
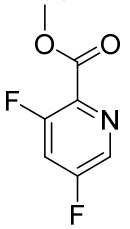
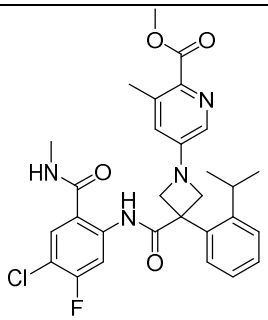
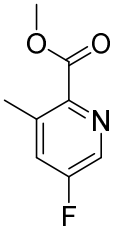
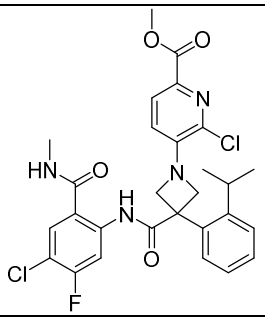
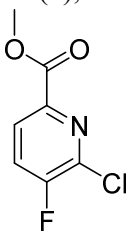
Retention time (LCMS conditions 1): 1.491 min.

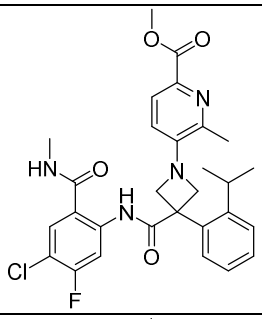
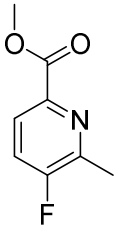
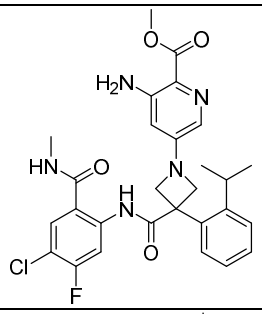
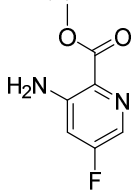
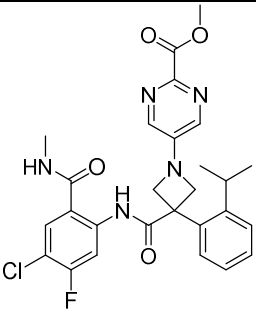
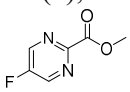
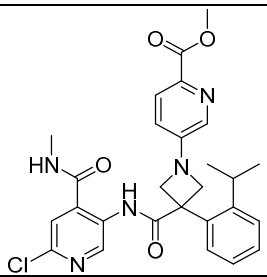
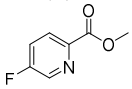
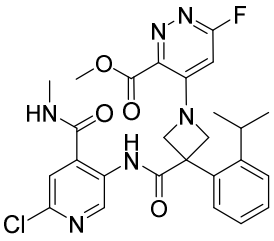
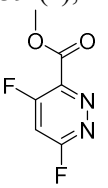
[0292] Example 103-(a) and the like

Compounds shown in Table 48 below were obtained by treating corresponding raw material compounds in the same manner as in Example 102-(a).

[Table 48]

Table 48

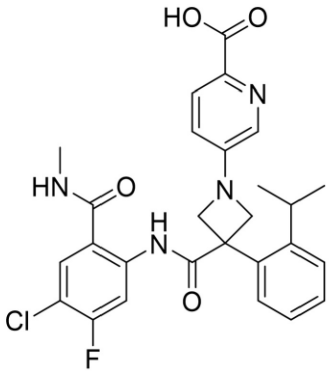
Example	Structural formula	Analysis data	Raw material
103-(a)		Mass spectrum (DUIS, m/z): 557 $[M+H]^+$ Retention time (LCMS conditions 1): 1.559 min	Example 11-(b), 
104-(a)		Mass spectrum (DUIS, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 1): 1.549 min	Example 11-(b), 
105-(a)		Mass spectrum (DUIS, m/z): 573 $[M+H]^+$ Retention time (LCMS conditions 1): 1.695 min	Example 11-(b), 

106-(a)		Mass spectrum (DUIS, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 1): 1.559 min	Example 11-(b), 
107-(a)		Mass spectrum (DUIS, m/z): 554 $[M+H]^+$ Retention time (LCMS conditions 1): 1.262 min	Example 11-(b), 
108-(a)		Mass spectrum (ESI, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 2): 1.381 min	Example 11-(b), 
320-(a)		Mass spectrum (DUIS, m/z): 522 $[M+H]^+$ Retention time (LCMS conditions 7): 0.813 min	Example 33-(b), 
386-(a)		Mass spectrum (DUIS, m/z): 541 $[M+H]^+$ Retention time (LCMS conditions 7): 0.821 min	Example 39-(a), 

[0293] Example 102-(b)

Production of 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid

[C146]



A water (0.1 ml) solution of 6 mg of lithium hydroxide monohydrate was added dropwise to a tetrahydrofuran (0.3 ml)/methanol (0.1 ml) solution of 26 mg of methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate produced in Example 102-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. The pH was adjusted to four by adding 1N hydrochloric acid to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 26 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 525 $[M+H]^+$

Retention time (LCMS conditions 1): 1.266 min.

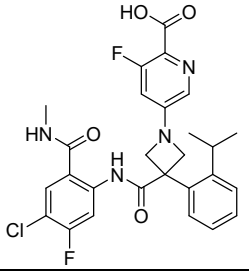
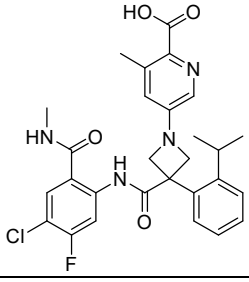
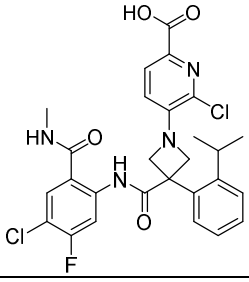
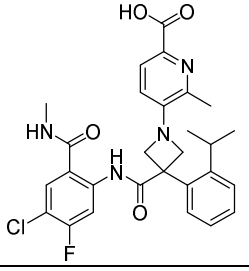
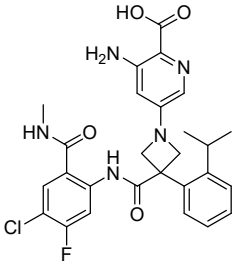
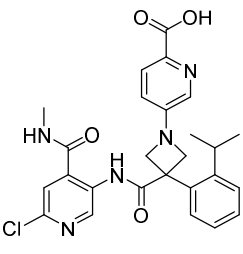
^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.45 (d, J = 12.2 Hz, 1H), 8.00 (d, J = 2.8 Hz, 1H), 7.92 - 7.85 (m, 2H), 7.55 - 7.50 (m, 1H), 7.42 - 7.32 (m, 3H), 7.05 (dd, J = 2.8, 8.7 Hz, 1H), 4.84 - 4.73 (m, 2H), 4.51 - 4.37 (m, 2H), 2.64 (s, 3H), 2.61 - 2.50 (m, 1H), 1.09 (d, J = 6.7 Hz, 6H)

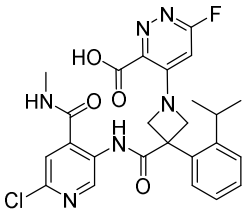
[0294] Example 103-(b) and the like

Compounds shown in Table 49 below were obtained by treating corresponding raw material compounds in the same manner as in Example 102-(b). The synthesis of Example 107-(b) was performed at 40°C as the reaction temperature.

[Table 49]

Table 49

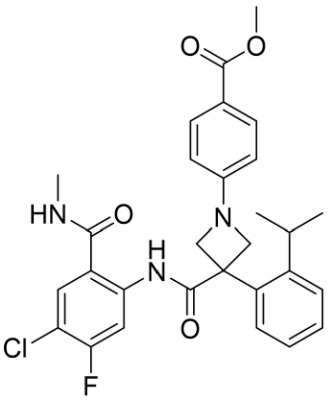
Example	Structural formula	Analysis data	Raw material
103-(b)		Mass spectrum (DUIS, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 1): 1.424 min	Example 103-(a)
104-(b)		Mass spectrum (DUIS, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 1): 1.383 min	Example 104-(a)
105-(b)		Mass spectrum (DUIS, m/z): 559 $[M+H]^+$ Retention time (LCMS conditions 1): 1.520 min	Example 105-(a)
106-(b)		Mass spectrum (DUIS, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 1): 1.284 min	Example 106-(a)
107-(b)		Mass spectrum (DUIS, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 1): 1.200 min	Example 107-(a)
320-(b)		Mass spectrum (DUIS, m/z): 508 $[M+H]^+$ Retention time (LCMS conditions 7): 0.691 min	Example 320-(a)

386-(b)		Mass spectrum (DUIS, m/z): 527 $[M+H]^+$ Retention time (LCMS conditions 7): 0.730 min	Example 386-(a)

[0295] Example 109-(a)

Production of methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate

[C147]



17 mg of 4-(methoxycarbonyl)phenylboronic acid, 0.019 ml of pyridine, 27 mg of copper (II) acetate, and 35 mg of a molecular sieve 4A were added to a dichloromethane (0.7 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an air atmosphere and stirred at room temperature for six hours. 17 mg of 4-(methoxycarbonyl)phenylboronic acid was added thereto at room temperature and stirred at room temperature for 17 hours. A reaction mixture was filtered and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) and then purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 5 mg of a title compound as a white oily substance.

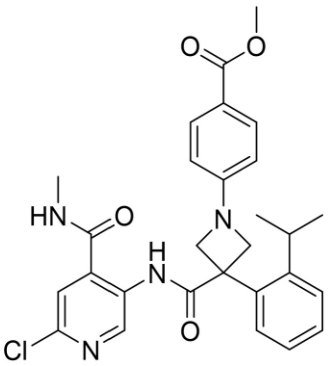
Mass spectrum (DUIS, m/z): 538 $[M+H]^+$

Retention time (LCMS conditions 1): 1.806 min.

[0296] Example 110-(a)

Production of methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate

[C148]



A 1,4-dioxane (5 ml) solution of 321 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b), 329 mg of tripotassium phosphate, and 250 mg of methyl 4-bromobenzoate was degassed and substituted with nitrogen. 74 mg of [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) was added at room temperature under an argon gas flow and stirred at 100°C for 5.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 381 mg of a title compound as a slightly yellow foamy substance.

Mass spectrum (DUIS, m/z): 521 $[M+H]^+$

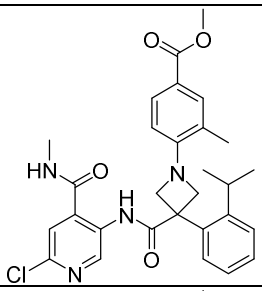
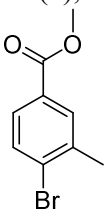
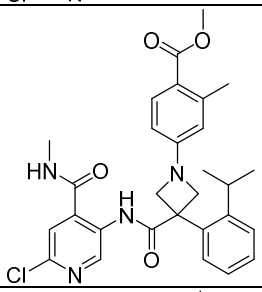
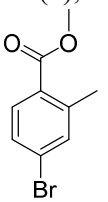
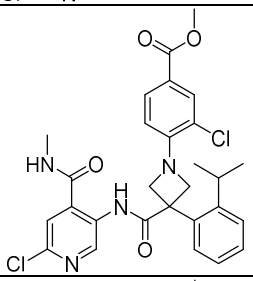
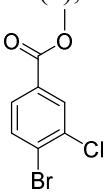
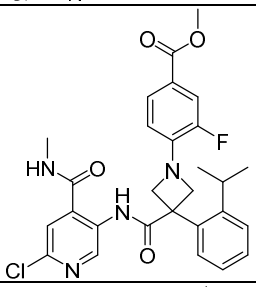
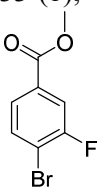
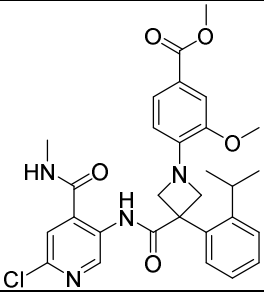
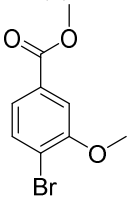
Retention time (LCMS conditions 1): 1.606 min.

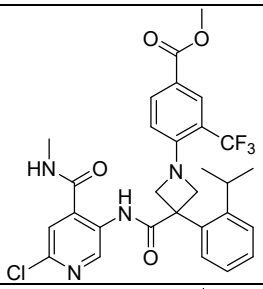
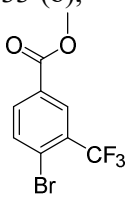
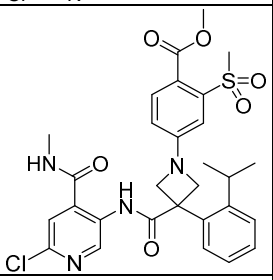
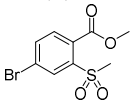
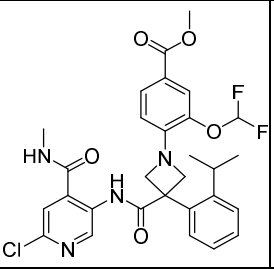
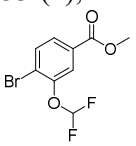
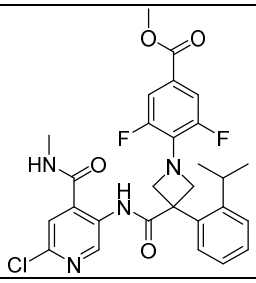
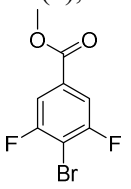
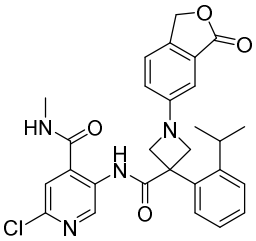
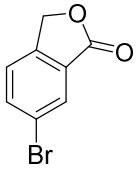
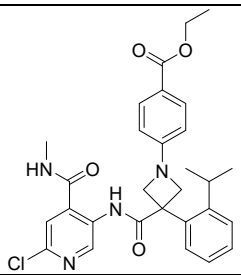
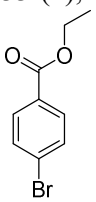
[0297] Example 299-(a) and the like

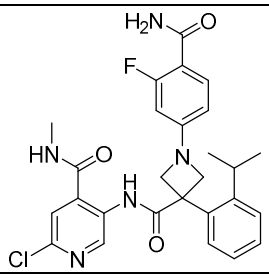
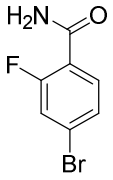
Compounds shown in Table 50 below were obtained by treating corresponding raw material compounds in the same manner as in Example 110-(a). In Example 305-(a) and Example 306-(a), potassium carbonate was used instead of tripotassium phosphate.

[Table 50]

Table 50

Example	Structural formula	Analysis data	Raw material
299-(a)		Mass spectrum (DUIS, m/z): 535 $[M+H]^+$ Retention time (LCMS conditions 7): 0.992 min	Example 33-(b), 
300-(a)		Mass spectrum (DUIS, m/z): 535 $[M+H]^+$ Retention time (LCMS conditions 7): 1.010 min	Example 33-(b), 
301-(a)		Mass spectrum (DUIS, m/z): 555 $[M+H]^+$ Retention time (LCMS conditions 8): 1.738 min	Example 33-(b), 
302-(a)		Mass spectrum (DUIS, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 7): 0.993 min	Example 33-(b), 
303-(a)		Mass spectrum (DUIS, m/z): 551 $[M+H]^+$ Retention time (LCMS conditions 7): 0.979 min	Example 33-(b), 

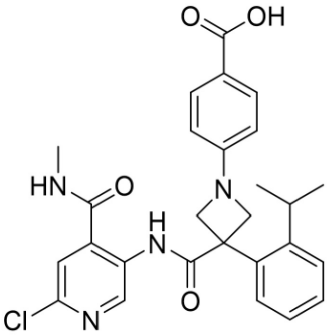
304-(a)		Mass spectrum (DUIS, m/z): 589 $[M+H]^+$ Retention time (LCMS conditions 6): 1.038 min	Example 33-(b), 
305-(a)		Mass spectrum (DUIS, m/z): 599 $[M+H]^+$ Retention time (LCMS conditions 7): 0.878 min	Example 33-(b), 
306-(a)		Mass spectrum (DUIS, m/z): 587 $[M+H]^+$ Retention time (LCMS conditions 7): 0.981 min	Example 33-(b), 
307-(a)		Mass spectrum (DUIS, m/z): 557 $[M+H]^+$ Retention time (LCMS conditions 7): 1.028 min	Example 33-(b), 
308-(a)		Mass spectrum (DUIS, m/z): 519 $[M+H]^+$ Retention time (LCMS conditions 7): 0.876 min	Example 33-(b), 
309-(a)		Mass spectrum (DUIS, m/z): 535 $[M+H]^+$ Retention time (LCMS conditions 8): 1.690 min	Example 33-(b), 

310-(a)		Mass spectrum (DUIS, m/z): 524 $[M+H]^+$ Retention time (LCMS conditions 8): 1.268 min	Example 33-(b), 

[0298] Example 110-(b)

Production of 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid

[C149]



88 mg of lithium hydroxide was added to a tetrahydrofuran (6 ml)/methanol (2 ml)/water (2 ml) solution of 381 mg of methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate produced in Example 110-(a) at room temperature under an argon gas flow and stirred at 50°C for 6.5 hours. 6 ml of a 1N sodium hydroxide aqueous solution was added to a reaction mixture, and the reaction mixture was washed with tert-butyl methyl ether twice. The pH was adjusted to one by adding 1N hydrochloric acid to an aqueous layer, and the aqueous layer was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 316 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 507 $[M+H]^+$

Retention time (LCMS conditions 8): 1.330 min.

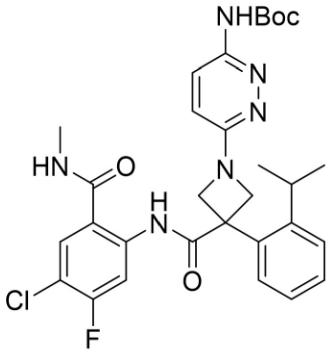
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.26 (br s, 1H), 10.67 (s, 1H), 9.37 (s, 1H), 9.01

- 8.93 (m, 1H), 7.80 - 7.75 (m, 2H), 7.71 (s, 1H), 7.56 - 7.49 (m, 1H),7.43 - 7.30 (m, 3H), 6.61 - 6.55 (m, 2H), 4.71 (br d, J = 7.8 Hz, 2H), 4.34 (br d, J = 7.8 Hz, 2H), 2.64 (d, J = 4.6 Hz, 3H), 2.62 - 2.54 (m, 1H), 1.09 (d, J = 6.7Hz, 6H)

[0299] Example 111-(a)

Production of tert-butyl (6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazin-3-yl)carbamate

[C150]



Reaction 1

0.003 ml of diphenylphosphoryl azide and 0.003 ml of triethylamine were added to a tert-butanol (0.1 ml) solution of 5 mg of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid produced in the same manner as in Example 76-(a) at room temperature under an argon gas flow and stirred at 80°C for four hours.

[0300] Reaction 2

0.018 ml of diphenylphosphoryl azide and 0.016 ml of triethylamine were added to a tert-butanol (0.6 ml) solution of 35 mg of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid produced in the same manner as in Example 76-(a) at room temperature under an argon gas flow and stirred at 80°C for four hours.

A mixture obtained by combining reaction mixtures of the reaction 1 and the reaction 2 was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone) to obtain 16 mg of a title compound as a white foamy substance.

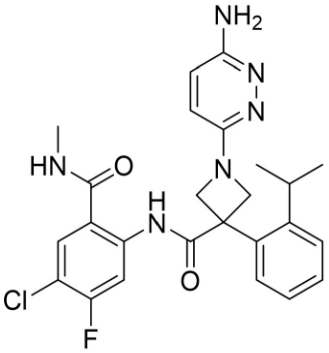
Mass spectrum (DUIS, m/z): 597 $[M+H]^+$

Retention time (LCMS conditions 1): 1.440 min.

[0301] Example 111-(b)

Production of 1-(6-aminopyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C151]



0.342 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to 16 mg of tert-butyl (6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazin-3-yl)carbamate produced in Example 111-(a) at room temperature under an argon gas flow and stirred at room temperature for two hours. A 2M sodium carbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 7 mg of a title compound as a white solid.

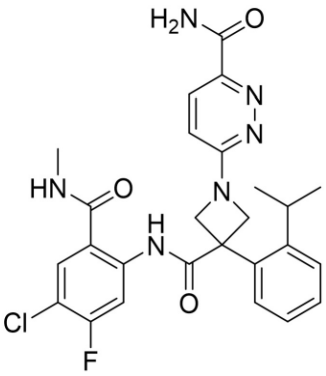
Mass spectrum (ESI, m/z): 497 $[M+H]^+$

Retention time (LCMS conditions 2): 1.033 min.

[0302] Example 112-(a)

Production of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide

[C152]



0.045 ml of N,N-diisopropylethylamine and 26 mg of HATU were added to a N,N-dimethylformamide (0.6 ml) solution of 30 mg of 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid produced in the same manner as in Example 76-(a) at room temperature under an argon gas flow and stirred at room temperature for five minutes. Next, 9 mg of ammonium chloride was added thereto at room temperature and stirred at room temperature for one hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 29 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 525 $[M+H]^+$

Retention time (LCMS conditions 1): 1.269 min.

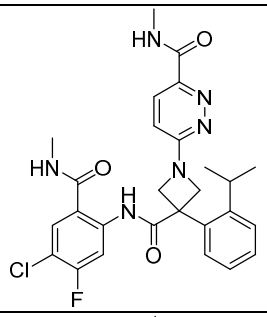
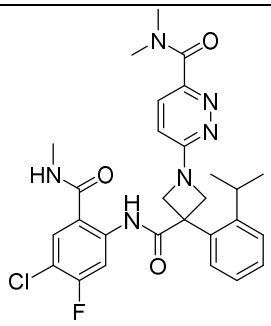
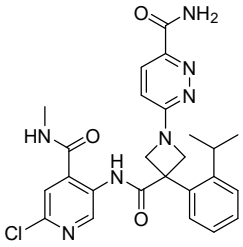
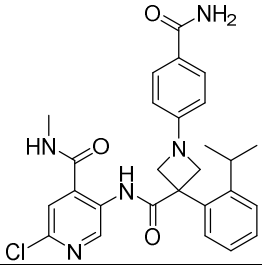
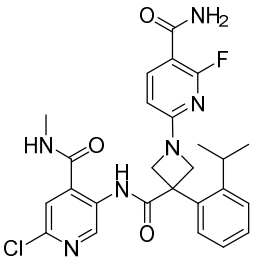
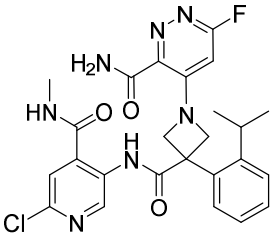
[0303] Example 113-(a) and the like

Compounds shown in Table 51 below were obtained by treating corresponding raw material compounds in the same manner as in Example 112-(a).

[Table 51]

Table 51

Example	Structural formula	Analysis data	Raw material

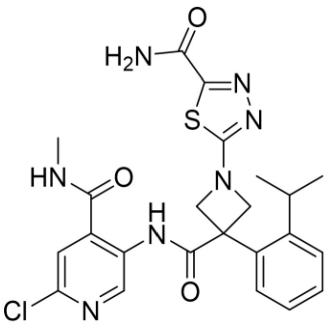
113-(a)		Mass spectrum (DUIS, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 1): 1.319 min	Example 76-(b), 2M methylamine/tetrahydrofuran solution
114-(a)		Mass spectrum (DUIS, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 1): 1.271 min	Example 76-(b), 2M dimethylamine/tetrahydrofuran solution
314-(a)		Mass spectrum (DUIS, m/z): 508 $[M+H]^+$ Retention time (LCMS conditions 8): 1.061 min	Example 87-(b), Ammonium chloride
315-(a)		Mass spectrum (DUIS, m/z): 506 $[M+H]^+$ Retention time (LCMS conditions 9): 1.246 min	Example 110-(b), Ammonium chloride
316-(c)		Mass spectrum (DUIS, m/z): 525 $[M+H]^+$ Retention time (LCMS conditions 8): 1.195 min	Example 316-(b), Ammonium chloride
386-(c)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 7): 0.729 min	Example 386-(b), Ammonium chloride

[0304] Example 115-(a)

Production of 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxamide

[C153]



0.3 ml of 28% ammonia water was added to a tetrahydrofuran (0.7 ml) solution of 57 mg of ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate produced in the same manner as in Example 89-(a) at room temperature under an argon gas flow and stirred at room temperature for four hours. A saturated aqueous sodium bicarbonate solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate) to obtain 49 mg of a title compound as a white solid.

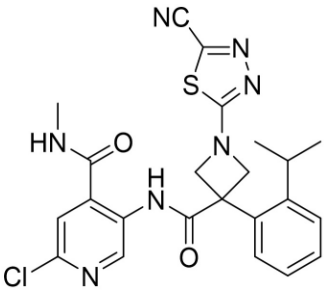
Mass spectrum (DUIS, m/z): 514 $[M+H]^+$

Retention time (LCMS conditions 1): 1.127 min.

[0305] Example 116-(a)

Production of 2-chloro-5-(1-(5-cyano-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C154]



0.016 ml of triethylamine and 0.007 ml of trifluoroacetic anhydride were added to a tetrahydrofuran (0.49 ml) solution of 25 mg of 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxamide produced in Example-115(a) at 0°C under an argon gas flow and stirred at room temperature for one hour. 0.007 ml of trifluoroacetic anhydride was added at 0°C and stirred at room temperature for two hours. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture cooled with ice water, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 8 mg of a title compound as a white solid.

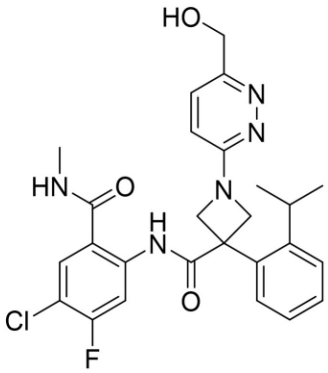
Mass spectrum (DUIS, m/z): 496 $[M+H]^+$

Retention time (LCMS conditions 1): 1.399 min.

[0306] Example 117-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C155]



An ethanol (0.8 ml) solution of 29 mg of sodium borohydride was added to a tetrahydrofuran (2.8 ml) solution of 30 mg of methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate produced in Example 75-(a) at 0°C under an argon gas flow, stirred at 0°C for 10 minutes, and stirred at 40°C for 30 minutes. 2M hydrochloric acid was added to a reaction mixture, a saturated sodium bicarbonate aqueous solution was then added thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 512 $[M+H]^+$

Retention time (LCMS conditions 1): 1.045 min.

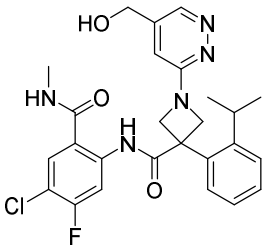
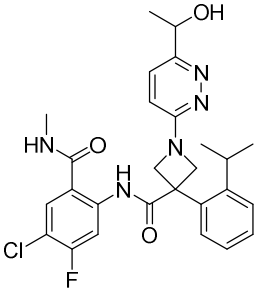
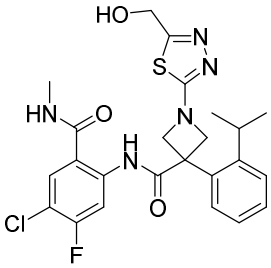
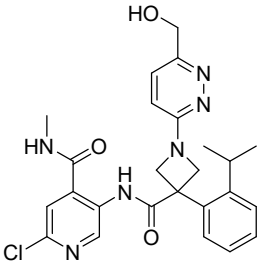
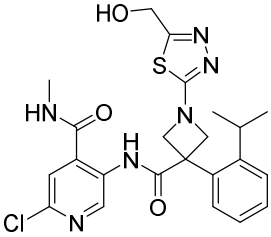
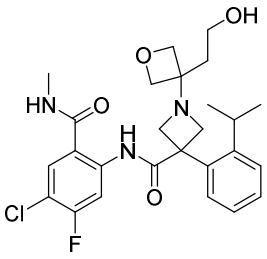
[0307] Example 118-(a) and the like

Compounds shown in Table 52 below were obtained by treating corresponding raw material compounds in the same manner as in Example 117-(a). The synthesis of Example 205-(a) was performed at room temperature as the reaction temperature.

[Table 52]

Table 52

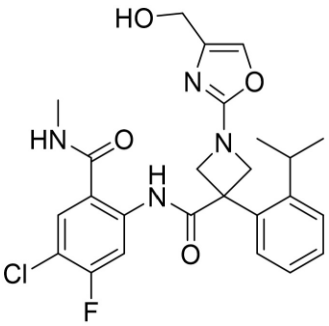
Example	Structural formula	Analysis data	Raw material

118-(a)		Mass spectrum (DUIS, m/z): 512 $[M+H]^+$ Retention time (LCMS conditions 1): 1.031 min	Example 77-(a)
119-(a)		Mass spectrum (DUIS, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 1): 1.084 min	Example 91-(a)
120-(a)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.273 min	Example 81-(a)
122-(a)		Mass spectrum (DUIS, m/z): 495 $[M+H]^+$ Retention time (LCMS conditions 1) : 0.864 min	Example 87-(a)
123-(a)		Mass spectrum (DUIS, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 1) : 1.063 min	Example 89-(a)
205-(a)		Mass spectrum (ESI, m/z): 504 $[M+H]^+$ Retention time (LCMS conditions 2): 1.004 min	Example 201-(a)

[0308] Example 121-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(4-(hydroxymethyl)oxazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C156]



35 mg of sodium borohydride was added to a tetrahydrofuran (0.8 ml) solution of 34 mg of methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylate produced in the same manner as in Example 80-(a) at 0°C under an argon gas flow, stirred at 0°C for 10 minutes, and then stirred at room temperature for two hours. 2N hydrochloric acid was added to a reaction mixture, a saturated sodium bicarbonate aqueous solution was added thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 19 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 501 $[M+H]^+$

Retention time (LCMS conditions 2): 1.298 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.52 (s, 1H), 8.79 - 8.70 (m, 1H), 8.47 (d, J = 12.2 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.51 - 7.28 (m, 5H), 5.03 (t, J = 5.6 Hz, 1H), 4.71 (br d, J = 7.8 Hz, 2H), 4.46 (br d, J = 7.8 Hz, 2H), 4.24 - 4.19 (m, 2H), 2.63 (d, J = 4.5 Hz, 3H), 2.47 - 2.41 (m, 1H), 1.05 (d, J = 6.7 Hz, 6H)

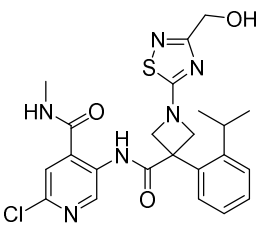
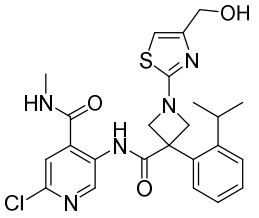
[0309] Example 124-(a) and the like

Compounds shown in Table 53 below were obtained by treating corresponding raw material compounds in the same manner as in Example 121-(a). The synthesis of Example 124-(a) was performed using ethanol instead of tetrahydrofuran. The synthesis of Example 125-(b) was performed

using ethanol instead of tetrahydrofuran and at 60°C as the reaction temperature.

[Table 53]

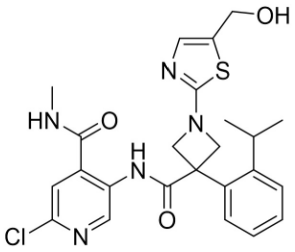
Table 53

Example	Structural formula	Analysis data	Raw material
124-(a)		Mass spectrum (ESI, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 2): 1.120 min	Example 88-(a)
125-(b)		Mass spectrum (ESI, m/z): 500 $[M+H]^+$ Retention time (LCMS conditions 2): 1.086 min	Example 125-(a)

[0310] Example 126-(b)

Production of 2-chloro-5-(1-(5-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C157]



9 mg of lithium borohydride was added to a tetrahydrofuran (1 ml) solution of 52 mg of methyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate produced in Example 126-(a) at room temperature under an argon gas flow and stirred at room temperature for 5.5 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, a saturated sodium bicarbonate solution was then added thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated

residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). Acetonitrile was added to the obtained purified product, and the precipitated solid was collected by filtration. The obtained solid was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 12 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 500 $[M+H]^+$

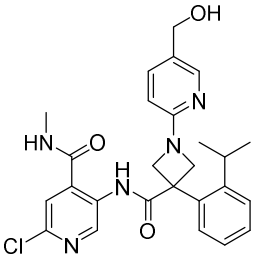
Retention time (LCMS conditions 2): 1.006 min.

[0311] Example 127-(a)

A compound shown in Table 54 below was obtained by treating a corresponding raw material compound in the same manner as in Example 126-(b).

[Table 54]

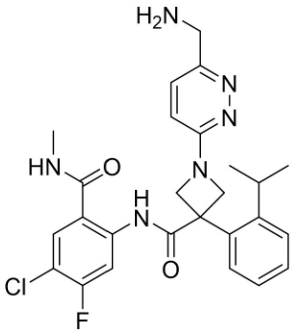
Table 54

Example	Structural formula	Analysis data	Raw material
127-(a)		Mass spectrum (ESI, m/z): 494 $[M+H]^+$ Retention time (LCMS conditions 2): 0.835 min	Example 86-(a)

[0312] Example 128-(a)

Production of 1-(6-(aminomethyl)pyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C158]



14 mg of phthalimide, 0.028 ml of tri-n-butylphosphine, and 20 mg of 1,1'-azobis(N,N-dimethylformamide) were added to a tetrahydrofuran (0.75 ml) solution of 39 mg of N-(4-chloro-5-

fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example-117(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone). 0.003 ml of hydrazine monohydrate was added dropwise to a dichloromethane (0.5 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at room temperature for two hours. 0.5 ml of ethanol was added thereto at room temperature and stirred at 40°C for four hours. The reaction mixture was filtered. A filtrate was diluted with dichloromethane and washed successively with a 1M sodium hydroxide aqueous solution and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by high performance liquid chromatography (column; XSelect CSH C18, mobile phase; 0.1% formic acid aqueous solution:acetonitrile:0.1% formic acid acetonitrile solution). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 10 mg of a title compound as a white solid.

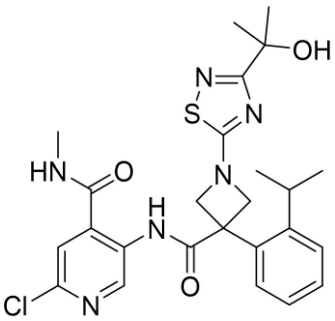
Mass spectrum (DUIS, m/z): 511 $[M+H]^+$

Retention time (LCMS conditions 4): 0.810 min.

[0313] Example 129-(a)

Production of 2-chloro-5-(1-(3-(2-hydroxypropan-2-yl)-1,2,4-thiadiazol-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C159]



0.68 ml of a 1M methylmagnesium bromide/tetrahydrofuran solution was added dropwise to a tetrahydrofuran (1 ml) solution of 37 mg of ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate produced in the same manner as in Example 88-(a) at 0°C under an argon gas flow and stirred at room temperature for 1.5 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; CHIRALPAK-IC, eluent; dichloromethane:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 529 $[M+H]^+$

Retention time (LCMS conditions 2): 1.321 min.

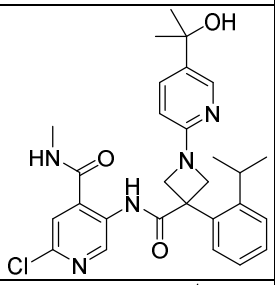
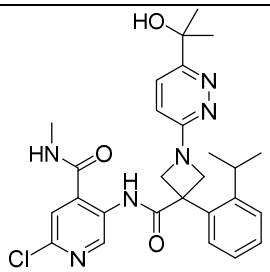
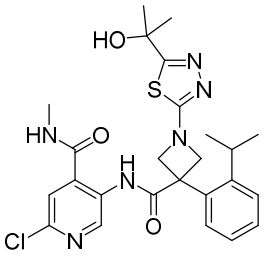
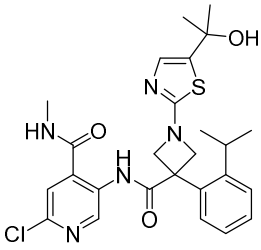
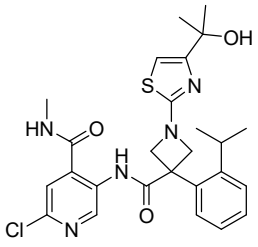
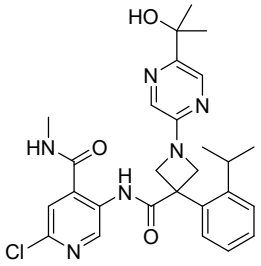
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.47 (s, 1H), 9.33 (s, 1H), 8.97 - 8.89 (m, 1H), 7.68 (s, 1H), 7.57 - 7.50 (m, 1H), 7.46 - 7.30 (m, 3H), 5.09 (s, 1H), 4.86- 4.76 (m, 2H), 4.66 - 4.53 (m, 2H), 2.60 (d, J = 4.5 Hz, 3H), 2.45 - 2.36 (m, 1H), 1.44 (s, 6H), 1.07 (d, J = 6.7 Hz, 6H)

[0314] Example 130-(a) and the like

Compounds shown in Table 55 below were obtained by treating corresponding raw material compounds in the same manner as in Example 129-(a). The synthesis of Example 132-(a) was performed at 40°C as the reaction temperature.

[Table 55]

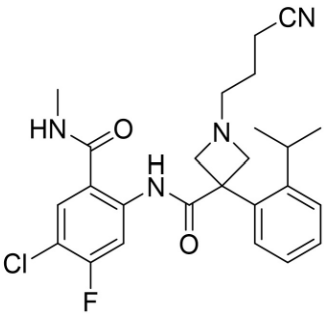
Table 55

Example	Structural formula	Analysis data	Raw material
130-(a)		Mass spectrum (ESI, m/z): 522 $[M+H]^+$ Retention time (LCMS conditions 2): 0.903 min	Example 86-(a)
131-(a)		Mass spectrum (ESI, m/z): 523 $[M+H]^+$ Retention time (LCMS conditions 2): 1.049 min	Example 87-(a)
132-(a)		Mass spectrum (DUIS, m/z): 529 $[M+H]^+$ Retention time (LCMS conditions 1): 1.178 min	Example 89-(a)
133-(a)		Mass spectrum (ESI, m/z): 528 $[M+H]^+$ Retention time (LCMS conditions 2): 1.082 min	Example 126-(a)
134-(a)		Mass spectrum (ESI, m/z): 528 $[M+H]^+$ Retention time (LCMS conditions 2): 1.227 min	Example 125-(a)
318-(a)		Mass spectrum (DUIS, m/z): 523 $[M+H]^+$ Retention time (LCMS conditions 8): 1.253 min	Example 295-(a)

[0315] Example 135-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C160]



0.007 ml of 4-bromobutyronitrile and 19 mg of potassium carbonate were added to a N,N-dimethylformamide (0.5 ml) solution of 29 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for 22 hours. A reaction mixture was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 21 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 471 $[M+H]^+$

Retention time (LCMS conditions 2): 0.951 min.

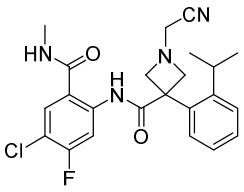
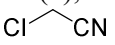
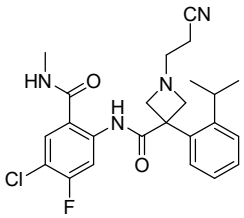
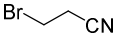
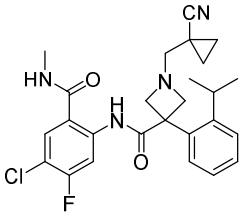
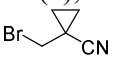
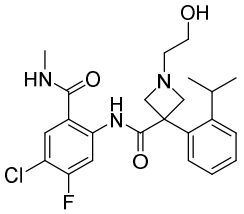
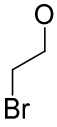
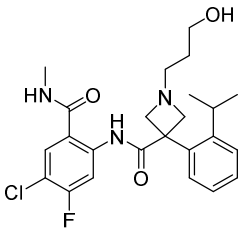
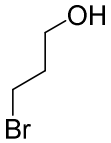
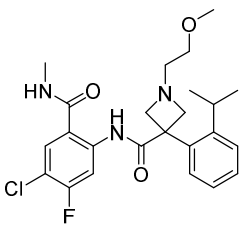
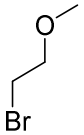
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.10 (s, 1H), 8.88 - 8.78 (m, 1H), 8.48 (d, J = 12.4 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.34 - 7.15 (m, 4H), 4.15 - 4.05(m, 2H), 3.44 - 3.36 (m, 2H), 2.75 (d, J = 4.5 Hz, 3H), 2.71 - 2.65 (m, 1H), 2.58 - 2.44 (m, 4H), 1.62 (quin, J = 6.9 Hz, 2H), 1.06 (d, J = 6.8 Hz, 6H)

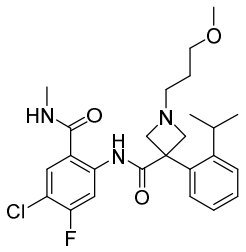
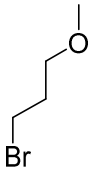
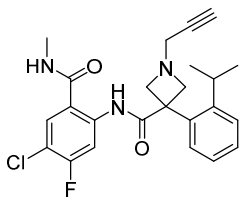
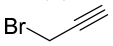
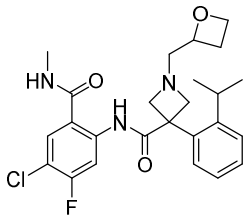
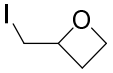
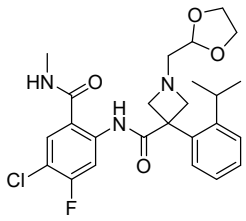
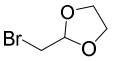
[0316] Example 136-(a) and the like

Compounds shown in Table 56 below were obtained by treating corresponding raw material compounds in the same manner as in Example 135-(a). The synthesis of Example 145-(a) was performed at 60°C as the reaction temperature.

[Table 56]

Table 56

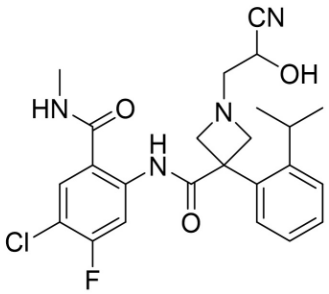
Example	Structural formula	Analysis data	Raw material
136-(a)		Mass spectrum (ESI, m/z): 443 $[M+H]^+$ Retention time (LCMS conditions 2): 1.437 min	Example 11-(b), 
137-(a)		Mass spectrum (DUIS, m/z): 457 $[M+H]^+$ Retention time (LCMS conditions 1): 0.995 min	Example 11-(b), 
138-(a)		Mass spectrum (ESI, m/z): 483 $[M+H]^+$ Retention time (LCMS conditions 2): 1.047 min	Example 11-(b), 
139-(a)		Mass spectrum (ESI, m/z): 448 $[M+H]^+$ Retention time (LCMS conditions 3): 0.743 min	Example 11-(b), 
140-(a)		Mass spectrum (ESI, m/z): 462 $[M+H]^+$ Retention time (LCMS conditions 2): 0.897 min	Example 11-(b), 
141-(a)		Mass spectrum (ESI, m/z): 462 $[M+H]^+$ Retention time (LCMS conditions 2): 0.975 min	Example 11-(b), 

142-(a)		Mass spectrum (ESI, m/z): 476 $[M+H]^+$ Retention time (LCMS conditions 2): 1.005 min	Example 11-(b), 
143-(a)		Mass spectrum (DUIS, m/z): 442 $[M+H]^+$ Retention time (LCMS conditions 1): 0.993 min	Example 11-(b), 
144-(a)		Mass spectrum (ESI, m/z): 474 $[M+H]^+$ Retention time (LCMS conditions 2): 0.963 min	Example 11-(b), 
145-(a)		Mass spectrum (DUIS, m/z): 490 $[M+H]^+$ Retention time (LCMS conditions 1): 1.013 min	Example 11-(b), 

[0317] Example 145-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyano-2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C161]



0.038 ml of 6N hydrochloric acid was added to a tetrahydrofuran (1 ml) solution of 28 mg of 1-((1,3-dioxolan-2-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-

isopropylphenyl)azetidine-3-carboxamide produced in Example 145-(a) at room temperature under an argon gas flow and stirred at 70°C for six hours. 1 ml of tetrahydrofuran and 2 ml of 6N hydrochloric acid were added thereto at room temperature and stirred at 70°C for 3.5 hours. A reaction mixture was poured into a saturated sodium bicarbonate aqueous solution, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 0.012 ml of triethylamine and 0.010 ml of trimethylsilylcyanide were added to a dichloromethane (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for 2.5 hours. A 2M potassium carbonate aqueous solution was added to the reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; connected in the order of YMC-GPC T-30000 → T-2000 → T-1000, eluent; dichloromethane). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 6 mg of a title compound as a white solid.

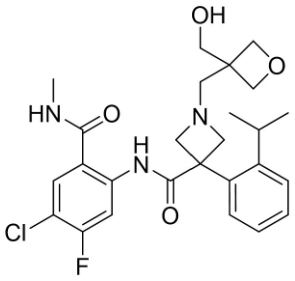
Mass spectrum (ESI, m/z): 473 $[M+H]^+$

Retention time (LCMS conditions 2): 1.035 min.

[0318] Example 146-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C162]



0.009 ml of 3-(bromomethyl)-3-oxetanemethanol and 50 mg of cesium carbonate were added to an acetonitrile (1 ml) solution of 33 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 85°C for two hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 29 mg of a title compound as a white solid.

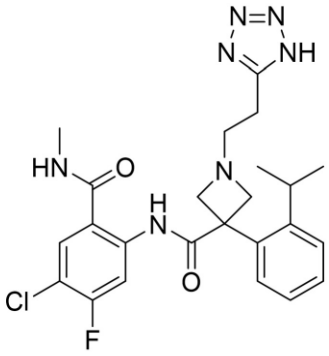
Mass spectrum (ESI, m/z): 504 $[M+H]^+$

Retention time (LCMS conditions 2): 0.904 min.

[0319] Example 147-(a)

Production of 1-(2-(1H-tetrazol-5-yl)ethyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C163]



32 mg of azidotrimethyltin (IV) was added to a toluene (1 ml) solution of 35 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyanoethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 137-(a) at room temperature under an argon gas flow and stirred at 120°C for 45 hours. A reaction mixture was purified by medium pressure preparative chromatography (DIOL silica gel, solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 36 mg of a title

compound as a white solid.

Mass spectrum (DUIS, m/z): 500 $[M+H]^+$

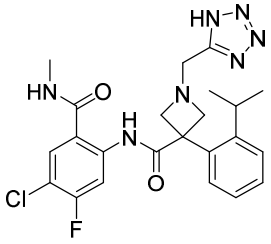
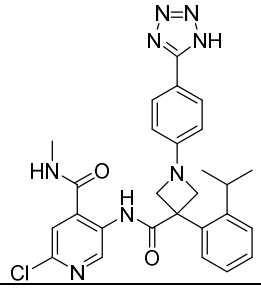
Retention time (LCMS conditions 1): 0.936 min.

[0320] Example 148-(a) and the like

Compounds shown in Table 57 below were obtained by treating corresponding raw material compounds in the same manner as in Example 147-(a).

[Table 57]

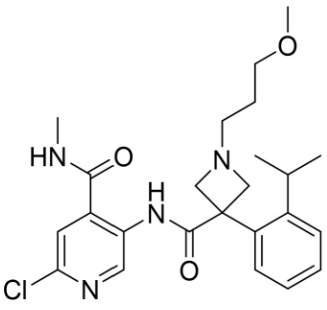
Table 57

Example	Structural formula	Analysis data	Raw material
148-(a)		Mass spectrum (DUIS, m/z): 486 $[M+H]^+$ Retention time (LCMS conditions 1): 1.028 min	Example 136-(a)
319-(a)		Mass spectrum (DUIS, m/z): 531 $[M+H]^+$ Retention time (LCMS conditions 8): 1.271 min	Example 313-(a)

[0321] Example 149-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methoxypropyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C164]



34 mg of potassium carbonate and 14 mg of 1-bromo-3-methoxypropane were added to a N,N-

dimethylformamide (0.5 ml) solution of 35 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a) at room temperature under an argon gas flow and stirred at room temperature for six hours. Water was added to a reaction mixture, and the reaction mixture was extracted with tert-butyl methyl ether. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 28 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 459 $[M+H]^+$

Retention time (LCMS conditions 1): 0.847 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.29 (s, 1H), 9.37 (s, 1H), 9.09 - 9.00 (m, 1H), 7.74 (s, 1H), 7.33 - 7.17 (m, 4H), 4.06 (br d, J = 7.2 Hz, 2H), 3.41 -3.29 (m, 4H), 3.20 (s, 3H), 2.75 (d, J = 4.5 Hz, 3H), 2.72 - 2.58 (m, 1H), 2.44 (t, J = 7.2 Hz, 2H), 1.63 - 1.49 (m, 2H), 1.06 (d, J = 6.7 Hz, 6H)

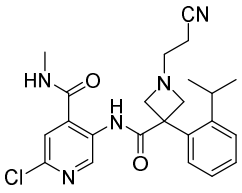
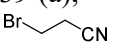
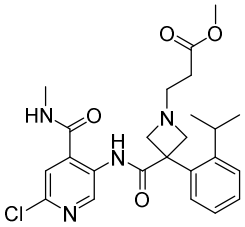
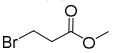
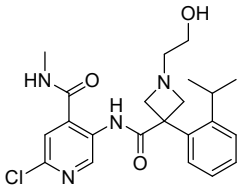
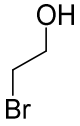
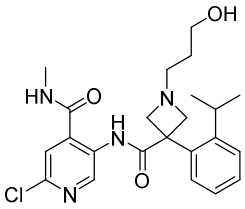
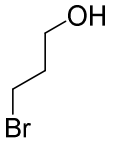
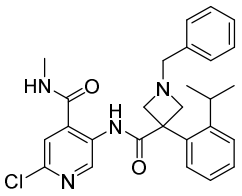
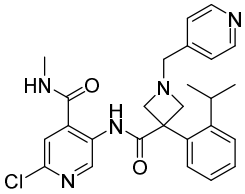
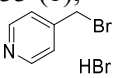
[0322] Example 150-(a) and the like

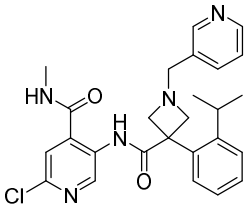
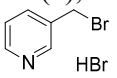
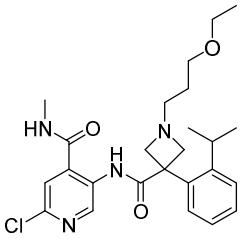
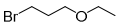
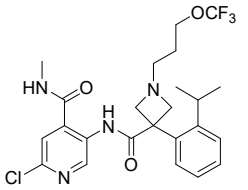
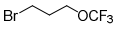
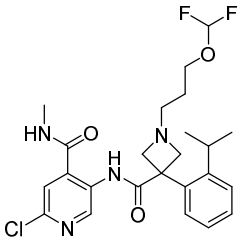
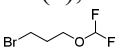
Compounds shown in Table 58 below were obtained by treating corresponding raw material compounds in the same manner as in Example 149-(a). The synthesis of Example 150-(a) was performed at 50°C as the reaction temperature. The synthesis of Example 152-(a) was performed using acetonitrile instead of N,N-dimethylformamide and at 70°C as the reaction temperature. The synthesis of Example 153-(a) was performed using tetrahydrofuran instead of N,N-dimethylformamide and at 70°C as the reaction temperature.

[Table 58]

Table 58

Example	Structural formula	Analysis data	Raw material

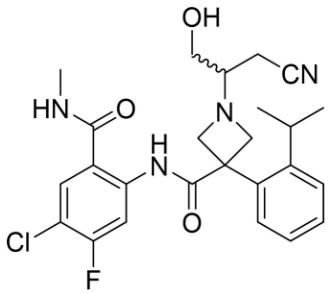
150-(a)		Mass spectrum (DUIS, m/z): 440 $[M+H]^+$ Retention time (LCMS conditions 1): 0.789 min	Example 39-(a), 
151-(a)		Mass spectrum (DUIS, m/z): 473 $[M+H]^+$ Retention time (LCMS conditions 1): 0.817 min	Example 39-(a), 
152-(a)		Mass spectrum (ESI, m/z): 431 $[M+H]^+$ Retention time (LCMS conditions 2): 0.697 min	Example 33-(b), 
153-(a)		Mass spectrum (ESI, m/z): 445 $[M+H]^+$ Retention time (LCMS conditions 2): 0.724 min	Example 33-(b), 
154-(a)		Mass spectrum (DUIS, m/z): 477 $[M+H]^+$ Retention time (LCMS conditions 1): 0.942 min	Example 33-(b), Benzyl bromide
155-(a)		Mass spectrum (DUIS, m/z): 478 $[M+H]^+$ Retention time (LCMS conditions 1): 0.741 min	Example 33-(b), 

156-(a)		Mass spectrum (DUIS, m/z): 478 $[M+H]^+$ Retention time (LCMS conditions 1): 0.751 min	Example 33-(b), 
328-(a)		Mass spectrum (DUIS, m/z): 473 $[M+H]^+$ Retention time (LCMS conditions 8): 0.922 min	Example 33-(b), 
329-(a)		Mass spectrum (DUIS, m/z): 513 $[M+H]^+$ Retention time (LCMS conditions 8): 0.965 min	Example 33-(b), 
330-(a)		Mass spectrum (DUIS, m/z): 495 $[M+H]^+$ Retention time (LCMS conditions 1): 0.944 min	Example 33-(b), 

[0323] Example 157-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide (enantiomer 1)

[C165]



0.008 ml of (R)-(+)-4-chloro-3-hydroxybutyronitrile and 14 mg of potassium carbonate were added to a N,N-dimethylformamide (0.5 ml) solution of 31 mg of N-(4-chloro-5-fluoro-2-

(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for 71 hours. A reaction mixture was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:acetonitrile). A saturated sodium bicarbonate aqueous solution was added to the obtained purified product, and the purified product was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 21 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 487 $[M+H]^+$

Retention time (LCMS conditions 2): 1.071 min.

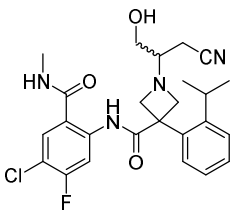
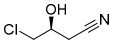
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.12 (s, 1H), 8.98 - 8.81 (m, 1H), 8.49 (d, J = 12.3 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.38 - 7.13 (m, 4H), 4.85 (t, J =5.5 Hz, 1H), 4.24 - 4.08 (m, 2H), 3.67 - 3.52 (m, 2H), 3.49 - 3.41 (m, 1H), 3.40 - 3.27 (m, 1H), 2.80 - 2.66 (m, 4H), 2.65 - 2.59 (m, 2H), 2.59 - 2.53 (m,1H), 1.12 - 1.00 (m, 6H)

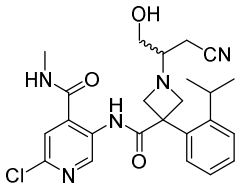
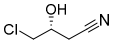
[0324] Example 158-(a) and the like

Compounds shown in Table 59 below were obtained by treating corresponding raw material compounds in the same manner as in Example 157-(a).

[Table 59]

Table 59

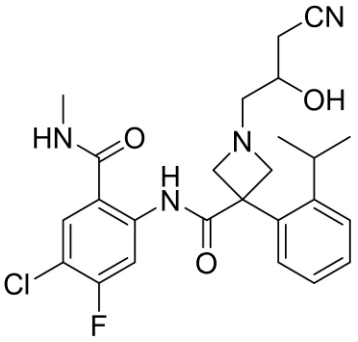
Example	Structural formula	Analysis data	Raw material
158-(a)	 Enantiomer 2	Mass spectrum (ESI, m/z): 487 $[M+H]^+$ Retention time (LCMS conditions 2): 1.074 min	Example 11-(b), 

159-(a)	 Enantiomer 1	Mass spectrum (ESI, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 2): 0.871 min	Example 33-(b), 

[0325] Example 160-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyano-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C166]



0.006 ml of epichlorohydrin was added to a tert-butanol (1 ml)/ethanol (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for 48 hours. A reaction mixture was concentrated under reduced pressure. 0.074 ml of a 1M potassium tert-butoxide/tetrahydrofuran solution was added to a tert-butanol (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for three hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 0.018 ml of trimethylsilylcyanide and 0.222 ml of a 1M tetrabutylammonium fluoride/tetrahydrofuran solution were added to a tetrahydrofuran (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at 75°C for 12 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed successively with

a saturated ammonium chloride aqueous solution and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 25 mg of a title compound as a white solid.

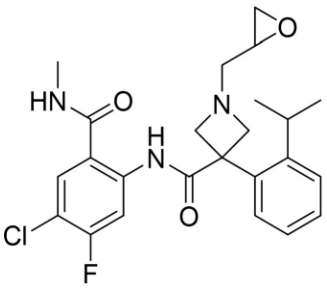
Mass spectrum (ESI, m/z): 487 $[M+H]^+$

Retention time (LCMS conditions 2): 0.909 min.

[0326] Example 161-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxirane-2-ylmethyl)azetidine-3-carboxamide

[C167]



0.010 ml of epichlorohydrin was added to an ethanol (1 ml) solution of 25 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for five hours. A reaction mixture was concentrated under reduced pressure.

0.12 ml of a 1M potassium tert-butoxide/tetrahydrofuran solution was added to a tert-butanol (1 ml) solution of a concentrated residue at room temperature under an argon gas flow and stirred at room temperature for 40 minutes. A reaction mixture was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) to obtain 23 mg of a title compound as a white foamy substance.

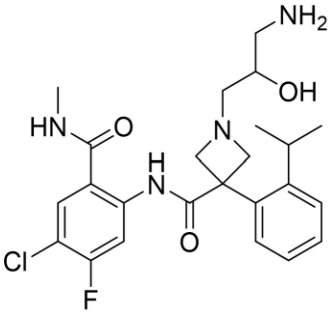
Mass spectrum (ESI, m/z): 460 $[M+H]^+$

Retention time (LCMS conditions 2): 0.942 min.

[0327] Example 161-(b)

Production of 1-(3-amino-2-hydroxypropyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C168]



0.050 ml of a 7M ammonia/methanol solution was added to a methanol (1 ml) solution of 23 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxiran-2-ylmethyl)azetidine-3-carboxamide produced in Example 161-(a) at room temperature under an argon gas flow and stirred at 60°C for 1.5 hours. 0.20 ml of a 7M ammonia/methanol solution was added thereto and stirred at 60°C for 2.5 hours. 0.20 ml of a 7M ammonia/methanol solution was added thereto, the system was sealed, and the components were stirred at 60°C for nine hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:acetonitrile). Ethyl acetate was added to the obtained purified product, and the purified product was washed with a saturated sodium carbonate aqueous solution. An organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 4 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 477 $[M+H]^+$

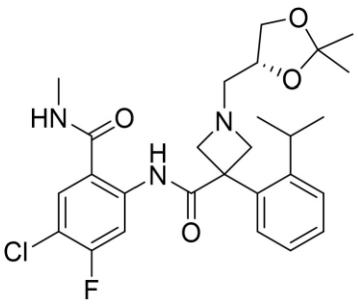
Retention time (LCMS conditions 1): 0.671 min.

[0328] Example 162-(a)

Production of (R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-

yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C169]



30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) and 0.026 ml of N,N-diisopropylethylamine were added to an acetonitrile (0.6 ml) solution of 24 mg of (S)-(2,2-dimethyl-1,3-dioxolan-4-yl)methyltrifluoromethanesulfonate at 0°C under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 37 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 518 $[M+H]^+$

Retention time (LCMS conditions 2): 1.051 min.

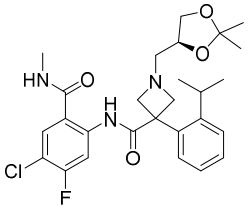
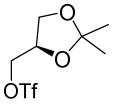
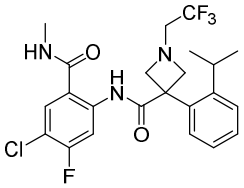
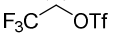
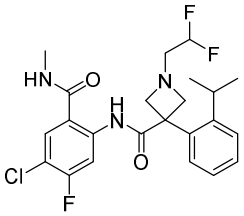
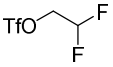
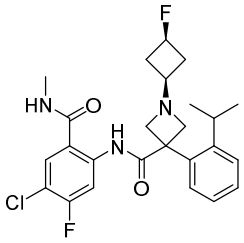
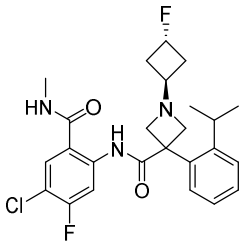
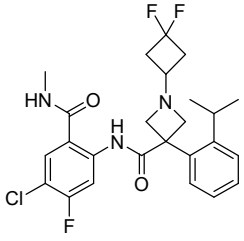
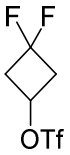
[0329] Example 163-(a) and the like

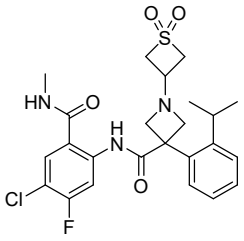
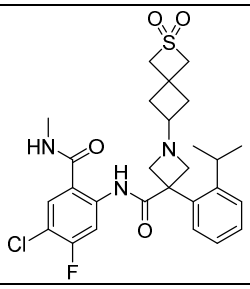
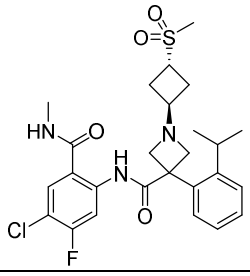
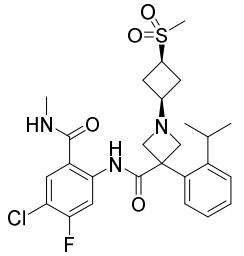
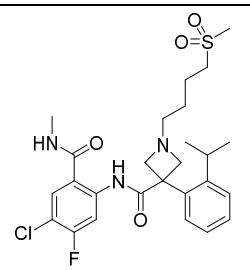
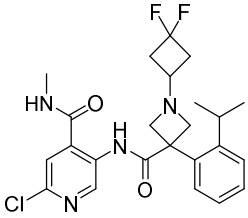
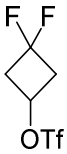
Compounds shown in Table 60 below were obtained by treating corresponding raw material compounds in the same manner as in Example 162-(a). The synthesis of Example 164-(a) was performed using tetrahydrofuran instead of acetonitrile and at 50°C as the reaction temperature. The synthesis of Example 165-(a) was performed using dichloromethane instead of acetonitrile and triethylamine instead of N,N-diisopropylethylamine.

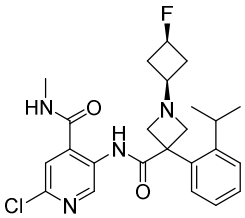
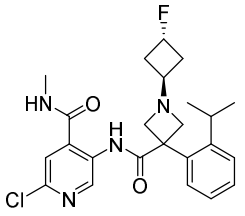
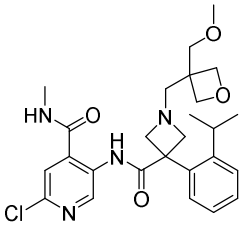
[Table 60]

Table 60

Example	Structural formula	Analysis data	Raw material

163-(a)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.062 min	Example 11-(b), 
164-(a)		Mass spectrum (ESI, m/z): 486 $[M+H]^+$ Retention time (LCMS conditions 2): 1.681 min	Example 11-(b), 
165-(a)		Mass spectrum (DUIS, m/z): 468 $[M+H]^+$ Retention time (LCMS conditions 1): 1.281 min	Example 11-(b), 
166-(a)		Mass spectrum (ESI, m/z): 476 $[M+H]^+$ Retention time (LCMS conditions 2): 1.009 min	Example 11-(b), Reference Example 166-(a)
167-(a)		Mass spectrum (ESI, m/z): 476 $[M+H]^+$ Retention time (LCMS conditions 2): 1.024 min	Example 11-(b), Reference Example 167-(a)
168-(a)		Mass spectrum (DUIS, m/z): 494 $[M+H]^+$ Retention time (LCMS conditions 1): 1.140 min	Example 11-(b), 

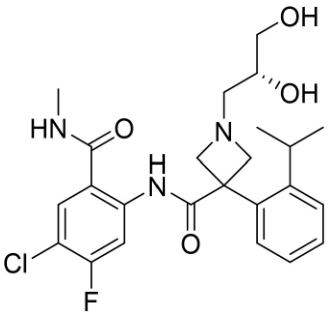
169-(a)		Mass spectrum (DUIS, m/z): 508 $[M+H]^+$ Retention time (LCMS conditions 1): 1.389 min	Example 11-(b), Reference Example 169-(a)
170-(a)		Mass spectrum (ESI, m/z): 548 $[M+H]^+$ Retention time (LCMS conditions 2): 0.955 min	Example 11-(b), Reference Example 170-(a)
171-(a)		Mass spectrum (ESI, m/z): 536 $[M+H]^+$ Retention time (LCMS conditions 2): 0.959 min	Example 11-(b), Reference Example 171-(a)
172-(a)		Mass spectrum (ESI, m/z): 536 $[M+H]^+$ Retention time (LCMS conditions 2): 0.912 min	Example 11-(b), Reference Example 172-(a)
173-(a)		Mass spectrum (ESI, m/z): 538 $[M+H]^+$ Retention time (LCMS conditions 2): 0.944 min	Example 11-(b), Reference Example 173-(a)
331-(a)		Mass spectrum (DUIS, m/z): 477 $[M+H]^+$ Retention time (LCMS conditions 8): 0.936 min	Example 33-(b), 

332-(a)		Mass spectrum (DUIS, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 8): 0.832 min	Example 33-(b), Reference Example 166-(a)
333-(a)		Mass spectrum (DUIS, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 8): 0.854 min	Example 33-(b), Reference Example 167-(a)
334-(a)		Mass spectrum (DUIS, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 8): 0.843 min	Example 33-(b), Reference Example 334-(a)

[0330] Example 162-(b)

Production of (R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C170]



0.020 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a methanol (0.6 ml) solution of 37 mg of (R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in Example 162-(a) at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 16 hours. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was

washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 478 $[M+H]^+$

Retention time (LCMS conditions 2): 0.866 min.

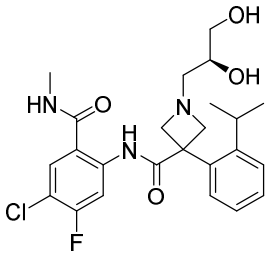
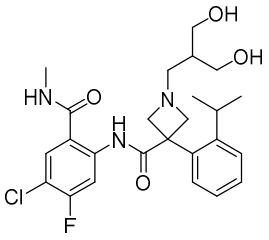
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.18 (s, 1H), 8.91 - 8.83 (m, 1H), 8.49 (d, J = 12.4 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.37 - 7.09 (m, 4H), 4.58 (d, J = 4.6 Hz, 1H), 4.47 (t, J = 5.5 Hz, 1H), 4.14 (br d, J = 7.4 Hz, 2H), 3.51 - 3.15 (m, 5H), 2.78 - 2.63 (m, 4H), 2.57 - 2.46 (m, 1H), 2.40 - 2.32 (m, 1H), 1.12 - 1.01 (m, 6H)

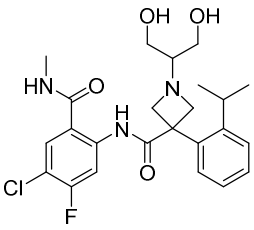
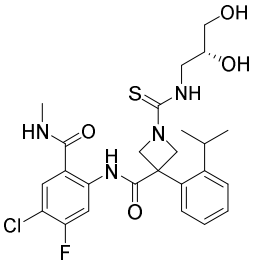
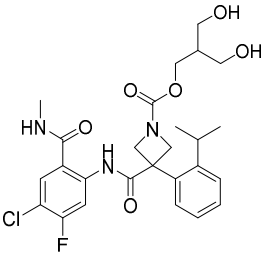
[0331] Example 163-(b) and the like

Compounds shown in Table 61 below were obtained by treating corresponding raw material compounds in the same manner as in Example 162-(b).

[Table 61]

Table 61

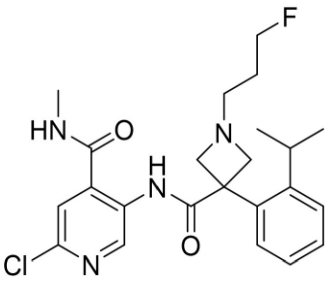
Example	Structural formula	Analysis data	Raw material
163-(b)		Mass spectrum (ESI, m/z): 478 $[M+H]^+$ Retention time (LCMS conditions 2): 0.853 min	Example 163-(a)
179-(b)		Mass spectrum (ESI, m/z): 492 $[M+H]^+$ Retention time (LCMS conditions 3): 0.741 min	Example 179-(a)

218-(b)		Mass spectrum (ESI, m/z): 478 $[M+H]^+$ Retention time (LCMS conditions 2): 0.875 min	Example 218-(a)
242-(b)		Mass spectrum (ESI, m/z): 537 $[M+H]^+$ Retention time (LCMS conditions 2): 1.202 min	Example 242-(a)
254-(b)		Mass spectrum (ESI, m/z): 536 $[M+H]^+$ Retention time (LCMS conditions 2): 1.195 min	Example 254-(a)

[0332] Example 174-(a)

Production of 2-chloro-5-(1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C171]



30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a) and 0.025 ml of N,N-diisopropylethylamine were added to an acetonitrile (1 ml)/tetrahydrofuran (0.1 ml) solution of 22 mg of 3-fluoropropyl trifluoromethanesulfonate in an ice bath under an argon gas flow and stirred at room temperature for 1.5 hours. 22 mg of 3-fluoropropyl trifluoromethanesulfonate was added thereto at room temperature and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The

obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 19 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 447 $[M+H]^+$

Retention time (LCMS conditions 1): 0.836 min.

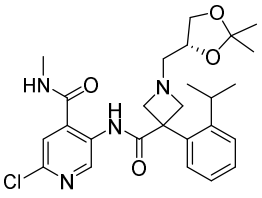
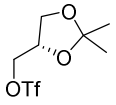
^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 9.35 (s, 1H), 7.72 (s, 1H), 7.38 - 7.12 (m, 4H), 4.49 (td, J = 6.0, 47.4 Hz, 2H), 4.15 - 4.02 (m, 2H), 3.48 - 3.32 (m, 2H), 2.74 (s, 3H), 2.72 - 2.57 (m, 1H), 2.55 - 2.48 (m, 2H), 1.83 - 1.61 (m, 2H), 1.06 (d, J = 6.7 Hz, 6H)

[0333] Example 175-(a)

A compound shown in Table 62 below was obtained by treating a corresponding raw material compound in the same manner as in Example 174-(a).

[Table 62]

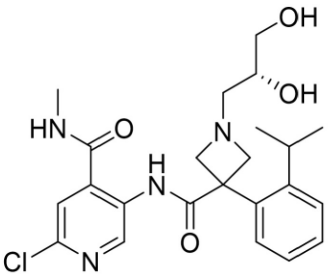
Table 62

Example	Structural formula	Analysis data	Raw material
175-(a)		Mass spectrum (DUIS, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 1): 0.870 min	Example 39-(a), 

[0334] Example 175-(b)

Production of (R)-2-chloro-5-(1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C172]



0.067 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a methanol (0.67 ml) solution of 27 mg of (R)-2-chloro-5-(1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-

isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in Example 175-(a) at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 15.5 hours. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 15 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 461 $[M+H]^+$

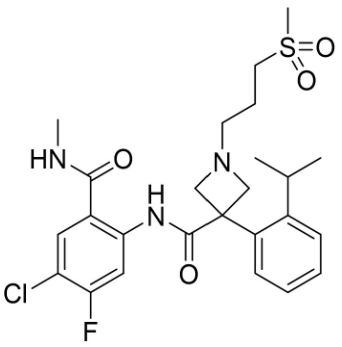
Retention time (LCMS conditions 1): 0.680 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.48 (s, 1H), 9.39 (s, 1H), 9.15 - 9.07 (m, 1H), 7.76 (s, 1H), 7.34 - 7.18 (m, 3H), 7.17 - 7.11 (m, 1H), 4.59 (d, J = 4.5 Hz, 1H), 4.55 - 4.46 (m, 1H), 4.20 - 4.05 (m, 2H), 3.55 - 3.23 (m, 5H), 2.76 (d, J = 4.6 Hz, 3H), 2.68 - 2.46 (m, 2H), 2.44 - 2.31 (m, 1H), 1.13 - 1.02 (m, 6H)

[0335] Example 176-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-(methylsulfonyl)propyl)azetidine-3-carboxamide

[C173]



21 mg of potassium carbonate and 24 mg of 3-(methylsulfonyl)propyl 4-methylbenzenesulfonate were added to a N,N-dimethylformamide (0.6 ml) solution of 30 mg of N-(4-

chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for one hour. A mixture was left to stand at room temperature for 14 hours and then stirred at 60°C for two hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone), and was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 10 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 524 $[M+H]^+$

Retention time (LCMS conditions 2): 0.922 min.

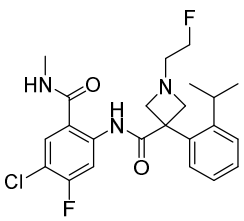
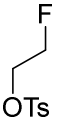
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.11 (s, 1H), 8.87 - 8.78 (m, 1H), 8.48 (d, J = 12.4 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.35 - 7.15 (m, 4H), 4.11 (br d, J = 7.2 Hz, 2H), 3.49 - 3.26 (m, 2H), 3.19 - 3.10 (m, 2H), 2.96 (s, 3H), 2.79 - 2.64 (m, 4H), 2.57 - 2.44 (m, 2H), 1.81 - 1.67 (m, 2H), 1.07 (d, J = 6.8 Hz, 6H)

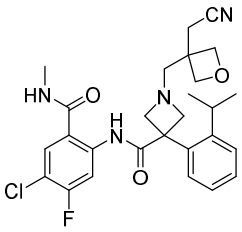
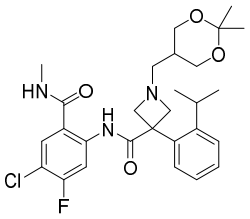
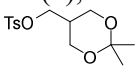
[0336] Example 177-(a) and the like

Compounds shown in Table 63 below were obtained by treating corresponding raw material compounds in the same manner as in Example 176-(a). The synthesis of Example 177-(a) was performed at 60°C as the reaction temperature. The synthesis of Example 179-(a) was performed using cesium carbonate instead of potassium carbonate and at 40°C as the reaction temperature.

[Table 63]

Table 63

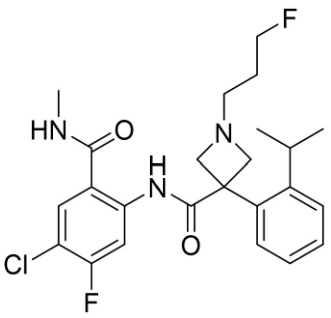
Example	Structural formula	Analysis data	Raw material
177-(a)		Mass spectrum (ESI, m/z): 450 $[M+H]^+$ Retention time (LCMS conditions 2): 0.963 min	Example 11-(b), 

178-(a)		Mass spectrum (ESI, m/z): 513 $[M+H]^+$ Retention time (LCMS conditions 2): 1.177 min	Example 11-(b), Reference Example 178-(a)
179-(a)		Mass spectrum (ESI, m/z): 532 $[M+H]^+$ Retention time (LCMS conditions 2): 1.020 min	Example 11-(b), 

[0337] Example 180-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C174]

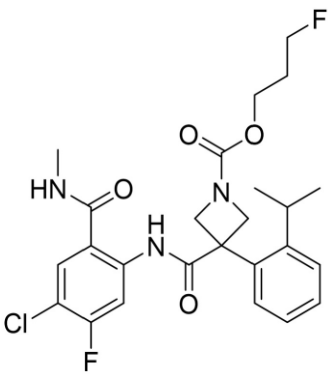


and

Example 181-(a)

3-fluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C175]



21 mg of potassium carbonate and 19 mg of 3-fluoropropyl 4-methylbenzenesulfonate were added to a N,N-dimethylformamide (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 60°C for five hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). A fraction containing Example 180-(a) eluted later was concentrated under reduced pressure, and the obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a compound of Example 180-(a) as a white solid.

In addition, a fraction containing Example 181-(a) eluted earlier was concentrated under reduced pressure, and the obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 6 mg of a compound of Example 181-(a) as a white solid.

Example 180-(a)

Rf value: 0.30 (hexane:ethyl acetate = 1:1 (V/V))

Mass spectrum (ESI, m/z): 464 $[M+H]^+$

Retention time (LCMS conditions 2): 0.980 min.

Example 181-(a)

Rf value: 0.40 (hexane:ethyl acetate = 1:1 (V/V))

Mass spectrum (ESI, m/z): 508 $[M+H]^+$

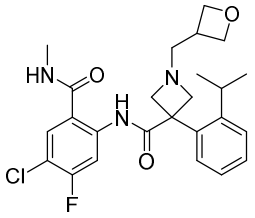
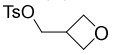
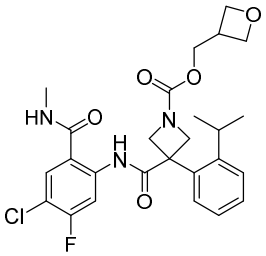
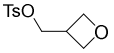
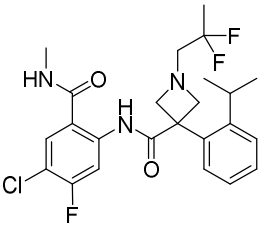
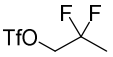
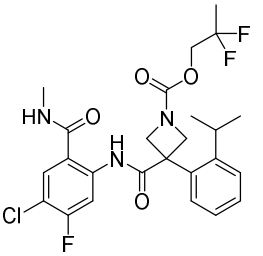
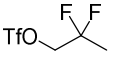
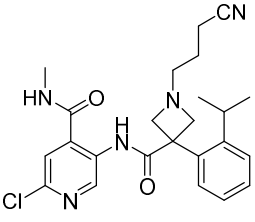
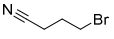
Retention time (LCMS conditions 2): 1.549 min.

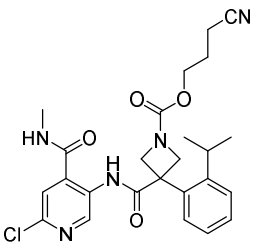
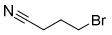
[0338] Example 182-(a) and the like

Compounds shown in Table 64 below were obtained by treating corresponding raw material compounds in the same manner as in Example 180-(a) and Example 181-(a). The syntheses of Example 182-(a), Example 183-(a), Example 184-(a), Example 185-(a), Example 186-(a), and Example 187-(a) were performed at room temperature as the reaction temperature.

[Table 64]

Table 64

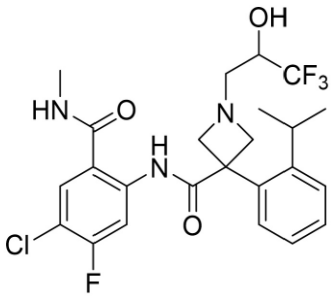
Example	Structural formula	Analysis data	Raw material
182-(a)		Mass spectrum (ESI, m/z): 474 $[M+H]^+$ Retention time (LCMS conditions 2): 0.923 min	Example 11-(b), 
183-(a)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.407 min	Example 11-(b), 
184-(a)		Mass spectrum (ESI, m/z): 482 $[M+H]^+$ Retention time (LCMS conditions 2): 1.289 min	Example 11-(b), 
185-(a)		Mass spectrum (ESI, m/z): 526 $[M+H]^+$ Retention time (LCMS conditions 2): 1.608 min	Example 11-(b), 
186-(a)		Mass spectrum (DUIS, m/z): 454 $[M+H]^+$ Retention time (LCMS conditions 1): 0.782 min	Example 33-(b), 

187-(a)		Mass spectrum (DUIS, m/z): 498 $[M+H]^+$ Retention time (LCMS conditions 1): 1.260 min	Example 33-(b), 

[0339] Example 188-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamide

[C176]



21 mg of 2-(trifluoromethyl)oxirane and 0.031 ml of triethylamine were added to an ethanol (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow, stirred at room temperature for 30 minutes, and then left to stand overnight at room temperature. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 36 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 516 $[M+H]^+$

Retention time (LCMS conditions 2): 1.062 min.

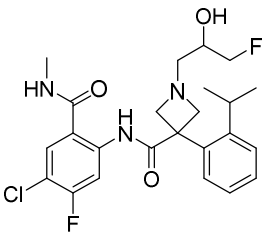
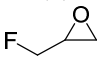
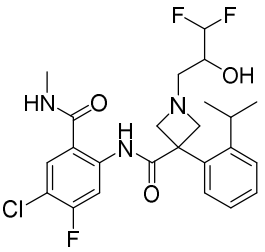
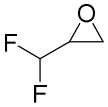
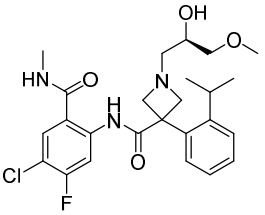
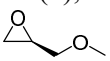
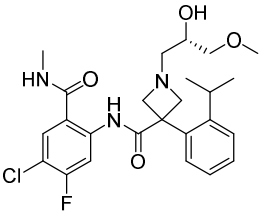
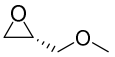
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 12.16 (s, 1H), 8.90 - 8.83 (m, 1H), 8.49 (d, J = 12.4 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.32 - 7.15 (m, 4H), 6.22 (d, J = 6.5 Hz, 1H), 4.23 - 4.14 (m, 2H), 4.12 - 4.01 (m, 1H), 3.59 - 3.48 (m, 2H), 2.79 - 2.68 (m, 5H), 2.59 - 2.52 (m, 1H), 1.12 - 1.01 (m, 6H)

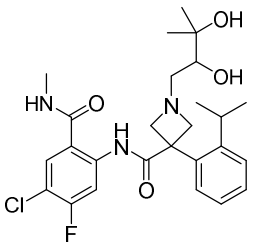
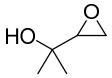
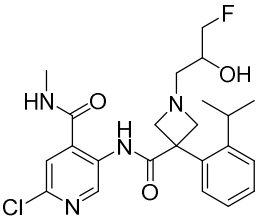
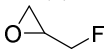
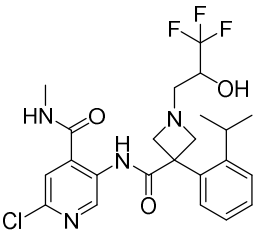
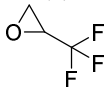
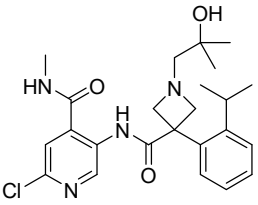
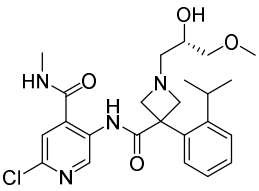
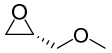
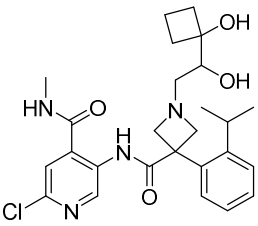
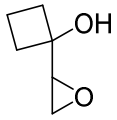
[0340] Example 191-(a) and the like

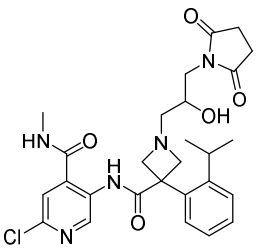
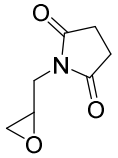
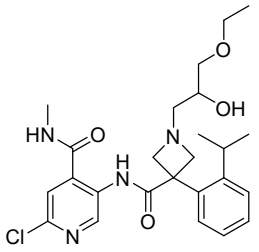
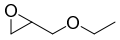
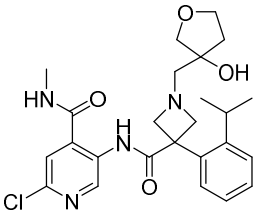
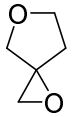
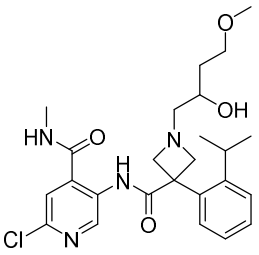
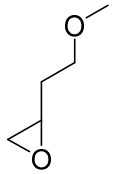
Compounds shown in Table 65 below were obtained by treating corresponding raw material compounds in the same manner as in Example 188-(a). The synthesis of Example 195-(a) was performed at 60°C as the reaction temperature. The syntheses of Example 196-(a) and Example 197-(a) were performed using N,N-dimethylformamide instead of ethanol. The synthesis of Example 338-(a) was performed using a mixed solvent of ethanol and N,N-dimethylformamide instead of ethanol. The synthesis of Example 342-(a) was performed using a mixed solvent of ethanol and N-methyl-2-pyrrolidinone instead of ethanol and at 50°C as the reaction temperature.

[Table 65]

Table 65

Example	Structural formula	Analysis data	Raw material
191-(a)		Mass spectrum (ESI, m/z): 480 $[M+H]^+$ Retention time (LCMS conditions 2): 0.933 min	Example 11-(b), 
192-(a)		Mass spectrum (ESI, m/z): 498 $[M+H]^+$ Retention time (LCMS conditions 2): 0.979 min	Example 11-(b), 
193-(a)		Mass spectrum (ESI, m/z): 492 $[M+H]^+$ Retention time (LCMS conditions 2): 0.941 min	Example 11-(b), 
194-(a)		Mass spectrum (ESI, m/z): 492 $[M+H]^+$ Retention time (LCMS conditions 2): 0.944 min	Example 11-(b), 

195-(a)		Mass spectrum (ESI, m/z): 506 $[M+H]^+$ Retention time (LCMS conditions 2): 0.933 min	Example 11-(b), 
196-(a)		Mass spectrum (DUIS, m/z): 463 $[M+H]^+$ Retention time (LCMS conditions 1): 0.766 min	Example 39-(a), 
197-(a)		Mass spectrum (DUIS, m/z): 499 $[M+H]^+$ Retention time (LCMS conditions 1): 0.911 min	Example 39-(a), 
198-(a)		Mass spectrum (ESI, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 2): 0.768 min	Example 33-(b), 
336-(a)		Mass spectrum (DUIS, m/z): 475 $[M+H]^+$ Retention time (LCMS conditions 8): 0.753 min	Example 33-(b), 
337-(a)		Mass spectrum (DUIS, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 8): 0.796 min	Example 33-(b), 

338-(a)		Mass spectrum (DUIS, m/z): 542 $[M+H]^+$ Retention time (LCMS conditions 9): 0.522 min	Example 33-(b), 
339-(a)		Mass spectrum (DUIS, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 8): 0.807 min	Example 33-(b), 
341-(a)		Mass spectrum (DUIS, m/z): 487 $[M+H]^+$ Retention time (LCMS conditions 8): 0.741 min	Example 33-(b), 
342-(a)		Mass spectrum (DUIS, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 8): 0.759 min	Example 33-(b), 

[0341] Example 189-(a)

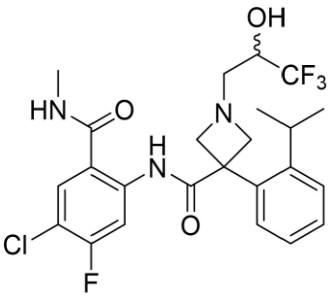
Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamide (enantiomer 1)

and

Example 190-(a)

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamide (enantiomer 2)

[C177]



268 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamide produced in the same manner as in Example 188-(a) was separated and purified by high performance liquid chromatography (column; CHIRALPAK IG, mobile phase; hexane:ethanol). A fraction containing an enantiomer eluted earlier was lyophilized to obtain 0.10 g of a compound of Example 189-(a) as a white solid. In addition, a fraction containing an enantiomer eluted later was lyophilized to obtain 0.13 g of a compound of Example 190-(a) as a white solid.

High performance liquid chromatography analysis:

Column; CHIRALPAK IF-3 4.6 × 150 mm

Eluent; hexane: ethanol: trifluoroacetic acid: dimethylamine = 90: 10: 0.1: 0.1

Flow rate; 0.8 mL/min.

Temperature; 40°C

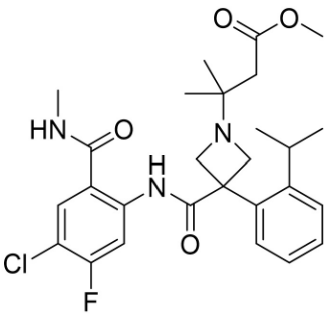
Detection wavelength; 254 nm

Retention time; Example 189-(a): 3.93 min, Example 190-(a): 5.15 min.

[0342] Example 199-(a)

Production of methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoate

[C178]



0.014 ml of methyl 3,3-dimethylacrylate and 0.017 ml of 1,8-diazabicyclo[5.4.0]-7-undecene were added to an acetonitrile (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 90°C for 5.5 hours. Ethyl acetate was added to a reaction mixture, the reaction mixture was washed successively with water and saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 24 mg of a title compound as a white foamy substance.

Mass spectrum (DUIS, m/z): 518 $[M+H]^+$

Retention time (LCMS conditions 1): 1.086 min.

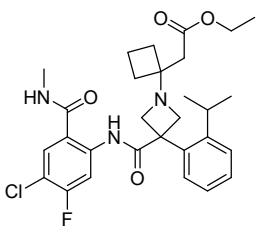
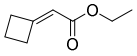
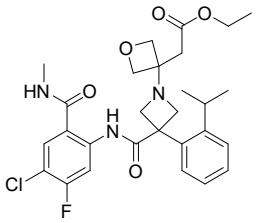
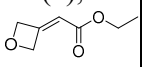
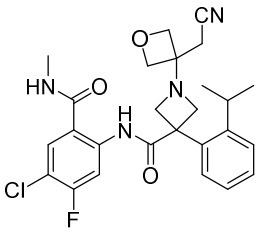
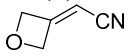
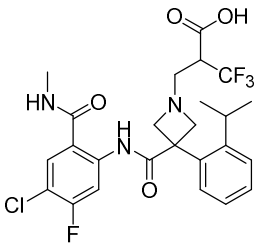
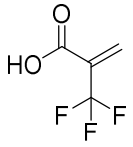
[0343] Example 200-(a) and the like

Compounds shown in Table 66 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 199-(a). The syntheses of Example 200-(a), Example 201-(a), Example 202-(a), and Example 203-(a) were performed at room temperature as the reaction temperature.

[Table 66]

Table 66

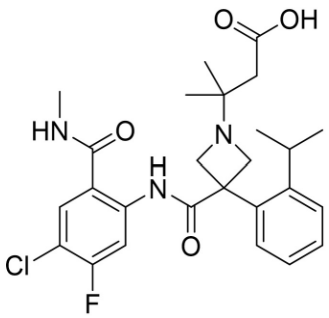
Example	Structural formula	Analysis data	Raw material

200-(a)		Mass spectrum (ESI, m/z): 544 $[M+H]^+$ Retention time (LCMS conditions 2): 1.149 min	Example 11-(b), 
201-(a)		Mass spectrum (ESI, m/z): 546 $[M+H]^+$ Retention time (LCMS conditions 2): 1.432 min	Example 11-(b), 
202-(a)		Mass spectrum (ESI, m/z): 499 $[M+H]^+$ Retention time (LCMS conditions 2): 1.422 min	Example 11-(b), 
203-(a)		Mass spectrum (ESI, m/z): 544 $[M+H]^+$ Retention time (LCMS conditions 2): 1.114 min	Example 11-(b), 

[0344] Example 199-(b)

Production of 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoic acid

[C179]



A water (0.25 ml) solution of 6 mg of lithium hydroxide monohydrate was added dropwise to a tetrahydrofuran (1 ml)/methanol (0.25 ml) solution of 24 mg of methyl 3-(3-((4-chloro-5-fluoro-2-

(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoate produced in Example 199-(a) at room temperature under argon gas and stirred at room temperature for 19 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 17 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 504 $[M+H]^+$

Retention time (LCMS conditions 2): 0.996 min.

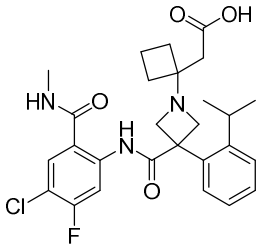
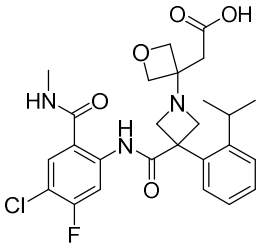
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.82 (br s, 1H), 8.90 - 8.66 (m, 1H), 8.47 (d, J = 12.3 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.39 - 7.22 (m, 4H), 4.04 -3.91 (m, 2H), 3.79 - 3.67 (m, 2H), 2.73 - 2.62 (m, 4H), 2.23 (s, 2H), 1.09 - 1.01 (m, 12H)

[0345] Example 200-(b) and the like

Compounds shown in Table 67 below were obtained by treating corresponding raw material compounds in the same manner as in Reference Example 199-(b).

[Table 67]

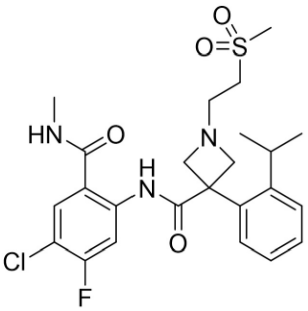
Table 67

Example	Structural formula	Analysis data	Raw material
200-(b)		Mass spectrum (ESI, m/z): 516 $[M+H]^+$ Retention time (LCMS conditions 2): 1.047 min	Example 200-(a)
201-(b)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.107 min	Example 201-(a)

[0346]Example 204-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-(methylsulfonyl)ethyl)azetidine-3-carboxamide

[C180]



An ethanol (0.6 ml) suspension of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) and 12 mg of methylvinylsulfone were stirred at room temperature for 30 minutes under an argon gas flow. A reaction mixture was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 33 mg of a title compound as a white solid.

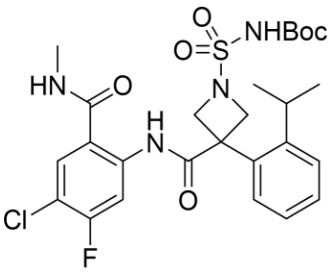
Mass spectrum (ESI, m/z): 510$[M+H]^+$

Retention time (LCMS conditions 2): 0.942 min.

[0347] Example 224-(a)

Production of tert-butyl ((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate

[C181]



0.017 ml of tert-butanol was added to a dichloromethane (1.2 ml) solution of 0.015 ml of chlorosulfonyl isocyanate in an ice bath under an argon gas flow and stirred in the ice bath for 30 minutes.

Next, 0.041 ml of triethylamine and 60 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) were added thereto in the ice bath and stirred at room temperature for 1.5 hours. Saturated sodium bicarbonate was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) to obtain 68 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 581[M-H]$^-$

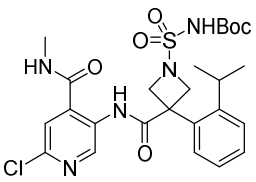
Retention time (LCMS conditions 2): 1.574 min.

[0348] Example 226-(a)

A compound shown in Table 68 below was obtained by treating a corresponding raw material compound in the same manner as in Example 224-(a).

[Table 68]

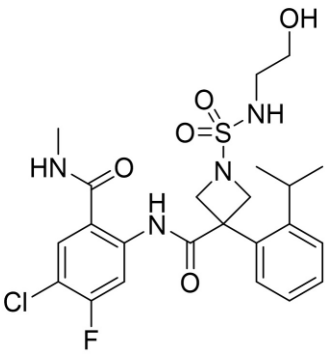
Table 68

Example	Structural formula	Analysis data	Raw material
226-(a)		Mass spectrum (ESI, m/z): 564 [M-H]$^-$ Retention time (LCMS conditions 2): 1.403 min	Example 33-(b)

[0349] Example 224-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2-hydroxyethyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C182]



9 mg of 2-((tetrahydropyran-2-yl)oxy)ethan-1-ol, 24 mg of triphenylphosphine, and 0.047 ml of a 40% diisopropyl azodicarboxylate/toluene solution were added to a tetrahydrofuran (1 ml) solution of 35 mg of tert-butyl ((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate produced in Example 224-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. 12 mg of triphenylphosphine and 0.024 ml of a 40% diisopropyl azodicarboxylate/toluene solution were added thereto at room temperature, stirred at room temperature for 30 minutes, and then left to stand at room temperature for 63 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 0.115 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a dichloromethane (0.575 ml) solution of the obtained purified product at room temperature under an argon gas flow, stirred at room temperature for six hours, and then left to stand at room temperature for 14 hours. A reaction mixture was concentrated under reduced pressure. 0.35 ml of trifluoroacetic acid was added to a dichloromethane (0.7 ml) solution of a concentrated residue at room temperature under an argon gas flow and stirred at room temperature for three hours. A reaction mixture was concentrated under reduced pressure. A 2M sodium carbonate aqueous solution was added to a concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 16 mg of a title compound as a white solid.

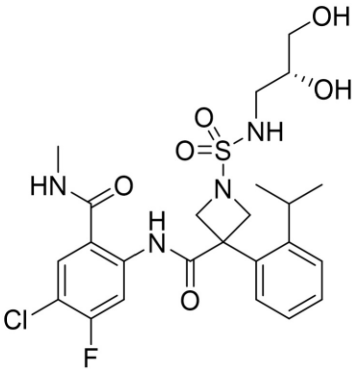
Mass spectrum (ESI, m/z): 527[M+H]$^+$

Retention time (LCMS conditions 2): 1.279 min.

[0350] Example 225-(a)

Production of (R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2,3-dihydroxypropyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C183]



0.013 ml of (R)-(-)-2,2-dimethyl-1,3-dioxolane-4-methanol, 32 mg of triphenylphosphine, and 0.065 ml of a 40% diisopropyl azodicarboxylate/toluene solution were added to a tetrahydrofuran (1 ml) solution of 48 mg of tert-butyl ((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate produced in the same manner as in Example 224-(a) at room temperature under an argon gas flow, stirred at room temperature for five hours, and left to stand at room temperature for 14 hours. 32 mg of triphenylphosphine and 0.065 ml of a 40% diisopropyl azodicarboxylate/toluene solution were added thereto at room temperature and stirred at room temperature for one hour. 32 mg of triphenylphosphine and 0.065 ml of a 40% diisopropyl azodicarboxylate/toluene solution were added thereto at room temperature and stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 0.056 ml of trifluoroacetate was added to a dichloromethane (0.558 ml) solution of the obtained purified product at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 15.5 hours. The reaction mixture

was concentrated under reduced pressure. A saturated sodium bicarbonate aqueous solution was added to a concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 14 mg of potassium carbonate was added to a methanol (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 28 mg of a title compound as a white solid.

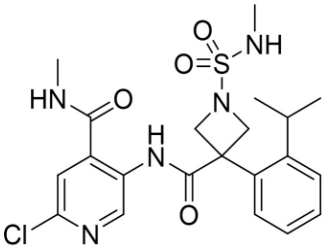
Mass spectrum (ESI, m/z): 557 $[M+H]^+$

Retention time (LCMS conditions 2): 1.197 min.

[0351] Example 226-(b)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(N-methylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C184]



0.004 ml of iodomethane and 26 mg of cesium carbonate were added to a N,N-dimethylformamide (0.5 ml) solution of 30 mg of tert-butyl ((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate produced in Example 226-(a) at room temperature under an argon gas flow and stirred at room temperature for 3.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer

was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 0.215 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a 1,4-dioxane (1 ml) solution of 25 mg of the obtained purified product at room temperature under an argon gas flow and stirred at room temperature for four hours. The reaction mixture was concentrated under reduced pressure. A saturated sodium bicarbonate aqueous solution was added to the concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 17 mg of a title compound as a white solid.

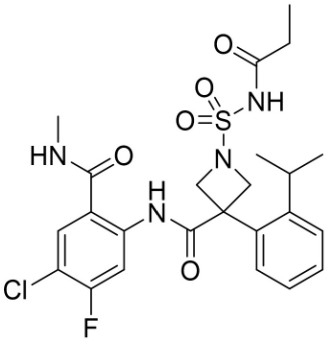
Mass spectrum (ESI, m/z): 480 $[M+H]^+$

Retention time (LCMS conditions 2): 1.201 min.

[0352] Example 227-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamide

[C185]



0.011 ml of N,N-diisopropylethylamine, 5 mg of 4-dimethylaminopyridine, and 0.008 ml of propionic anhydride were added to an acetonitrile (0.5 ml) suspension of 15 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide produced in

the same manner as in Example 4-(a) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. 1M hydrochloric acid was added to the reaction mixture thus obtained, and the reaction mixture was extracted with ethyl acetate. The resulting organic layer was washed successively with water and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 14 mg of the title compound as a white solid.

Mass spectrum (ESI, m/z): 539 $[M+H]^+$

Retention time (LCMS conditions 2): 1.410 min.

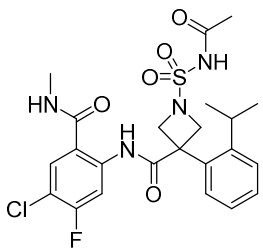
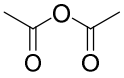
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.54 (br s, 1H), 11.51 (s, 1H), 8.80 - 8.71 (m, 1H), 8.43 (d, J = 12.2 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.46 - 7.24 (m, 4H), 4.70 (br d, J = 8.4 Hz, 2H), 4.47 (br d, J = 8.4 Hz, 2H), 2.63 (d, J = 4.5 Hz, 3H), 2.47 - 2.35 (m, 1H), 2.15 (q, J = 7.5 Hz, 2H), 1.04 (d, J = 6.7 Hz, 6H), 0.81 (t, J = 7.5 Hz, 3H)

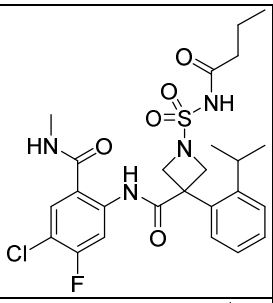
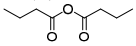
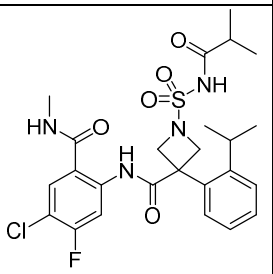
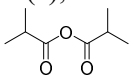
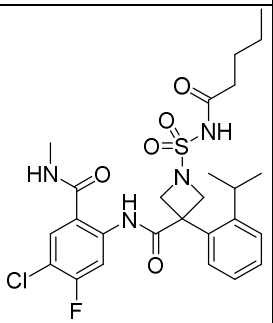
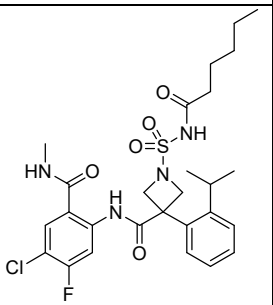
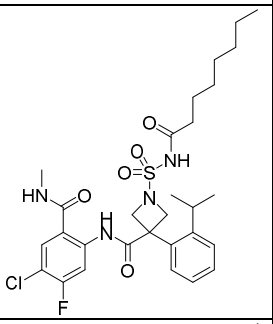
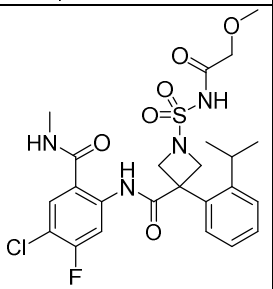
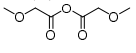
[0353] Example 228-(a) and the like

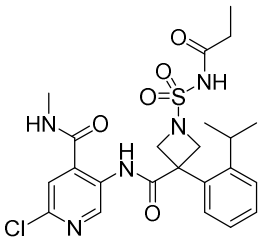
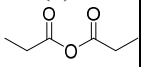
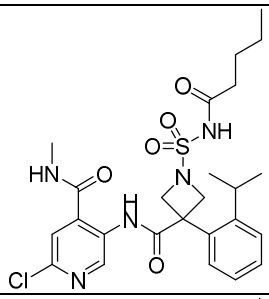
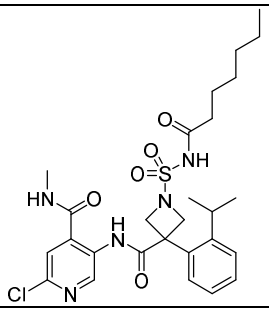
Compounds shown in Table 69 below were obtained by treating corresponding raw material compounds in the same manner as in Example 227-(a).

[Table 69]

Table 69

Example	Structural formula	Analysis data	Raw material
228-(a)		Mass spectrum (DUIS, m/z): 525 $[M+H]^+$ Retention time (LCMS conditions 1): 1.320 min	Example 4-(a), 

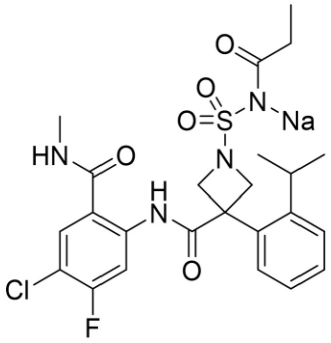
229-(a)		Mass spectrum (DUIS, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 1): 1.477 min	Example 4-(a), 
230-(a)		Mass spectrum (ESI, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 2): 1.481 min	Example 4-(a), 
231-(a)		Mass spectrum (ESI, m/z): 567 $[M+H]^+$ Retention time (LCMS conditions 2): 1.542 min	Example 4-(a), n-Pentanoic anhydride
232-(a)		Mass spectrum (ESI, m/z): 581 $[M+H]^+$ Retention time (LCMS conditions 2): 1.624 min	Example 4-(a), n-Hexanoic anhydride
233-(a)		Mass spectrum (ESI, m/z): 609 $[M+H]^+$ Retention time (LCMS conditions 2): 1.760 min	Example 4-(a), n-Octanoic anhydride
234-(a)		Mass spectrum (DUIS, m/z): 555 $[M+H]^+$ Retention time (LCMS conditions 1): 1.380 min	Example 4-(a), 

235-(a)		Mass spectrum (DUIS, m/z): 522 $[M+H]^+$ Retention time (LCMS conditions 1): 1.206 min	Example 10-(a), 
236-(a)		Mass spectrum (ESI, m/z): 550 $[M+H]^+$ Retention time (LCMS conditions 2): 1.361 min	Example 10-(a), n-Pentanoic anhydride
237-(a)		Mass spectrum (ESI, m/z): 578 $[M+H]^+$ Retention time (LCMS conditions 2): 1.534 min	Example 10-(a), n-Heptanoic anhydride

[0354] Example 227-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamide sodium salt

[C186]



0.158 ml of a 1M sodium hydroxide aqueous solution was added to an acetonitrile (2 ml)/water (2 ml) solution of 89 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamide produced in the same manner as in Example 227-(a) at room temperature and lyophilized to obtain 87 mg of the title compound as a white solid.

Mass spectrum (ESI, m/z): 539 $[M+H]^+$

Retention time (LCMS conditions 2): 1.422 min.

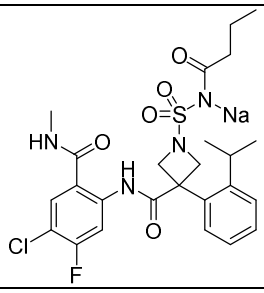
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.94 (s, 1H), 8.89 - 8.80 (m, 1H), 8.45 (d, J = 12.3 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.34 - 7.22 (m, 4H), 4.22 (d, J = 7.7 Hz, 2H), 4.13 (br d, J = 7.7 Hz, 2H), 2.77 - 2.68 (m, 4H), 1.88 (q, J = 7.6 Hz, 2H), 1.06 (d, J = 6.7 Hz, 6H), 0.80 (t, J = 7.6 Hz, 3H)

[0355] Example 229-(b)

A compound shown in Table 70 below was obtained by treating a corresponding raw material compound in the same manner as in Example 227-(b).

[Table 70]

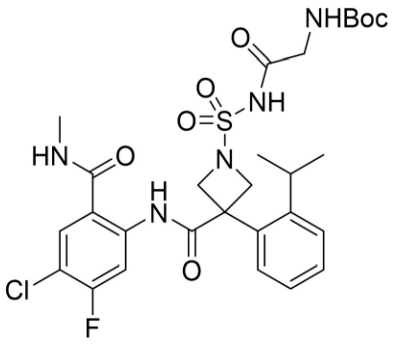
Table 70

Example	Structural formula	Analysis data	Raw material
229-(b)		Mass spectrum (ESI, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 2): 1.475 min	Example 229-(a)

[0356] Example 238-(a)

Production of tert-butyl (2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine)-1-sulfonamido)-2-oxoethyl)carbamate

[C187]



0.022 ml of N,N-diisopropylethylamine and 36 mg of 2,5-dioxopyrrolidin-1-yl(tert-butoxycarbonyl)glycinate were added to an acetonitrile (1 ml) suspension of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide

produced in the same manner as in Example 4-(a) at room temperature under an argon gas flow, stirred at room temperature for eight hours, and left to stand at room temperature for 15 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate:methanol). Ethyl acetate was added to the obtained purified product, washed successively with water, a 2M sodium carbonate aqueous solution, and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 30 mg of a title compound as a white solid.

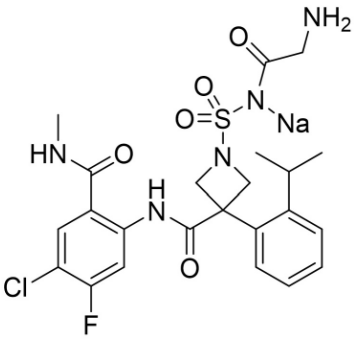
Mass spectrum (ESI, m/z): 638 $[M-H]^-$

Retention time (LCMS conditions 2): 1.487 min.

[0357] Example 238-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-glycylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide sodium salt

[C188]



0.234 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to 30 mg of tert-butyl (2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine)-1-sulfonamido)-2-oxoethyl)carbamate produced in Example 238-(a) at room temperature under an argon gas flow, stirred at room temperature for two hours, and left to stand at room temperature for 15 hours. A 2M sodium carbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 17 mg of a title compound as a white

solid.

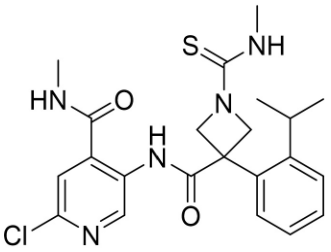
Mass spectrum (ESI, m/z): 540 $[M+H]^+$

Retention time (LCMS conditions 2): 0.973 min.

[0358] Example 239-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C189]



0.011 ml of triethylamine and an acetonitrile (0.3 ml) solution of 6 mg of methyl isothiocyanate were added to an acetonitrile (0.3 ml) suspension of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a) at room temperature under argon gas and stirred at room temperature for one hour. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 30 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 460 $[M+H]^+$

Retention time (LCMS conditions 1): 1.190 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.51 (s, 1H), 9.34 (s, 1H), 9.00 - 8.90 (m, 1H), 7.81 - 7.73 (m, 1H), 7.69 (s, 1H), 7.51 - 7.30 (m, 4H), 4.74 - 4.61 (m,2H), 4.44 - 4.28 (m, 2H), 2.86 (d, J = 4.3 Hz, 3H), 2.62 (d, J = 4.4 Hz, 3H), 2.55 - 2.40 (m, 1H), 1.07 (d, J = 6.7 Hz, 6H)

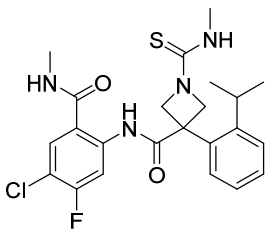
[0359] Example 240-(a)

A compound shown in Table 71 below was obtained by treating a corresponding raw material compound in the same manner as in Example 239-(a). In the synthesis of Example 240-(a), the reaction

was performed without using triethylamine.

[Table 71]

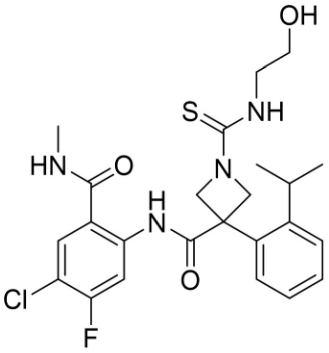
Table 71

Example	Structural formula	Analysis data	Raw material
240-(a)		Mass spectrum (ESI, m/z): 477 $[M+H]^+$ Retention time (LCMS conditions 2): 1.394 min	Example 11-(b)

[0360] Example 241-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C190]



0.016 ml of triethylamine and 16 mg of 1,1'-thiocarbonyldiimidazole were added to a tetrahydrofuran (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for two hours. Next, 0.0090 ml of 2-aminoethanol was added thereto at room temperature, stirred at room temperature for four hours, and left to stand at room temperature for 16.5 hours. A reaction mixture was concentrated under reduced pressure. Water was added to a concentrated residue, and the concentrated residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The

obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 25 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 507 $[M+H]^+$

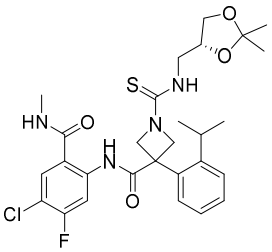
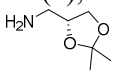
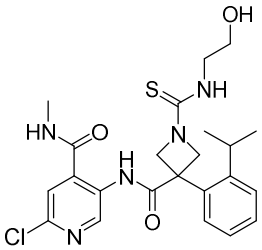
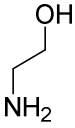
Retention time (LCMS conditions 2): 1.278 min.

[0361] Example 242-(a) and the like

Compounds shown in Table 72 below were obtained by treating corresponding raw material compounds in the same manner as in Example 241-(a). The synthesis of Example 242-(a) was performed at 60°C as the reaction temperature.

[Table 72]

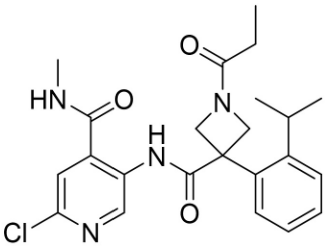
Table 72

Example	Structural formula	Analysis data	Raw material
242-(a)		Mass spectrum (DUIS, m/z): 577 $[M+H]^+$ Retention time (LCMS conditions 1): 1.534 min	Example 11-(b), 
243-(a)		Mass spectrum (ESI, m/z): 490 $[M+H]^+$ Retention time (LCMS conditions 2): 1.082 min	Example 33-(b), 

[0362] Example 244-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-propionylazetidine-3-carboxamido)-N-methylisonicotinamide

[C191]



0.027 ml of N,N-diisopropylethylamine, 9 mg of 4-dimethylaminopyridine, and 0.020 ml of propionic anhydride were added to an acetonitrile (1 ml) solution of 31 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for one hour. 1N hydrochloric acid was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed successively with water and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; ethyl acetate:methanol). 1.2 ml of methanol and 0.3 ml of a 1N sodium hydroxide aqueous solution were added to the obtained purified product at room temperature and stirred at room temperature for one hour. The reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 30 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 443 $[M+H]^+$

Retention time (LCMS conditions 2): 1.180 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.46 (s, 1H), 9.34 (s, 1H), 8.99 - 8.90 (m, 1H), 7.68 (s, 1H), 7.53 - 7.28 (m, 4H), 4.86 - 4.75 (m, 1H), 4.62 - 4.47 (m, 2H), 4.33 - 4.21 (m, 1H), 2.61 (d, J = 4.5 Hz, 3H), 2.48 - 2.39 (m, 1H), 2.13 (q, J = 7.5 Hz, 2H), 1.11 - 1.01 (m, 6H), 0.97 (t, J = 7.5 Hz, 3H)

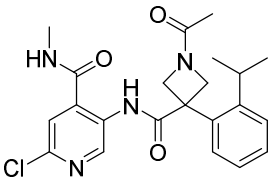
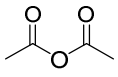
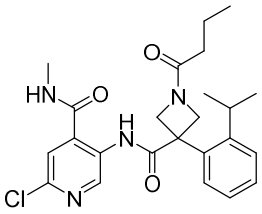
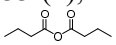
[0363] Example 245-(a) and the like

Compounds shown in Table 73 below were obtained by treating corresponding raw material compounds in the same manner as in Example 244-(a).

[Table 73]

Table 73

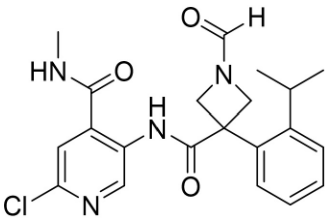
Example	Structural formula	Analysis data	Raw material

245-(a)		Mass spectrum (ESI, m/z): 429 $[M+H]^+$ Retention time (LCMS conditions 2): 1.071 min	Example 33-(b), 
246-(a)		Mass spectrum (ESI, m/z): 457 $[M+H]^+$ Retention time (LCMS conditions 2): 1.267 min	Example 33-(b), 

[0364] Example 247-(a)

Production of 2-chloro-5-(1-formyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C192]



0.016 ml of N,N-diisopropylethylamine and 0.011 ml of 2,2,2-trifluoroethyl formate were added to a N,N-dimethylformamide (0.5 ml) solution of 31 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow, stirred at room temperature for two hours, and then left to stand at room temperature for 15.5 hours. 0.009 ml of acetic acid and water were added to a reaction mixture, and the reaction mixture was extracted with tert-butyl methyl ether. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 29 mg of a title compound as a white solid.

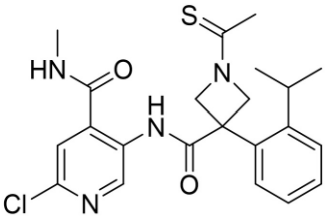
Mass spectrum (ESI, m/z): 415 $[M+H]^+$

Retention time (LCMS conditions 2): 1.069 min.

[0365] Example 248-(a)

Production of 2-chloro-5-(1-ethanethioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C193]



63 mg of HATU and 0.113 ml of N,N-diisopropylethylamine were added to a N,N-dimethylformamide (2 ml) solution of 47 mg of 2-chloro-5-(1-ethanethioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)isonicotinic acid produced in Reference Example 248-(c) at room temperature under an argon gas flow and stirred at room temperature for 10 minutes. Next, 22 mg of methylamine hydrochloride was added thereto at room temperature and stirred at room temperature for 15 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 33 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 445 $[M+H]^+$

Retention time (LCMS conditions 2): 1.289 min.

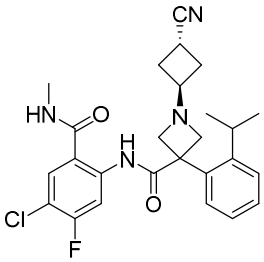
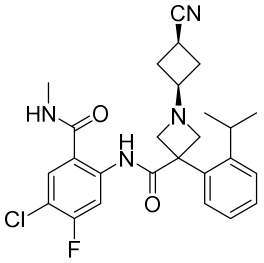
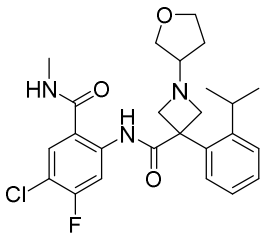
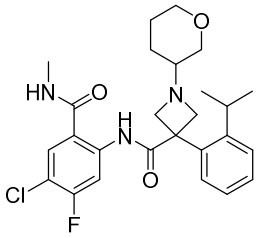
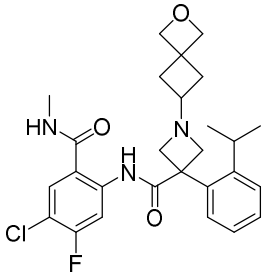
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.46 (s, 1H), 9.34 (s, 1H), 8.99 - 8.88 (m, 1H), 7.68 (s, 1H), 7.57 - 7.49 (m, 1H), 7.47 - 7.31 (m, 3H), 5.09 - 4.98 (m,1H), 4.89 - 4.74 (m, 2H), 4.51 - 4.37 (m, 1H), 2.60 (d, J = 4.6 Hz, 3H), 2.47 - 2.39 (m, 1H), 2.35 (s, 3H), 1.12 - 1.03 (m, 6H)

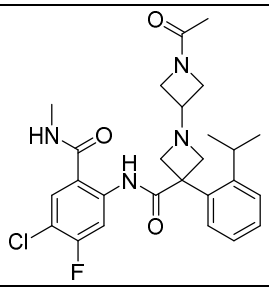
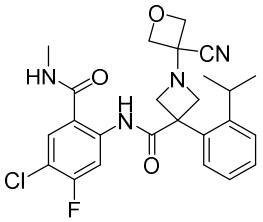
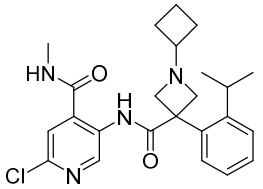
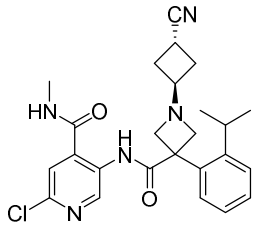
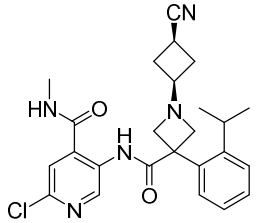
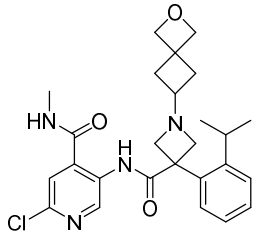
[0366] Example 211-(a) and the like

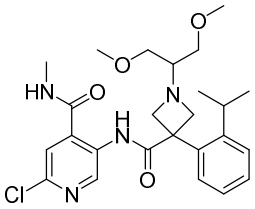
Compounds shown in Table 74 below were obtained by treating corresponding raw material compounds in the same manner as in Example 248-(a). The synthesis of Example 343-(a) was performed using acetonitrile instead of N,N-dimethylformamide.

[Table 74]

Table 74

Example	Structural formula	Analysis data	Raw material
211-(a)		Mass spectrum (ESI, m/z): 483 $[M+H]^+$ Retention time (LCMS conditions 2): 0.986 min	Reference Example 211-(b)
212-(a)		Mass spectrum (ESI, m/z): 483 $[M+H]^+$ Retention time (LCMS conditions 2): 0.963 min	Reference Example 212-(b)
213-(a)		Mass spectrum (ESI, m/z): 474 $[M+H]^+$ Retention time (LCMS conditions 2): 0.939 min	Reference Example 213-(b)
214-(a)		Mass spectrum (ESI, m/z): 488 $[M+H]^+$ Retention time (LCMS conditions 2): 0.985 min	Reference Example 214-(b)
216-(a)		Mass spectrum (ESI, m/z): 500 $[M+H]^+$ Retention time (LCMS conditions 3): 0.798 min	Reference Example 216-(b)

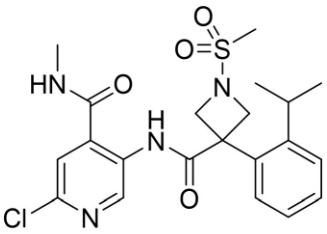
217-(a)		Mass spectrum (ESI, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 2): 0.929 min	Reference Example 217-(b)
219-(a)		Mass spectrum (ESI, m/z): 485 $[M+H]^+$ Retention time (LCMS conditions 2): 1.494 min	Reference Example 219-(b)
220-(a)		Mass spectrum (ESI, m/z): 441 $[M+H]^+$ Retention time (LCMS conditions 2): 0.985 min	Reference Example 220-(b)
221-(a)		Mass spectrum (DUIS, m/z): 466 $[M+H]^+$ Retention time (LCMS conditions 1): 0.824 min	Reference Example 221-(b)
222-(a)		Mass spectrum (DUIS, m/z): 466 $[M+H]^+$ Retention time (LCMS conditions 1): 0.810 min	Reference Example 222-(b)
223-(a)		Mass spectrum (DUIS, m/z): 483 $[M+H]^+$ Retention time (LCMS conditions 1): 0.794 min	Reference Example 223-(b)

343-(a)		Mass spectrum (DUIS, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 8): 0.918 min	Reference Example 343-(b)

[0367] Example 249-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(methylsulfonyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C194]



0.007 ml of methanesulfonyl chloride and 0.016 ml of triethylamine were added to a dichloromethane (1 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 32 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 465 $[M+H]^+$

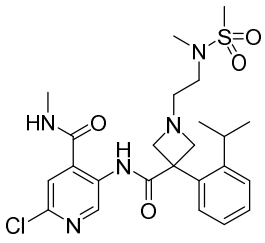
Retention time (LCMS conditions 2): 1.224 min.

[0368] Example 346-(a)

A compound shown in Table 75 below was obtained by treating a corresponding raw material compound in the same manner as in Example 249-(a).

[Table 75]

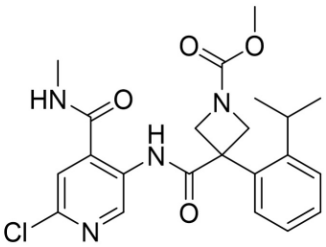
Table 75

Example	Structural formula	Analysis data	Raw material
346-(a)		Mass spectrum (ESI, m/z): 522 $[M+H]^+$ Retention time (LCMS conditions 3): 0.621 min	Example 345-(a)

[0369] Example 250-(a)

Production of methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C195]



0.022 ml of triethylamine and 0.007 ml of methyl chloroformate were added to a dichloromethane (1 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. 0.003 ml of methyl chloroformate was added thereto at room temperature and stirred at room temperature for 2.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 31 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 445 $[M+H]^+$

Retention time (LCMS conditions 2): 1.271 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.40 (s, 1H), 9.34 (s, 1H), 8.97 - 8.88 (m, 1H), 7.67 (s, 1H), 7.50 - 7.29 (m, 4H), 4.67 - 4.49 (m, 2H), 4.47 - 4.26 (m, 2H), 3.59 (s, 3H), 2.60 (d, J = 4.6

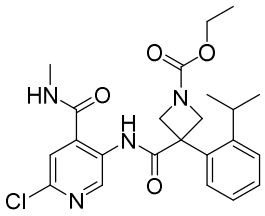
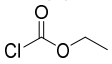
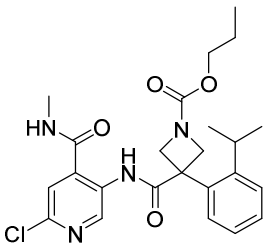
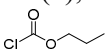
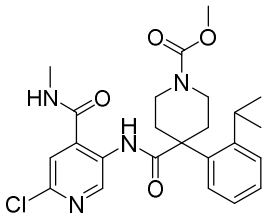
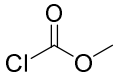
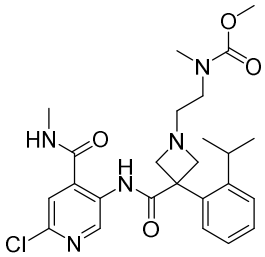
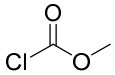
Hz, 3H), 2.42 - 2.34 (m, 1H), 1.04 (d, J = 6.7 Hz, 6H)

[0370] Example 251-(a) and the like

Compounds shown in Table 76 below were obtained by treating corresponding raw material compounds in the same manner as in Example 250-(a).

[Table 76]

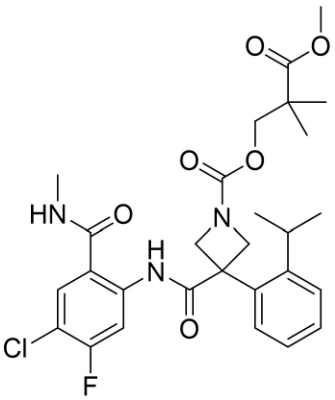
Table 76

Example	Structural formula	Analysis data	Raw material
251-(a)		Mass spectrum (ESI, m/z): 459 $[M+H]^+$ Retention time (LCMS conditions 2): 1.377 min	Example 33-(b), 
252-(a)		Mass spectrum (ESI, m/z): 473 $[M+H]^+$ Retention time (LCMS conditions 2): 1.481 min	Example 33-(b), 
292-(c)		Mass spectrum (ESI, m/z): 473 $[M+H]^+$ Retention time (LCMS conditions 2): 1.364 min	Example 292-(b), 
347-(a)		Mass spectrum (ESI, m/z): 502 $[M+H]^+$ Retention time (LCMS conditions 3): 0.637 min	Example 345-(a), 

[0371] Example 253-(a)

Production of 3-methoxy-2,2-dimethyl-3-oxopropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C196]



24 mg of 1,1'-carbonyldiimidazole was added to a dichloromethane (0.5 ml) solution of 0.019 ml of methyl hydroxypivalate at room temperature under an argon gas flow and stirred at room temperature for four hours. 0.25 ml of the obtained solution was added to a 1,4-dioxane (1 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 90°C for one hour. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 44 mg of a title compound as a white foamy substance.

Mass spectrum (DUIS, m/z): 562 $[M+H]^+$

Retention time (LCMS conditions 1): 1.631 min.

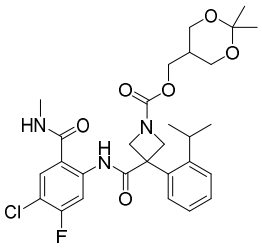
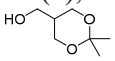
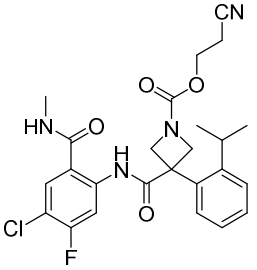
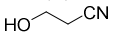
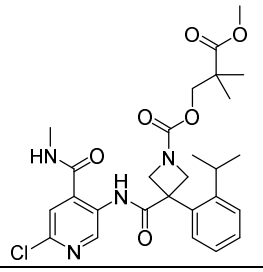
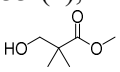
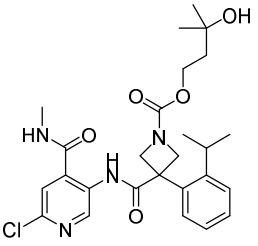
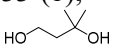
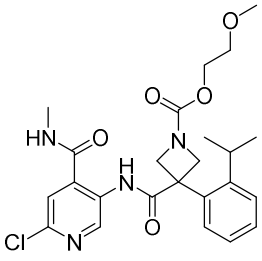
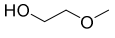
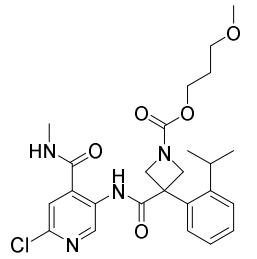
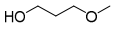
[0372] Example 254-(a) and the like

Compounds shown in Table 77 below were obtained by treating corresponding raw material compounds in the same manner as in Example 253-(a).

[Table 77]

Table 77

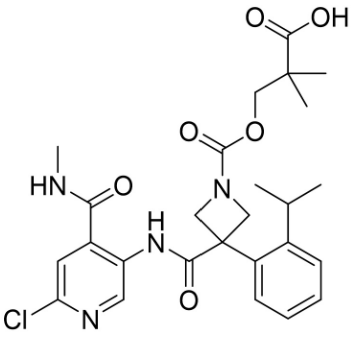
Example	Structural formula	Analysis data	Raw material

254-(a)		Mass spectrum (DUIS, m/z): 576 $[M+H]^+$ Retention time (LCMS conditions 1): 1.586 min	Example 11-(b), 
255-(a)		Mass spectrum (ESI, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 2): 1.420 min	Example 11-(b), 
256-(a)		Mass spectrum (ESI, m/z): 545 $[M+H]^+$ Retention time (LCMS conditions 2): 1.463 min	Example 33-(b), 
257-(a)		Mass spectrum (ESI, m/z): 517 $[M+H]^+$ Retention time (LCMS conditions 2): 1.239 min	Example 33-(b), 
258-(a)		Mass spectrum (ESI, m/z): 489 $[M+H]^+$ Retention time (LCMS conditions 2): 1.271 min	Example 33-(b), 
259-(a)		Mass spectrum (ESI, m/z): 503 $[M+H]^+$ Retention time (LCMS conditions 2): 1.349 min	Example 33-(b), 

[0373] Example 256-(b)

Production of 3-((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid

[C197]



0.514 ml of a 1N sodium hydroxide aqueous solution was added to a tetrahydrofuran (1 ml) solution of 56 mg of 3-methoxy-2,2-dimethyl-3-oxopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate produced in Example 256-(a) at room temperature under an argon gas flow and stirred at 50°C for 6.5 hours. 1N hydrochloric acid was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with tert-butyl methyl ether. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 38 mg of a title compound as a white solid.

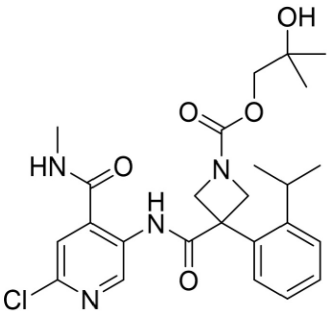
Mass spectrum (ESI, m/z): 531 $[M+H]^+$

Retention time (LCMS conditions 2): 1.252 min.

[0374] Example 260-(a)

Production of 2-hydroxy-2-methylpropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate

[C198]



18 mg of 1,1'-carbonyldiimidazole was added to a dichloromethane (0.5 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). A tetrahydrofuran (0.2 ml) solution of 31 mg of 2-methylpropane-1,2-diol and 18 mg of sodium hydride [manufactured by FUJIFILM Wako Pure Chemical Industries, Ltd., oily, 63.1 wt%] were added to a tetrahydrofuran (0.8 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 25 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 503 $[M+H]^+$

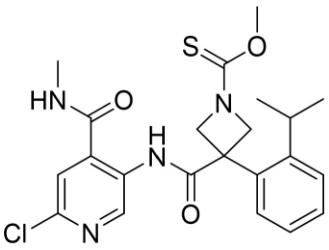
Retention time (LCMS conditions 2): 1.205 min.

[0375] Example 261-(a)

Production of O-methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidine-1-carbothioate

[C199]



A dichloromethane (0.5 ml) solution of 0.049 ml of thiophosgene was added to a dichloromethane (0.5 ml) solution of 25 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. Next, 0.65 ml of a 5M sodium methoxide/methanol solution was added dropwise thereto at room temperature and stirred at room temperature for 45 minutes. A reaction mixture was poured into a saturated ammonium chloride aqueous solution and extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 25 mg of a title compound as a white solid.

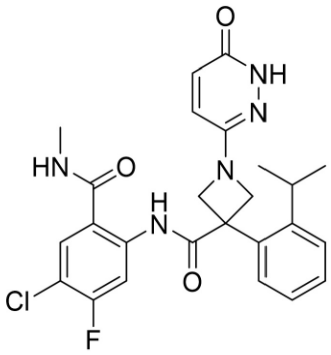
Mass spectrum (ESI, m/z): 461 $[M+H]^+$

Retention time (LCMS conditions 2): 1.487 min.

[0376] Example 262-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide

[C200]



An acetic acid (0.75 ml) solution of 32 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in Example 262-(a) was stirred at 120°C under an argon gas flow for 11 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol) to obtain 19 mg of a title compound as a slightly yellow solid.

Mass spectrum (ESI, m/z): 498 $[M+H]^+$

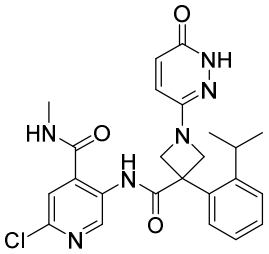
Retention time (LCMS conditions 2): 1.252 min.

[0377] Example 263-(a)

A compound shown in Table 78 below was obtained by treating a corresponding raw material compound in the same manner as in Example 262-(b).

[Table 78]

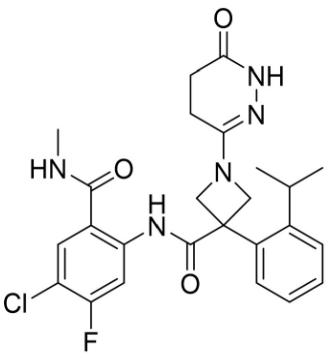
Table 78

Example	Structural formula	Analysis data	Raw material
263-(a)		Mass spectrum (ESI, m/z): 481 $[M+H]^+$ Retention time (LCMS conditions 2): 1.050 min	Example 94-(a)

[0378] Example 264-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)azetidine-3-carboxamide

[C201]



2 mg of zinc was added to an acetic acid (0.75 ml) solution of 12 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide produced in Example 262-(b) at 60°C under an argon gas flow and stirred at 60°C for 4.5 hours. 2 mg of zinc was added thereto and stirred at 60°C for four hours. 2 mg of zinc was added thereto and stirred at 60°C for 30 minutes. 2 mg of zinc was added thereto and stirred at 60°C for one hour. 2 mg of zinc was added thereto and stirred at 60°C for one hour. 2 mg of zinc was added thereto and stirred at 60°C for 1.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol) to obtain 10 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 500 $[M+H]^+$

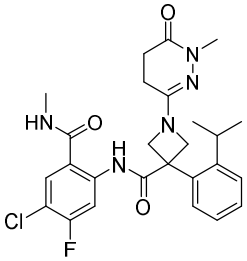
Retention time (LCMS conditions 2): 1.225 min.

[0379] Example 266-(a)

A compound shown in Table 79 below was obtained by treating a corresponding raw material compound in the same manner as in Example 264-(a).

[Table 79]

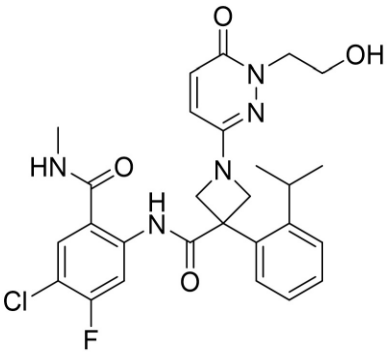
Table 79

Example	Structural formula	Analysis data	Raw material
266-(a)		Mass spectrum (ESI, m/z): 514 $[M+H]^+$ Retention time (LCMS conditions 2): 1.323 min	Example 265-(a)

[0380] Example 268-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

[C202]



0.010 ml of (2-bromoethoxy)-tert-butyldimethylsilane and 20 mg of cesium carbonate were added to a N,N-dimethylformamide (0.5 ml) solution of 15 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide produced in Example 262-(b) at room temperature under an argon gas flow and stirred at room temperature for five hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 0.1 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to a dichloromethane (0.2 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at room temperature for two hours. A reaction mixture was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; ethyl acetate:methanol) to obtain 8 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 542 $[M+H]^+$

Retention time (LCMS conditions 2): 1.265 min.

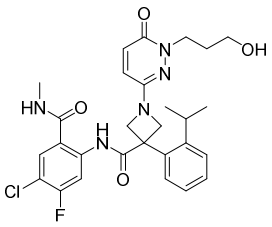
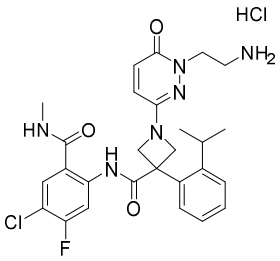
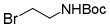
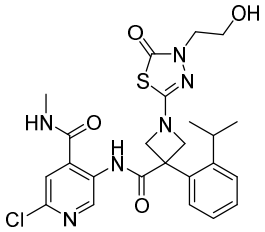
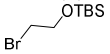
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.72 (s, 1H), 8.83 - 8.73 (m, 1H), 8.47 (d, J = 12.3 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.44 (dd, J = 1.2, 7.5 Hz, 1H), 7.40 - 7.27 (m, 3H), 7.16 (d, J = 9.8 Hz, 1H), 6.84 (d, J = 9.8 Hz, 1H), 4.74 (t, J = 5.9 Hz, 1H), 4.63 (br d, J = 7.8 Hz, 2H), 4.31 (br d, J = 7.8 Hz, 2H), 3.96 (t, J = 6.3 Hz, 2H), 3.69 - 3.61 (m, 2H), 2.67 (d, J = 4.4 Hz, 3H), 2.66 - 2.57 (m, 1H), 1.07 (d, J = 6.7 Hz, 6H)

[0381] Example 269-(a) and the like

Compounds shown in Table 80 below were obtained by treating corresponding raw material compounds in the same manner as in Example 268-(a).

[Table 80]

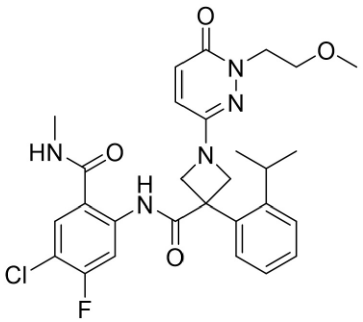
Table 80

Example	Structural formula	Analysis data	Raw material
269-(a)		Mass spectrum (ESI, m/z): 556 $[M+H]^+$ Retention time (LCMS conditions 2): 1.297 min	Example 262-(b),
270-(a)		Mass spectrum (ESI, m/z): 541 $[M+H]^+$ Retention time (LCMS conditions 2): 0.989 min	Example 262-(b), 
284-(a)		Mass spectrum (DUIS, m/z): 531 $[M+H]^+$ Retention time (LCMS conditions 1): 1.191 min	Example 281-(a), 

[0382] Example 271-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-(2-methoxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide

[C203]



0.006 ml of 2-bromoethyl methyl ether and 26 mg of cesium carbonate were added to a N,N-

dimethylformamide (0.5 ml) solution of 20 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide produced in Example 262-(b) at room temperature under an argon gas flow and stirred at room temperature for two hours. 0.006 ml of 2-bromoethyl methyl ether was added thereto and stirred at room temperature for 2.5 hours. 0.006 ml of 2-bromoethyl methyl ether and 26 mg of cesium carbonate were added thereto and stirred at room temperature for seven hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 6 mg of a title compound as a white foamy substance.

Mass spectrum (ESI, m/z): 556 $[M+H]^+$

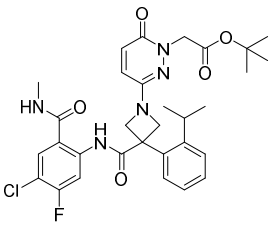
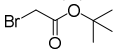
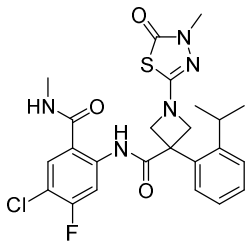
Retention time (LCMS conditions 2): 1.411 min.

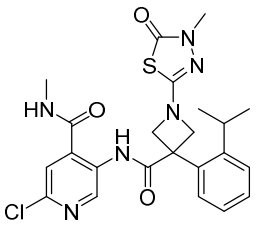
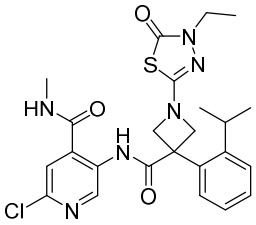
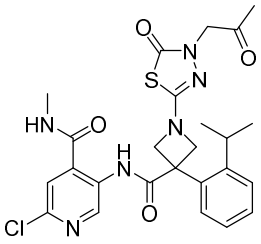
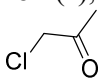
[0383] Example 272-(a) and the like

Compounds shown in Table 81 below were obtained by treating corresponding raw material compounds in the same manner as in Example 271-(a). The synthesis of Example 286-(a) was performed at 60°C as the reaction temperature.

[Table 81]

Table 81

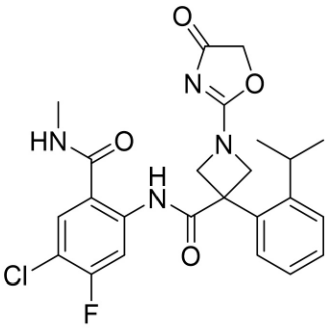
Example	Structural formula	Analysis data	Raw material
272-(a)		Mass spectrum (ESI, m/z): 612 $[M+H]^+$ Retention time (LCMS conditions 2): 1.616 min	Example 262-(b), 
282-(a)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.573 min	Example 280-(a), Iodomethane

283-(a)		Mass spectrum (DUIS, m/z): 501 $[M+H]^+$ Retention time (LCMS conditions 1): 1.356 min	Example 281-(a), Iodomethane
285-(a)		Mass spectrum (DUIS, m/z): 515 $[M+H]^+$ Retention time (LCMS conditions 1): 1.472 min	Example 281-(a), Iodoethane
286-(a)		Mass spectrum (DUIS, m/z): 543 $[M+H]^+$ Retention time (LCMS conditions 1): 1.296 min	Example 281-(a), 

[0384] Example 273-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamide

[C204]



0.006 ml of chloroacetylisocyanate was added to a dichloromethane (0.3 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for one hour. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. 0.022

ml of 1,8-diazabicyclo[5.4.0]-7-undecene was added to a tetrahydrofuran (0.3 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for 18 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate:methanol) to obtain 32 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 487 $[M+H]^+$

Retention time (LCMS conditions 1): 1.249 min.

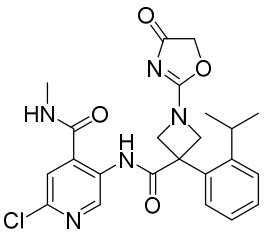
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.34 (s, 1H), 8.74 - 8.66 (m, 1H), 8.47 (d, J = 12.2 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.52 - 7.46 (m, 1H), 7.43 - 7.32 (m, 3H), 4.90 - 4.77 (m, 2H), 4.74 - 4.55 (m, 4H), 2.59 (d, J = 4.4 Hz, 3H), 2.43 - 2.30 (m, 1H), 1.05 (d, J = 6.7 Hz, 6H)

[0385] Example 274-(a)

A compound shown in Table 82 below was obtained by treating a corresponding raw material compound in the same manner as in Example 273-(a).

[Table 82]

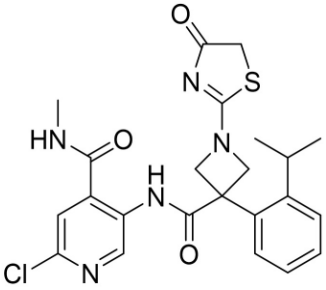
Table 82

Example	Structural formula	Analysis data	Raw material
274-(a)		Mass spectrum (DUIS, m/z): 470 $[M+H]^+$ Retention time (LCMS conditions 1): 1.034 min	Example 33-(b)

[0386] Example 275-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrothiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C205]



13 mg of 2-(methylthio)thiazol-4(5H)-one and 0.019 ml of N,N-diisopropylethylamine were added to a methanol (0.5 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) to obtain 35 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 486 $[M+H]^+$

Retention time (LCMS conditions 1): 1.088 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.41 (s, 1H), 9.33 (s, 1H), 8.96 - 8.89 (m, 1H), 7.68 (s, 1H), 7.55 - 7.50 (m, 1H), 7.45 - 7.41 (m, 2H), 7.40 - 7.33 (m, 1H), 4.96 - 4.84 (m, 2H), 4.77 - 4.61 (m, 2H), 4.11 - 4.01 (m, 2H), 2.59 (d, J = 4.5 Hz, 3H), 2.42 - 2.31 (m, 1H), 1.11 - 1.01 (m, 6H)

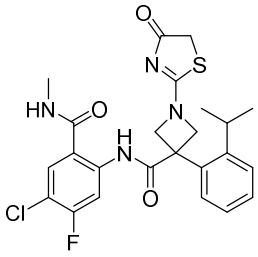
[0387] Example 276-(a)

A compound shown in Table 83 below was obtained by treating a corresponding raw material compound in the same manner as in Example 275-(a). In the synthesis of Example 276-(a), the reaction was performed without using N,N-diisopropylethylamine.

[Table 83]

Table 83

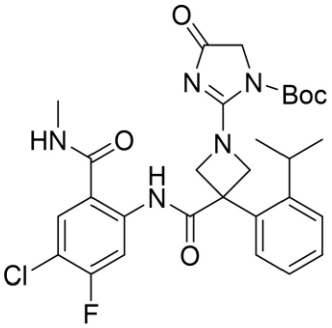
Example	Structural formula	Analysis data	Raw material

276-(a)		Mass spectrum (DUIS, m/z): 503 $[M+H]^+$ Retention time (LCMS conditions 1): 1.310 min	Example 11-(b)

[0388] Example 277-(a)

Production of tert-butyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate

[C206]



17 mg of tert-butyl 2-(methylthio)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate as described in WO 2014/188193 was added to a methanol (0.8 ml) solution of 30 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for two hours. A reaction mixture was concentrated under reduced pressure, and 0.8 ml of ethanol and 17 mg of tert-butyl 2-(methylthio)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate were added thereto and stirred at room temperature for one hour. The reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone) to obtain 30 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 586 $[M+H]^+$

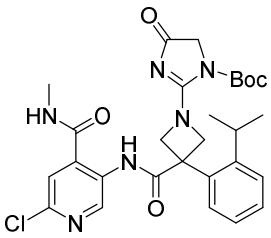
Retention time (LCMS conditions 1): 1.510 min.

[0389] Example 279-(a)

A compound shown in Table 84 below was obtained by treating a corresponding raw material compound in the same manner as in Example 277-(a). In the synthesis of Example 279-(a), the reaction was performed by adding N,N-diisopropylethylamine.

[Table 84]

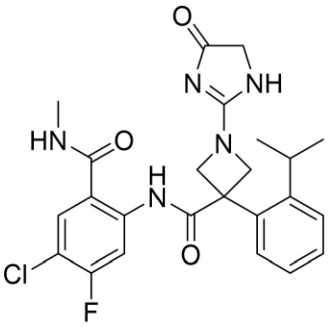
Table 84

Example	Structural formula	Analysis data	Raw material
279-(a)		Mass spectrum (DUIS, m/z): 569 $[M+H]^+$ Retention time (LCMS conditions 1): 1.325 min	Example 39-(a)

[0390] Example 277-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide

[C207]



0.6 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to 30 mg of tert-butyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate produced in Example 277-(a) at room temperature under an argon gas flow and stirred at room temperature for one hour. A 2M sodium carbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate:methanol). The

obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 25 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 486 $[M+H]^+$

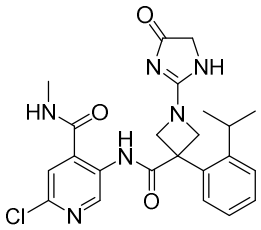
Retention time (LCMS conditions 1): 0.960 min.

[0391] Example 279-(b)

A compound shown in Table 85 below was obtained by treating a corresponding raw material compound in the same manner as in Example 277-(b).

[Table 85]

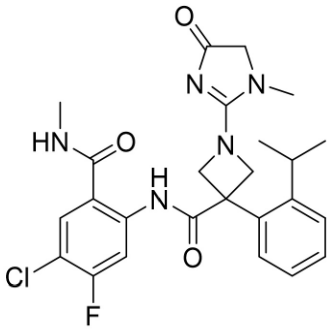
Table 85

Example	Structural formula	Analysis data	Raw material
279-(b)		Mass spectrum (DUIS, m/z): 469 $[M+H]^+$ Retention time (LCMS conditions 1): 0.757 min	Example 279-(a)

[0392] Example 278-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide

[C208]



0.004 ml of N,N-diisopropylethylamine and 0.002 ml of iodomethane were added to a N,N-dimethylformamide (0.5 ml) solution of 5 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide produced in Example 277-(b) at room temperature under an argon gas flow and stirred at room temperature for seven

hours. A mixture was left to stand at room temperature for 15 hours and stirred at room temperature for 4.5 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 3 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 500 $[M+H]^+$

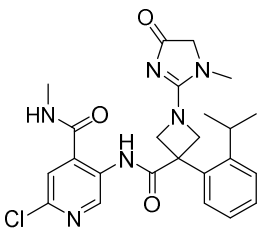
Retention time (LCMS conditions 1): 1.003 min.

[0393] Example 279-(c)

A compound shown in Table 86 below was obtained by treating a corresponding raw material compound in the same manner as in Example 278-(a).

[Table 86]

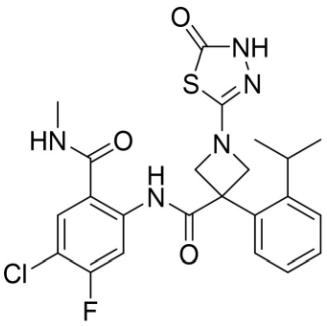
Table 86

Example	Structural formula	Analysis data	Raw material
279-(c)		Mass spectrum (DUIS, m/z): 483 $[M+H]^+$ Retention time (LCMS conditions 1): 0.830 min	Example 279-(b)

[0394] Example 280-(a)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide

[C209]



0.104 ml of triethylamine and 44 mg of 1,1'-thiocarbonyldiimidazole were added to a tetrahydrofuran (1.2 ml) solution of 50 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for two hours. Next, 0.012 ml of hydrazine monohydrate was added thereto at room temperature and stirred at room temperature for two hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 0.052 ml of triethylamine and 60 mg of 1,1'-carbonyldiimidazole were added to a dichloromethane (1.2 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for one hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 50 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 504 $[M+H]^+$

Retention time (LCMS conditions 2): 1.426 min.

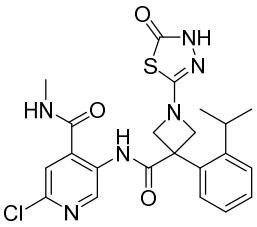
[0395] Example 281-(a)

A compound shown in Table 87 below was obtained by treating a corresponding raw material compound in the same manner as in Example 280-(a).

[Table 87]

Table 87

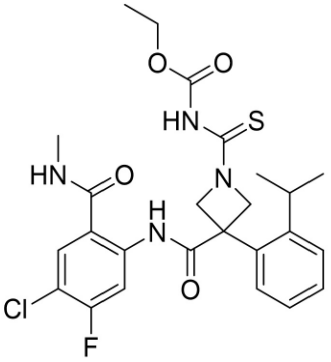
Example	Structural formula	Analysis data	Raw material

281-(a)		Mass spectrum (DUIS, m/z): 487 $[M+H]^+$ Retention time (LCMS conditions 1): 1.201 min	Example 33-(b)

[0396] Example 287-(a)

Production of ethyl (3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonothioyl)carbamate

[C210]



0.036 ml of ethoxycarbonyl isothiocyanate was added to a dichloromethane (2.5 ml) solution of 100 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at room temperature for two hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 122 mg of a title compound as a slightly yellow solid.

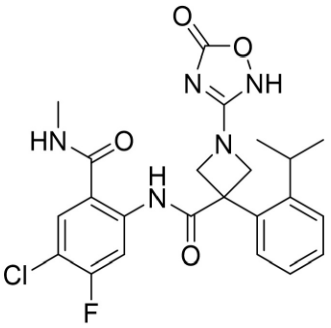
Mass spectrum (DUIS, m/z): 535 $[M+H]^+$

Retention time (LCMS conditions 1): 1.519 min.

[0397] Example 287-(b)

Production of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-2,5-dihydro-1,2,4-oxadiazol-3-yl)azetidine-3-carboxamide

[C211]



0.011 ml of iodomethane was added to a N,N-dimethylformamide (1.1 ml) solution of 60 mg of ethyl (3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonothioyl)carbamate produced in Example 287-(a) at room temperature under an argon gas flow and stirred at room temperature for nine hours. A mixture was left to stand at room temperature for 15 hours and stirred at room temperature for two hours. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 3 mg of hydroxylamine hydrochloride was added to a pyridine (0.4 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at 60°C for nine hours. The reaction mixture was concentrated under reduced pressure, water was then added thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 9 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 488 $[M+H]^+$

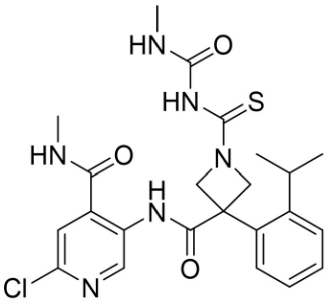
Retention time (LCMS conditions 2): 1.327 min.

[0398] Example 288-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-

carboxamido)-N-methylisonicotinamide

[C212]



An ethyl acetate (1 ml) solution of 0.14 ml of 4-chlorophenyl chloroformate was added to an ethyl acetate (2.5 ml) solution of 107 mg of potassium thiocyanate at 0°C under an argon gas flow and stirred at 0°C for two hours. A mixture was left to stand at room temperature for 15 hours and then stirred at 40°C for nine hours. The mixture was left to stand at room temperature for 15 hours and then stirred at 40°C for 4.5 hours. A reaction mixture was concentrated under reduced pressure, and 1 ml of dichloromethane was added thereto. 0.192 ml of the obtained solution was added to a dichloromethane (1.4 ml) solution of 60 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at 0°C under an argon gas flow, stirred at 0°C for 30 minutes, and stirred at room temperature for 30 minutes. Next, 0.215 ml of a 2M methylamine/tetrahydrofuran solution was added thereto at room temperature and stirred at room temperature for two hours. 0.350 ml of a 2M methylamine/tetrahydrofuran solution was added thereto and stirred at room temperature for one hour. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone) to obtain 48 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 503 $[M+H]^+$

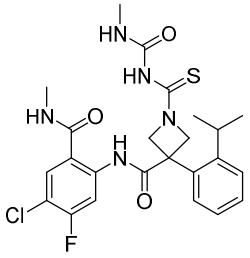
Retention time (LCMS conditions 1): 1.271 min.

[0399] Example 289-(a)

A compound shown in Table 88 below was obtained by treating a corresponding raw material compound in the same manner as in Example 288-(a).

[Table 88]

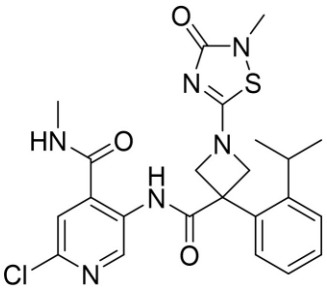
Table 88

Example	Structural formula	Analysis data	Raw material
289-(a)		Mass spectrum (DUIS, m/z): 520 $[M+H]^+$ Retention time (LCMS conditions 1): 1.463 min	Example 11-(b)

[0400] Example 288-(b)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C213]



160 mg of bromine was added to 1 ml of dichloromethane. 0.23 ml of the obtained solution was added to a dichloromethane (0.8 ml) solution of 48 mg of 2-chloro-5-(3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in Example 288-(a) at room temperature under an argon gas flow and stirred at room temperature for 15 minutes. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of

acetonitrile/water and lyophilized to obtain 33 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 501 $[M+H]^+$

Retention time (LCMS conditions 1): 1.093 min.

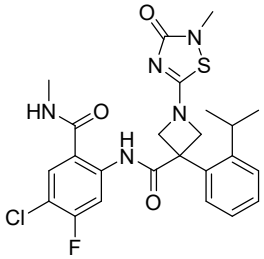
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.44 (s, 1H), 9.33 (s, 1H), 8.96 - 8.89 (m, 1H), 7.68 (s, 1H), 7.53 - 7.48 (m, 1H), 7.45 - 7.33 (m, 3H), 4.87 - 4.71 (m, 2H), 4.68 - 4.51 (m, 2H), 3.10 (s, 3H), 2.60 (d, J = 4.5 Hz, 3H), 2.40 - 2.31 (m, 1H), 1.06 (d, J = 6.5 Hz, 6H)

[0401] Example 289-(b)

A compound shown in Table 89 below was obtained by treating a corresponding raw material compound in the same manner as in Example 288-(b).

[Table 89]

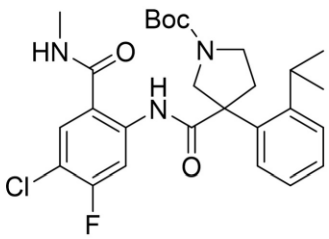
Table 89

Example	Structural formula	Analysis data	Raw material
289-(b)		Mass spectrum (ESI, m/z): 518 $[M+H]^+$ Retention time (LCMS conditions 2): 1.305 min	Example 289-(a)

[0402] Example 290-(a)

Production of tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)pyrrolidine-1-carboxylate

[C214]



0.015 ml of oxalyl chloride and 0.001 ml of N,N-dimethylformamide were added to a dichloromethane (1 ml) solution of 50 mg of 1-(tert-butoxycarbonyl)-3-(2-isopropylphenyl)pyrrolidine-3-carboxylate produced in Reference Example 290-(d) at room temperature under an argon gas flow and

stirred at room temperature for one hour. A reaction mixture was concentrated under reduced pressure. 28 mg of 2-amino-5-chloro-4-fluoro-N-methylbenzamide produced in the same manner as in Reference Example 11-(a) and 0.013 ml of pyridine were added to a dichloromethane (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow, stirred at room temperature for 1.5 hours, and stirred at 45°C for 7.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 36 mg of a title compound as a white foamy substance.

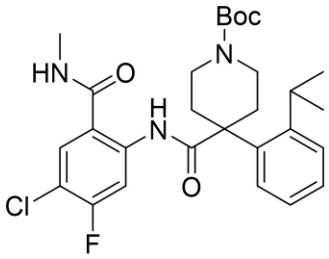
Mass spectrum (ESI, m/z): 516 $[M-H]^-$

Retention time (LCMS conditions 2): 1.763 min.

[0403] Example 291-(a)

Production of tert-butyl 4-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate

[C215]



0.015 ml of oxalyl chloride and 0.001 ml of N,N-dimethylformamide were added to a dichloromethane (1 ml) solution of 50 mg of 1-(tert-butoxycarbonyl)-4-(2-isopropylphenyl)piperidine-4-carboxylic acid as described in WO 2019/234115 at room temperature under an argon gas flow and stirred at room temperature for 40 minutes. A reaction mixture was concentrated under reduced pressure. 27 mg of 2-amino-5-chloro-4-fluoro-N-methylbenzamide produced in the same manner as in Reference Example 11-(a) and 0.046 ml of N,N-diisopropylethylamine were added to a dichloromethane (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow, stirred at room temperature for one hour, and stirred at 45°C for 12 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain

38 mg of a title compound as a white foamy substance.

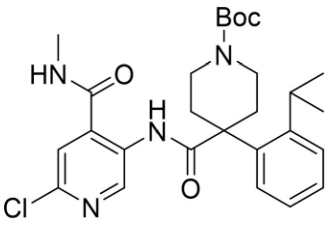
Mass spectrum (ESI, m/z): 530 $[M-H]^-$

Retention time (LCMS conditions 2): 1.855 min.

[0404] Example 292-(a)

Production of tert-butyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate

[C216]



An operation of adding toluene to 57 mg of 1-(tert-butoxycarbonyl)-4-(2-isopropylphenyl)piperidine-4-carboxylic acid as described in WO 2019/234115 and concentrating a mixture under reduced pressure was performed. A concentrated residue and a dichloromethane (1 ml) solution of 0.014 ml of pyridine was added dropwise to a dichloromethane (1 ml) solution of 0.015 ml of oxalyl chloride and 0.001 ml of N,N-dimethylformamide at room temperature under an argon gas flow and stirred at room temperature for one hour. Next, 28 mg of 5-amino-2-chloro-N-methylisonicotinamide produced in the same manner as in Reference Example 33-(a) and 0.014 ml of pyridine were added thereto at room temperature and stirred at 45°C for 19.5 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 32 mg of a title compound as a white foamy substance.

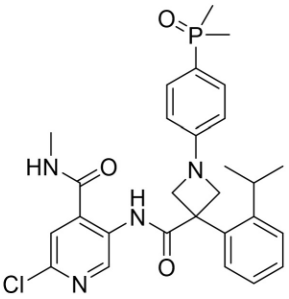
Mass spectrum (ESI, m/z): 513 $[M-H]^-$

Retention time (LCMS conditions 2): 1.654 min.

[0405] Example 311-(a)

Production of 2-chloro-5-(1-(4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C217]



7.4 mg of [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) was added to a 1,4-dioxane (0.8 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b), 27 mg of (4-bromophenyl)dimethylphosphine oxide, and 33 mg of tripotassium phosphate at room temperature under an argon gas flow and stirred at 110°C for eight hours. Water was added to the reaction mixture thus obtained allowed to cool to room temperature, and the reaction mixture was extracted with ethyl acetate. The resulting organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 35 mg of the title compound as a white solid.

Mass spectra (DUIS, m/z): 539 $[M+H]^+$

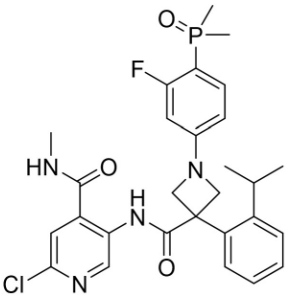
Retention time (LCMS conditions 8): 1.161 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.71 (s, 1H), 9.38 (s, 1H), 9.03 - 8.93 (m, 1H), 7.71 (s, 1H), 7.59 - 7.50 (m, 3H), 7.42 - 7.29 (m, 3H), 6.69 - 6.63 (m, 2H), 4.68 (br d, J = 7.4 Hz, 2H), 4.29 (br d, J = 7.4 Hz, 2H), 2.69 - 2.55 (m, 4H), 1.55 (d, J = 13.2Hz, 6H), 1.09 (d, J = 6.7 Hz, 6H)

[0406] Example 312-(a)

Production of 2-chloro-5-(1-(4-(dimethylphosphoryl)-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C218]



A 1,4-dioxane (1 ml)/water (0.2 ml) suspension of 40 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a), 26 mg of (4-bromo-2-fluorophenyl)dimethylphosphine oxide, and 60 mg of tripotassium phosphate was degassed and substituted with nitrogen. 9 mg of [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) was added thereto at room temperature under an argon gas flow and stirred at 110°C for eight hours. Water was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and filtered. DNH silica gel was added to a filtrate at room temperature, stirred at room temperature for 30 minutes, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 39 mg of a title compound as a white solid.

Mass spectrum(DUIS, m/z): 557 $[M+H]^+$

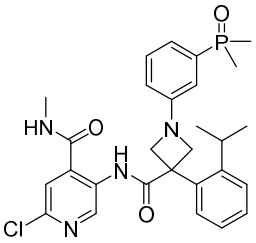
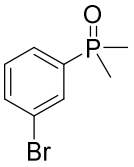
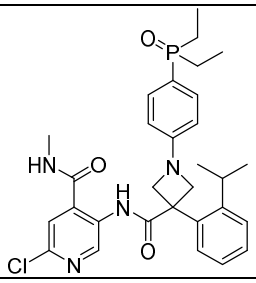
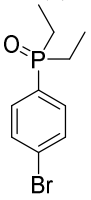
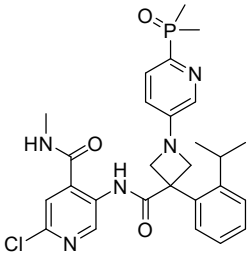
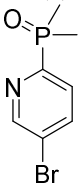
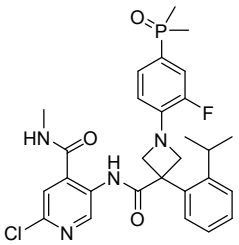
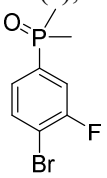
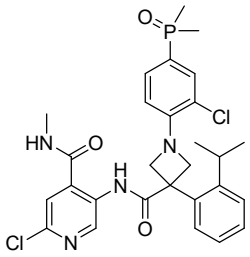
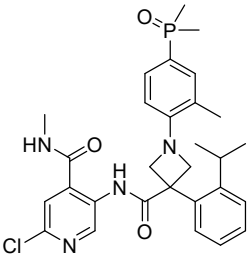
Retention time (LCMS conditions 8): 1.238 min.

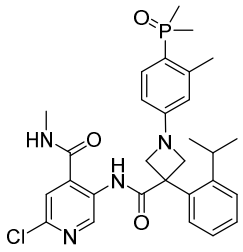
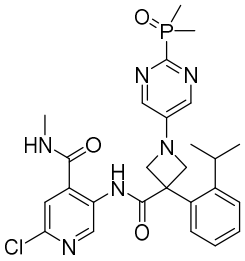
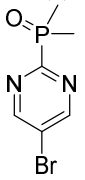
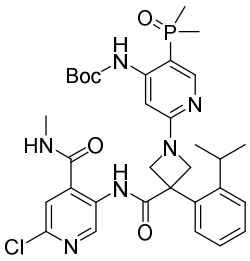
[0407] Example 369-(a) and the like

Compounds shown in Table 90 below were obtained by treating corresponding raw material compounds in the same manner as in Example 312-(a).

[Table 90]

Table 90

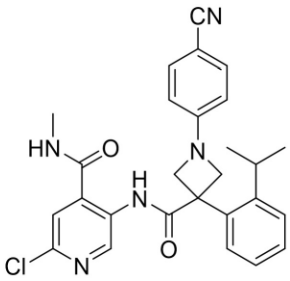
Example	Structural formula	Analysis data	Raw material
369-(a)		Mass spectrum (DUIS, m/z): 539 $[M+H]^+$ Retention time (LCMS conditions 8): 1.184 min	Example 39-(a), 
370-(a)		Mass spectrum (DUIS, m/z): 567 $[M+H]^+$ Retention time (LCMS conditions 8): 1.272 min	Example 39-(a), 
371-(a)		Mass spectrum (DUIS, m/z): 540 $[M+H]^+$ Retention time (LCMS conditions 8): 1.088 min	Example 39-(a), 
376-(a)		Mass spectrum (DUIS, m/z): 557 $[M+H]^+$ Retention time (LCMS conditions 8): 1.202 min	Example 39-(a), 
377-(a)		Mass spectrum (DUIS, m/z): 573 $[M+H]^+$ Retention time (LCMS conditions 8): 1.242 min	Example 39-(a), Reference Example 377-(a)
378-(a)		Mass spectrum (DUIS, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 8): 1.201 min	Example 39-(a), Reference Example 378-(a)

379-(a)		Mass spectrum (DUIS, m/z): 553 $[M+H]^+$ Retention time (LCMS conditions 8): 1.205 min	Example 39-(a), Reference Example 379-(a)
380-(a)		Mass spectrum (DUIS, m/z): 541 $[M+H]^+$ Retention time (LCMS conditions 8): 1.053 min	Example 39-(a), 
381-(a)		Mass spectrum (DUIS, m/z): 655 $[M+H]^+$ Retention time (LCMS conditions 7): 0.822 min	Example 39-(a), Reference Example 381-(a)

[0408] Example 313-(a)

Production of 2-chloro-5-(1-(4-cyanophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C219]



52 mg of 4-bromobenzonitrile, 168 mg of cesium carbonate, and 22 mg of (2-dicyclohexylphosphino-2',6'-diisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: RuPhos Pd G3) were added to a 1,4-dioxane (2 ml) solution of 101 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at 100°C for eight hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium

sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 58 mg of a title compound as a yellow foamy substance.

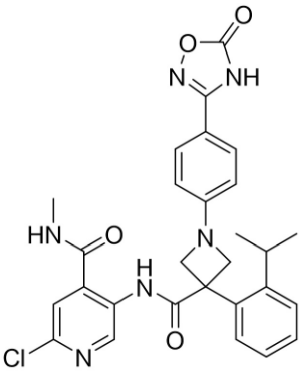
Mass spectrum(DUIS, m/z): 488[M+H]$^+$

Retention time (LCMS conditions 7): 0.934 min.

[0409] Example 313-(b)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide

[C220]



0.042 ml of a 50% hydroxylamine aqueous solution was added to a dimethyl sulfoxide (1.5 ml) solution of 35 mg of 2-chloro-5-(1-(4-cyanophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in Example 313-(a) at room temperature under an argon gas flow and stirred at 80°C for seven hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 24 mg of 1,1'-carbonyldiimidazole and 0.027 ml of 1,8-diazabicyclo[5.4.0]-7-undecene were added to a dimethyl sulfoxide (1.5 ml) solution of a concentrated residue at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. 1N hydrochloric acid was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A

concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 10 mg of a title compound as a white solid.

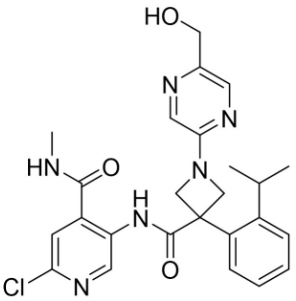
Mass spectrum (DUIS, m/z): 547 $[M+H]^+$

Retention time (LCMS conditions 8): 1.363 min.

[0410] Example 317-(a)

Production of 2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide

[C221]



An ethanol (0.15 ml) solution of 4.3 mg of sodium borohydride was added to a tetrahydrofuran (0.53 ml) solution of 30 mg of methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate produced in the same manner as in Example 295-(a) at 0°C under an argon gas flow, stirred at 0°C for 10 minutes, and then stirred at 40°C for one hour. 2M hydrochloric acid was added to a reaction mixture, a saturated sodium carbonate aqueous solution was then added thereto, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:acetone). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 8 mg of a title compound as a white solid.

Mass spectra (DUIS, m/z): 495 $[M+H]^+$

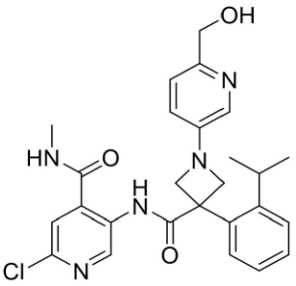
Retention time (LCMS conditions 8): 1.085 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.65 (s, 1H), 9.36 (s, 1H), 9.01 - 8.92 (m, 1H), 8.14 - 8.11 (m, 1H), 7.97 (d, J = 1.3 Hz, 1H), 7.70 (s, 1H), 7.55 - 7.49 (m, 1H), 7.43 - 7.31 (m, 3H), 5.26 (t, J = 5.8 Hz, 1H), 4.78 (br d, J = 8.2 Hz, 2H), 4.50 - 4.43 (m, 4H), 2.63 (d, J = 4.5 Hz, 3H), 2.59 - 2.53 (m, 1H), 1.09 (d, J = 6.7 Hz, 6H)

[0411] Example 320-(c)

Production of 2-chloro-5-(1-(6-(hydroxymethyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C222]



0.024 ml of triethylamine and 0.023 ml of isobutyl chloroformate were added to a tetrahydrofuran (1 ml) solution of 83 mg of 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid produced in Example 320-(b) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. A reaction mixture was filtered, a water (0.05 ml) solution of 13 mg of sodium borohydride was added to a filtrate and stirred at room temperature for one hour. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed successively with a saturated sodium bicarbonate aqueous solution and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; Xselect CSH C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to

obtain 14 mg of a title compound as a white solid.

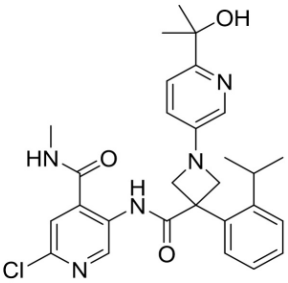
Mass spectrum (DUIS, m/z): 494 $[M+H]^+$

Retention time (LCMS conditions 8): 0.872 min.

[0412] Example 321-(a)

Production of 2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide

[C223]



1.7 ml of a 1M methylmagnesium bromide/tetrahydrofuran solution was added to a tetrahydrofuran (1 ml) suspension of 90 mg of methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate produced in the same manner as in Example 320-(a) at 0°C under an argon gas flow and stirred at room temperature for 1.5 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) and then purified by high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 21 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 522 $[M+H]^+$

Retention time (LCMS conditions 8): 0.953 min.

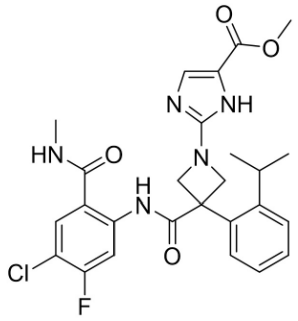
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.82 (br s, 1H), 9.38 (s, 1H), 9.01 (br s, 1H), 7.86

(d, J = 2.5 Hz, 1H), 7.72 (s, 1H), 7.53 - 7.42 (m, 2H), 7.41 - 7.24 (m,3H), 7.04 - 6.95 (m, 1H), 5.02 (br s, 1H), 4.72 - 4.60 (m, 2H), 4.30 - 4.16 (m, 2H), 2.73 - 2.59 (m, 4H), 1.38 (s, 6H), 1.08 (d, J = 6.8 Hz, 6H)

[0413] Example 322-(a)

Production of methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylate

[C224]



26 mg of sodium hydride [manufactured by FUJIFILM Wako Pure Chemical Industries, Ltd., oily, 60 wt%] was added to a tetrahydrofuran (2 ml) solution of 85 mg of methyl 2-bromo-1H-imidazole-5-carboxylate at 0°C under an argon gas flow and stirred at 0°C for 30 minutes. Next, 0.111 ml of 2-(chloromethoxy)ethyltrimethylsilane was added thereto at 0°C and stirred at room temperature for 30 minutes. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product, 297 mg of cesium carbonate, and 19 mg of (2-dicyclohexylphosphino-2',6'-diisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: RuPhosPdG3) were added to a 1,4-dioxane (1.5 ml) suspension of 100 mg of N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropyl phenyl)azetidine-3-carboxamide hydrochloride produced in the same manner as in Example 11-(b) at room temperature under an argon gas flow and stirred at 100°C for eight hours. A mixture was left to stand at room

temperature overnight. 19 mg of (2-dicyclohexylphosphino-2',6'-diisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: RuPhosPdG3) was added thereto at room temperature and stirred at 100°C for 10 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 2.5 ml of a 4M hydrogen chloride/ethyl acetate solution was added to an ethyl acetate (2 ml) solution of the resulting purified product at room temperature under an argon gas flow, stirred at room temperature for 16 hours, stirred at 60°C for six hours, and left to stand at room temperature overnight. 2 ml of a 4M hydrogen chloride/ethyl acetate solution was added thereto at room temperature and stirred at 60°C for six hours. The reaction mixture was concentrated under reduced pressure. A saturated sodium bicarbonate aqueous solution was added to the obtained residue, and the residue was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) to obtain 29 mg of a title compound as a slightly yellow solid.

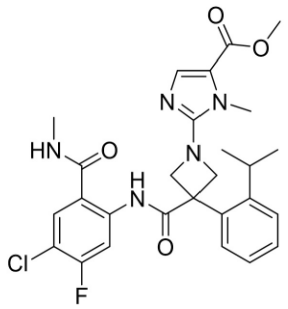
Mass spectrum (DUIS, m/z): 528 $[M+H]^+$

Retention time (LCMS conditions 7): 0.687 min.

[0414] Example 323-(a)

Methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylate

[C225]

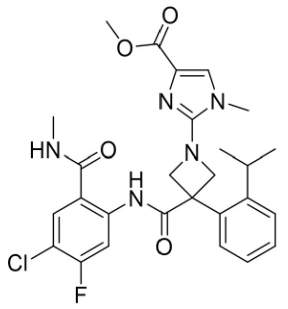


and

Example 324-(a)

Production of methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylate

[C226]



68 mg of potassium carbonate and 0.026 ml of iodomethane were added to a N,N-dimethylformamide (2 ml) solution of 200 mg of methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylate produced in the same manner as in Example 322-(a) at room temperature under an argon gas flow and stirred at room temperature for 23 hours. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed successively with water and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was separated and purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). A fraction eluting earlier was concentrated under reduced pressure, whereby 68 mg of a compound of Example 323-(a) was obtained as a slightly yellow oily substance. In addition, a fraction eluting later was concentrated under reduced

pressure, whereby 74 mg of a compound of Example 324-(a) was obtained as a slightly yellow oily substance.

(Example 323-(a))

Mass spectrum (DUIS, m/z): 542 $[M+H]^+$

Retention time (LCMS conditions 7): 0.811 min.

(Example 324-(a))

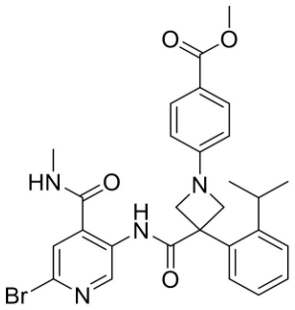
Mass spectrum (DUIS, m/z): 542 $[M+H]^+$

Retention time (LCMS conditions 7): 0.767 min.

[0415] Example 325-(a)

Production of methyl 4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate

[C227]



0.011 ml of pyridine, 0.002 ml of N,N-dimethylformamide, and 0.012 ml of oxalyl chloride were added to a dichloromethane (1 ml) solution of 50 mg of 3-(2-isopropylphenyl)-1-(4-(methoxycarbonyl)phenyl)azetidine-3-carboxylic acid produced in Reference Example 325-(c) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. A reaction mixture was concentrated under reduced pressure. 30 mg of 5-amino-2-bromo-N-methylisonicotinamide produced in the same manner as in Reference Example 25-(b), and 0.011 ml of pyridine were added to a dichloromethane (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for 18 hours. Water was added to the reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with water,

dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 41 mg of a title compound as a white foamy substance.

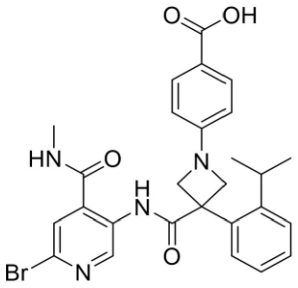
Mass spectrum (DUIS, m/z): 565, 567 $[M+H]^+$

Retention time (LCMS conditions 7): 0.980 min.

[0416] Example 325-(b)

Production of 4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid

[C228]



A water (0.5 ml) solution of 10 mg of lithium hydroxide monohydrate was added to a tetrahydrofuran (1.5 ml)/methanol (0.5 ml) solution of 41 mg of methyl 4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate produced in Example 325-(a) at room temperature under an argon gas flow, stirred at room temperature for two hours, and stirred at 40°C for 14.5 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 34 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 551, 553 $[M+H]^+$

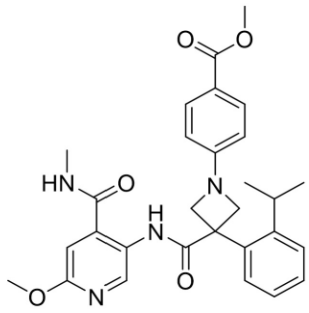
Retention time (LCMS conditions 8): 1.358 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 9.33 (s, 1H), 7.83 - 7.75 (m, 3H), 7.55 - 7.49 (m, 1H), 7.44 - 7.31 (m, 3H), 6.61 (d, J = 8.9 Hz, 2H), 4.75 - 4.65 (m, 2H),4.38 - 4.27 (m, 2H), 2.63 (s, 3H), 2.59 - 2.47 (m, 1H), 1.08 (d, J = 6.7 Hz, 6H)

[0417] Example 326-(a)

Production of methyl 4-(3-(2-isopropylphenyl)-3-((6-methoxy-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoate

[C229]



0.011 ml of pyridine, 0.002 ml of N,N-dimethylformamide, and 0.012 ml of oxalyl chloride were added to a dichloromethane (1 ml) solution of 50 mg of 3-(2-isopropylphenyl)-1-(4-(methoxycarbonyl)phenyl)azetidine-3-carboxylic acid produced in the same manner as in Reference Example 325-(c) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. A reaction mixture was concentrated under reduced pressure. 23 mg of 5-amino-2-methoxy-N-methylisonicotinamide produced in Reference Example 326-(a) and 0.011 ml of pyridine were added to a dichloromethane (1 ml) solution of the obtained concentrated residue at room temperature under an argon gas flow and stirred at room temperature for five hours. Water was added to the reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate) to obtain 38 mg of a title compound as a slightly yellow oily substance.

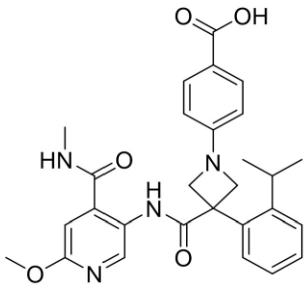
Mass spectrum (DUIS, m/z): 517 $[M+H]^+$

Retention time (LCMS conditions 7): 0.935 min.

[0418] Example 326-(b)

Production of 4-(3-(2-isopropylphenyl)-3-((6-methoxy-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoic acid

[C230]



A water (0.5 ml) solution of 10 mg of lithium hydroxide monohydrate was added to a tetrahydrofuran (1.5 ml)/methanol (0.5 ml) solution of 38 mg of methyl 4-(3-(2-isopropylphenyl)-3-((6-methoxy-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoate produced in Example 326-(a) at room temperature under an argon gas flow, stirred at 40°C for five hours, and stirred at 50°C for 10 hours. A saturated ammonium chloride aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 28 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 503 $[M+H]^+$

Retention time (LCMS conditions 8): 1.255 min.

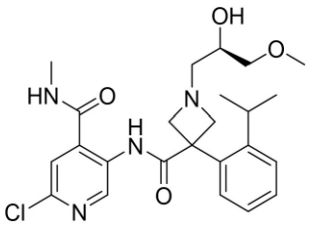
^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 8.97 (s, 1H), 7.80 (d, J = 8.8 Hz, 2H), 7.55 - 7.48 (m, 1H), 7.44 - 7.29 (m, 3H), 6.96 (s, 1H), 6.61 (d, J = 8.8 Hz, 2H), 4.73 - 4.63 (m, 2H), 4.37 - 4.24 (m, 2H), 3.85 (s, 3H), 2.64 - 2.48 (m, 4H), 1.09 (d, J = 6.7 Hz, 6H)

[0419] Example 335-(a)

Production of (R)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-

carboxamido)-N-methylisonicotinamide

[C231]



0.011 ml of (R)-glycidyl methyl ether and 0.032 ml of triethylamine were added to an ethanol (0.5 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for 27 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 24 mg of a title compound as a white solid.

Mass spectrum(DUIS, m/z): 475 $[M+H]^+$

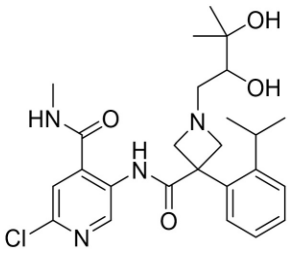
Retention time (LCMS conditions 8): 0.777 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 9.34 (s, 1H), 7.71 (s, 1H), 7.36 - 7.19 (m, 3H), 7.18 - 7.12 (m, 1H), 4.17 - 4.08 (m, 2H), 3.70 - 3.61 (m, 1H), 3.56 - 3.42 (m, 2H), 3.30 - 3.20 (m, 5H), 2.76 (s, 3H), 2.64 - 2.49 (m, 2H), 2.47 - 2.39 (m, 1H), 1.12 - 1.01 (m, 6H)

[0420] Example 340-(a)

Production of 2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C232]



0.032 ml of triethylamine and 12 mg of 2-(oxiran-2-yl)propan-2-ol were added to an ethanol (0.4 ml)/N,N-dimethylformamide (0.1 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow, stirred at room temperature for eight hours, and left to stand at room temperature for 15 hours. The resulting mixture was further stirred at room temperature for eight hours and left to stand at room temperature for 16 hours. Water was added to the reaction mixture thus obtained, and the reaction mixture was extracted with ethyl acetate. The resulting organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting concentrated residue was purified by medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution) and subjected to high performance liquid chromatography (column: Xselect CSH C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing the target substance was lyophilized to obtain 18 mg of the target compound as a white solid.

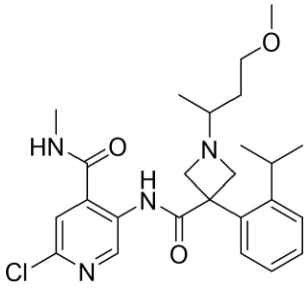
Mass spectra (DUIS, m/z): 489 $[M+H]^+$

Retention time (LCMS conditions 9): 0.520 min.

[0421] Example 344-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methoxybutan-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C233]



7 mg of 4-methoxybutan-2-one was added to a tetrahydrofuran (1 ml) solution of 20 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. Next, 16 mg of sodium triacetoxyborohydride was added thereto at room temperature and stirred at room temperature for three hours. 16 mg of sodium triacetoxyborohydride was added thereto at room temperature and stirred at room temperature for one hour. A saturated sodium bicarbonate aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate) and then subjected to medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 19 mg of a target compound as a white solid.

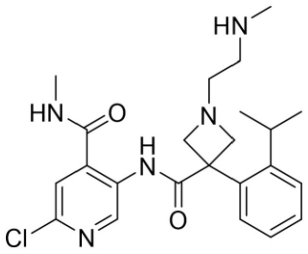
Mass spectrum (ESI, m/z): 473 $[M+H]^+$

Retention time (LCMS conditions 3): 0.708 min.

[0422] Example 345-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(methylamino)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C234]



11 mg of 2-chloro-N-methylethan-1-amine hydrochloride and 0.017 ml of N,N-diisopropylethylamine were added to an ethanol (1 ml) suspension of 25 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 33-(b) in an ice bath under an argon gas flow, stirred in the ice bath for three hours, stirred at 60°C for three hours, left to stand at room temperature for 14 hours, and stirred at 60°C for nine hours. A 10% citric acid aqueous solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 30 mg of a title compound as a white foamy substance.

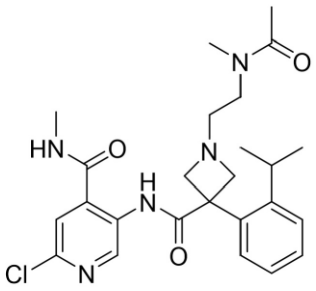
Mass spectrum (ESI, m/z): 444 $[M+H]^+$

Retention time (LCMS conditions 7): 0.440 min.

[0423] Example 345-(b)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylacetamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C235]



0.014 ml of triethylamine and 0.0095 ml of acetic anhydride were added to a dichloromethane (1 ml) solution of 30 mg of 2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(methylamino)ethyl)azetidine-3-

carboxamido)-N-methylisonicotinamide produced in Example 345-(a) at room temperature under an argon gas flow and stirred at room temperature for 30 minutes. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DNH silica gel, eluting solvent; hexane:ethyl acetate) and then subjected to medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 23 mg of a title compound as a white solid.

Mass spectrum (ESI, m/z): 486 $[M+H]^+$

Retention time (LCMS conditions 3): 0.512 min.

[0424] Example 348-(a)

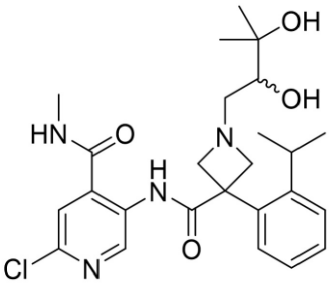
Production of 2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide (enantiomer 1)

and

Example 349-(a)

Production of 2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide (enantiomer 2)

[C236]



101 mg of 2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 340-(a) was optically split by high performance liquid chromatography (column: CHIRALPAK IF, mobile phase: dichloromethane (containing 0.2% of diethylamine):ethanol = 99:1). A fraction containing an enantiomer eluting earlier was concentrated under reduced pressure and subjected to high performance

liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing the target substance was lyophilized to obtain 27 mg of a compound of Example 348-(a) as a white solid. In addition, a fraction containing the enantiomer eluting later was concentrated under reduced pressure and subjected to high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), a fraction containing the target substance was lyophilized to obtain 37 mg of a compound of Example 349-(a) as a white solid.

(High performance liquid chromatography analysis)

Column: CHIRALPAK IF 4.6 × 150 mm

Mobile phase: Dichloromethane (containing 0.2% of diethylamine)

Flow rate: 1 mL/min.

Temperature: Room temperature

Detection wavelength: 254 nm

Retention time: 3.78 min in Example 348-(a) and 4.44 min in Example 349-(a)

(Example 348-(a))

Mass spectra (DUIS, m/z): 489 $[M+H]^+$

Retention time (LCMS conditions 8): 0.736 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 9.33 (s, 1H), 7.69 (s, 1H), 7.41 - 7.11 (m, 4H), 4.24 - 4.14 (m, 2H), 3.67 - 3.49 (m, 2H), 3.33 - 3.26 (m, 1H), 2.80 - 2.70 (m, 4H), 2.61 - 2.44 (m, 2H), 1.13 - 1.04 (m, 9H), 1.02 (s, 3H)

(Example 349-(a))

Mass spectra (DUIS, m/z): 489 $[M+H]^+$

Retention time (LCMS conditions 8): 0.734 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6+D_2O) δ: 9.34 (s, 1H), 7.70 (s, 1H), 7.39 - 7.13 (m, 4H), 4.25 - 4.14 (m, 2H), 3.64 - 3.48 (m, 2H), 3.32 - 3.25 (m, 1H), 2.79 - 2.70 (m, 4H), 2.62 - 2.42 (m, 2H), 1.13 - 1.03 (m, 9H), 1.01 (s, 3H)

[0425] Example 350-(a)

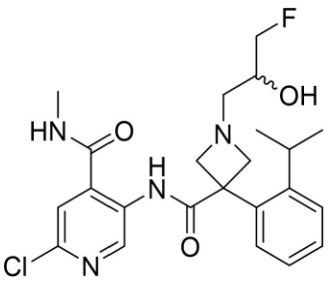
Production of 2-chloro-5-(1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide (enantiomer 1)

and

Example 351-(a)

Production of 2-chloro-5-(1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide (enantiomer 2)

[C237]



66 mg of 2-chloro-5-(1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide produced in the same manner as in Example 196-(a) was optically split by high performance liquid chromatography (column: CHIRALPAK IF, mobile phase: dichloromethane (containing 0.2% of diethylamine):ethanol = 99:1). A fraction containing an enantiomer eluting earlier was concentrated under reduced pressure and subjected to high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 22 mg of a compound of Example 350-(a) as a white solid. In addition, a fraction containing an enantiomer eluting later was concentrated under reduced pressure and subjected to high performance liquid chromatography (column; XBridge C18, mobile phase; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), a fraction containing a target substance was lyophilized to obtain 23 mg of a compound of Example 351-(a) as a white solid.

(High performance liquid chromatography analysis)

Column: CHIRALPAK IF 4.6 × 150 mm

Mobile phase A: diethylamine: ethanol = 1: 500

Mobile phase B: diethylamine: ethanol: hexane = 1: 10: 490

Gradient: 0 to 10 min; A/B= 100/0 → 50/50, 10 min to 15 min; A/B = 50/50

Flow rate: 1 mL/min.

Temperature: Room temperature

Detection wavelength: 254 nm

Retention time: 8.43 min in Example 350-(a) and 9.06 min in Example 351-(a)

(Example 350-(a))

Mass spectra (DUIS, m/z): 463 $[M+H]^+$

Retention time (LCMS conditions 8): 0.734 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.43 (br s, 1H), 9.38 (s, 1H), 9.18 - 9.01 (m, 1H), 7.75 (s, 1H), 7.33 - 7.18 (m, 3H), 7.17 - 7.12 (m, 1H), 5.13 - 4.98 (m, 1H), 4.48 - 4.21 (m, 2H), 4.18 - 4.08 (m, 2H), 3.81 - 3.67 (m, 1H), 3.53 - 3.45 (m, 2H), 2.76 (d, J = 4.5 Hz, 3H), 2.66 - 2.43 (m, 3H), 1.07 (d, J = 6.7 Hz, 6H)

(Example 351-(a))

Mass spectra (DUIS, m/z): 463 $[M+H]^+$

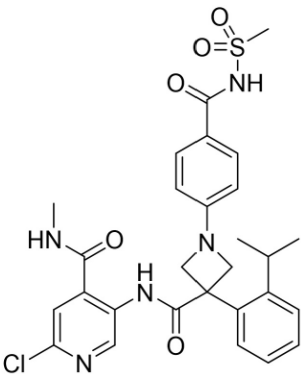
Retention time (LCMS conditions 8): 0.748 min.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.43 (br s, 1H), 9.38 (s, 1H), 9.16 - 9.03 (m, 1H), 7.75 (s, 1H), 7.33 - 7.18 (m, 3H), 7.17 - 7.12 (m, 1H), 5.12 - 4.99 (m, 1H), 4.49 - 4.20 (m, 2H), 4.18 - 4.08 (m, 2H), 3.82 - 3.66 (m, 1H), 3.53 - 3.46 (m, 2H), 2.76 (d, J = 4.4 Hz, 3H), 2.66 - 2.42 (m, 3H), 1.07 (d, J = 6.7 Hz, 6H)

[0426] Example 352-(a)

Production of 2-chloro-5-(3-(2-isopropylphenyl)-1-(4-((methylsulfonyl)carbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C238]



10 mg of methanesulfonamide, 23 mg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and 15 mg of 4-dimethylaminopyridine were added to a dichloromethane (1 ml) suspension of 30 mg of 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid produced in the same manner as in Example 110-(b) at room temperature under an argon gas flow, stirred at room temperature for eight hours, and left to stand at room temperature overnight. A reaction mixture was diluted with ethyl acetate, washed successively with 1N hydrochloric acid and saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 21 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 584 $[M+H]^+$

Retention time (LCMS conditions 8): 1.316 min.

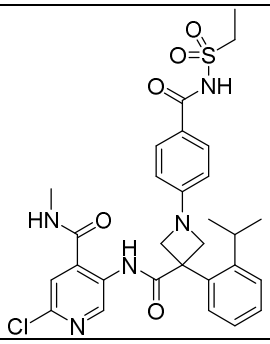
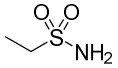
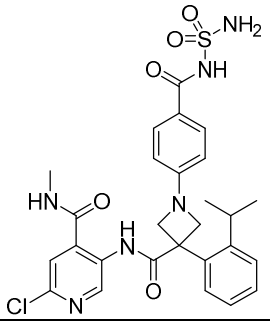
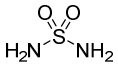
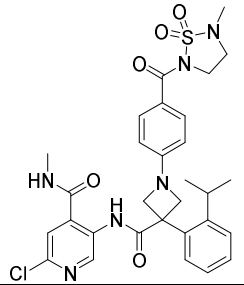
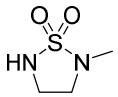
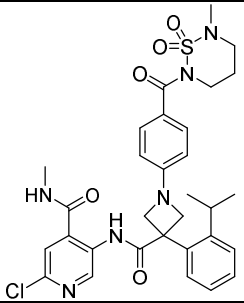
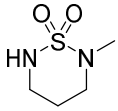
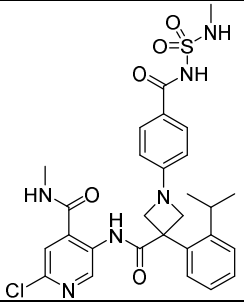
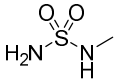
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.69 (br s, 1H), 10.66 (s, 1H), 9.37 (s, 1H), 9.00 - 8.94 (m, 1H), 7.86 - 7.81 (m, 2H), 7.71 (s, 1H), 7.55 - 7.50 (m, 1H), 7.42 - 7.31 (m, 3H), 6.61 - 6.56 (m, 2H), 4.72 (br d, J = 7.7 Hz, 2H), 4.36 (br d, J = 7.7 Hz, 2H), 3.28 (s, 3H), 2.64 (d, J = 4.5 Hz, 3H), 2.62 - 2.54 (m, 1H), 1.09 (d, J = 6.7 Hz, 6H)

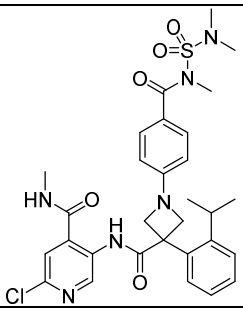
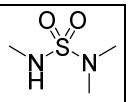
[0427] Example 353-(a) and the like

Compounds shown in Table 91 below were obtained by treating corresponding raw material compounds in the same manner as in Example 352-(a).

[Table 91]

Table 91

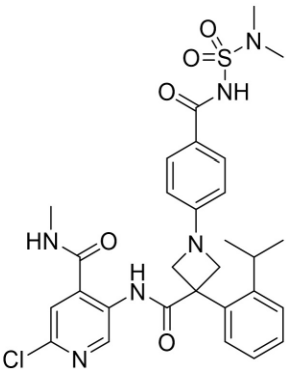
Example	Structural formula	Analysis data	Raw material
353-(a)		Mass spectrum (DUIS, m/z): 598 $[M+H]^+$ Retention time (LCMS conditions 8): 1.356 min	
354-(a)		Mass spectrum (DUIS, m/z): 585 $[M+H]^+$ Retention time (LCMS conditions 8): 1.235 min	
362-(a)		Mass spectrum (DUIS, m/z): 625 $[M+H]^+$ Retention time (LCMS conditions 8): 1.431 min	
363-(a)		Mass spectrum (DUIS, m/z): 639 $[M+H]^+$ Retention time (LCMS conditions 8): 1.500 min	
364-(a)		Mass spectrum (DUIS, m/z): 599 $[M+H]^+$ Retention time (LCMS conditions 8): 1.308 min	

365-(a)		Mass spectrum (DUIS, m/z): 627 $[M+H]^+$ Retention time (LCMS conditions 8): 1.497 min	

[0428] Example 355-(a)

Production of 2-chloro-5-(1-(4-((N,N-dimethylsulfamoyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide

[C239]



11 mg of N,N-dimethylsulfamide, 23 mg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and 15 mg of 4-dimethylaminopyridine were added to a dichloromethane (1 ml) suspension of 30 mg of 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid produced in the same manner as in Example 110-(b) at room temperature under an argon gas flow, stirred at room temperature for three hours, left to stand at room temperature overnight, and then further stirred at room temperature for three hours. A reaction mixture was diluted with ethyl acetate, washed successively with 1N hydrochloric acid and saturated saline, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 18 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 613 $[M+H]^+$

Retention time (LCMS conditions 8): 1.397 min.

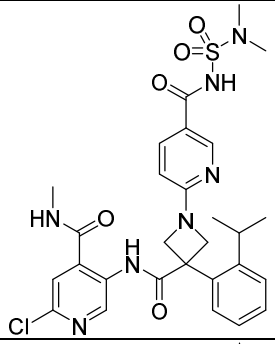
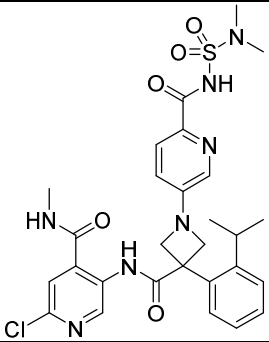
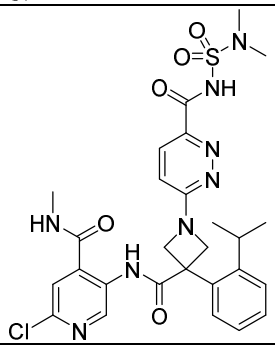
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 11.40 (br s, 1H), 10.66 (s, 1H), 9.37 (s, 1H), 9.01 - 8.93 (m, 1H), 7.86 - 7.80 (m, 2H), 7.71 (s, 1H), 7.55 - 7.51 (m, 1H), 7.43 - 7.31 (m, 3H), 6.62 - 6.56 (m, 2H), 4.71 (br d, J = 7.7 Hz, 2H), 4.35 (br d, J = 7.7 Hz, 2H), 2.84 (s, 6H), 2.64 (d, J = 4.6 Hz, 3H), 2.60 - 2.53 (m, 1H), 1.09 (d, J = 6.7 Hz, 6H)

[0429] Example 366-(a) and the like

Compounds shown in Table 92 below were obtained by treating corresponding raw material compounds in the same manner as in Example 355-(a).

[Table 92]

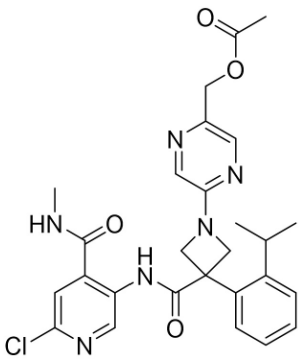
Table 92

Example	Structural formula	Analysis data	Raw material
366-(a)		Mass spectrum (DUIS, m/z): 614 $[M+H]^+$ Retention time (LCMS conditions 8): 1.242 min	Example 86-(b)
367-(a)		Mass spectrum (DUIS, m/z): 614 $[M+H]^+$ Retention time (LCMS conditions 8): 1.429 min	Example 320-(b)
368-(a)		Mass spectrum (DUIS, m/z): 615 $[M+H]^+$ Retention time (LCMS conditions 8): 1.278 min	Example 87-(b)

[0430] Example 356-(a)

Production of (5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl acetate

[C240]



0.0078 ml of pyridine and 0.009 ml of acetic anhydride were added to a dichloromethane (1 ml) solution of 40 mg of 2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 317-(a) at room temperature under an argon gas flow, stirred at room temperature for one hour, and left to stand at room temperature for 14 hours. Next, 1.5 mg of 4-dimethylaminopyridine was added thereto at room temperature and stirred at room temperature for 30 minutes. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 22 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 537 $[M+H]^+$

Retention time (LCMS conditions 8): 1.309 min.

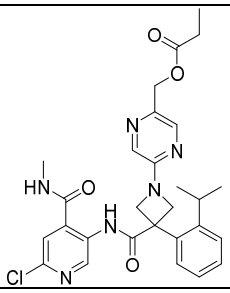
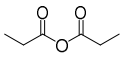
[0431] Example 357-(a)

A compound shown in Table 93 below was obtained by treating a corresponding raw material compound in the same manner as in Example 356-(a).

[Table 93]

Table 93

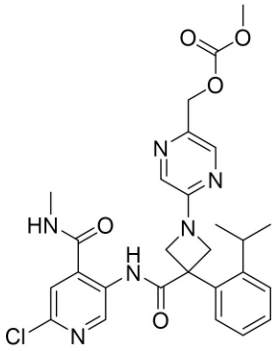
Example	Structural formula	Analysis data	Raw material

357-(a)		Mass spectrum (DUIS, m/z): 551 $[M+H]^+$ Retention time (LCMS conditions 8): 1.409 min	

[0432] Example 358-(a)

Production of (5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl methyl carbonate

[C241]



0.0078 ml of pyridine and 0.0075 ml of methyl chloroformate were added to a dichloromethane (1 ml) solution of 40 mg of 2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 317-(a) at room temperature under argon gas and stirred at room temperature for two hours. 0.016 ml of pyridine and 0.015 ml of methyl chloroformate were then added thereto at room temperature and stirred at room temperature for two hours. 0.024 ml of pyridine and 0.023 ml of methyl chloroformate were added thereto at room temperature and stirred at room temperature for 30 minutes. Water was added to a reaction mixture, and the reaction mixture was extracted with dichloromethane. An organic layer was washed with a 5% potassium hydrogen sulfate aqueous solution, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 28 mg of a title compound as a white solid. s

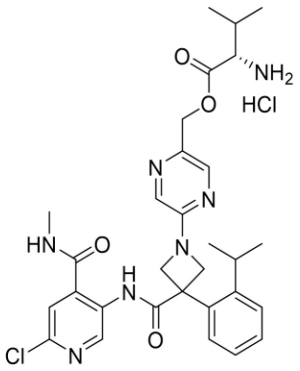
Mass spectrum (DUIS, m/z): 553 $[M+H]^+$

Retention time (LCMS conditions 8): 1.329 min.

[0433] Example 359-(a)

Production of (5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl L-valinate hydrochloride

[C242]



23 mg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride was added to a dichloromethane (1 ml) solution of 40 mg of 2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 317-(a), 23 mg of (tert-butoxycarbonyl)-L-valine, and 1.7 mg of 4-dimethylaminopyridine at room temperature under an argon gas flow, stirred at room temperature for three hours, and left to stand at room temperature for 17 hours. A reaction mixture was purified by medium pressure preparative chromatography (silica gel, eluting solvent; hexane:ethyl acetate). 0.56 ml of a 4M hydrogen chloride/1,4-dioxane solution was added to an ethyl acetate (0.28 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at room temperature for two hours. A reaction mixture was concentrated under reduced pressure. The obtained concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 24 mg of a title compound as a white solid.

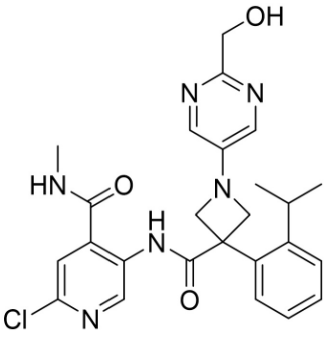
Mass spectrum (DUIS, m/z): 594 $[M+H]^+$

Retention time (LCMS conditions 8): 0.962 min.

[0434] Example 360-(a)

Production of 2-chloro-5-(1-(2-(hydroxymethyl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C243]



75 mg of tripotassium phosphate and 27 mg of (5-bromopyrimidin-2-yl)methanol were added to a 1,4-dioxane (1 ml)/water (0.2 ml) suspension of 50 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a) at room temperature, degassed, and substituted with nitrogen. 11 mg of [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) was added at room temperature under an argon gas flow, stirred at 110°C for eight hours, left to stand at room temperature for 14 hours, stirred at 110°C for 10 hours, left to stand at room temperature for 14 hours, and stirred at 110°C for 10 hours. Water was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and filtered. DNH silica gel was added to a filtrate at room temperature, stirred at room temperature for 30 minutes, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; hexane:ethyl acetate). The obtained purified product was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 26 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 495 $[M+H]^+$

Retention time (LCMS conditions 8): 1.057 min.

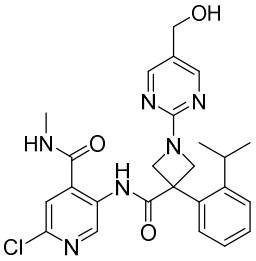
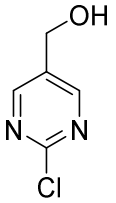
^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 10.80 (s, 1H), 9.38 (s, 1H), 9.04 - 8.95 (m, 1H), 8.17 (s, 2H), 7.72 (s, 1H), 7.51 - 7.45 (m, 1H), 7.43 - 7.28 (m, 3H), 5.10 (t, J = 6.2 Hz, 1H), 4.74 (br d, J = 7.6 Hz, 2H), 4.47 (d, J = 6.2 Hz, 2H), 4.37 (br d, J = 7.6 Hz, 2H), 2.69 - 2.55 (m, 4H), 1.09 (d, J = 6.7 Hz, 6H)

[0435] Example 361-(a)

A compound shown in Table 94 below was obtained by treating a corresponding raw material compound in the same manner as in Example 360-(a).

[Table 94]

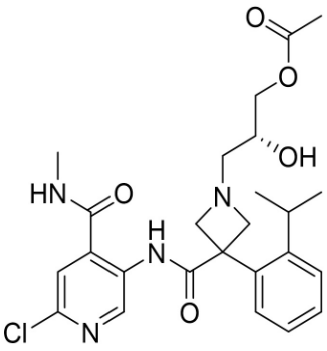
Table 94

Example	Structural formula	Analysis data	Raw material
361-(a)		Mass spectrum (DUIS, m/z): 495 $[M+H]^+$ Retention time (LCMS conditions 8): 1.057 min	

[0436] Example 372-(a)

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-hydroxypropylacetate

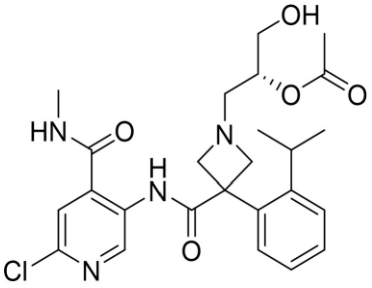
[C244]



Example 373-(a)

Production of (R)-1-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-hydroxypropan-2-yl acetate

[C245]

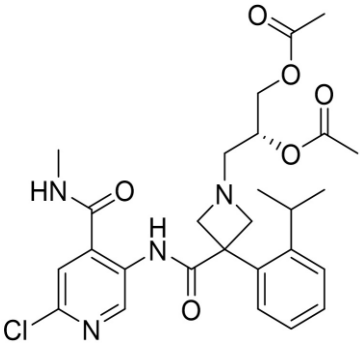


and

Example 374-(a)

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propane-1,2-diyl diacetate

[C246]



Reaction 1

0.0058 ml of pyridine and 0.0068 ml of acetic anhydride were added to a dichloromethane (1 ml) solution of 30 mg of (R)-2-chloro-5-(1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 175-(b) at room temperature under an argon gas flow, stirred at room temperature for seven hours, and left to stand at room temperature for 16 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was subjected to (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 18 mg of a mixture of Example 372-(a) and Example 373-(a) and 5 mg of Example 374-(a), which were target compounds, as white solids.

Reaction 2

0.0058 ml of pyridine and 0.0068 ml of acetic anhydride were added to a dichloromethane (1 ml) solution of 30 mg of (R)-2-chloro-5-(1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide produced in the same manner as in Example 175-(b) at room temperature under an argon gas flow, stirred at room temperature for three hours, and left to stand at room temperature for 69 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was subjected to (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 17 mg of a mixture of Example 372-(a) and Example 373-(a).

The mixtures of the reaction 1 and the reaction 2 were combined together and separated and purified by high performance liquid chromatography (column; XBridge C18, mobile phase; 10 mM ammonium bicarbonate aqueous solution:acetonitrile). Formic acid was added to a fraction eluting earlier, and the fraction was lyophilized to obtain 8 mg of Example 373-(a), which was a title compound, as a white solid. In addition, formic acid was added to a fraction eluting later and lyophilized to obtain 10 mg of Example 372-(a), which was a title compound, as a white solid.

(Example 372-(a))

Mass spectrum (DUIS, m/z): 503 $[M+H]^+$

Retention time (LCMS conditions 8): 0.793 min.

(Example 373-(a))

Mass spectrum (DUIS, m/z): 503 $[M+H]^+$

Retention time (LCMS conditions 8): 0.793 min.

(Example 374-(a))

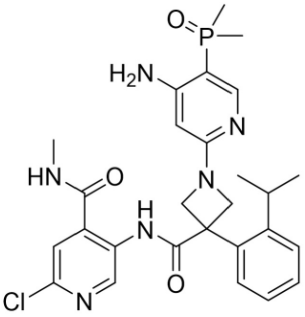
Mass spectrum (DUIS, m/z): 545 $[M+H]^+$

Retention time (LCMS conditions 8): 0.926 min.

[0437] Example 381-(b)

Production of 5-(1-(4-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide

[C247]



2 ml of trifluoroacetic acid was added to a dichloromethane (2 ml) solution of 109 mg of tert-butyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-(dimethylphosphoryl)pyridin-4-yl)carbamate produced in Example 381-(a) at room temperature under an argon gas flow and stirred at room temperature for 1.5 hours. A reaction mixture was concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), a saturated sodium hydrogencarbonate aqueous solution was added to a fraction containing a target substance, and the fraction was extracted with ethyl acetate. An organic layer was washed successively with a saturated sodium bicarbonate aqueous solution and a saturated saline aqueous solution, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 82 mg of a title compound as a slightly yellow foamy substance. A part (41 mg) of the obtained solid was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 38 mg of a title compound as a white solid.

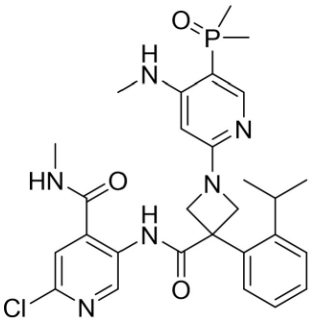
Mass spectrum (DUIS, m/z): 555 $[M+H]^+$

Retention time (LCMS conditions 8): 0.751 min.

[0438] Example 382-(a)

Production of 2-chloro-5-(1-(5-(dimethylphosphoryl)-4-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C248]



4 mg of paraformaldehyde was added to an acetic acid (0.5 ml) solution of 41 mg of 5-(1-(4-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide produced in Example 381-(b) at room temperature under an argon gas flow and stirred at 40°C for 2.5 hours. Next, 34 mg of sodium triacetoxyborohydride was added thereto at 40°C and stirred at 40°C for 2.5 hours. 34 mg of sodium triacetoxyborohydride was added thereto at 40°C, stirred at 40°C for 1.5 hours, and left to stand at room temperature overnight. 0.5 ml of acetic acid and 34 mg of sodium triacetoxyborohydride were added thereto at 40°C and stirred at 40°C for seven hours. A saturated aqueous sodium bicarbonate solution was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed successively with a saturated sodium bicarbonate aqueous solution and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), a saturated sodium hydrogencarbonate aqueous solution was added to a fraction containing a target substance, and the fraction was extracted with ethyl acetate. An organic layer was washed successively with a saturated sodium bicarbonate aqueous solution and saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The concentrated residue was dissolved in a mixed solvent of acetonitrile/water and lyophilized to obtain 27 mg of a title compound as a white solid.

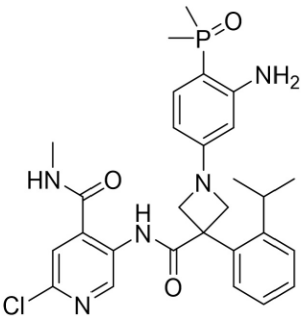
Mass spectrum (DUIS, m/z): 569 $[M+H]^+$

Retention time (LCMS conditions 8): 0.926 min.

[0439] Example 383-(a)

Production of 5-(1-(3-amino-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide

[C249]



53 mg of tripotassium phosphate and 40 mg of tert-butyl (5-bromo-2-(dimethylphosphoryl)phenyl)(tert-butoxycarbonyl)carbamate produced in Reference Example 383-(b) were added to a 1,4-dioxane (1 ml)/water (0.2 ml) suspension of 35 mg of 2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide hydrochloride produced in the same manner as in Example 39-(a) at room temperature, degassed, and substituted with nitrogen. 8 mg of [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2'-amino-1,1'-biphenyl)] palladium (II) methanesulfonate (trade name: XantPhos Pd G3) was added at room temperature under an argon gas flow, stirred at 110°C for one hour, left to stand at room temperature for 14 hours, stirred at 110°C for 10 hours, left to stand at room temperature for 14 hours, stirred at 110°C for 10 hours, left to stand at room temperature for 14 hours, and stirred at 110°C for four hours. Water was added to a reaction mixture allowed to cool to room temperature, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, and filtered. DNH silica gel was added to a filtrate at room temperature, stirred at room temperature for 30 minutes, filtered, and concentrated under reduced pressure. A concentrated residue was purified by medium pressure preparative chromatography (silica gel, eluting solvent; ethyl acetate:methanol) and then purified by medium pressure preparative chromatography (DIOL silica gel, eluting solvent; ethyl acetate:methanol). 0.032 ml of trifluoroacetic acid was added to a dichloromethane (0.32 ml) solution of the obtained purified product at room temperature under an argon gas flow and stirred at room

temperature for five hours. The reaction mixture was concentrated under reduced pressure. The concentrated residue was subjected to medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 4 mg of a title compound as a white solid.

Mass spectrum (DUIS, m/z): 554 $[M+H]^+$

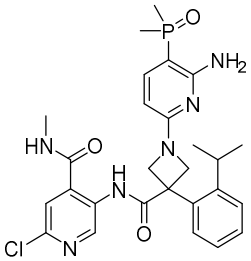
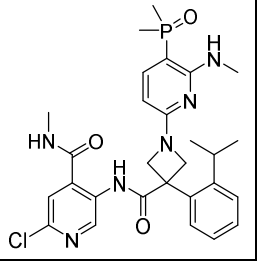
Retention time (LCMS conditions 8): 1.159 minutes

[0440] Example 384-(a) and the like

Compounds shown in Table 95 below were obtained by treating corresponding raw material compounds in the same manner as in Example 383-(a).

[Table 95]

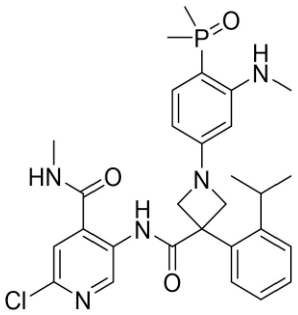
Table 95

Example	Structural formula	Analysis data	Raw material
384-(a)		Mass spectrum (DUIS, m/z): 555 $[M+H]^+$ Retention time (LCMS conditions 8): 0.923 min	Reference Example 384-(b)
388-(a)		Mass spectrum (DUIS, m/z): 569 $[M+H]^+$ Retention time (LCMS conditions 8): 1.262 min	Reference Example 388-(a)

[0441] Example 387-(a)

Production of 2-chloro-5-(1-(4-(dimethylphosphoryl)-3-(methylamino)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide

[C250]



0.0035 ml of pyridine and 0.6 mg of 4-dimethylaminopyridine were added to a tetrahydrofuran (1 ml) solution of 20 mg of 5-(1-(3-amino-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-2-chloro-N-methylisonicotinamide produced in the same manner as in Example 383-(a) at room temperature under an argon gas flow. Next, 0.0061 ml of trifluoroacetic anhydride was added thereto in an ice bath and stirred in the ice bath for 30 minutes. 0.0070 ml of pyridine and 0.012 ml of trifluoroacetic anhydride were added thereto in the ice bath and stirred in the ice bath for 30 minutes. Water was added to a reaction mixture, and the reaction mixture was extracted with ethyl acetate. An organic layer was washed with saturated saline, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. 10 mg of potassium carbonate and 0.0054 ml of iodomethane were added to a N,N-dimethylformamide (0.5 ml) solution of the obtained concentrated residue at room temperature under a flow of argon, stirred at room temperature for 30 minutes, and left to stand at room temperature for 14 hours. Next, 1 ml of a 1M sodium hydroxide aqueous solution was added thereto at room temperature and stirred at room temperature for one hour. 0.5 ml of 2M hydrochloric acid was added to the reaction mixture. The obtained solution was subjected to medium pressure preparative chromatography (ODS column, eluting solvent; 0.1% formic acid aqueous solution:0.1% formic acid acetonitrile solution), and a fraction containing a target substance was lyophilized to obtain 3 mg of a title compound as a white solid.

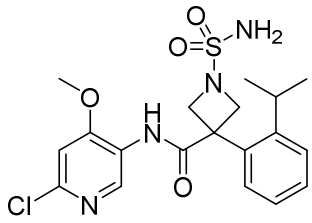
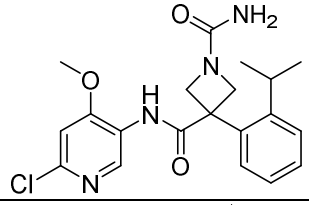
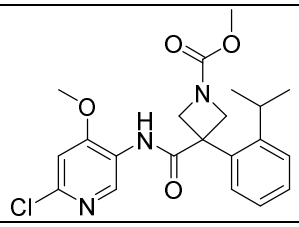
Mass spectrum (DUIS, m/z): 568 $[M+H]^+$

Retention time (LCMS conditions 8): 1.255 min.

[0442]

[Table 96]

Table 96. Comparative compound

Comparison No.	Compound structure	Note
C1		WO 2020/254408 Ex 21-2
C2		WO 2020/254408 Ex 22-1
C3		WO 2020/254408 Ex 23-1

[0443] Pharmacological test examples

(Test Example 1) LPA1 receptor GTP γS binding test

A membrane fraction of a CHO-K1 cell expressing a human LPA1 receptor (A324, manufactured by Charles River Laboratories, final concentration: 50 μg/mL) was suspended in a reaction buffer (20 mM HEPES, 100 mM NaCl, 10 mM $MgCl_2$, 10 μM GDP, 50 μg/mL of saponin, 0.2% BSA (all final concentrations), pH 7.4), and a test compound (final concentration: 1 μM) dissolved in DMSO was added thereto. After pre-incubation at 30°C for 15 minutes, an LPA (L7260, manufactured by Sigma-Aldrich, final concentration: 100 nM) solution containing [^{35}S] GTP γS (NEG 030X, manufactured by Perkin Elmer, Inc., final concentration: 0.1 nM) was added thereto and incubated at 30°C for 30 minutes. The membrane fraction was recovered using a cell harvester (M30, manufactured by Brandel) on glass fiber filter paper (GF/B, manufactured by Whatman) and washed with a 10 mM phosphate buffer (pH 7.4). The radioactivity of the membrane fraction was measured using a liquid scintillation analyzer (LSC-8000, manufactured by Hitachi). The inhibition (%) of the test compound for binding of the LPA1 receptor and [^{35}S] GTP γS was calculated by the following formula.

· Inhibition (%)= [1-{(test compound + radioactivity with LPA added) - (radioactivity with only DMSO added)}/{(radioactivity with DMSO and LPA added) - (radioactivity with only DMSO added)}] × 100

[0444] In the present test, the compound of the present invention exhibited excellent binding inhibitory activity, and for example, for the compounds of Examples 1-(a), 2-(a), 3-(a), 4-(a), 5-(a), 6-(a), 7-(c), 8-(a), 9-(a), 10-(a), 11-(b), 12-(a), 13-(a), 14-(a), 15-(a), 16-(b), 17-(b), 18-(a), 19-(a), 20-(a), and 21-(b), the inhibitions were 50% or higher at a compound concentration of 1 μM.

[0445] (Test Example 2) Suppression test of rat Schwann cell dedifferentiation

A rat Schwann cell line IFRS1 cell (SWN-IFRS 1C, obtained from Cosmo Bio) was suspended in Schwann Cell (IFRS1) Medium (manufactured by Cosmo Bio) and seeded into 24-well plates at 4.8 × 10^4 cells/well. The cell was cultured for 24 hours, the medium was then removed, a differentiation medium containing 1% FBS (8-CPT-cAMP (final concentration: 250 nM), 1 × N2 supplement, 1 × B27 supplement, 1% penicillin-streptomycin, DMEM/F12) was added thereto, and differentiation was induced for 48 hours. After the medium was removed, the differentiation medium containing 0.1% of BSA was added thereto, and subsequently, the test compound at each concentration dissolved in DMSO and LPA (final concentration: 10 μM) dissolved in PBS containing 0.1% of BSA were added thereto. After 24 hours, the cells were subjected to RNA extraction and purification using RNeasy (registered trademark) 96 QIAcube (registered trademark) HT Kit (manufactured by QIAGEN), cDNA was then synthesized using PrimeScript (registered trademark) RT reagent Kit with gDNA Eraser (manufactured by Takara Bio) and TaKaRa PCR Thermal Cycler Dice (registered trademark) Gradient (manufactured by Takara Bio), quantitative PCR was performed using TB Green (registered trademark) Premix Ex Taq (registered trademark) II (manufactured by Takara Bio) and Thermal Cycler Dice (registered trademark) Real Time System II or IV (manufactured by Takara Bio), and the expression levels of Myelin basic protein (Mbp) mRNA and Ribosomal protein lateral protein stalk subunit P0 (Rplp0) mRNA in IFRS1 cells were measured.

The expression level of Mbp mRNA was corrected by the expression level of Rplp0 mRNA.

Reduction in Mbp mRNA expression due to LPA induction was used as an indicator of dedifferentiation, and the inhibition (%) of the test compound against the reduction of Mbp mRNA expression was obtained by the following formula.

· Inhibition (%) = [1-{(test compound + Mbp mRNA expression level with LPA added) - (Mbp mRNA expression level with only DMSO added)}/{(Mbp mRNA expression level with DMSO + LPA added) - (Mbp mRNA expression level with only DMSO added)}] × 100

Based on the calculated inhibition (%), the compound concentration (IC_{50} value), which exhibited an inhibition of 50%, was obtained using EXSUS (manufactured by EPS).

[0446] The results of the individual test compounds in the present test are shown in Tables 97A and 97B below. A: $IC_{50} < 30$ nM, B: 30 nM $\leq IC_{50} < 100$ nM, C: 100 nM $\leq IC_{50} < 300$ nM, D: 300 nM $\leq IC_{50} < 1000$ nM, or E: $IC_{50} \geq 1000$ nM.

[Table 97]

Table 97A. Results of suppression tests of rat Schwann cell dedifferentiation for Example compounds

Example	IC50	Example	IC50	Example	IC50
1-(a)	A	2-(a)	A	3-(a)	A
4-(a)	A	5-(a)	B	6-(a)	A
7-(c)	A	8-(a)	B	9-(a)	A
10-(a)	A	11-(b)	A	12-(a)	B
13-(a)	A	14-(a)	A	15-(a)	A
16-(b)	B	17-(b)	B	18-(a)	B
19-(a)	A	20-(a)	A	21-(b)	B
22-(a)	A	23-(c)	B	24-(c)	B
25-(c)	D	26-(c)	A	27-(c)	C
28-(c)	B	29-(c)	A	30-(c)	A
31-(c)	A	32-(a)	A	33-(b)	B
33-(c)	C	34-(a)	C	35-(a)	B
36-(a)	B	37-(b)	B	38-(a)	D
39-(b)	A	40-(b)	C	41-(b)	B
42-(b)	B	43-(b)	B	44-(b)	C
45-(b)	B	46-(b)	C	47-(b)	B
48-(b)	D	49-(b)	D	50-(b)	B

51-(b)	B	52-(b)	C	53-(b)	B
54-(a)	A	55-(a)	B	56-(a)	B
57-(a)	B	58-(a)	A	59-(a)	B
60-(a)	B	61-(a)	B	62-(a)	A
63-(a)	B	64-(b)	C	65-(a)	B
66-(b)	B	67-(b)	B	68-(b)	B
69-(b)	B	70-(b)	A	71-(b)	B
72-(b)	C	73-(b)	B	74-(a)	A
75-(a)	A	76-(a)	A	77-(b)	A
78-(b)	D	79-(b)	B	80-(b)	B
81-(b)	A	82-(b)	B	83-(b)	B
84-(b)	C	85-(b)	C	86-(b)	C
87-(b)	B	88-(b)	C	89-(b)	A
90-(a)	C	91-(a)	A	92-(a)	A
93-(a)	A	94-(a)	A	95-(a)	A
96-(a)	A	97-(a)	A	98-(a)	A
99-(a)	A	100-(a)	A	101-(a)	A
102-(b)	B	103-(b)	C	104-(b)	C
105-(b)	B	106-(b)	C	107-(b)	C
108-(b)	C	109-(b)	A	110-(b)	B
111-(b)	A	112-(a)	B	113-(a)	B
114-(a)	B	115-(a)	A	116-(a)	A
117-(a)	B	118-(a)	A	119-(a)	A
120-(a)	A	121-(a)	A	122-(a)	B
123-(a)	A	124-(a)	A	125-(b)	A
126-(b)	A	127-(a)	A	128-(a)	A
129-(a)	A	130-(a)	A	131-(a)	B
132-(a)	A	133-(a)	A	134-(a)	A
135-(a)	A	136-(a)	A	137-(a)	A
138-(a)	D	139-(a)	B	140-(a)	B
141-(a)	C	142-(a)	A	143-(a)	B
144-(a)	B	145-(b)	A	146-(a)	B
147-(a)	B	148-(a)	D	149-(a)	A
150-(a)	A	151-(b)	C	152-(a)	B
153-(a)	B	154-(a)	D	155-(a)	C
156-(a)	C	157-(a)	A	158-(a)	B

159-(a)	B	160-(a)	A	161-(b)	B
162-(b)	A	163-(b)	B	164-(a)	B
165-(a)	A	166-(a)	A	167-(a)	A
168-(a)	A	169-(a)	A	170-(a)	C
171-(a)	A	172-(a)	B	173-(a)	B
174-(a)	A	175-(b)	B	176-(a)	A
177-(a)	A	178-(a)	C	179-(b)	D
180-(a)	A	181-(a)	A	182-(a)	B
183-(a)	B	184-(a)	B	185-(a)	A
186-(a)	A	187-(a)	B	188-(a)	A
189-(a)	A	190-(a)	A	191-(a)	A
192-(a)	A	193-(a)	A	194-(a)	B
195-(a)	B	196-(a)	A	197-(a)	A
198-(a)	B	199-(b)	A	200-(b)	C
201-(b)	C	202-(a)	B	203-(a)	C
204-(a)	C	205-(a)	D	206-(a)	A
207-(a)	D	208-(a)	A	209-(a)	A
210-(a)	A	211-(a)	A	212-(a)	A
213-(a)	A	214-(a)	A	215-(a)	A
216-(a)	A	217-(a)	A	218-(b)	A
219-(a)	A	220-(a)	A	221-(a)	A
222-(a)	B	223-(a)	B	224-(b)	A
225-(a)	B	226-(b)	B	239-(a)	A
240-(a)	A	241-(a)	A	242-(b)	A
243-(a)	B	244-(a)	A	245-(a)	B
246-(a)	A	247-(a)	A	248-(a)	A
249-(a)	B	250-(a)	A	251-(a)	A
252-(a)	B	253-(b)	B	254-(b)	B
255-(a)	A	256-(b)	C	257-(a)	D
258-(a)	B	259-(a)	B	260-(a)	B
261-(a)	A	262-(b)	A	263-(a)	A
264-(a)	B	265-(a)	A	266-(a)	A
267-(a)	A	268-(a)	A	269-(a)	B
270-(a)	D	271-(a)	B	272-(b)	C
273-(a)	A	274-(a)	A	275-(a)	A
276-(a)	A	277-(b)	B	278-(a)	B

279-(c)	A	280-(a)	A	281-(a)	A
282-(a)	A	283-(a)	A	284-(a)	A
285-(a)	A	286-(a)	A	287-(b)	A
288-(b)	A	289-(b)	A	290-(c)	A
291-(c)	C	292-(c)	A	293-(b)	D
294-(b)	A	295-(b)	C	296-(a)	B
297-(a)	A	298-(a)	B	299-(b)	A
300-(b)	B	301-(b)	A	302-(b)	A
303-(b)	B	304-(b)	B	305-(b)	C
306-(b)	B	307-(b)	B	308-(b)	B
309-(a)	B	310-(a)	A	311-(a)	A
312-(a)	A	313-(b)	B	314-(a)	B
315-(a)	A	316-(c)	B	317-(a)	A
318-(a)	A	319-(a)	B	320-(c)	B
321-(a)	A	322-(b)	B	323-(b)	B
324-(b)	C	325-(b)	B	326-(b)	B
327-(b)	C	328-(a)	A	329-(a)	A
330-(a)	A	331-(a)	B	332-(a)	B
333-(a)	A	334-(a)	B	335-(a)	B
336-(a)	A	337-(a)	B	338-(a)	B
339-(a)	B	340-(a)	B	341-(a)	B
342-(a)	B	343-(a)	A	344-(a)	A
345-(b)	B	346-(a)	A	347-(a)	B
348-(a)	B	349-(a)	A	350-(a)	A
351-(a)	A	352-(a)	C	353-(a)	C
354-(a)	C	355-(a)	B	360-(a)	A
361-(a)	A	362-(a)	A	363-(a)	A
364-(a)	C	365-(a)	A	366-(a)	C
367-(a)	A	368-(a)	C	369-(a)	B
370-(a)	A	371-(a)	B	372-(a)	A
373-(a)	A	374-(a)	B	375-(a)	C
376-(a)	A	377-(a)	A	378-(a)	A
379-(a)	B	380-(a)	C	381-(b)	B
382-(a)	D	383-(a)	B	385-(a)	B

Table 97B. Results of suppression test of rat Schwann cell dedifferentiation for comparative compounds

Comparative compound	IC50	Comparative compound	IC50	Comparative compound	IC50
C1	C	C2	E	C3	C

[0447] (Test Example 3) Multiple dose pain test for four days using type 2 diabetes model mice

In order to evaluate the anti-pain effect of the test compound in diabetic peripheral neuropathy, a plantar test (Hargreaves test) was performed using male C57BLKS/J Iar-+Lepr^{db}/+Lepr^{db} mice (db/db mouse, supplied by Japan SLC, Inc.).

Mice were housed in cages on glass plates and conditioned for at least one hour before the start of measurement. In the plantar test, the left hind paw of the mouse was thermally stimulated using a plantar calorimetric analyzer (390G, manufactured by IITC Life Science), and the paw withdrawal latency (PWL) was measured. The intensity of the thermal stimulation was set such that the PWL of male C57BL/6JJmsSlc mouse (C57BL/6 mouse, supplied from Japan SLC, Inc.) reached about 10 seconds. The cut-off time was set to 20 seconds. The thermal stimulation was performed three times at intervals of five minutes or longer, and the average value thereof was used as PWL.

The plantar test was performed on the beginning day of the test (Day 1) and db/db mouse with PWL of eight seconds or shorter was selected and used for the test.

The test compound was suspended in a 0.5% methylcellulose solution (133-17815, manufactured by FUJIFILM Wako Pure Chemical Industries, Ltd.) and orally administered once on Day 1 (after the plantar test) and twice per day from Day 2 to Day 4.

The plantar test was performed on Day 5 to calculate a difference (ΔPWL) between Day 5 PWL and Day 1 PWL.

[0448] In the present test, the compound of the present invention exhibited an excellent anti-pain effect. Results with the administration of 30 mg/kg of each test compound are shown in Tables 98A and 98B below. A: ΔPWL > three seconds, B: two seconds < ΔPWL ≤ three seconds, C: one second < ΔPWL ≤ two seconds, or D: ΔPWL ≤ one second.

[Table 98]

Table 98A. Results of multiple dose pain tests for four days using type 2 diabetes model mice for

Example compounds

Example	ΔPWL
2-(a)	C
3-(a)	C
4-(a)	A
6-(a)	C
7-(c)	A
9-(a)	B
10-(a)	C
14-(a)	B
20-(a)	C
21-(b)	A
39-(b)	A
66-(b)	A
73-(b)	C
76-(a)	B
83-(b)	B
121-(a)	B
135-(a)	C
157-(a)	A
162-(b)	A
176-(a)	D
188-(a)	A
199-(b)	B
227-(b)	A
250-(a)	A
268-(a)	B
273-(a)	B

Table 98B. Results of multiple dose pain tests for four days using type 2 diabetes model mice for comparative compounds

Comparative compound	ΔPWL
C1	D
C3	C

[0449] (Test Example 4) 14-day repeated dose pain test using type 2 diabetes model mice

In order to evaluate the therapeutic effect of test compounds on diabetic peripheral neuropathy, PWL after multiple dose and rest of the test compound was measured.

PWL was measured by the same method as in the four-day repeated dose pain test described above. The test compound was suspended in a 0.5% methylcellulose solution (vehicle) and orally administered twice per day from the beginning day of the test (Day 1) to Day 14. The plantar test was performed on Day 1 (pre-dose), Day 15 (the day after the final dose), and Day 22 (Day 7 after the beginning of stoppage). The pain threshold improvement rates on Day 15 and Day 22 were calculated based on the following formula.

· Pain threshold improvement rate (%) = {(PWL of db/db mice dosed with test compound) - (PWL of db/db mice dosed with vehicle)}/{(PWL of C57BL/6 mice dosed with vehicle) - (PWL of db/db mice dosed with vehicle)} × 100

In the present test, the compound of the present invention exhibited an excellent anti-pain effect, and the effect was observed even seven days after the stoppage, indicating a sustained anti-pain effect.

[0450] (Test Example 5) Intracellular calcium mobilization test

The test was performed using cells expressing the human LPA1 receptor (HTS 089RTA, obtained from Eurofins) and a Fluo-8 Medium Removal Calcium Assay Kit (36308, manufactured by AAT Bioquest).

Cells suspended in a Media Component (manufactured by Eurofins) were seeded on black and clear-bottom 96-well microplates at 100 μL/well and cultured overnight at 5% CO_2 and 37°C. The next day, the Media Component was removed, and a Fluo-8 NW dye loading solution (HBSS containing 0.1% BSA, 1X Pluronic F127Plus, and 20 mM Hepes) was added thereto at 100 μL/well and incubated at 37°C for 30 minutes. The test compound dissolved in DMSO was diluted with Assay Buffer (HBSS containing 0.1% BSA and 20 mM Hepes) to a final concentration of 1 μM, and 50 μL was added to the cells and incubated at 37°C for 30 minutes. LPA (L7260, manufactured by Sigma-Aldrich) was prepared on Assay Buffer to a final concentration of EC80, and 50 μL was added to the cells using FlexStation 3 (manufactured by Molecular Devices), and the fluorescence intensity at an excitation

wavelength of 490 nm and a measuring wavelength of 525 nm was measured at 37°C. The increase in fluorescence intensity was obtained by subtracting the fluorescence intensity prior to the addition of LPA from the maximum value of the fluorescence intensity increased by the addition of LPA, and the inhibition (%) of the test compound on intracellular calcium mobilization of LPA1 receptor-expressing cells induced by LPA was calculated by the following formula.

· Inhibition (%) = [1 - {(increase in fluorescence intensity with test compound + LPA added) - (increase in fluorescence intensity with only DMSO added)}/{(increase in fluorescence intensity with DMSO + LPA added) - (increase in fluorescence intensity with only DMSO added)}] × 100

In the present test, the compound of the invention exhibited excellent intracellular calcium mobilization inhibitory activity, and for example, for the compounds of Examples 3-(a), 4-(a), 7-(c), 22-(a), 26-(c), 30-(c), 31-(c), 32-(a), 39-(b), 54-(a), 58-(a), 66-(b), 73-(b), 76-(a), 79-(b), 83-(b), 91-(a), 92-(a), 93-(a), 95-(a), 96-(a), 99-(a), 100-(a), 102-(b), 109-(b), 121-(a), 123-(a), 129-(a), 130-(a), 135-(a), 157-(a), 158-(a), 162-(b), 163-(b), 167-(a), 169-(a), 174-(a), 176-(a), 188-(a), 189-(a), 190-(a), 211-(a), 213-(a), 216-(a), 217-(a), 224-(b), 239-(a), 241-(a), 244-(a), 245-(a), 247-(a), 248-(a), 249-(a), 250-(a), 251-(a), 261-(a), 263-(a), 268-(a), 273-(a), 275-(a), 283-(a), 288-(b), 290-(c), 291-(c), and 292-(c), the inhibitions were 50% or higher at a compound concentration of 1 μM.

[0451] (Test Example 6) Single dose pain test using paclitaxel-induced model mice

In order to evaluate the anti-pain effect of a single dose of the test compound in peripheral neuropathy associated with chemotherapeutic agents, a plantar test was performed using paclitaxel-induced model mice.

The peripheral neuropathy associated with chemotherapeutic agents is induced by the fact that paclitaxel (P1632, manufactured by Tokyo Chemical Industries, Ltd.) dissolved in a liquid mixture of ethanol and Kolliphor (registered trademark) ELP (30906, manufactured by Sigma-Aldrich) (1:1) was diluted 10-fold with saline and intraperitoneally administered to male C57BL/6 mice at a dosage of 5.5 mg/kg once and three times per two days.

PWL was measured by the above-described method. The test compound was suspended in a

0.5% methylcellulose solution and dosed 150 minutes prior to the plantar test. The anti-pain effect was evaluated by calculating the difference (ΔPWL) between the pre-dose PWL and the PWL after 150 minutes.

[0452] In the present test, the compound of the present invention exhibited an excellent anti-pain effect. The results of administration of the individual test compounds are shown in Table 99 below. A: ΔPWL > three seconds, B: two seconds < ΔPWL ≤ three seconds, C: one second < ΔPWL ≤ two seconds, or D: ΔPWL ≤ one second.

[Table 99]

Table 99. Results of single dose pain tests using paclitaxel-induced model mice for Example compounds

Example	Dosage	ΔPWL
4-(a)	10 mg/kg	A
10-(a)	30 mg/kg	B
36-(a)	30 mg/kg	C
39-(b)	30 mg/kg	A
66-(b)	30 mg/kg	B
73-(b)	30 mg/kg	B
83-(b)	30 mg/kg	B
102-(b)	30 mg/kg	C
110-(b)	30 mg/kg	A
123-(a)	30 mg/kg	C
129-(a)	30 mg/kg	C
130-(a)	30 mg/kg	B
149-(a)	30 mg/kg	C
174-(a)	30 mg/kg	C
175-(b)	30 mg/kg	C
239-(a)	30 mg/kg	C
244-(a)	30 mg/kg	C
245-(a)	30 mg/kg	C
247-(a)	30 mg/kg	C
248-(a)	30 mg/kg	C
250-(a)	30 mg/kg	B
275-(a)	30 mg/kg	C

288-(b)	30 mg/kg	C
292-(c)	30 mg/kg	C
299-(b)	30 mg/kg	C
301-(b)	30 mg/kg	C
311-(a)	30 mg/kg	B
312-(a)	30 mg/kg	C
313-(b)	30 mg/kg	C
317-(a)	30 mg/kg	C
321-(a)	30 mg/kg	B
326-(b)	30 mg/kg	C
335-(a)	30 mg/kg	C
336-(a)	30 mg/kg	C
348-(a)	30 mg/kg	B
352-(a)	30 mg/kg	A
355-(a)	30 mg/kg	A
360-(a)	30 mg/kg	A
361-(a)	30 mg/kg	B
362-(a)	30 mg/kg	A

[0453] (Test Example 7) 14-day repeated dose pain test using paclitaxel-induced model mice

In order to evaluate the therapeutic effect of the test compound in peripheral neuropathy associated with chemotherapeutic agents, post-repeated and after drug withdrawal paw withdrawal threshold (PWT) was measured.

Paclitaxel-induced model mice were prepared as described above. As control mice, a medium containing paclitaxel dissolved therein was administered to C57BL/6 mice in the same manner. PWT was measured using Electronic Von Frey (2390, manufactured by IITC Life Science). That is, mice were housed in a cage on a wire net and conditioned for at least one hour prior to the beginning of measurement, and the left hind paw of the mouse was stimulated with Electronic Von Frey from below the wire net. The measurement was performed three times at intervals of 5 minutes or longer, and the average value was calculated as PWT. The Electronic Von Frey test was performed on Day 8 from the first dose of paclitaxel, and mice with PWT of 8 g or less were selected and used for the test.

The test compound was suspended in a 0.5% methylcellulose solution (vehicle) and orally

administered twice per day from Day 8 to Day 21.

PWT was measured on Day 22 (the day after the final dose) and Day 29 (Day 7 after the beginning of stoppage). The pain threshold improvement rate on Day 22 or Day 29 was calculated based on the following formula.

· Pain threshold improvement rate (%) = {(PWT of paclitaxel-induced model mouse group dosed with test compound) - (PWT of paclitaxel-induced model mouse group dosed with vehicle)}/{(PWT of control mouse group dosed with vehicle) - (PWT of paclitaxel-induced model mouse group dosed with vehicle)} × 100

In the present test, the compound of the present invention exhibited an excellent anti-pain effect, and the effect was observed even seven days after the stoppage, indicating a sustained anti-pain effect.

[0454] (Test Example 8) 14-day repeated dose pain test using streptozotocin-induced diabetic rats

In order to evaluate the therapeutic effect of the test compound on diabetic peripheral neuropathy, PWT after multiple dose and rest of the test compound was measured.

Streptozotocin (S0130, manufactured by Merck) (hereinafter abbreviated as STZ) was dissolved in 0.1M citrate buffer (pH 4.5, 21081, manufactured by Muto Pure Chemicals Co., Ltd.) and intraperitoneally administered to male Slc:Wistar rats (Wistar rats, supplied by Japan SLC, Inc.) once at a dose of 50 mg/kg. A control rat was dosed with a 0.1M citrate buffer in the same manner.

The rats were housed in cages on a wire net and conditioned for at least 15 minutes before the beginning of the measurement. 0.4, 0.6, 1, 2, 4, 6, 8, 15 g of eight von Frey filaments (514000-20C, manufactured by IITC Life Science) were vertically applied to the sole of the hind limb from below the wire net. PWT was calculated by an up-down method according to a method by Chaplan et al. (J Neurosci Methods. 1994;53(1):55 to 63).

A von Frey test was performed on Day 15 from STZ administration, rats with PWT of 8 g or less and a blood sugar value of 350 mg/dL or more as measured with MediSafe Fit Pro II (MS-FKP02, manufactured by Terumo Corporation) were selected and used for the test.

The test compound was suspended in a 0.5% methylcellulose solution (vehicle) and orally

administered once per day from Day 15 to Day 28.

The pain threshold improvement rate was calculated based on the following formula after the von Frey test was performed on Day 29 (the day after the final dose) and Day 36 (Day 7 after the beginning of stoppage).

· Pain threshold improvement rate (%) = {(PWT of STZ-induced rat group dosed with test compound) - (PWT of STZ-induced rat group dosed with vehicle)}/{(PWT of control rat group dosed with vehicle) - (PWT of STZ-induced rat group dosed with vehicle)} × 100

In the present test, the compound of the present invention exhibited an excellent anti-pain effect, and the effect was observed even seven days after the stoppage, indicating a sustained anti-pain effect.

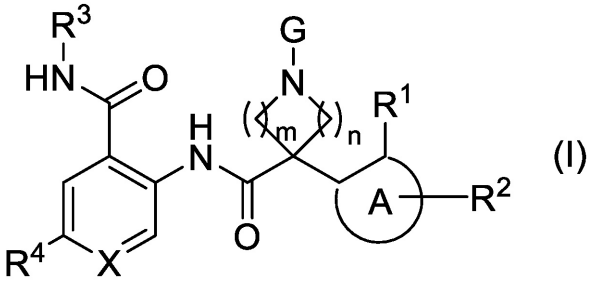
Industrial Applicability

[0455] The compound represented by the general formula (I) of the present invention, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof has excellent LPA receptor antagonism and is useful for the prevention, amelioration, and/or treatment of diseases of which symptoms are ameliorated by antagonizing an LPA receptor.

CLAIMS

1. A compound represented by the following general formula (I):

[C1]



(I)

[wherein

a ring A is a benzene ring or a 5- or 6-membered aromatic heterocycle,

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

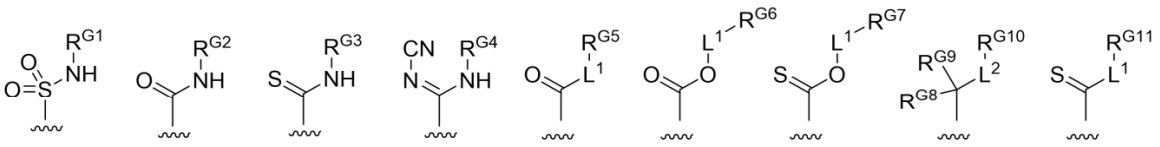
R^4 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, or a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom, a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from a group Q1, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from a group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C2]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

G is the C_3-C_6 cycloalkyl group optionally substituted with one to five substituents independently selected from the group Q1, the C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, or the 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, in which in a case where adjacent two carbon atoms on a ring of the cycloalkyl group, the aryl group, or the heteroaryl group have been substituted with a carboxy group and a C_1-C_6 alkyl group substituted with one hydroxy group, respectively, the carboxy group and the C_1-C_6 alkyl group substituted with one hydroxy group optionally form a lactone ring together with the carbon atoms to which the carboxy group and the C_1-C_6 alkyl group bind,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of a halogen atom, a hydroxy group, an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group optionally substituted with one to five substituents independently selected from the group Q3, a cyano group, $NR^{N7}R^{N8}$, and a 3- to 12-membered non-aromatic heterocyclyl group,

R^{N7} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N8} is a hydrogen atom or a C_1-C_6 alkyl group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, a $NR^{N9}R^{N10}$, and a C_6-C_{10} aryl group,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1}, R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q4, a C_2-C_{10} acyl group optionally substituted with one to five substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_1-C_6 alkyl group substituted with one hydroxy group, and a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5}, R^{G6}, R^{G7}, and R^{G11} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group optionally substituted with one to five halogen atoms, and a C_2-C_6 acyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom, a halogen atom, or a C_1-C_6 alkyl group,

the C_1-C_6 alkyl group may be substituted with one to five substituents independently selected from a halogen atom, a hydroxy group, and a C_1-C_6 alkoxy group,

R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_2-C_6 alkenyl group, a C_1-C_6 alkoxy group

optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a C_6-C_{10} aryl group optionally substituted with one to five substituents independently selected from the group Q1, a 5- to 10-membered heteroaryl group optionally substituted with one to five substituents independently selected from the group Q1, or a 3- to 12-membered non-aromatic heterocyclyl group optionally substituted with one to five substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

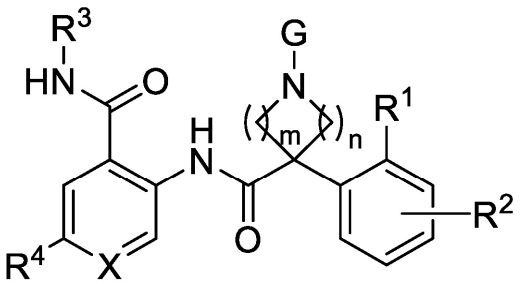
R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group,

m and n are each independently an integer of any of 1 or 2],

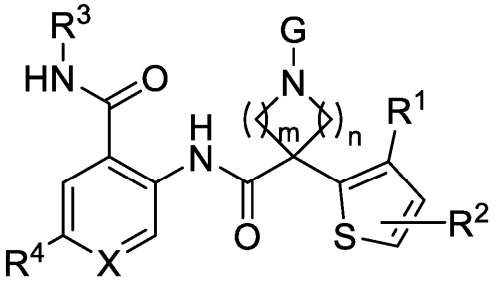
a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, which is represented by the following general formula (I-a) or (I-b):

[C3]



(I-a)



(I-b)

[wherein

R^1 is a C_1-C_6 alkyl group or a C_3-C_6 cycloalkyl group,

R^2 is a hydrogen atom or a halogen atom,

R^3 is a hydrogen atom or a C_1-C_6 alkyl group,

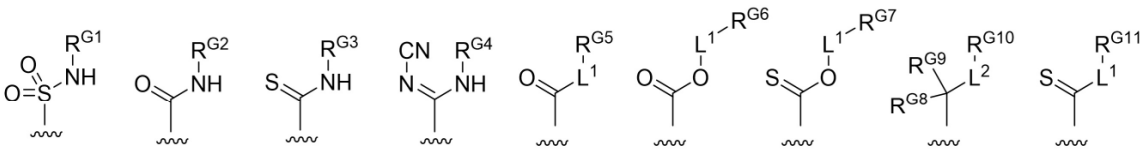
R^4 is a halogen atom, a C_1-C_6 alkyl group, or a C_1-C_6 alkoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a formyl group, a C_1-C_6 alkyl-SO_2 group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one to three substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 4- to 12-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C4]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from a group Q3, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_1-C_6 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $SO_2NR^{N5}R^{N6}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N2} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_1-C_6 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_6 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{N5} and R^{N6} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

R^{P1} and R^{P2} are each independently a C_1-C_6 alkyl group,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, and a cyano group,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, a C_2-C_6 acyl group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, and a $NR^{N9}R^{N10}$,

R^{Q3} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N9} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N10} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_1-C_6 alkoxy-carbonyl group,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 akylamino-carbonyl group,

the group Q4 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a cyano group, $NR^{N11}R^{N12}$, and a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

R^{N11} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, or a C_1-C_6 alkoxy-carbonyl group,

R^{N12} is a hydrogen atom or a C_1-C_6 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, and a C_1-C_6 alkyl group substituted with one hydroxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, a carboxy group, or a C_1-C_6 alkoxy-carbonyl group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two C_1-C_6 alkyl groups,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, a C_1-C_6 alkoxy group, and a C_2-C_6 acyloxy group,

wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_6 alkyl group,

the C_1-C_6 alkyl group may be substituted with one to five substituents independently selected from a hydroxy group, and a C_1-C_6 alkoxy group,

R^{G10} is a hydroxy group, a C_2-C_6 alkynyl group, a C_1-C_6 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, a C_1-C_6 alkyl-SO_2 group, a phenyl group optionally substituted with

one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, or a 3- to 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2,

R^{N13} is a hydrogen atom, a C_1-C_6 alkyl group, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

R^{N14} is a hydrogen atom or a C_1-C_6 alkyl group,

m and n are each independently an integer of any of 1 or 2],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2, wherein R^{N1} is a hydrogen atom or a C_1-C_6 alkyl group,

R^{N2} is a hydrogen atom,

R^{N5} and R^{N6} are hydrogen atoms,

the group Q2 is a group consisting of an oxo group, a C_1-C_6 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, and a C_2-C_6 acyl group,

R^{N9} and R^{N10} are hydrogen atoms,

R^{G1} is a hydrogen atom, a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_6 alkyl group optionally substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group, a C_1-C_6 alkoxy group, and an amino group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a halogen atom, a hydroxy group, a C_1-C_6 alkoxy group, a carboxy group, a C_1-C_6 alkoxy-carbonyl group, a cyano group, or a 4- to 6-membered non-aromatic heterocyclyl group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group may be substituted with one to three substituents independently selected from the group consisting of a halogen atom, a hydroxy group, a C_1-C_6 alkyl group optionally substituted with one to five halogen atoms, an alkyl group substituted with one hydroxy group, and a C_2-C_6 acyloxy group,

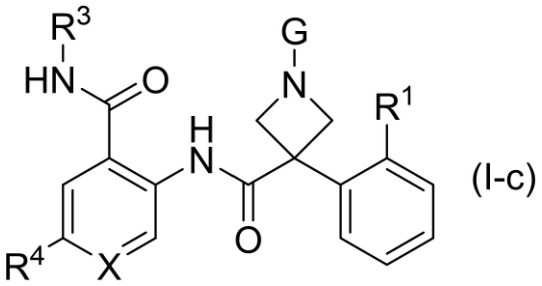
wherein in a case where any one carbon atom of the linear C_1-C_4 alkylene group has been substituted with two C_1-C_6 alkyl groups, the two C_1-C_6 alkyl groups optionally form a C_3-C_6 cycloalkane ring together with a carbon atom to which the two C_1-C_6 alkyl groups bind, and

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_6 alkoxy-carbonyl group, or a C_1-C_6 alkyl-SO_2 group,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 1, which is represented by the following general formula (I-c):

[C5]



(I-c)

[wherein

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom or a C_1-C_4 alkyl group,

R^4 is a halogen atom, a C_1-C_4 alkyl group, or a C_1-C_4 alkoxy group,

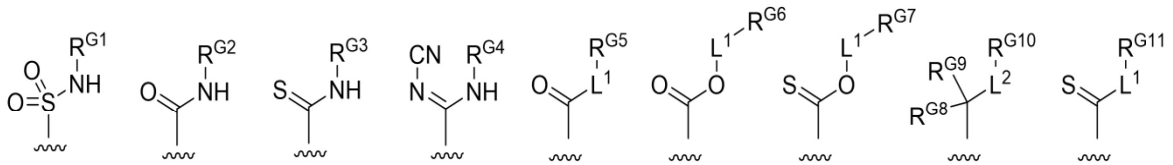
X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a halogen atom,

G is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, a C_1-C_4 alkyl group optionally substituted with

one to three halogen atoms, a C_3-C_6 cycloalkyl group optionally substituted with one or two substituents independently selected from the group Q1, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from the group Q2, or a group indicated by any of the following formulae (II-1) to (II-9),

[C6]



(II-1) (II-2) (II-3) (II-4) (II-5) (II-6) (II-7) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a hydroxy group, a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3, a C_1-C_4 alkoxy group optionally substituted with one to three halogen atoms, a carboxy group, a C_1-C_4 alkoxy-carbonyl group, a C_1-C_4 alkyl-SO_2 group, a cyano group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, $POR^{P1}R^{P2}$, a 3- to 12-membered non-aromatic heterocyclyl group substituted with an oxo group, and a 5- to 10-membered heteroaryl group,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one to five substituents independently selected from the group Q3,

the group Q3 is a group consisting of a halogen atom, OR^{Q3}, and a carboxy group,

R^{Q3} is a hydrogen atom, a C_2-C_6 acyl group optionally substituted with one amino group, or a C_1-C_4 alkoxy-carbonyl group,

R^{G1} is a hydrogen atom, a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4, or a C_2-C_{10} acyl group optionally substituted with one or two substituents independently selected from the group Q4,

R^{G2}, R^{G3}, and R^{G4} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one or two substituents independently selected from the group Q4,

the group Q4 is a group consisting of a hydroxy group and a C_1-C_4 alkoxy group,

L^1 is a linear C_1-C_4 alkylene group optionally substituted with one to three C_1-C_4 alkyl groups,

R^{G5} and R^{G11} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

R^{G6} and R^{G7} are each independently a hydrogen atom, a hydroxy group, or a carboxy group,

L^2 is a single bond or a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a C_2-C_6 acyloxy group, a cyano group, $NR^{N13}R^{N14}$, or a C_1-C_4 alkyl-SO_2 group,

R^{N13} is a hydrogen atom, a C_2-C_6 acyl group, a C_1-C_4 alkoxy-carbonyl group, or a C_1-C_4 alkyl-SO_2 group,

R^{N14} is a hydrogen atom or a C_1-C_4 alkyl group],

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 4, wherein in the formula (I-c),

R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

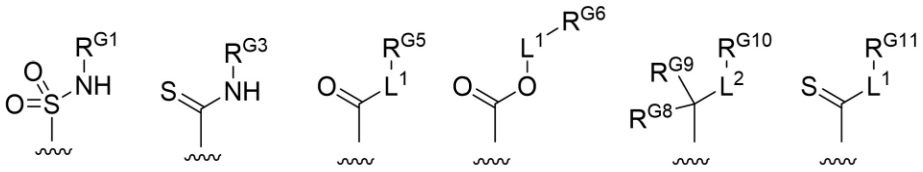
R^4 is a halogen atom or a methoxy group,

X is CR^5 or a nitrogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9),

[C7]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally

substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents independently selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally substituted with one hydroxy group, and

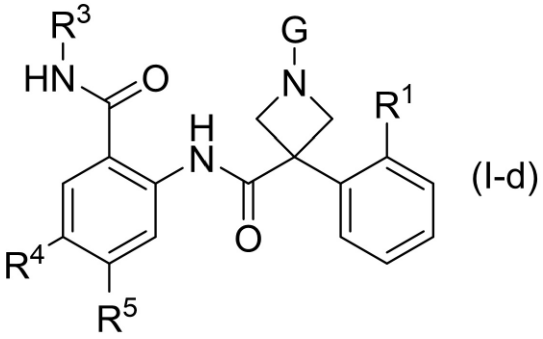
R^{G10} is a hydroxy group, a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group,

or

a pharmaceutically acceptable salt thereof.

6. The compound according to claim 5, which is represented by the following general formula (I-d):

[C8]



(I-d)

[wherein symbols are as defined in claim 5] or

a pharmaceutically acceptable salt thereof.

7. The compound according to claim 6, wherein in the formula (I-d),

R^1 is a C_1-C_4 alkyl group,

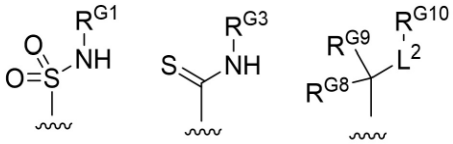
R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom,

R^5 is a hydrogen atom or a fluorine atom,

G is a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), or (II-8),

[C9]



(II-1) (II-3) (II-8)

the group Q1 is a group consisting of a C_1-C_4 alkyl group optionally substituted with one hydroxy group and a carboxy group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group optionally substituted with one hydroxy group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one substituent selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are each independently a hydrogen atom or a C_1-C_4 alkyl group optionally

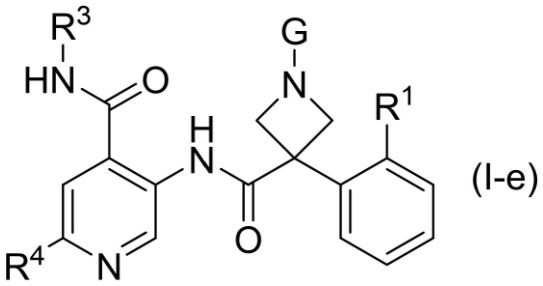
substituted with one hydroxy group, and

R^{G10} is a hydroxy group, a carboxy group, a cyano group, or a C_1-C_4 alkyl-SO_2 group, or

a pharmaceutically acceptable salt thereof.

8. The compound according to claim 5, which is represented by the following general formula (I-e):

[C10]



[wherein symbols are as defined in claim 5] or

a pharmaceutically acceptable salt thereof.

9. The compound according to claim 8, wherein in the formula (I-e),

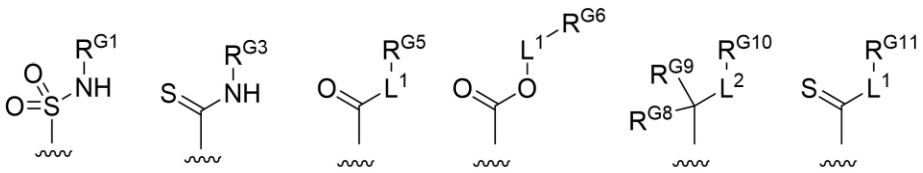
R^1 is a C_1-C_4 alkyl group,

R^3 is a hydrogen atom, a methyl group, or a CD_3 group,

R^4 is a halogen atom or a methoxy group,

G is a C_1-C_4 alkyl group optionally substituted with one to three halogen atoms, a phenyl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered heteroaryl group optionally substituted with one or two substituents independently selected from the group Q1, a 5- or 6-membered non-aromatic heterocyclyl group optionally substituted with one or two substituents independently selected from group Q2, or a group indicated by any of the following formula (II-1), (II-3), (II-5), (II-6), (II-8), or (II-9),

[C11]



(II-1) (II-3) (II-5) (II-6) (II-8) (II-9)

the group Q1 is a group consisting of a halogen atom, a C_1-C_4 alkyl group optionally substituted with one hydroxy group, a carboxy group, $NR^{N1}R^{N2}$, $CONR^{N3}R^{N4}$, and $POR^{P1}R^{P2}$,

R^{N1} is a hydrogen atom or a C_1-C_4 alkyl group,

R^{N2} is a hydrogen atom,

R^{N3} is a hydrogen atom, a C_1-C_4 alkyl-SO_2 group, or $SO_2NR^{N15}R^{N16}$,

R^{N15} and R^{N16} are each independently a hydrogen atom or a C_1-C_4 alkyl group,

R^{N4} is a hydrogen atom or a C_1-C_4 alkyl group,

when R^{N3} is $SO_2NR^{N15}R^{N16}$, R^{N4} and R^{N15} optionally form a C_2-C_3 alkylene group together,

R^{P1} and R^{P2} are each independently a C_1-C_4 alkyl group,

the group Q2 is a group consisting of an oxo group and a C_1-C_4 alkyl group,

R^{G1} is a hydrogen atom or a C_2-C_{10} acyl group,

R^{G3} is a hydrogen atom or a C_1-C_4 alkyl group,

L^1 is a linear C_1-C_4 alkylene group,

R^{G5} and R^{G11} are hydrogen atoms,

R^{G6} is a hydrogen atom,

L^2 is a linear C_1-C_4 alkylene group,

wherein the linear C_1-C_4 alkylene group is optionally substituted with one to three substituents selected from the group consisting of a hydroxy group and a C_1-C_4 alkyl group optionally substituted with one to three fluorine atoms,

R^{G8} and R^{G9} are hydrogen atoms, and

R^{G10} is a hydroxy group or a C_1-C_4 alkoxy group optionally substituted with one to three fluorine atoms,

or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 1, which is selected from the group consisting of N-(2-carbamoyl-4-chlorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-carbamoyl-4-chloro-5-fluorophenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-chloro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-bromo-2-carbamoylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(4-bromo-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-bromo-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-carbamoyl-5-fluoro-4-methylphenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(5-fluoro-4-methyl-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N^3-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide;

1-carbamothioyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)nicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

N-(4-chloro-5-fluoro-2-((methyl-d3)carbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4,5-difluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4,5-difluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4,5-difluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-bromo-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-bromo-5-(3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-fluoro-6-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-fluoro-6-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-fluoro-6-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-ethylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-ethylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-ethylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-propylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-propylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-propylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isobutylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isobutylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isobutylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-cyclopentylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-cyclopentylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-cyclopentylphenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(3-isopropylthiophen-2-yl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)azetidine-3-

carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(3-isopropylthiophen-2-yl)-1-sulfamoylazetidine-3-carboxamide;

3-(5-chloro-3-isopropylthiophen-2-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-sulfamoylazetidine-3-carboxamide;

tert-butyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxyacetyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-hydroxypropanoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N^3-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-1,3-dicarboxamide;

2-chloro-5-(1-(N'-cyanocarbamimidoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

2-chloro-5-(1-(3-hydroxy-3-methylbutanoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-carbamothioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-2-chloro-N-methylisonicotinamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)acetate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)acetic acid;

ethyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)butanoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)butanoic acid;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoate

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pentanoate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pentanoic acid;

methyl 1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclobutane-1-carboxylate;

1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclobutane-1-carboxylic acid;

methyl 2-(1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclopropyl)acetate;

2-(1-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)cyclopropyl)acetic acid;

methyl 4-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

4-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoate;

2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)benzoic acid;

methyl 6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)nicotinate;

6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)nicotinic acid;

methyl 5-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)picolinate;

5-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)picolinic acid;

methyl 6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)pyridazine-3-carboxylate;

6-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)pyridazine-3-carboxylic acid;

tert-butyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutane-1-carboxylic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-methylazetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydropyran-4-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-fluoro-3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoro-3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

3-hydroxypropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxypropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxyethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,4-dihydroxybutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(trans-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-hydroxycyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

ethyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-5-carboxylic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-methylnicotinic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)isonicotinate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)isonicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylnicotinic acid;

methyl 2-amino-6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

2-amino-6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-methylnicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-methylnicotinic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methoxynicotinate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methoxynicotinic acid;

methyl 2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

2-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(thiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid;

methyl 6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylate;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylic acid;

ethyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-4-carboxylic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-4-carboxylic acid;

ethyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylic acid;

ethyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxylic acid;

ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,2,4-thiadiazole-3-carboxylic acid;

ethyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-cyanopyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(6-acetylpyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-(methylsulfonyl)pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-sulfamoylpyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-chloro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methyl-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-(trifluoromethyl)-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(5-amino-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-methyl-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluoropicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluoropicolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylpicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylpicolinic acid;

methyl 6-chloro-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

6-chloro-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-methylpicolinate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-methylpicolinic acid;

methyl 3-amino-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

3-amino-5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

methyl 5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-2-carboxylate;

5-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrimidine-2-carboxylic acid;

methyl 4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

tert-butyl (6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazin-3-yl)carbamate;

1-(6-aminopyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-methylpyridazine-3-carboxamide;

6-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N,N-dimethylpyridazine-3-carboxamide;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1,3,4-thiadiazole-2-carboxamide;

2-chloro-5-(1-(5-cyano-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-(1-hydroxyethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(4-(hydroxymethyl)oxazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(6-(hydroxymethyl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(hydroxymethyl)-1,2,4-thiadiazol-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

ethyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-4-carboxylate;

2-chloro-5-(1-(4-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)thiazole-5-carboxylate;

2-chloro-5-(1-(5-(hydroxymethyl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

1-(6-(aminomethyl)pyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-(2-hydroxypropan-2-yl)-1,2,4-thiadiazol-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(2-hydroxypropan-2-yl)thiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cyanomethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyanoethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((1-cyanocyclopropyl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-methoxyethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-methoxypropyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(prop-2-yn-1-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-2-ylmethyl)azetidine-3-carboxamide;

1-((1,3-dioxolan-2-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-cyano-2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(2-(1H-tetrazol-5-yl)ethyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-((1H-tetrazol-5-yl)methyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-methoxypropyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-cyanoethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoate;

3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)propanoic acid;

2-chloro-5-(1-(2-hydroxyethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-benzyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(pyridin-4-ylmethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(pyridin-3-ylmethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(1-cyano-3-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyano-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxirane-2-ylmethyl)azetidine-3-carboxamide;

1-(3-amino-2-hydroxypropyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2,2,2-trifluoroethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoroethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3,3-difluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,1-dioxidothietan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-dioxido-2-thiaspiro[3.3]heptan-6-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(trans-3-(methylsulfonyl)cyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(cis-3-(methylsulfonyl)cyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-(methylsulfonyl)butyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-(2,3-dihydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3-(methylsulfonyl)propyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-fluoroethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((3-(cyanomethyl)oxetan-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,2-dimethyl-1,3-dioxan-5-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-hydroxy-2-(hydroxymethyl)propyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

3-fluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(oxetan-3-ylmethyl)azetidine-3-carboxamide;

oxetan-3-ylmethyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-difluoropropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2,2-difluoropropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-chloro-5-(1-(3-cyanopropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

3-cyanopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3,3-difluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(S)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-(3-fluoro-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3,3,3-trifluoro-2-hydroxypropyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-2-methylpropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoate;

3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbutanoic acid;

ethyl 2-(1-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutyl)acetate;

2-(1-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)cyclobutyl)acetic acid;

ethyl 2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxetan-3-yl)acetate;

2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)oxetan-3-yl)acetic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-(cyanomethyl)oxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)methyl)-3,3,3-trifluoropropanoic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-(methylsulfonyl)ethyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-(2-hydroxyethyl)oxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-hydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methoxypropan-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-cyclobutyl-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(trans-3-methoxycyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(cis-3-methoxycyclobutyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(trans-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(cis-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydrofuran-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(tetrahydropyran-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,1-dioxidotetrahydrothiopyran-4-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-oxaspiro[3.3]heptan-6-yl)azetidine-3-carboxamide;

1'-acetyl-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-[1,3'-biazetidine]-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1,3-dihydroxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(3-cyanooxetan-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-cyclobutyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(trans-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-cyanocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-oxaspiro[3.3]heptan-6-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl ((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2-hydroxyethyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-(2,3-dihydroxypropyl)sulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

tert-butyl ((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)sulfonyl)carbamate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-methylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamide;

1-(N-acetylsulfamoyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(N-butyrylsulfamoyl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-isobutyrylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-pentanoylsulfamoyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-hexanoylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-octanoylsulfamoyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(N-(2-methoxyacetyl)sulfamoyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-propionylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(N-pentanoylsulfamoyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(N-heptanoylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl (2-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine)-1-sulfonamido)-2-oxoethyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(N-glycylsulfamoyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(methylcarbamothioyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

(R)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-((2,3-dihydroxypropyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

2-chloro-5-(1-((2-hydroxyethyl)carbamothioyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-propionylazetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-acetyl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

5-(1-butyryl-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-formyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-ethanethioyl-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(methylsulfonyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

ethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

propyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxy-2,2-dimethyl-3-oxopropyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-((3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid;

(2,2-dimethyl-1,3-dioxan-5-yl)methyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-hydroxy-2-(hydroxymethyl)propyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-cyanoethyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxy-2,2-dimethyl-3-oxopropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-((3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonyl)oxy)-2,2-dimethylpropanoic acid;

3-hydroxy-3-methylbutyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-methoxyethyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

3-methoxypropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

2-hydroxy-2-methylpropyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carboxylate;

O-methyl 3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbothioate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(6-chloropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-1-(1-(3-hydroxypropyl)-6-oxo-1,6-dihydropyridazin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

1-(1-(2-aminoethyl)-6-oxo-1,6-dihydropyridazin-3-yl)-N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-(2-methoxyethyl)-6-oxo-1,6-dihydropyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-oxopyridazin-1(6H)-yl)acetate;

2-(3-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-oxopyridazin-1(6H)-yl)acetic acid;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrooxazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrothiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydrothiazol-2-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide;

tert-butyl 2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-4-oxo-4,5-dihydro-1H-imidazole-1-carboxylate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(4-methyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(2-hydroxyethyl)-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(1-(4-ethyl-5-oxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-oxo-4-(2-oxopropyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)azetidine-3-carboxamide)-N-methylisonicotinamide;

ethyl (3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidine-1-carbonothioyl)carbamate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(5-oxo-2,5-dihydro-1,2,4-oxadiazol-3-yl)azetidine-3-carboxamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-((methylcarbamoyl)carbamothioyl)azetidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-(2-methyl-3-oxo-2,3-dihydro-1,2,4-thiadiazol-5-yl)azetidine-3-carboxamide;

tert-butyl 3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)pyrrolidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)pyrrolidine-3-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-3-(2-isopropylphenyl)-1-sulfamoylpyrrolidine-3-carboxamide;

tert-butyl 4-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-4-(2-isopropylphenyl)piperidine-4-carboxamide;

N-(4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)-4-(2-isopropylphenyl)-1-sulfamoylpiperidine-4-carboxamide;

tert-butyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

2-chloro-5-(4-(2-isopropylphenyl)piperidine-4-carboxamido)-N-methylisonicotinamide;

methyl 4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidine-1-carboxylate;

methyl 4-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinate;

4-amino-6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)nicotinic acid;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylamino)nicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylamino)nicotinic acid;

methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazine-2-carboxylic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(6-(methylsulfonyl)pyridazin-3-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-(methylsulfonyl)pyridin-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(5-sulfamoylpyridin-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methylbenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-2-methylbenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-methylbenzoic acid;

methyl 3-chloro-4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

3-chloro-4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluorobenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-fluorobenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methoxybenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-methoxybenzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(trifluoromethyl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(trifluoromethyl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylsulfonyl)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(methylsulfonyl)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-(difluoromethoxy)benzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-

1-yl)-3-(difluoromethoxy)benzoic acid;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3,5-difluorobenzoate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3,5-difluorobenzoic acid;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-oxo-1,3-dihydroisobenzofuran-5-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-(hydroxymethyl)benzoic acid;

ethyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

5-(1-(4-carbamoyl-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-cyanophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyridazine-3-carboxamide;

5-(1-(4-carbamoylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

methyl 6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-2-fluoronicotinate;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinic acid;

6-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-fluoronicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(2-hydroxypropan-2-yl)pyrazin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(4-(1H-tetrazol-5-yl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

methyl 5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinate;

5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)picolinic acid;

2-chloro-5-(1-(6-(hydroxymethyl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1H-imidazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-5-carboxylic acid;

methyl 2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylate;

2-(3-((4-chloro-5-fluoro-2-(methylcarbamoyl)phenyl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-1-methyl-1H-imidazole-4-carboxylic acid;

methyl 4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoate;

4-(3-((6-bromo-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)benzoic acid;

methyl 4-(3-(2-isopropylphenyl)-3-((6-methoxy-2-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoate;

4-(3-(2-isopropylphenyl)-3-((6-methoxy-2-(methylcarbamoyl)pyridin-3-yl)carbamoyl)azetidin-1-yl)benzoic acid;

methyl 6-(4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidin-1-yl)nicotinate;

6-(4-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-4-(2-isopropylphenyl)piperidin-1-yl)nicotinic acid;

2-chloro-5-(1-(3-ethoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(3-(trifluoromethoxy)propyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(difluoromethoxy)propyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3,3-difluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(cis-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(1-(trans-3-fluorocyclobutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-((3-(methoxymethyl)oxetan-3-yl)methyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(S)-2-chloro-5-(1-(2-hydroxy-3-methoxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-2-(1-hydroxycyclobutyl)ethyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-(2,5-dioxopyrrolidin-1-yl)-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(3-ethoxy-2-hydroxypropyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2,3-dihydroxy-3-methylbutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-((3-hydroxytetrahydrofuran-3-yl)methyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-hydroxy-4-methoxybutyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(1,3-dimethoxypropan-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-methoxybutan-2-yl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(methylamino)ethyl)azetidine-3-carboxamido)-N-

methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylacetamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(2-(N-methylmethylsulfonamido)ethyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

methyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)ethyl)(methyl)carbamate;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-((methylsulfonyl)carbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-((ethylsulfonyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(sulfamoylcarbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-((N,N-dimethylsulfamoyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl acetate;

(5-(3-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl propionate;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl methyl carbonate;

(5-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)pyrazin-2-yl)methyl L-valinate;

2-chloro-5-(1-(2-(hydroxymethyl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(5-(hydroxymethyl)pyrimidin-2-yl)-3-(2-isopropylphenyl)azetidine-3-

carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(5-methyl-1,1-dioxido-1,2,5-thiadiazolidine-2-carbonyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(6-methyl-1,1-dioxido-1,2,6-thiadiazinane-2-carbonyl)phenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

2-chloro-5-(3-(2-isopropylphenyl)-1-(4-(N-methylsulfamoylcarbamoyl)phenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(N,N-dimethylsulfamoyl)(methyl)carbamoyl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-N-methylisonicotinamide;

6-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)nicotinamide;

5-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)picolinamide;

6-(3-(1-(6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-N-(N,N-dimethylsulfamoyl)pyridazine-3-carboxamide;

2-chloro-5-(1-(3-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(diethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(6-(dimethylphosphoryl)pyridin-3-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2-hydroxypropylacetate;

(R)-1-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-3-hydroxypropan-2-yl acetate;

(R)-3-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)propane-1,2-diyl diacetate;

2-chloro-5-(1-(5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-2-fluorophenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-chloro-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-2-methylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-methylphenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

2-chloro-5-(1-(2-(dimethylphosphoryl)pyrimidin-5-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

tert-butyl (2-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-5-(dimethylphosphoryl)pyridin-4-yl)carbamate;

5-(1-(4-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

2-chloro-5-(1-(5-(dimethylphosphoryl)-4-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide;

5-(1-(3-amino-4-(dimethylphosphoryl)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

5-(1-(6-amino-5-(dimethylphosphoryl)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamide)-2-chloro-N-methylisonicotinamide;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoronicotinamide;

methyl 4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-

isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxylate;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxylic acid;

4-(3-((6-chloro-4-(methylcarbamoyl)pyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-6-fluoropyridazine-3-carboxamide;

2-chloro-5-(1-(4-(dimethylphosphoryl)-3-(methylamino)phenyl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide; and

2-chloro-5-(1-(5-(dimethylphosphoryl)-6-(methylamino)pyridin-2-yl)-3-(2-isopropylphenyl)azetidine-3-carboxamido)-N-methylisonicotinamide,

a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition comprising the compound according to any one of claims 1 to 10, a deuterated compound thereof, or a pharmaceutically acceptable salt thereof.

12. The pharmaceutical composition according to claim 11, for preventing, ameliorating, and/or treating a disease, the symptom of which is ameliorated by antagonizing a lysophosphatidic acid receptor.

13. The pharmaceutical composition according to claim 12, wherein the disease in which symptoms are ameliorated by antagonizing a lysophosphatidic acid receptor is pain or fibrosis.