



(51) International Patent Classification:

C07D 401/14 (2006.01) A61P 35/00 (2006.01)
A61K 31/506 (2006.01) C07D 403/14 (2006.01)

(21) International Application Number:

PCT/KR2024/007677

(22) International Filing Date:

05 June 2024 (05.06.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

10-2023-0073928 09 June 2023 (09.06.2023) KR

(71) Applicant: YUHAN CORPORATION [KR/KR]; 74, No-ryangjin-ro, Dongjak-gu, Seoul 06927 (KR).

(72) Inventors: JEONG, Jaewon; 323-501, 117, Dongtan-daero 24-gil, Hwaseong-si, Gyeonggi-do 18466 (KR). JUNG, Eun Hye; 113-2804, 10, Seonbok 2-ro, Sujigu, Yongin-si, Gyeonggi-do 16847 (KR). LEE, Soyeon; 303, 35-16, Deogyong-daero 439beon-gil, Jangnang-gu, Suwon-si, Gyeonggi-do 16357 (KR). CHO, Hyokjun; 1710-702, 951, Dongbu-daero, Hwaseong-si, Gyeonggi-do 18487 (KR). HYUN, Kwan Hoon; 119-1103, 16, Seowolcheon-ro, Bupyeong-gu, Incheon 21312 (KR). KIM, Suhwa; 105-2403, 15, Tapsil-ro, Giheung-gu, Yongin-si, Gyeonggi-do 17084 (KR). CHONG, Wonce; 126-705, 31, Byongjeomnoeul-ro, Hwaseong-si, Gyeonggi-do 18367 (KR). KIM, Tae Kyun; 432-901, 70, Dongtanbanseok-ro, Hwaseong-si, Gyeonggi-do 18456 (KR).

(74) Agent: OH, Kook-Jin; 302, Doocon Bldg., 24, Beobwon-ro 3-gil, Seocho-gu, Seoul 06595 (KR).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV,

GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: PYRIMIDINE/PYRIDINE DERIVATIVES OR SALTS THEREOF AND PHARMACEUTICAL COMPOSITIONS COMPRISING THE SAME

(57) Abstract: The present invention provides a novel pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof, a process for the preparation thereof, a pharmaceutical composition comprising the same and a use thereof. The pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof can be usefully applied for preventing or treating various blood cancers or solid tumors through excellent inhibitory activity against hematopoietic progenitor kinase 1 (HPK1).



Description

Title of Invention: PYRIMIDINE/PYRIDINE DERIVATIVES OR SALTS THEREOF AND PHARMACEUTICAL COMPOSITIONS COMPRISING THE SAME

Technical Field

- [1] The present invention relates to a pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof having an excellent inhibitory activity against hematopoietic progenitor kinase 1 (HPK1), a process for the preparation thereof, a pharmaceutical composition comprising the same, and a use thereof.

Background Art

- [2] Antibody-based cancer immunotherapy shows continuous anti-tumor effects in a significant proportion of cancer patients and thus the development of cancer immunotherapy will be one of the effective anti-cancer platforms in the future. Antibody-based cancer immunotherapy has been shown to improve survival rates compared to conventional standard therapies. However, the response rate thereof varies widely depending on tumor types, ranging from 15% in head and neck cancer patients to 87% in leukemia patients (Science 2018;23;359(6382):1350-1355). Such a limitation makes it difficult to utilize cancer immunotherapy as a broad-spectrum anticancer therapy and requires developing the biomarkers that can predict responsiveness (Nature 2017;18;541(7637):321-330; Nat. Rev. Cancer 2019; Mar;19(3):133-150). Therefore, in addition to the cancer immunotherapy, there is an urgent need for alternative approaches that modulate the response of immune cells.
- [3] Recently, there are being re-examined approaches for targeting the intracellular pathway that regulates immune function by small molecules. For increasing the efficacy of cancer immunotherapy based on said approaches, it is required to control immunosuppression in the tumor microenvironment and peripheral tolerance to tumor antigens. In addition, since most of cancer immunotherapies are based on the antibody and target the receptors present on the surface of cell membranes, it is difficult to develop antibody-based cancer immunotherapy that can act on the targets present within tumor cells or immune cells.
- [4] Hematopoietic progenitor kinase 1 (HPK1), a member of the MAP4K family, is a serine/threonine kinase and is mainly expressed only in the hematopoietic cell lineage (T cells, B cells, DC cells, mononuclear cells, NK cells, etc.). HPK1 involves in various signaling mechanisms such as JNK, AP-1, and NK- κ B to regulate the function of immune cells (Genes Devel. 1996; 10:2251-2264, EMBO J. 1996; 15:7013-7025, Proc Nat Acad Sci USA. 2009; 106(34):14508-14513). For example, HPK1 plays a

role in suppressing excessive activity of T cells through phosphorylation and activation of the T cell receptor adapter protein SLP-76 when the T cell receptor is activated by binding to a ligand (J. Exp. Med. 2007; 204:681). In addition, HPK1 inhibits the activity of B cells by interfering with signaling of the B cell receptor through phosphorylation of BLNK protein (J. Biol. Chem. 2012; 287:11037). Therefore, increase in proliferation of T cells and increase in inflammatory cytokines can be observed in HPK1 KO/KD mice in which the function of HPK1 is suppressed. And, decrease in tumor growth rate and increase in efficacy of cancer immunotherapy can be also observed in a tumor model using HPK1 KO/KD mice (Cell Rep. 2018; 25(1):80-94). In addition, it has been reported that the activity of COX-2 and PGE2/adenosine is an important cause of reducing the efficacy of immunotherapy in the tumor microenvironment; and that tumor growth rate according to the immune response is decreased in HPK1 KD mice, even in the presence of high level of PGE2 (Cancer Immunol Immunother. 2010; 59(3):419-429). These mechanisms mean that, when HPK1 is inhibited in most of tumor patients, the activity of immune cells increases and the immunosuppression in the tumor microenvironment can also be improved. Therefore, the materials that inhibit HPK1 can be usefully applied to the prevention and treatment of any types of carcinomas, including various blood cancers and solid tumors.

Disclosure of Invention

Technical Problem

- [5] The present inventors carried out various studies to develop a material having an excellent inhibitory activity against HPK1. As a result, the present inventors have found that a pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof has an excellent inhibitory activity against HPK1. Therefore, the pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof inhibits HPK1 to activate immune cells and improve the tumor microenvironment in which the immune system is suppressed, thereby being able to be usefully applied to the prevention and treatment of various blood cancers and solid tumors.

- [6] Therefore, the present invention provides said pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof, a process for the preparation thereof, a pharmaceutical composition comprising the same, and a use thereof.

Solution to Problem

- [7] According to an aspect of the present invention, there is provided a pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof.

- [8] According to another aspect of the present invention, there is provided a process for preparing said pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof.
- [9] According to still another aspect of the present invention, there is provided a pharmaceutical composition comprising said pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof as an active ingredient.
- [10] According to still another aspect of the present invention, there is provided a therapeutic method comprising administering said pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof.
- [11] According to still another aspect of the present invention, there is provided a use of said pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof for the manufacture of a medicament for inhibiting hematopoietic progenitor kinase 1.

Advantageous Effects of Invention

- [12] It has been found by the present invention that the pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof has an excellent inhibitory activity against HPK1. Therefore, the compound or pharmaceutically acceptable salt thereof according to the present invention can be usefully applied for preventing or treating various blood cancers and solid tumors, through inhibiting the activity of HPK1.

Best Mode for Carrying out the Invention

- [13] As used herein, the term 'alkyl' refers to an aliphatic hydrocarbon radical, including a straight or branched aliphatic hydrocarbon radical. For example, the C₁~C₆ alkyl means aliphatic hydrocarbon having 1 to 6 carbon atoms, including methyl, ethyl, propyl, n-butyl, n-pentyl, n-hexyl, isopropyl, isobutyl, sec-butyl, tert-butyl, neopentyl, and isopentyl.
- [14] The term 'hydroxy' refers to the -OH group. The term 'alkoxy' refers to a radical formed by substituting the hydrogen atom in the hydroxyl group with an alkyl, unless otherwise defined. For example, the C₁~C₆ alkoxy includes methoxy, ethoxy, propoxy, n-butoxy, n-pentyloxy, isopropoxy, sec-butoxy, tert-butoxy, neopentyloxy, and isopentyloxy.
- [15] The term 'halogen' refers to the fluoro, bromo, chloro, or iodo group.
- [16] The term 'amino' refers to the -NH₂ group. The term 'alkylamino' refers to an amino group substituted with mono- or di-alkyl. For example, the C₁~C₆ alkylamino includes an amino group substituted with mono- or di- C₁~C₆ alkyl.
- [17] The term 'carbonyl' refers to -C(=O)-. The term 'aminocarbonyl' refers to a carbonyl group substituted with amino. The term 'alkylcarbonyl' refers to a carbonyl group substituted with alkyl. The term 'hydroxycarbonyl' refers to a carbonyl group substituted with hydroxy. The term 'alkoxycarbonyl' refers to a carbonyl group

substituted with alkoxy. The term 'heterocycloalkylcarbonyl' refers to a carbonyl group substituted with heterocycloalkyl.

[18] The term 'sulfonyl' refers to $-\text{SO}_2-$. The term 'alkylsulfonyl' refers to a sulfonyl group substituted with alkyl.

[19] The term 'cyano' refers to the $-\text{CN}$.

[20] The term 'cycloalkyl' refers to a cyclic alkyl group, where the 'alkyl' is the same as defined in the above. For example, the cycloalkyl includes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, etc., but not limited thereto.

[21] The term 'heterocycloalkyl' refers to a 3- to 12-membered cycloalkyl or spirocycloalkyl group having one to three heteroatoms selected from N, O and S. For example, the heterocycloalkyl includes azetidiny, pyrrolidiny, piperidiny, N-methylpiperidiny, pyrazolidiny, morpholiny, piperaziny, tetrahydropyrany, tetrahydrofurany, oxazolidin-2-onyl, 2,8-diazaspiro[4.5]decanyl, etc., but not limited thereto.

[22] The term 'aryl' refers to a 3- to 12-membered aromatic ring and may be a single ring or multiple rings. For examples, the aryl includes phenyl, naphthyl, biphenyl, etc., but not limited thereto.

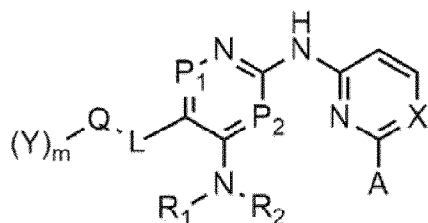
[23] The term 'heteroaryl' refers to a 3- to 12-membered aromatic ring having one to three heteroatoms selected from N, O and S and may be a single ring or multiple rings. For example, the heteroaryl includes thienyl, furyl, pyrrolyl, pyrazolyl, thiazolyl, oxazolyl, pyridiny, pyrimidiny, quinoliny, quinazoliny, quinoxaliny, [1,2,4]triazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyridiny, imidazo[1,2-a]pyridiny, [1,2,4]triazolo[4,3-a]pyridin-6-yl, etc., but not limited thereto.

[24] The term 'substituted' refers to being substituted at one or more substitutable positions. For example, the expression ' $\text{C}_1\sim\text{C}_6$ alkyl substituted with halogen' includes a $\text{C}_1\sim\text{C}_6$ alkyl group substituted with one or more halogens, for example, 1, 2 or 3 halogens.

[25] The present invention provides a pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof having an excellent inhibitory activity against HPK1, i.e., the following compound of Formula 1 or pharmaceutically acceptable salt thereof:

[26] <Formula 1>

[27]



[28] wherein,

- [29] P_1 and P_2 are, independently each other, $-\text{CH}=\text{}$ or $-\text{N}=\text{}$,
- [30] R_1 and R_2 are, independently each other, a $\text{C}_1\sim\text{C}_6$ alkyl group; a $\text{C}_3\sim\text{C}_6$ cycloalkyl group optionally substituted with hydroxy or amino; or a heterocycloalkyl optionally substituted with hydroxy or amino, or
- [31] R_1 and R_2 form a heterocycloalkyl together with the nitrogen atom to which they are bonded, wherein the heterocycloalkyl is optionally substituted with one or two groups selected from the group consisting of halogen, amino, hydroxy, $\text{C}_1\sim\text{C}_6$ alkyl, $\text{C}_1\sim\text{C}_6$ alkoxy, $\text{C}_1\sim\text{C}_6$ alkyl substituted with halogen, $\text{C}_1\sim\text{C}_6$ alkyl substituted with hydroxy, $\text{C}_3\sim\text{C}_6$ cycloalkyl, $\text{C}_3\sim\text{C}_6$ cycloalkyl substituted with hydroxy, mono- or di- $\text{C}_1\sim\text{C}_6$ alkylamino, aminocarbonyl, $\text{C}_1\sim\text{C}_6$ alkylcarbonylamino, and mono- or di- $\text{C}_1\sim\text{C}_6$ alkylamino- $\text{C}_1\sim\text{C}_6$ alkyl,
- [32] X is $-\text{C}(\text{R}_3)=$ or $-\text{N}=\text{}$,
- [33] R_3 is hydrogen, halogen, cyano, nitro, amino, $\text{C}_1\sim\text{C}_3$ alkyl, $\text{C}_1\sim\text{C}_3$ alkyl substituted with halogen, hydroxycarbonyl, $\text{C}_1\sim\text{C}_3$ alkoxy carbonyl, aminocarbonyl, mono- or di- $\text{C}_1\sim\text{C}_3$ alkylaminocarbonyl, or $\text{C}_1\sim\text{C}_3$ alkylsulfonyl,
- [34] A is a 5- to 12-membered aryl group; a 5- to 12-membered heteroaryl group having one to three heteroatoms selected from N, O and S; or a 5- to 12-membered heterocycloalkyl group having one to three heteroatoms selected from N, O and S, wherein the aryl group, the heteroaryl group, or the heterocycloalkyl group is optionally substituted with one to three groups selected from the group consisting of halogen, amino, hydroxy, $\text{C}_1\sim\text{C}_6$ alkyl, $\text{C}_1\sim\text{C}_6$ alkyl substituted with hydroxy, $\text{C}_1\sim\text{C}_6$ alkoxy, $\text{C}_3\sim\text{C}_6$ cycloalkyl, aldehyde, mono- or di- $\text{C}_1\sim\text{C}_3$ alkylamino, mono- or di- $\text{C}_1\sim\text{C}_3$ alkylamino- $\text{C}_1\sim\text{C}_6$ alkyl, $\text{C}_1\sim\text{C}_6$ alkoxy carbonyl, mono- or di- $\text{C}_1\sim\text{C}_6$ alkylaminocarbonyl, $\text{C}_1\sim\text{C}_6$ alkylaminocarbonyl substituted with halogen, $\text{C}_3\sim\text{C}_6$ cycloalkylaminocarbonyl, $\text{C}_3\sim\text{C}_6$ cycloalkylaminocarbonyl substituted with halogen, $\text{C}_3\sim\text{C}_6$ cycloalkylaminocarbonyl substituted with hydroxy, heterocycloalkyl- $\text{C}_1\sim\text{C}_3$ alkyl optionally substituted with hydroxy, heterocycloalkylcarbonyl optionally substituted with halogen, and oxo,
- [35] L is a bond, $-\text{C}(\text{O})-$, $-(\text{CH}_2)_n-$, $-\text{C}(\text{O})\text{NH}-$, or $-\text{C}\equiv\text{C}-$,
- [36] n is 1, 2, or 3,
- [37] Q is a bond; $\text{C}_3\sim\text{C}_6$ cycloalkyl; a 3- to 12-membered heterocycloalkyl having one to three heteroatoms selected from N, O and S; a 5- to 12-membered heteroaryl having one to three heteroatoms selected from N, O and S; or a 5- to 12-membered aryl,
- [38] m is 1, 2, or 3,
- [39] Y is, independently each other, hydrogen, hydroxy, halogen, amino, $\text{C}_1\sim\text{C}_6$ alkyl, $\text{C}_1\sim\text{C}_6$ alkyl substituted with hydroxy, $\text{C}_1\sim\text{C}_6$ alkyl substituted with halogen, $\text{C}_1\sim\text{C}_6$ alkyl substituted with mono- or di- $\text{C}_1\sim\text{C}_3$ alkylamino, $\text{C}_1\sim\text{C}_6$ alkoxy, $\text{C}_1\sim\text{C}_6$ alkoxy

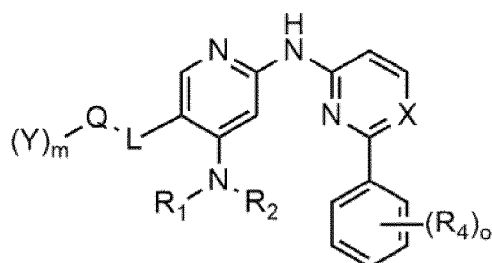
- substituted with C₁~C₃ alkoxy, C₁~C₆ alkoxy substituted with halogen, C₁~C₆ alkoxy substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy-C₁~C₆ alkyl, C₃~C₆ cycloalkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl substituted with halogen, C₁~C₃ alkylcarbonyl, C₃~C₆ cycloalkyl-aminocarbonyl substituted with hydroxy, mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkylamino substituted with mono- or di-C₁~C₃ alkylamino, aminocarbonyl-C₁~C₆ alkyl, C₁~C₃ alkoxycarbonyl-C₁~C₆ alkyl, C₁~C₃ alkylcarbonylamino, mono- or di-C₁~C₆ alkylaminocarbonyl, mono- or di-C₁~C₆ alkylaminocarbonylamino, or mono- or di-C₁~C₆ alkylaminocarbonyl-C₁~C₆ alkyl, or
- [40] a heterocycloalkyl-containing group selected from the group consisting of azetidiny; azetidiny-C₁~C₆ alkyl; tetrahydropyranyl; tetrahydrofuranyl; pyrrolidiny; pyrrolidiny-C₁~C₃ alkyl; piperidiny; piperidiny-C₁~C₃ alkyl; piperidiny carbonyl; piperidinyloxy; piperaziny; piperaziny-C₁~C₃ alkyl; piperaziny carbonyl; oxetanyl; morpholiny; morpholiny-C₁~C₃ alkyl; and morpholiny carbonyl, wherein the heterocycloalkyl of the heterocycloalkyl-containing group is optionally substituted with one to four groups selected from the group consisting of halogen, hydroxy, amino, oxo, C₁~C₃ alkyl, C₁~C₃ alkyl substituted with hydroxy, and mono- or di-C₁~C₃ alkylamino.
- [41] In an embodiment of the present invention, P₁ may be -CH= and P₂ may be -CH= or -N=. In another embodiment of the present invention, P₁ may be -N= and P₂ may be -CH=.
- [42] In the compound of Formula 1 or pharmaceutically acceptable salt thereof according to the present invention, R₁ and R₂ may form piperidine, azetidine, pyrrolidine, piperazine, or 2,8-diazaspiro[4.5]decane together with the nitrogen atom to which they are bonded. In an embodiment, R₁ may be a C₁~C₆ alkyl group and R₂ may be a C₃~C₆ cycloalkyl group substituted with hydroxy.
- [43] In an embodiment of the present invention, X may be -N=.
- [44] In another embodiment of the present invention, X may be -C(R₃)= and R₃ may be H, -F, -Cl, -CH₃, -CN, -NO₂, -NH₂, -C(O)OH, -C(O)OCH₃, -C(O)NH₂, -C(O)N(CH₃)₂, or -SO₂CH₃.
- [45] In the compound of Formula 1 or pharmaceutically acceptable salt thereof according to the present invention, A may be preferably phenyl, pyridiny, thienyl, [1,2,4]triazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyridiny, quinoliny, quinoxaliny, or oxazolidiny. In an embodiment, A may be optionally substituted with one to three groups selected from the group consisting of halogen, amino, hydroxy, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkoxy, aldehyde, mono- or di-C₁~C₃ alkylamino-C₁~C₆ alkyl, C₁~C₆ alkoxycarbonyl, mono- or di-C₁~C₆ alkylaminocarbonyl, azetidiny-C₁~C₃ alkyl substituted with

hydroxy, azetidinyldicarbonyl optionally substituted with one or two halogens, pyrrolidinylcarbonyl optionally substituted with one or two halogens, and oxo,

[46] In the compound of Formula 1 or pharmaceutically acceptable salt thereof according to the present invention, A may be particularly preferably phenyl. That is, particularly preferably, the present invention includes a compound of Formula 1a or pharmaceutically acceptable salt thereof:

[47] <Formula 1a>

[48]



[49] wherein,

[50] R_1 and R_2 form a heterocycloalkyl together with the nitrogen atom to which they are bonded, wherein the heterocycloalkyl is optionally substituted with one or two groups selected from the group consisting of halogen, amino, hydroxy, $C_1\sim C_6$ alkyl, $C_1\sim C_6$ alkoxy, $C_1\sim C_6$ alkyl substituted with halogen, $C_1\sim C_6$ alkyl substituted with hydroxy, $C_3\sim C_6$ cycloalkyl, $C_3\sim C_6$ cycloalkyl substituted with hydroxy, mono- or di- $C_1\sim C_6$ alkylamino, aminocarbonyl, $C_1\sim C_6$ alkylcarbonylamino, and mono- or di- $C_1\sim C_6$ alkylamino- $C_1\sim C_6$ alkyl,

[51] X is $-C(R_3)=$ or $-N=$,

[52] R_3 is hydrogen, halogen, cyano, nitro, amino, $C_1\sim C_3$ alkyl, $C_1\sim C_3$ alkyl substituted with halogen, hydroxycarbonyl, $C_1\sim C_3$ alkoxy, aminocarbonyl, mono- or di- $C_1\sim C_3$ alkylaminocarbonyl, or $C_1\sim C_3$ alkylsulfonyl,

[53] R_4 is, independently each other, halogen, amino, hydroxy, $C_1\sim C_6$ alkyl, $C_1\sim C_6$ alkyl substituted with hydroxy, $C_1\sim C_6$ alkoxy, $C_3\sim C_6$ cycloalkyl, aldehyde, mono- or di- $C_1\sim C_3$ alkylamino, mono- or di- $C_1\sim C_3$ alkylamino- $C_1\sim C_6$ alkyl, $C_1\sim C_6$ alkoxy, mono- or di- $C_1\sim C_6$ alkylaminocarbonyl, $C_1\sim C_6$ alkylaminocarbonyl substituted with halogen, $C_3\sim C_6$ cycloalkylaminocarbonyl, $C_3\sim C_6$ cycloalkylaminocarbonyl substituted with halogen, $C_3\sim C_6$ cycloalkylaminocarbonyl substituted with hydroxy, heterocycloalkyl- $C_1\sim C_3$ alkyl optionally substituted with hydroxy, or heterocycloalkylcarbonyl optionally substituted with halogen,

[54] o is 0, 1, 2, or 3,

[55] L is a bond, $-C(O)-$, $-(CH_2)_n-$, $-C(O)NH-$, or $-C\equiv C-$,

[56] n is 1, 2, or 3,

- [57] Q is a bond; C₃~C₆ cycloalkyl; a 3- to 12-membered heterocycloalkyl having one to three heteroatoms selected from N, O and S; a 5- to 12-membered heteroaryl having one to three heteroatoms selected from N, O and S; or a 5- to 12-membered aryl,
- [58] m is 1, 2, or 3,
- [59] Y is, independently each other, hydrogen, hydroxy, halogen, amino, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkyl substituted with halogen, C₁~C₆ alkyl substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy, C₁~C₆ alkoxy substituted with C₁~C₃ alkoxy, C₁~C₆ alkoxy substituted with halogen, C₁~C₆ alkoxy substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy-C₁~C₆ alkyl, C₃~C₆ cycloalkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl substituted with halogen, C₁~C₃ alkylcarbonyl, C₃~C₆ cycloalkyl-aminocarbonyl substituted with hydroxy, mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkylamino substituted with mono- or di-C₁~C₃ alkylamino, aminocarbonyl-C₁~C₆ alkyl, C₁~C₃ alkoxycarbonyl-C₁~C₆ alkyl, C₁~C₃ alkylcarbonylamino, mono- or di-C₁~C₆ alkylaminocarbonyl, mono- or di-C₁~C₆ alkylaminocarbonylamino, or mono- or di-C₁~C₆ alkylaminocarbonyl-C₁~C₆ alkyl, or
- [60] a heterocycloalkyl-containing group selected from the group consisting of azetidiny; azetidiny-C₁~C₆ alkyl; tetrahydropyranyl; tetrahydrofuranyl; pyrrolidiny; pyrrolidiny-C₁~C₃ alkyl; piperidiny; piperidiny-C₁~C₃ alkyl; piperidinylcarbonyl; piperidinylloxy; piperaziny; piperaziny-C₁~C₃ alkyl; piperazinylcarbonyl; oxetanyl; morpholiny; morpholiny-C₁~C₃ alkyl; and morpholinylcarbonyl, wherein the heterocycloalkyl of the heterocycloalkyl-containing group is optionally substituted with one to four groups selected from the group consisting of halogen, hydroxy, amino, oxo, C₁~C₃ alkyl, C₁~C₃ alkyl substituted with hydroxy, and mono- or di-C₁~C₃ alkylamino.
- [61] In the compound of Formula 1a or pharmaceutically acceptable salt thereof, R₁ and R₂ may form preferably piperidine, azetidine, pyrrolidine, piperazine, or 2,8-diazaspiro[4.5]decane together with the nitrogen atom to which they are bonded.
- [62] In the compound of Formula 1a or pharmaceutically acceptable salt thereof, X may be preferably -N=.
- [63] In the compound of Formula 1a or pharmaceutically acceptable salt thereof, X may be -C(R₃)= and R₃ may be preferably H, -F, -Cl, -CH₃, -CN, -NO₂, -NH₂, -C(O)OH, -C(O)OCH₃, -C(O)NH₂, -C(O)N(CH₃)₂, or -SO₂CH₃.
- [64] In the compound of Formula 1a or pharmaceutically acceptable salt thereof, R₄ may be, independently each other, preferably halogen, amino, hydroxy, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkoxy, aldehyde, mono- or di-C₁~C₃ alkylamino-C₁~C₆ alkyl, C₁~C₆ alkoxycarbonyl, mono- or di-C₁~C₆ alkylaminocarbonyl, azetidiny-C₁~C₃ alkyl substituted with

hydroxy, azetidinyldicarbonyl optionally substituted with one or two halogens, or pyrrolidinylcarbonyl optionally substituted with one or two halogens.

- [65] In the compound of Formula 1 (preferably Formula 1a) or pharmaceutically acceptable salt thereof of the present invention, when Q is a ring such as C₃~C₆ cycloalkyl; a 3- to 12-membered heterocycloalkyl having one to three heteroatoms selected from N, O and S; a 5- to 12-membered heteroaryl having one to three heteroatoms selected from N, O and S; or a 5- to 12-membered aryl, Y may be substituted at any substitutable position(s) within the ring.
- [66] In the compound of Formula 1 (preferably Formula 1a) or pharmaceutically acceptable salt thereof of the present invention, Q may be a bond, C₃~C₆ cycloalkyl, tetrahydropyranyl, pyrrolidinyl, phenyl, pyridinyl, pyrazolyl, thiazolyl, imidazo[1,2-a]pyridinyl, [1,2,4]triazolo[4,3-a]pyridin-6-yl, 2H-benzo[b][1,4]oxazin-3(4H)-onyl, 3,4-dihydroquinolin-2(1H)-onyl, 3,4-dihydro-2H-benzo[b][1,4]oxazinyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-onyl, 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-onyl, or 3,4-dihydro-1,8-naphthyridin-2(1H)-onyl.
- [67] In the compound of Formula 1 (preferably Formula 1a) or pharmaceutically acceptable salt thereof of the present invention, Y may be, independently each other, hydrogen, hydroxy, halogen, amino, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkyl substituted with halogen, C₁~C₆ alkyl substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy, C₁~C₆ alkoxy substituted with C₁~C₃ alkoxy, C₁~C₆ alkoxy substituted with halogen, C₁~C₆ alkoxy substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy-C₁~C₆ alkyl, C₃~C₆ cycloalkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl substituted with halogen, C₁~C₃ alkylcarbonyl, C₃~C₆ cycloalkyl-aminocarbonyl substituted with hydroxy, mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkylamino substituted with mono- or di-C₁~C₃ alkylamino, aminocarbonyl-C₁~C₆ alkyl, C₁~C₃ alkoxycarbonyl-C₁~C₆ alkyl, C₁~C₃ alkylcarbonylamino, mono- or di-C₁~C₆ alkylaminocarbonyl, mono- or di-C₁~C₆ alkylaminocarbonylamino, or mono- or di-C₁~C₆ alkylaminocarbonyl-C₁~C₆ alkyl.
- [68] In the compound of Formula 1 (preferably Formula 1a) or pharmaceutically acceptable salt thereof of the present invention, one of Y may be a heterocycloalkyl-containing group selected from the group consisting of azetidinyldicarbonyl; tetrahydropyranyl; tetrahydrofuranyl; pyrrolidinyl; pyrrolidinylmethyl; pyrrolidinylethyl; piperidinyl; piperidinylmethyl; piperidinylcarbonyl; piperidinylalkoxy; piperazinyl; piperazinylmethyl; piperazinylcarbonyl; oxetanyl; morpholinyl; morpholinylmethyl; morpholinylethyl; and morpholinylcarbonyl, and the remaining Y may be hydrogen. In addition, the heterocycloalkyl of the heterocycloalkyl-containing group may be substituted with one to four groups selected from the group consisting of

halogen, hydroxy, amino, oxo, C₁~C₃ alkyl, C₁~C₃ alkyl substituted with hydroxy, and mono- or di-C₁~C₃ alkylamino.

- [69] In the compound of Formula 1 or pharmaceutically acceptable salt, preferable compounds include the following compound or pharmaceutically acceptable salt thereof selected from the group consisting of:
- [70] (S)-cyclopropyl(4-(3-hydroxypiperidin-1-yl)-6-((2-(5-methylpyridin-3-yl)pyrimidin-4-yl)amino)pyridin-3-yl)methanone;
- [71] (S)-(6-((2-(5-aminopyridin-3-yl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone;
- [72] (S)-cyclopropyl(4-(3-hydroxypiperidin-1-yl)-6-((2-(5-methoxypyridin-3-yl)pyrimidin-4-yl)amino)pyridin-3-yl)methanone;
- [73] (S)-cyclopropyl(6-((2-(3-hydroxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)methanone;
- [74] (S)-cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)methanone;
- [75] cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxyazetidin-1-yl)pyridin-3-yl)methanone;
- [76] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [77] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [78] (R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [79] 1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)azetidin-3-ol;
- [80] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [81] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [82] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [83] (3S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [84] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [85] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

- [86] (S)-1-(5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [87] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(tetrahydro-2H-pyran-4-yl)phenyl)pyridin-4-yl)piperidin-3-ol;
- [88] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(4-methylpiperazin-1-yl)phenyl)pyridin-4-yl)piperidin-3-ol;
- [89] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [90] (S)-1-(2-((2-(4-(hydroxymethyl)thiophen-2-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [91] (S)-1-(2-((2-(2,6-difluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [92] (S)-1-(2-((2-(3,6-difluoro-2-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [93] (S)-1-(2-((2-(2,3-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [94] (S)-1-(2-((2-(2-ethoxy-6-fluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [95] (S)-1-(2-((2-([1,2,4]triazolo[1,5-a]pyridin-7-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [96] (S)-1-(2-((2-(pyrazolo[1,5-a]pyridin-3-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [97] (S)-1-(2-((2-(quinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [98] (S)-1-(2-((2-(8-fluoroquinolin-7-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [99] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((4-methylpiperazin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [100] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [101] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(morpholinomethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [102] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((4-hydroxypiperidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [103] 1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide;
- [104] (S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

- [105] (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-methylpiperazin-1-yl)methanone;
- [106] (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(morpholino)methanone;
- [107] (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone;
- [108] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(((S)-3-fluoropyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [109] (3S)-1-(2-((5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [110] (3S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [111] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [112] (3S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((3-hydroxypyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [113] N-(4-(3-(dimethylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [114] (1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-3-methylpyrrolidin-3-yl)methanol;
- [115] N-(4-(4-((dimethylamino)methyl)-4-fluoropiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [116] (4-(2,2-difluoroethyl)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)methanol;
- [117] (3S)-1-(6'-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [118] 1-((6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)methyl)piperidin-3-ol;
- [119] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide;
- [120] (R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide;
- [121] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [122] (R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [123] (6'-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone;
- [124] (S)-1-(6'-((4-aminopiperidin-1-yl)methyl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [125] (S)-1-(6'-ethoxy-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [126] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(trifluoromethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [127] (3S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)-5-methylpyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [128] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;
- [129] methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate;
- [130] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(imidazo[1,2-a]pyridin-6-yl)pyridin-4-yl)piperidin-3-ol;
- [131] (S)-1-(5-([1,2,4]triazolo[4,3-a]pyridin-6-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [132] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-yl)amino)nicotinonitrile;
- [133] N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [134] 1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)cyclopropan-1-ol;
- [135] 1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)ethan-1-ol;
- [136] 2-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-2-methylpropan-1-ol;
- [137] 2-(2-fluoro-6-methoxyphenyl)-N-(4-(4-methylpiperazin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [138] (S)-1-(2-((2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [139] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [140] methyl 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinate;
- [141] (S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;

- [142] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [143] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [144] (3S)-1-(2-((5-chloro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [145] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine;
- [146] (R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [147] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [148] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [149] (S)-3-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)pyridin-2-ol;
- [150] (S)-1-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-methylpiperidin-4-yl)oxy)-[2,3'-bipyridin]-4'-yl)piperidin-3-ol;
- [151] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-6-amine;
- [152] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(1-methylpiperidin-4-yl)-[3,3'-bipyridin]-6-amine;
- [153] 2-(2-fluoro-6-methoxyphenyl)-N-(5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(3-(2,2,2-trifluoroethyl)piperidin-1-yl)pyridin-2-yl)pyrimidin-4-amine;
- [154] 2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(fluoromethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [155] N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)acetamide;
- [156] 2-(2-fluoro-6-methoxyphenyl)-N-(5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(4-(trifluoromethyl)piperidin-1-yl)pyridin-2-yl)pyrimidin-4-amine;
- [157] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;
- [158] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;
- [159] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;
- [160] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [161] N-(4-(2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [162] N-(4-(2,8-diazaspiro[4.5]decan-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [163] (3R,4R)-4-fluoro-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [164] (3R,4R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-(hydroxymethyl)piperidin-3-ol;
- [165] (R)-N-(4-(3-aminopyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [166] (S)-N-(4-(3-aminopyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [167] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(2-(1-methylpiperidin-4-yl)thiazol-5-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [168] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-6-amine;
- [169] 4-((S)-3-aminopiperidin-1-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [170] (S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol;
- [171] (S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol;
- [172] (S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol;
- [173] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [174] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [175] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [176] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [177] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [178] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [179] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [180] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [181] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
- [182] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-N,N-dimethylnicotinamide;
- [183] 4-((S)-3-aminopiperidin-1-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-amine;
- [184] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;
- [185] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-methoxypropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [186] 2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [187] (S)-4-(3-aminopiperidin-1-yl)-N⁶-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-N⁶',N⁶'-dimethyl-[3,3'-bipyridin]-6,6'-diamine;
- [188] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(pyrrolidin-1-yl)-[3,3'-bipyridin]-6-amine;
- [189] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperidin-1-yl)-[3,3'-bipyridin]-6-amine;
- [190] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine;
- [191] (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(methylamino)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [192] (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(methylamino)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [193] (S)-2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(methylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [194] (S)-N-(4-(3-(ethylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [195] (R)-N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide;
- [196] (S)-3-(6-((4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyridin-2-yl)oxazolidin-2-one;

- [197] (S)-N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide;
- [198] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;
- [199] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-N,N-dimethylnicotinamide;
- [200] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [201] (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-N,N-dimethylacetamide;
- [202] (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)ethan-1-ol;
- [203] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [204] N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [205] 2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [206] N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine;
- [207] (S)-3-(6-((4-(3-aminopiperidin-1-yl)-6'-morpholino-[3,3'-bipyridin]-6-yl)amino)pyridin-2-yl)oxazolidin-2-one;
- [208] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinic acid;
- [209] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinamide;
- [210] 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-N,N-dimethylnicotinamide;
- [211] 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;
- [212] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
- [213] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
- [214] (3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [215] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;

- [216] N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [217] N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [218] 4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine;
- [219] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [220] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [221] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
- [222] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [223] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [224] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-amine;
- [225] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-amine;
- [226] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [227] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [228] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [229] 6-((5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;
- [230] (S)-1-(2-((2-(2-fluoro-4-(hydroxymethyl)-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [231] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [232] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [233] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [234] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [235] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [236] (S)-3-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)propanamide;
- [237] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(azetidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [238] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [239] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [240] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [241] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [242] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [243] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [244] (S)-5-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridazin-3-amine;
- [245] (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(4-methylpiperazin-1-yl)methanone;
- [246] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [247] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [248] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [249] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [250] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [251] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [252] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [253] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

- [254] methyl (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate;
- [255] (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N-methylbenzamide;
- [256] (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N,N-dimethylbenzamide;
- [257] (S)-1-(2-((2-(4-((3-hydroxyazetidin-1-yl)methyl)thiophen-2-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [258] (S)-3-fluoro-4-(4-((4-(3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-5-methoxybenzaldehyde;
- [259] (S)-1-(2-((2-(2-fluoro-6-methoxy-4-((methylamino)methyl)phenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [260] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [261] 6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide;
- [262] 6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [263] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [264] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3S)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [265] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-(3-hydroxycyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [266] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,2R)-2-hydroxycyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [267] N-(3,3-difluorocyclobutyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [268] N-((1R,3R)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [269] N-((1R,3S)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [270] 6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [271] 6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-N-((1R,3S)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

- [272] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide;
- [273] N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [274] N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [275] (S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [276] N-(4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [277] N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [278] (3R,4R)-3-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-4-ol;
- [279] N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [280] N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [281] (S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [282] (3R,4R)-3-amino-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-ol;
- [283] (1S,4S)-4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)(methyl)amino)cyclohexan-1-ol;
- [284] N²-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [285] N²-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [286] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [287] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [288] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [289] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

- [290] (3S)-1-(5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [291] (3S)-1-(5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [292] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [293] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [294] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [295] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [296] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [297] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(2-(tetrahydro-2H-pyran-4-yl)ethyl)pyridin-4-yl)piperidin-3-ol;
- [298] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [299] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(2-methoxyethoxy)-[3,3'-bipyridin]-6-amine;
- [300] (S)-(3,3-difluoroazetidin-1-yl)(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanone;
- [301] (4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((S)-3-fluoropyrrolidin-1-yl)methanone;
- [302] (4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone;
- [303] (S)-(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)(3,3-difluoropyrrolidin-1-yl)methanone;
- [304] (S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropan-2-ol;
- [305] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-(dimethylamino)propyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [306] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(azetidin-3-ylmethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [307] N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-pyrrolidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [308] N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-pyrrolidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [309] (S)-4-(3-aminopiperidin-1-yl)-N⁶-(2-(dimethylamino)ethyl)-N⁶-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-[3,3'-bipyridin]-6,6'-diamine;
- [310] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperazin-1-yl)-[3,3'-bipyridin]-6-amine;
- [311] (S)-(2-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluorophenyl)methanol;
- [312] (S)-(2-(4-((4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluorophenyl)methanol;
- [313] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methoxy-2-methylpropan-2-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [314] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-((3,3-difluorocyclobutyl)methyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [315] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-(dimethylamino)ethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [316] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(fluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [317] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperidin-4-yl)-[3,3'-bipyridin]-6-amine;
- [318] (S)-4-(3-aminopiperidin-1-yl)-6'-(2-(dimethylamino)ethoxy)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-[3,3'-bipyridin]-6-amine;
- [319] (S)-1-(4'-(3-aminopiperidin-1-yl)-6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-6-yl)-3-ethylurea;
- [320] (4-(4-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone;
- [321] N-(4-((2R,5S)-5-amino-2-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [322] N-(4-((3R,4S)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [323] N-(4-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [324] (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(morpholino)methanone;

- [325] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [326] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [327] (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one;
- [328] (S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)pyrrolidin-2-one;
- [329] (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one;
- [330] (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one;
- [331] (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-8-methyl-3,4-dihydroquinolin-2(1H)-one;
- [332] (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1-methyl-3,4-dihydroquinolin-2(1H)-one;
- [333] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [334] (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(piperazin-1-yl)methanone;
- [335] (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [336] (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [337] N-(4-((3R,4R)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [338] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [339] 6-(4-((S)-3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one;
- [340] (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-methylpiperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [341] (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(fluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [342] (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(difluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [343] (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one;

- [344] (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one;
- [345] (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-3,4-dihydro-1,8-naphthyridin-2(1H)-one;
- [346] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [347] methyl (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropanoate;
- [348] (S)-N-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)acetamide;
- [349] (S)-3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-N,N-dimethylbenzamide;
- [350] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-(trifluoromethoxy)phenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [351] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-fluoro-3-methylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [352] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [353] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-isopropoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [354] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [355] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [356] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [357] (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(4-(2-hydroxyethyl)piperazin-1-yl)methanone;
- [358] 4-(4-((S)-3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-N-((1R,4S)-4-hydroxycyclohexyl)benzamide;
- [359] (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-fluoro-N,N-dimethylbenzamide;
- [360] (S)-1-(3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)ethan-1-one;
- [361] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-chloro-4-fluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [362] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [363] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3,4-difluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [364] (3R,4R)-4-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [365] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-(dimethylamino)-4-fluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [366] N-(4-((3R,4S)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [367] N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [368] N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [369] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [370] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [371] N-(4-((3S,4S)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [372] N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [373] N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [374] N-(4-((3S,5R)-3-amino-5-(trifluoromethyl)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [375] (3S,5S)-5-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [376] N-(4-((3R,4S)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [377] N-(4-((3S,4R)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [378] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [379] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [380] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((4-methyltetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [381] (S)-4-((4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)ethynyl)tetrahydro-2H-pyran-4-ol;

- [382] (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methylbut-3-yn-2-ol;
- [383] (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)but-3-yn-1-ol;
- [384] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-(methylsulfonyl)pyridin-2-yl)pyridin-2-amine;
- [385] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;
- [386] 2-(2,4-difluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;
- [387] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [388] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [389] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [390] 6-((4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [391] 6-((4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [392] 6-((4-((S)-3-aminopiperidin-1-yl)-6'-morpholino-[3,3'-bipyridin]-6-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [393] N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(2-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [394] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;
- [395] 6-((4-((3R,4R)-4-amino-3-hydroxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [396] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-ethyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [397] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [398] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [399] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [400] 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

- [401] N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [402] N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [403] 4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
- [404] N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [405] N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [406] 6-((4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-nicotinonitrile;
- [407] 6-((4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [408] N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [409] 6-((4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile; and
- [410] 4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine.
- [411] In the compound of Formula 1 or pharmaceutically acceptable salt, more preferable compounds include the following compound or pharmaceutically acceptable salt thereof selected from the group consisting of:
- [412] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [413] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [414] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [415] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [416] (3S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [417] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [418] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

- [419] (S)-1-(5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [420] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(tetrahydro-2H-pyran-4-yl)phenyl)pyridin-4-yl)piperidin-3-ol;
- [421] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(4-methylpiperazin-1-yl)phenyl)pyridin-4-yl)piperidin-3-ol;
- [422] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [423] (S)-1-(2-((2-(2,6-difluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [424] (S)-1-(2-((2-(2,3-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [425] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [426] (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone;
- [427] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(((S)-3-fluoropyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [428] (3S)-1-(2-((5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [429] (3S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [430] N-(4-(4-((dimethylamino)methyl)-4-fluoropiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [431] (4-(2,2-difluoroethyl)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)methanol;
- [432] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [433] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;
- [434] methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate;
- [435] N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [436] 1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)cyclopropan-1-ol;

- [437] 1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)ethan-1-ol;
- [438] 2-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-2-methylpropan-1-ol;
- [439] (S)-1-(2-((2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [440] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [441] methyl 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinate;
- [442] (S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [443] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [444] (3S)-1-(2-((5-chloro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [445] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine;
- [446] (R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [447] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [448] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [449] 2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(fluoromethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [450] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;
- [451] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [452] (3R,4R)-4-fluoro-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [453] (3R,4R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-(hydroxymethyl)piperidin-3-ol;
- [454] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [455] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [456] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [457] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [458] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
- [459] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-methoxypropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [460] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [461] N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [462] 2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
- [463] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinamide;
- [464] 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;
- [465] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
- [466] (3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [467] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
- [468] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [469] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [470] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
- [471] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [472] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [473] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-amine;
- [474] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [475] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [476] (S)-1-(2-((2-(2-fluoro-4-(hydroxymethyl)-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [477] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [478] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [479] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [480] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [481] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [482] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [483] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [484] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [485] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [486] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [487] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [488] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [489] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [490] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [491] methyl (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate;
- [492] (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N,N-dimethylbenzamide;
- [493] (S)-3-fluoro-4-(4-((4-(3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-5-methoxybenzaldehyde;

- [494] 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,2R)-2-hydroxy cyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;
- [495] N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [496] N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [497] (S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [498] N-(4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [499] N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [500] (3R,4R)-3-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-4-ol;
- [501] N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [502] (3R,4R)-3-amino-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-ol;
- [503] (1S,4S)-4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)(methyl)amino)cyclohexan-1-ol;
- [504] N²-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [505] N²-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [506] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(difluoro methyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [507] (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;
- [508] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [509] (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [510] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [511] (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

- [512] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [513] (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(2-methoxyethoxy)-[3,3'-bipyridin]-6-amine;
- [514] (S)-(3,3-difluoroazetidin-1-yl)(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanone;
- [515] (4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone;
- [516] (S)-(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)(3,3-difluoropyrrolidin-1-yl)methanone;
- [517] (S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropan-2-ol;
- [518] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methoxy-2-methylpropan-2-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [519] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-((3,3-difluorocyclobutyl)methyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [520] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(fluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [521] N-(4-((2R,5S)-5-amino-2-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [522] N-(4-((3R,4S)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [523] N-(4-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [524] (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one;
- [525] (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-8-methyl-3,4-dihydroquinolin-2(1H)-one;
- [526] (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1-methyl-3,4-dihydroquinolin-2(1H)-one;
- [527] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [528] (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [529] (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [530] N-(4-((3R,4R)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [531] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [532] (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(fluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [533] (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(difluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [534] methyl (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropanoate;
- [535] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [536] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [537] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [538] (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-fluoro-N,N-dimethylbenzamide;
- [539] (S)-1-(3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)ethan-1-one;
- [540] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3,4-difluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [541] (3R,4R)-4-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [542] N-(4-((3R,4S)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [543] N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [544] N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [545] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [546] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [547] N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [548] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [549] (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methylbut-3-yn-2-ol;
- [550] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [551] 6-((4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile; and
- [552] 6-((4-((3R,4R)-4-amino-3-hydroxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile.
- [553] In the compound of Formula 1 or pharmaceutically acceptable salt, still more preferable compounds include the following compound or pharmaceutically acceptable salt thereof selected from the group consisting of:
- [554] (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [555] (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;
- [556] (3S)-1-(2-((5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [557] (3S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [558] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [559] methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate;
- [560] (S)-1-(2-((2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [561] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [562] (S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [563] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [564] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine;
- [565] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

- [566] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [567] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [568] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [569] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [570] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [571] 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
- [572] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-methoxypropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [573] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [574] 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;
- [575] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
- [576] (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
- [577] 4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
- [578] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
- [579] 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-amine;
- [580] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [581] (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [582] N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [583] (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N,N-dimethylbenzamide;
- [584] (3R,4R)-3-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-4-ol;

- [585] N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [586] (3R,4R)-3-amino-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-ol;
- [587] N²-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [588] N²-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;
- [589] (S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropan-2-ol;
- [590] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(fluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [591] N-(4-((3R,4R)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [592] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [593] (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3,4-difluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [594] (3R,4R)-4-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;
- [595] N-(4-((3R,4S)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [596] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
- [597] N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
- [598] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [599] (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methylbut-3-yn-2-ol;
- [600] 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;
- [601] 6-((4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile; and
- [602] 6-((4-((3R,4R)-4-amino-3-hydroxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile.

[603] The compound of Formula 1 or pharmaceutically acceptable salt thereof may be in the form of structural isomer such as tautomer and in the form of stereoisomer such as R or S isomer having with asymmetric carbon center(s), cis- or trans-geometrical isomer, or optical isomer (enantiomer). Therefore, the compound of Formula 1 or pharmaceutically acceptable salt thereof includes said all forms, such as a cis- or trans-geometrical isomer, a (R)- or (S)-optical isomer, and a racemic mixture (RS), unless otherwise indicated.

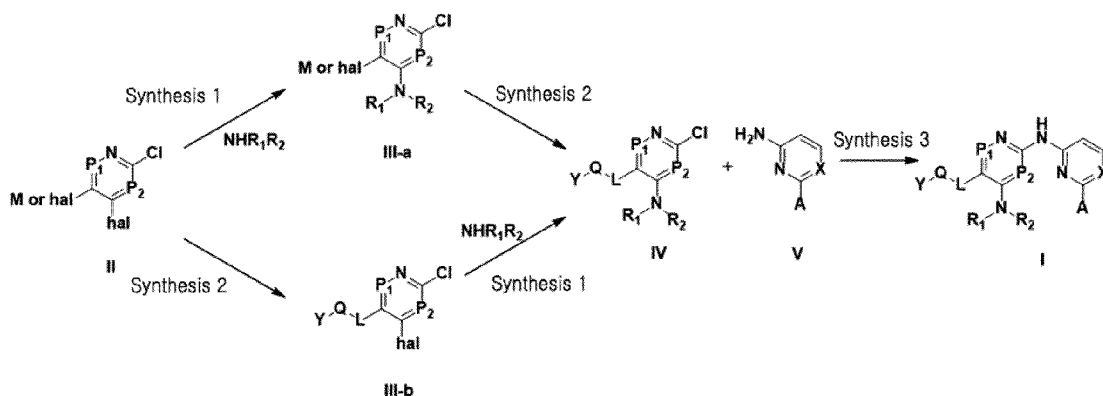
[604] The compound of Formula 1 of the present invention may be in a pharmaceutically acceptable salt form. The salt may be a conventional acid addition salt form, which includes e.g., salts derived from an inorganic acid such as hydrochloric acid, sulfuric acid, nitric acid, phosphoric acid, perchloric acid, or hydrobromic acid; and salts derived from an organic acid such as formic acid, acetic acid, propionic acid, oxalic acid, succinic acid, benzoic acid, citric acid, maleic acid, malonic acid, malic acid, tartaric acid, gluconic acid, lactic acid, gentisic acid, fumaric acid, lactobionic acid, salicylic acid, phthalic acid, embonic acid, aspartic acid, glutamic acid, or acetylsalicylic acid. And, the salt includes a salt derived from amino acids such as glycine, alanine, valine, isoleucine, serine, cysteine, cystine, aspartic acid, glutamine, lysine, arginine, tyrosine, and proline. In addition, the salt includes a salt derived from sulfonic acids, such as methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, or toluenesulfonic acid.

[605] The present invention includes, within its scope, a process for preparing the compound of Formula 1 or pharmaceutically acceptable salt thereof.

[606] For example, the compound of Formula 1 or pharmaceutically acceptable salt thereof according to the present invention may be prepared by a process which comprises preparing a compound of Formula IV from a compound of Formula II, via a compound of Formula III-a or III-b, through Synthesis 1 or Synthesis 2; and reacting the compound of Formula IV with a compound of Formula V through Synthesis 3 to prepare a compound of Formula 1, as shown in the following Reaction Scheme 1:

[607] <Reaction Scheme 1>

[608]

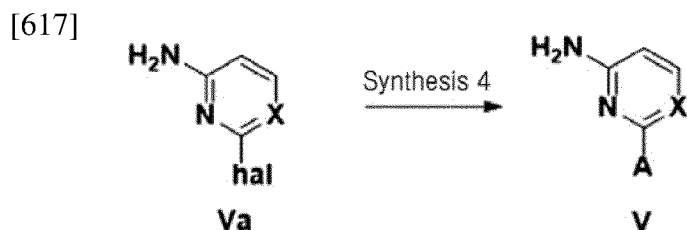


- [609] In the Reaction Scheme 1, hal is halogen; M is $-B(OH)_2$ or pinacolborane ($-BPin$); and P_1 , P_2 , R_1 , R_2 , L, Q, Y, X, and A are the same as defined in the above.
- [610] In the Reaction Scheme 1, the reaction of Synthesis 1 may be carried out by reacting the commercially available compound of Formula II or III-b with NHR_1R_2 . The reaction may be carried out with a base such as cesium carbonate (Cs_2CO_3), potassium carbonate (K_2CO_3), triethylamine (TEA), or diisopropylethylamine (DIPEA), in an organic solvent such as dimethylformamide, acetonitrile, dichloromethane, or dimethyl sulfoxide. And, the reaction may be carried out at room temperature or under heating conditions (60 °C to 110 °C), but is not limited thereto.
- [611] In the Reaction Scheme 1, the reaction of Synthesis 2 may be carried out by reacting the compound of Formula II or III-a having the substituent M with Y-Q-L-halide or reacting the compound of Formula II or III-a having the substituent hal with Y-Q-L- $B(OH)_2$ or pinacolborane.
- [612] The reaction of Synthesis 2 may be carried out through the Suzuki reaction, using a palladium catalyst. The palladium catalyst includes palladium diacetate ($Pd(OAc)_2$), tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$), palladium di[1,1'-bis(diphenylphosphino)ferrocene]dichloride ($PdCl_2(dppf)_2$), or dichlorobis(triphenylphosphine)palladium(II) ($PdCl_2(PPh_3)_2$), etc. And, the reaction may be carried out in the presence of a base such as cesium carbonate (Cs_2CO_3) or potassium carbonate (K_2CO_3), in an organic solvent such as 1,4-dioxane, tetrahydrofuran, acetonitrile, 1,2-dimethoxyethane, or dimethylformamide and water, at 80 °C to 110 °C.
- [613] In addition, the reaction of Synthesis 2 may be also carried out through the Sonogashira reaction using a palladium and copper catalyst. The palladium and copper catalyst includes e.g., tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$), dichlorobis(triphenylphosphine)palladium(II) ($PdCl_2(PPh_3)_2$), and copper(I) iodide (CuI). And, the reaction may be carried out in the presence of a base such as triethylamine (TEA) or diisopropylethylamine (DIPEA), in an organic solvent such as dimethylformamide or tetrahydrofuran, at 60 °C to 110 °C.
- [614] In the Reaction Scheme 1, the reaction of Synthesis 3 may be carried out by reacting the compound of Formula IV with the compound of Formula V, using a palladium catalyst, through the Buchwald-hartwig reaction. The palladium catalyst includes palladium diacetate ($Pd(OAc)_2$), tris(dibenzylideneacetone)dipalladium ($Pd_2(dba)_3$), tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$), or palladium di[1,1'-bis(diphenylphosphino)ferrocene]dichloride ($PdCl_2(dppf)_2$), etc. The reaction may be carried out using a ligand and a base, in addition to the palladium catalyst. The ligand includes 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

l (XPhos), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos), (S)-2,2-bis(diphenylphosphino)-1,1-binaphthyl (BINAP), or 1,1'-bis(diphenylphosphino)ferrrocene (dppf), etc. The base includes cesium carbonate (Cs_2CO_3), potassium carbonate (K_2CO_3), potassium fluoride (KF), potassium phosphate (K_3PO_4), sodium tert-butoxide (NaOtBu), etc. The reaction may be carried out in an organic solvent such as benzene, toluene, 1,4-dioxane, tetrahydrofuran, acetonitrile, 1,2-dimethoxyethane, or dimethylformamide, at 60 °C to 110 °C.

[615] The compound of Formula V in the Reaction Scheme 1 may be prepared from e.g., a compound of Formula Va, according to the following Reaction Scheme 2.

[616] <Reaction Scheme 2>



[618] In the Reaction Scheme 2, hal is halogen and X and A are the same as defined in the above.

[619] In the Reaction Scheme 2, the reaction of Synthesis 4 may be carried out by reacting the compound of Formula Va with A-boronic acid or A-pinacolborane through the Suzuki reaction, using a palladium catalyst. The palladium catalyst includes palladium diacetate ($\text{Pd}(\text{OAc})_2$), tetrakis(triphenylphosphine)palladium ($\text{Pd}(\text{PPh}_3)_4$), palladium di[1,1'-bis(diphenylphosphino)ferrocene]dichloride ($\text{PdCl}_2(\text{dppf})_2$), or dichlorobis(triphenylphosphine)palladium(II) ($\text{PdCl}_2(\text{PPh}_3)_2$), etc. And, the reaction may be carried out in the presence of a base such as cesium carbonate (Cs_2CO_3) or potassium carbonate (K_2CO_3), in an organic solvent such as 1,4-dioxane, tetrahydrofuran, acetonitrile, 1,2-dimethoxyethane, or dimethylformamide and water, at 80 °C to 110 °C.

[620] The pyrimidine/pyridine derivative or pharmaceutically acceptable salt thereof according to the present invention, i.e., the compound of Formula 1 or pharmaceutically acceptable salt thereof has an excellent inhibitory activity against hematopoietic progenitor kinase 1 (HPK1) and thus can be usefully applied for the prevention or treatment of various diseases mediated by HPK1.

[621] Therefore, the present invention includes, within its scope, a pharmaceutical composition for inhibiting hematopoietic progenitor kinase 1 comprising a therapeutically effective amount of the compound of Formula 1 or pharmaceutically acceptable salt thereof as an active ingredient. In an embodiment, the present invention provides a pharmaceutical composition for preventing or treating the diseases

associated with HPK1 such as a cancer including a blood cancer or a solid tumor, for example melanoma, blastoma, sarcoma, lymphoma, leukemia, bladder cancer, brain tumor, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, endometrioma, hepatic cancer, laryngeal cancer, lung cancer, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, thyroid cancer, ependymoma, glioblastoma, bullous cell tumor, neuroblastoma, osteosarcoma, rhabdomyosarcoma, or nephroblastoma, comprising a therapeutically effective amount of the compound of Formula 1 or pharmaceutically acceptable salt thereof as an active ingredient.

- [622] The pharmaceutical composition of the present invention may comprise a pharmaceutically acceptable carrier, such as diluents, disintegrants, sweeteners, lubricants, or flavoring agents, which is conventionally used in the art. The pharmaceutical composition may be formulated to an oral dosage form such as tablets, capsules, powders, granules, suspensions, emulsions, or syrups; or a parenteral dosage form such as solutions for external use, suspensions for external use, emulsions for external use, gels (e.g., ointment), inhalations, nebulizations, injections, according to conventional methods. The dosage form may be formulated to various forms, e.g., dosage forms for single administration or for multiple administrations.
- [623] The pharmaceutical composition of the present invention may comprise, for example, a diluent (e.g., lactose, corn starch, etc.); a lubricant (e.g., magnesium stearate); an emulsifying agent; a suspending agent; a stabilizer; and/or an isotonic agent. If necessary, the composition further comprises sweeteners and/or flavoring agents.
- [624] The composition of the present invention may be administered orally or parenterally, including inhalant, intravenous, intraperitoneal, subcutaneous, rectal and topical routes of administration. Therefore, the composition of the present invention may be formulated into various forms such as tablets, capsules, aqueous solutions or suspensions. In the case of tablets for oral administration, carriers such as lactose, corn starch, and lubricating agents, e.g. magnesium stearate, are conventionally used. In the case of capsules for oral administration, lactose and/or dried corn starch can be used as a diluent. When an aqueous suspension is required for oral administration, the active ingredient may be combined with emulsifying and/or suspending agents. If desired, certain sweetening and/or flavoring agents may be used. For intramuscular, intraperitoneal, subcutaneous and intravenous administration, sterile solutions of the active ingredient are usually prepared, and the pH of the solutions should be suitably adjusted and buffered. For intravenous administration, the total concentration of solutes should be controlled in order to render the preparation isotonic. The composition of the present invention may be in the form of an aqueous solution containing pharmaceutically acceptable carriers, e.g., saline having a pH level of 7.4.

The solutions may be introduced into a patient's intramuscular bloodstream by local bolus injection.

- [625] The compound of Formula 1 or pharmaceutically acceptable salt thereof may be singly or multiply administered in an effective amount ranging from about 1 mg/kg per day to about 1000 mg/kg per day, preferably from about 100 mg/kg per day to about 800 mg/kg per day, to a subject patient. Of course, the dosage may be changed according to the patient's age, weight, susceptibility, symptom, or activity of the compound.
- [626] The present invention includes, within its scope, a method for inhibiting hematopoietic progenitor kinase 1 in a mammal, comprising administering a therapeutically effective amount of the compound of Formula 1 or pharmaceutically acceptable salt thereof to the mammal in need thereof. In an embodiment, the present invention provides a method for treating the diseases associated with HPK1 such as a cancer including a blood cancer or a solid tumor, for example melanoma, blastoma, sarcoma, lymphoma, leukemia, bladder cancer, brain tumor, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, endometrioma, hepatic cancer, laryngeal cancer, lung cancer, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, thyroid cancer, ependymoma, glioblastoma, bullous cell tumor, neuroblastoma, osteosarcoma, rhabdomyosarcoma, or nephroblastoma, comprising administering a therapeutically effective amount of the compound of Formula 1 or pharmaceutically acceptable salt thereof to the mammal in need thereof.
- [627] The present invention also provides a use of the compound of Formula 1 or pharmaceutically acceptable salt thereof for the manufacture of a medicament for inhibiting hematopoietic progenitor kinase 1 in a mammal. In an embodiment, the present invention provides a use of the compound of Formula 1 or pharmaceutically acceptable salt thereof for the manufacture of a medicament for preventing or treating the diseases associated with HPK1 such as a cancer including a blood cancer or a solid tumor, for example melanoma, blastoma, sarcoma, lymphoma, leukemia, bladder cancer, brain tumor, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, endometrioma, hepatic cancer, laryngeal cancer, lung cancer, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, thyroid cancer, ependymoma, glioblastoma, bullous cell tumor, neuroblastoma, osteosarcoma, rhabdomyosarcoma, or nephroblastoma.
- [628] Hereinafter, the present invention will be described in more detail through examples and test examples. However, these examples and test examples are provided for illustration purposes only and are not intended to limit the scope of the invention.
- [629] The analyses of the compounds prepared below were carried out as follows: Nuclear magnetic resonance (NMR) spectrum analysis was carried out using Bruker 400 MHz

spectrometer and the chemical shifts thereof were analyzed in ppm. And, the indicated molecular weights were measured by using liquid chromatograph/mass selective detector (MSD) of Agilent 1260 Infinity series equipped with an electrostatic spray interface, which depicts the m/z ratio values in ESI+ (electrospray ionization (cation)) by using Single Quadrupole, with the $[M+H]^+$ peak represented. The purification of the compounds synthesized below was carried out with medium pressure liquid chromatography (MPLC) using the CombiFlash NextGen 300+ (Teledyne ISCO, USA). In addition, the starting materials for each example were known compounds that were synthesized according to literatures or purchased from the commercial markets.

- [630] The following Preparations show the methods for synthesizing the intermediates for preparing the compounds or salts thereof of the present invention (i.e., the compounds of Examples).
- [631] Preparation A1-1: (S)-(6-((2-chloropyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone
- [632] Step 1: (S)-(6-chloro-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone
- [633] Cyclopropyl(4,6-dichloropyridin-3-yl)methanone (3.0 g, 13.89 mmol) was dissolved in anhydrous acetonitrile (70.0 mL) and then (S)-3-hydroxypiperidine hydrochloride (2.1 g, 15.27 mmol) and diisopropylethylamine (3.8 mL, 27.77 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature overnight. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (2.24 g). (Yield: 57.4%) ^1H NMR (CDCl_3 , 400MHz) δ 8.34 (s, 1H), 6.85 (s, 1H), 3.93-3.38 (m, 1H), 3.36-3.35 (m, 1H), 3.19-3.17 (m, 1H), 3.12-3.05 (m, 2H), 2.54-2.51 (m, 1H), 1.96-1.92 (m, 2H), 1.65-1.62 (m, 2H), 1.31-1.30 (m, 2H), 1.29-1.28 (m, 2H)
- [634] Step 2: (S)-(6-((2-chloropyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone (A1-1)
- [635] (S)-(6-Chloro-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone (1.0 g, 23.56 mmol) was dissolved in anhydrous 1,4-dioxane (24.0 mL) and then 4-amino-2-chloropyrimidine (507.6 mg, 3.92 mmol), tris(dibenzylideneacetone)dipalladium (326.2 mg, 3.92 mmol), and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (412.2 mg, 0.71 mmol) were added dropwise thereto. Then, 1.0M lithium bis(trimethylsilyl)amide (7.1 mL, 7.12 mmol) dissolved in tetrahydrofuran was added to the mixed solution, which was then refluxed under stirring at 110°C for 2 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with

ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (400.0 mg). (Yield: 30.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.39 (s, 1H), 8.32 (d, 1H), 7.45 (d, 1H), 7.3 (s, 1H), 3.97 (s, 1H), 3.44-3.43 (m, 1H), 3.27-3.24 (m, 1H), 3.23-3.10 (m, 2H), 2.63-2.60 (m, 1H), 2.59-2.41 (m, 1H), 2.01-1.91 (m, 2H), 1.70-1.58 (m, 2H), 1.32-1.25 (m, 2H), 1.07-1.04 (m, 2H)

[636] Preparation A1-2: (3S)-1-[2-[(2-chloropyrimidin-4-yl)amino]-5-(1-tetrahydropyran-4-ylpyrazol-4-yl)-4-pyridyl]piperidin-3-ol

[637] (S)-1-(2-Chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol (A2-1) was dissolved in anhydrous 1,4-dioxane (27.0 mL) and then 4-amino-2-chloropyrimidine (1.07 g, 8.27 mmol), tris(dibenzylideneacetone)dipalladium (504.7 mg, 0.55 mmol), 2-dicyclohexylphosphino-2',6'-diisopropoxybiphenyl (514.4 mg, 1.10 mmol), and sodium tert-butoxide (794.5 mg, 8.27 mmol) were added thereto. The reaction mixture was refluxed under stirring at 110°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (317.0 mg). (Yield: 25.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.26 (s, 1H), 8.16 (s, 1H), 8.06 (d, 1H), 7.83 (s, 1H), 6.99 (s, 1H), 6.06 (d, 1H), 4.46-4.44 (m, 1H), 4.21-4.13 (m, 3H), 3.62-3.54 (m, 3H), 3.11-3.05 (m, 1H), 2.94-2.84 (m, 2H), 2.52-2.34 (m, 1H), 2.28-2.01 (m, 4H), 2.05-1.86 (m, 2H), 1.84-1.16 (m, 2H)

[638] Preparation A2-1: (S)-1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[639] Step 1: (S)-1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-ol (A2)

[640] 2-Chloro-4-fluoro-5-iodopyridine (1.0 g, 3.88 mmol) was dissolved in anhydrous dimethylformamide (20.0 mL) and then (S)-3-hydroxypiperidine hydrochloride (588.0 mg, 4.27 mmol) and diisopropylethylamine (1.6 mL, 11.65 mmol) were added dropwise thereto. The reaction mixture was stirred at 50°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (800 mg). (Yield: 60.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.57 (s, 1H), 6.87 (s, 1H), 4.04-3.99 (m, 1H), 3.34-3.31 (m, 1H), 3.07-3.04 (m, 2H), 3.01-2.96 (m, 1H), 2.24 (d, 1H), 2.06-1.99 (m, 1H), 1.92-1.86 (m, 1H), 1.80-1.73 (m, 2H)

- [641] Step 2: (S)-1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol (A2-1)
- [642] (S)-1-(2-Chloro-5-iodopyridin-4-yl)piperidin-3-ol (2.1 g, 6.29 mmol) was dissolved in anhydrous 1,4-dioxane (31.4 mL) and then 1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-boronic acid pinacol ester (1.75 g, 6.29 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (257.0 mg, 0.31 mmol), 2.0M sodium carbonate solution (10.0 mL, 20.0 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 6 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (1.61 g). (Yield: 70.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.80 (d, 2H), 6.88 (s, 1H), 4.44-4.37 (m, 1H), 4.16-4.13 (m, 2H), 3.87-3.82 (m, 1H), 3.61-3.54 (m, 2H), 3.26-3.23 (m, 1H), 3.01-2.98 (m, 1H), 2.78-2.69 (m, 2H), 2.18-2.05 (m, 4H), 1.94-1.91 (m, 1H), 1.84-1.80 (m, 1H), 1.66-1.49 (m, 3H)
- [643] Preparation A2-2: (S)-1-(2-chloro-5-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [644] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-methylpyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.11 (s, 1H), 7.78 (s, 1H), 7.67 (s, 1H), 6.87 (s, 1H), 3.97 (s, 3H), 3.86-3.72 (m, 1H), 3.27-3.25 (m, 1H), 3.03-3.00 (m, 1H), 2.78-2.66 (m, 2H), 1.95-1.92 (m, 1H), 1.82-1.80 (m, 1H), 1.79-1.65 (m, 1H), 1.50-1.48 (m, 1H)
- [645] Preparation A2-3: (S)-1-(2-chloro-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [646] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-isopropylpyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.76 (s, 2H), 6.86 (s, 1H), 4.58 (septet, 1H), 3.92-3.85 (m, 1H), 3.27-3.24 (m, 1H), 3.01-2.98 (m, 1H), 2.76-2.66 (m, 2H), 1.94-1.91 (m, 1H), 1.87-1.82 (m, 1H), 1.81-1.79 (m, 1H), 1.68 (d, 6H), 1.52-1.50 (m, 1H)
- [647] Preparation A2-4: (3S)-1-(2-chloro-5-(1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [648] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-(oxolan-3-yl)-1H-pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (s, 1H), 7.84 (s, 1H),

- 7.78 (s, 1H), 6.87 (s, 1H), 5.05-5.04 (m, 1H), 4.18-4.12 (m, 3H), 4.07-4.04 (m, 1H), 3.99-3.93 (m, 1H), 3.84-3.72 (m, 1H), 3.24-3.21 (m, 1H), 3.00-2.98 (m, 1H), 2.78-2.69 (m, 2H), 2.55-2.48 (m, 1H), 2.40-2.36 (m, 1H), 1.93-1.90 (m, 1H), 1.81-1.72 (m, 1H), 1.69-1.67 (m, 1H), 1.51-1.49 (m, 1H)
- [649] Preparation A2-5: (S)-1-(2-chloro-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [650] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-methyl-4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.88 (d, 2H), 6.91 (s, 1H), 4.82-4.76 (m, 2H), 3.88-3.85 (m, 1H), 3.28-3.24 (m, 1H), 3.03-2.99 (m, 1H), 2.78-2.69 (m, 2H), 1.98-1.94 (m, 1H), 1.84-1.80 (m, 1H), 1.64-1.62 (m, 1H), 1.56-1.49 (m, 2H)
- [651] Preparation A2-6: (S)-1-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [652] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (s, 1H), 7.96 (s, 2H), 6.89 (s, 1H), 4.80-4.74 (q, 2H), 3.85-3.84 (m, 1H), 3.26-3.23 (m, 1H), 3.01-2.98 (m, 1H), 2.76-2.67 (m, 2H), 1.95-1.92 (m, 1H), 1.81-1.79 (m, 1H), 1.62-1.60 (m, 1H), 1.50-1.47 (m, 1H)
- [653] Preparation A2-7: (S)-1-(2-chloro-5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [654] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-(cyclopropylmethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.85 (s, 1H), 7.77 (s, 1H), 6.87 (s, 1H), 4.05 (d, 2H), 3.92-3.86 (m, 1H), 3.28-3.25 (m, 1H), 3.03-3.00 (m, 1H), 2.78-2.67 (m, 2H), 1.94-1.91 (m, 1H), 1.82-1.80 (m, 1H), 1.75-1.71 (m, 1H), 1.55-1.54 (m, 2H), 1.52-1.50 (m, 1H), 0.92-0.71 (m, 2H), 0.69-0.68 (m, 2H)
- [655] Preparation A2-8: (S)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [656] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.18 (d, 2H), 7.99 (s, 1H), 7.26 (t, 1H), 6.93 (s, 1H), 3.91-3.86 (m, 1H), 3.27-3.23 (m, 1H), 3.04-2.99 (m, 1H), 3.80 (s, 2H), 2.07-1.94 (m, 1H), 1.88-1.82 (m, 1H), 1.63-1.62 (m, 1H), 1.55-1.50 (m, 2H)

- [657] Preparation A2-9: (S)-1-(2-chloro-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [658] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-(2-methoxyethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 7.91 (s, 1H), 7.78 (s, 1H), 6.88 (s, 1H), 4.37-4.31 (m, 2H), 3.87-3.78 (m, 3H), 3.39 (s, 3H), 3.14 (d, 1H), 3.04-2.99 (m, 1H), 2.86-2.81 (m, 1H), 2.78-2.73 (m, 1H), 1.90-1.88 (m, 2H), 1.71-1.68 (m, 1H), 1.58-1.53 (m, 1H)
- [659] Preparation A2-10: (S)-1-(2-chloro-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [660] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 1-(2,2-difluoroethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.86-7.85 (m, 2H), 6.91 (s, 1H), 6.32-6.02 (m, 1H), 4.58-4.50 (m, 2H), 3.90-3.84 (m, 1H), 3.27-3.23 (m, 1H), 3.04-3.00 (m, 1H), 2.79-2.67 (m, 2H), 1.98-1.94 (m, 1H), 1.86-1.80 (m, 1H), 1.57-1.48 (m, 3H)
- [661] Preparation A2-11: (S)-1-(2-chloro-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [662] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(trifluoromethyl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 6.85 (s, 1H), 4.58-4.52 (m, 1H), 4.37-4.35 (m, 2H), 3.81-3.79 (m, 3H), 3.40-3.35 (m, 4H), 3.05-3.02 (m, 1H), 2.61-2.56 (m, 1H), 1.93-1.92 (m, 1H), 1.65-1.63 (m, 1H), 1.46 (s, 9H), 1.41-1.31 (m, 1H)
- [663] Preparation A2-12: (S)-1-(2-chloro-5-(4-(tetrahydro-2H-pyran-4-yl)phenyl)pyridin-4-yl)piperidin-3-ol
- [664] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 4-(4-tetrahydropyranyl)phenylboronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.44-7.42 (m, 2H), 7.32-7.30 (m, 2H), 6.86 (s, 1H), 4.12-4.10 (m, 2H), 3.71-3.70 (m, 1H), 3.59-3.53 (m, 2H), 3.13-3.11 (m, 1H), 2.92-2.90 (m, 1H), 2.84-2.70 (m, 3H), 1.87-1.82 (m, 5H), 1.79-1.68 (m, 1H), 1.56-1.44 (m, 3H)
- [665] Preparation A2-13: (S)-1-(2-chloro-5-(4-(4-methylpiperazin-1-yl)phenyl)pyridin-4-yl)piperidin-3-ol
- [666] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 4-(4-methyl-1-piperazinyl)phenylboronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.01 (s, 1H), 7.39 (d,

- 2H), 7.00 (d, 2H), 6.84 (s, 1H), 3.82-3.74 (m, 1H), 3.30-3.27 (m, 4H), 3.16-3.13 (m, 1H), 2.94-2.92 (m, 1H), 2.79-2.71 (m, 2H), 2.63-2.61 (m, 4H), 2.38 (s, 3H), 1.74-1.70 (m, 2H), 1.48-1.46 (m, 2H)
- [667] Preparation A2-14: (S)-1-(6-chloro-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [668] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 6-(morpholin-4-yl)pyridin-3-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.31 (s, 1H), 8.00 (s, 1H), 7.71 (d, 1H), 6.87 (s, 1H), 6.72 (d, 1H), 3.86-3.84 (m, 4H), 3.78-3.77 (m, 1H), 3.58-3.55 (m, 4H), 3.23-3.21 (m, 1H), 3.01-2.99 (m, 1H), 2.80-2.69 (m, 2H), 1.92-1.87 (m, 1H), 1.82-1.72 (m, 1H), 1.49-1.45 (m, 2H)
- [669] Preparation A2-15: (S)-1-(6-chloro-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [670] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 3-pyridylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.81 (s, 1H), 8.70-8.68 (m, 1H), 8.06 (s, 1H), 7.88-7.87 (m, 1H), 7.45-7.42 (m, 1H), 6.93 (s, 1H), 3.82-3.75 (m, 1H), 3.21-3.18 (m, 1H), 2.75-2.73 (m, 1H), 2.72-2.70 (m, 2H), 1.72-1.70 (m, 2H), 1.48-1.47 (m, 1H)
- [671] Preparation A2-16: (S)-1-(6-chloro-6'-ethoxy-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [672] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 6-ethoxypyridin-3-boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.27 (s, 1H), 8.03 (s, 1H), 7.77 (d, 1H), 6.89 (s, 1H), 6.83 (d, 1H), 4.41 (q, 2H), 3.77-3.75 (m, 1H), 3.24-3.22 (m, 1H), 2.98-2.97 (m, 1H), 2.76-2.68 (m, 2H), 1.90-1.87 (m, 1H), 1.74-1.72 (m, 2H), 1.68 (t, 3H)
- [673] Preparation A2-17: (S)-1-(6-chloro-6'-(trifluoromethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [674] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 2-(trifluoromethyl)pyridin-5-boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.93 (s, 1H), 8.07 (s, 1H), 8.05 (d, 1H), 7.82 (d, 1H), 6.97 (s, 1H), 3.78-3.76 (m, 1H), 3.23-3.22 (m, 1H), 3.20-3.19 (m, 1H), 2.96-2.73 (m, 2H), 1.95-1.92 (m, 1H), 1.91-1.88 (m, 1H), 1.69-1.49 (m, 2H)
- [675] Preparation A2-18: (S)-1-(2-chloro-5-(imidazo[1,2-a]pyridin-6-yl)pyridin-4-yl)piperidin-3-ol
- [676] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to imidazo[1,2-a]pyridin-6-ylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.28 (s, 1H), 8.08 (s, 1H), 7.62-7.59 (m, 1H), 7.52-7.51 (m, 1H), 7.40-7.38 (m, 2H), 6.92 (s, 1H), 3.82-3.78 (m, 1H), 3.34-3.20

- (m, 1H), 3.05-2.92 (m, 1H), 2.81-2.73 (m, 2H), 2.12-2.05 (m, 1H), 1.91-1.84 (m, 1H), 1.49-1.47 (m, 2H)
- [677] Preparation A2-19: (S)-1-(5-([1,2,4]triazolo[4,3-a]pyridin-6-yl)-2-chloropyridin-4-yl)piperidin-3-ol
- [678] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to [1,2,4]triazolo[4,3-a]pyridin-6-ylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.80 (s, 1H), 8.30 (s, 1H), 8.08 (s, 1H), 7.79 (d, 1H), 7.54 (d, 1H), 6.95 (s, 1H), 3.92-3.81 (m, 1H), 3.33-3.30 (m, 1H), 3.12-3.10 (m, 1H), 2.90-2.88 (m, 1H), 2.79-2.74 (m, 1H), 1.96-1.93 (m, 1H), 1.82-1.73 (m, 1H), 1.51-1.48 (m, 2H)
- [679] Preparation A2-20: (3S)-1-[2-chloro-5-[1-(2,2,6,6-tetramethyltetrahydropyran-4-yl)pyrazol-4-yl]-4-pyridyl]piperidin-3-ol
- [680] The titled compound was prepared in accordance with the same procedures as in Preparation A2-1, changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,6,6-tetramethyltetrahydropyran-4-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.82 (s, 1H), 7.77 (s, 1H), 6.90 (s, 1H), 4.80-4.70 (m, 1H), 3.95-3.85 (m, 1H), 3.70-3.65 (m, 1H), 3.30-3.20 (m, 1H), 3.10-3.00 (m, 1H), 2.80-2.65 (m, 2H), 2.20-2.10 (m, 2H), 2.00-1.90 (m, 1H), 1.90-1.80 (m, 2H), 1.70-1.60 (m, 1H), 1.60-1.50 (m, 1H), 1.42 (s, 6H), 1.34 (s, 6H)
- [681] Preparation A3-1: tert-butyl (S)-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [682] Step 1: tert-butyl (S)-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-yl)carbamate (A3)
- [683] 2-Chloro-4-fluoro-5-iodopyridine (5.0 g, 19.42 mmol) was dissolved in anhydrous dimethylformamide (90.6 mL) and then (S)-3-(tert-butoxycarbonylamino)piperidine (4.28 g, 21.36 mmol) and diisopropylethylamine (7.9mL, 58.26mmol) were added dropwise thereto. The reaction mixture was stirred at 50°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (5.9 g). (Yield: 69.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.57 (s, 1H), 6.85 (s, 1H), 4.92 (brs, 1H), 3.95-3.94 (m, 1H), 3.34 (d, 1H), 3.08-3.04 (m, 2H), 2.90-2.85 (m, 1H), 2.06-1.94 (m, 3H), 1.46 (s, 9H)
- [684] Step 2: tert-butyl (S)-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate (A3-1)
- [685] tert-Butyl (S)-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-yl)carbamate (3.0 g, 6.85 mmol) was dissolved in anhydrous 1,4-dioxane (34.3 mL) and then 1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-boronic acid pinacol ester (2.9 g, 10.28 mmol), [1,1'-

bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (559.7 mg, 0.68 mmol), and 2.0M sodium carbonate solution (12.1 mL, 24.2 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (2.3 g). (Yield: 73.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.81 (s, 1H), 7.77 (s, 1H), 6.86 (s, 1H), 4.55-4.45 (m, 1H), 4.45-4.35 (m, 1H), 4.20-4.10 (m, 2H), 3.80-3.70 (m, 1H), 3.61 (t, 2H), 3.50-3.40 (m, 1H), 3.15-3.00 (m, 1H), 2.65-2.55 (m, 1H), 2.55-2.45 (m, 1H), 2.25-2.05 (m, 4H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.45 (s, 9H), 1.40-1.30 (m, 1H)

[686] Preparation A3-2: tert-butyl (S)-(1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[687] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (d, 2H), 7.94 (s, 1H), 7.26 (t, 1H), 6.90 (s, 1H), 4.48-4.47 (m, 1H), 3.76-3.67 (m, 1H), 3.46-3.43 (m, 1H), 3.08-3.05 (m, 1H), 2.62-2.52 (m, 2H), 1.98-1.96 (m, 1H), 1.73-1.64 (m, 1H), 1.45 (s, 9H), 1.38-1.31 (m, 2H)

[688] Preparation A3-3: tert-butyl (S)-(1-(2-chloro-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[689] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-methyl-4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.79-7.75 (m, 2H), 6.85 (s, 1H), 4.57-4.48 (m, 1H), 4.23-4.16 (m, 1H), 3.76-3.70 (m, 1H), 3.42 (d, 1H), 3.07-3.03 (m, 3H), 2.58-2.55 (m, 2H), 2.36 (s, 3H), 2.23-2.12 (m, 7H), 1.96-1.94 (m, 1H), 1.65-1.54 (m, 2H), 1.43 (s, 9H)

[690] Preparation A3-4: tert-butyl (S)-(1-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[691] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.88 (s, 1H), 7.82 (s, 1H), 6.88 (s, 1H), 4.83-4.78 (m, 2H), 4.50-4.42 (m, 1H), 3.73-3.69 (m, 1H), 3.44-3.41 (m, 1H), 3.11-3.09 (m, 1H), 2.63-2.58 (m, 1H), 2.45-2.43 (m, 1H), 2.00-1.94 (m, 1H), 1.73-1.70 (m, 1H), 1.44 (s, 9H), 1.35-1.28 (m, 1H)

- [692] Preparation A3-5: tert-butyl (S)-(1-(2-chloro-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [693] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(2-methoxyethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 6.85 (s, 1H), 4.58-4.52 (m, 1H), 4.37-4.35 (m, 2H), 3.81-3.79 (m, 3H), 3.40-3.35 (m, 4H), 3.05-3.02 (m, 1H), 2.61-2.56 (m, 1H), 1.93-1.92 (m, 1H), 1.65-1.63 (m, 1H), 1.46 (s, 9H), 1.41-1.31 (m, 1H)
- [694] Preparation A3-6: tert-butyl (S)-(1-(2-chloro-5-(1-(3-methoxypropyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [695] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(3-methoxypropyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CD₃OD, 400MHz) δ 8.07 (s, 1H), 8.00 (s, 1H), 7.81 (s, 1H), 7.02 (s, 1H), 4.30 (t, 2H), 3.59 (brs, 1H), 3.43-3.32 (m, 3H), 3.32 (s, 3H), 3.22 (d, 1H), 2.62 (t, 1H), 2.51 (t, 1H), 2.17-2.11 (m, 2H), 1.96-1.93 (m, 1H), 1.73 (brs, 1H), 1.70-1.62 (m, 1H), 1.59 (s, 9H), 1.51-1.43 (m, 1H)
- [696] Preparation A3-7: tert-butyl (S)-(1-(2-chloro-5-(1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [697] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-methyl-3-(trifluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CD₃OD, 400MHz) δ 7.91 (s, 1H), 7.88 (s, 1H), 7.03 (s, 1H), 4.09 (s, 1H), 3.34-3.32 (m, 2H), 3.27-3.23 (m, 1H), 2.71 (t, 1H), 2.38 (t, 1H), 1.90-1.86 (m, 1H), 1.71 (brs, 1H), 1.60-1.54 (m, 2H), 1.44 (s, 9H)
- [698] Preparation A3-8: tert-butyl (S)-(1-(2-chloro-5-(1-(2-(dimethylamino)-2-oxoethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [699] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to N,N-dimethyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)acetamide. ¹H NMR (CD₃OD, 400MHz) δ 8.13 (s, 1H), 8.04 (s, 1H), 7.85 (s, 1H), 5.24-5.14(m, 2H), 3.63-3.59 (m, 1H), 3.45-3.41 (m, 2H), 3.17 (s, 3H), 3.01 (s, 3H), 2.65-2.55 (m, 2H), 2.03-1.97 (m, 1H), 1.96-1.92 (m, 1H), 1.74-1.66 (m, 1H), 1.46 (s, 9H), 1.40 (brs, 1H)
- [700] Preparation A3-9: tert-butyl (S)-(1-(2-chloro-5-(1-(2-(methoxymethoxy)ethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [701] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(2-(methoxymethoxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.09 (d, 2H), 7.85 (s, 1H), 7.04 (s, 1H), 4.60 (s, 2H), 4.43-4.42 (m,

2H), 3.94 (t, 2H), 3.63-3.61 (m, 1H), 3.43-3.41 (m, 1H), 3.26 (s, 3H), 3.25 (brs, 1H), 2.62-2.53 (m, 2H), 1.97-1.93 (m, 2H), 1.73-1.69 (m, 2H), 1.45 (s, 9H), 1.39-1.31 (m, 1H)

[702] Preparation A3-10: tert-butyl (S)-(1-(2-chloro-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[703] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(2,2-difluoroethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.83 (s, 1H), 7.82 (s, 1H), 6.88 (s, 1H), 6.34-6.19 (m, 1H), 4.60-4.53 (m, 2H), 3.82-3.70 (m, 1H), 3.46-3.43 (m, 1H), 3.12-3.09 (m, 1H), 2.64-2.61 (m, 1H), 2.53-2.42 (m, 1H), 1.98-1.92 (m, 1H), 1.83-1.74 (m, 1H), 1.72-1.62 (m, 1H), 1.57 (s, 9H), 1.45-1.43 (m, 1H)

[704] Preparation A3-11: tert-butyl (S)-(1-(2-chloro-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[705] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(trifluoromethyl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 8.12 (s, 1H), 8.06 (s, 1H), 6.92 (s, 1H), 4.47 (brs, 1H), 3.81-3.71 (m, 1H), 3.49-3.47 (m, 1H), 3.09-3.06 (m, 1H), 2.65-2.53 (m, 2H), 1.99-1.96 (m, 1H), 1.73-1.68 (m, 1H), 1.46 (s, 9H), 1.45-1.37 (m, 2H)

[706] Preparation A3-12: tert-butyl (S)-(1-(2-chloro-5-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[707] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-[2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-1-yl]ethyl]morpholine. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.81 (s, 1H), 7.77 (s, 1H), 6.87 (s, 1H), 4.55-4.45 (m, 1H), 4.33 (t, 2H), 3.80-3.75 (m, 1H), 3.72 (t, 4H), 3.50-3.40 (m, 1H), 3.15-3.05 (m, 1H), 2.89 (t, 2H), 2.65-2.60 (m, 1H), 2.60-2.45 (m, 5H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.46 (s, 9H), 1.40-1.30 (m, 1H)

[708] Preparation A3-13: tert-butyl (S)-(1-(2-chloro-5-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[709] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(2-pyrrolidin-1-ylethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.80 (s, 1H), 7.74 (s, 1H), 6.84 (s, 1H), 4.60-4.50 (m, 1H), 4.30 (t, 2H), 3.80-3.70 (m, 1H), 3.45-3.35 (m, 1H), 3.10-2.90 (m, 3H), 2.70-2.50 (m, 6H), 2.00-1.90 (m, 1H), 1.85-1.70 (m, 4H), 1.70-1.60 (m, 1H), 1.44 (s, 9H), 1.40-1.30 (m, 1H)

- [710] Preparation A3-14: tert-butyl N-[(3S)-1-[2-chloro-5-[1-(2-cyanoethyl)pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate
- [711] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-1-yl]propanenitrile. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.86 (s, 1H), 7.83 (s, 1H), 6.89 (s, 1H), 4.50 (t, 2H), 4.50-4.40 (m, 1H), 3.75-3.65 (m, 1H), 3.50-3.40 (m, 1H), 3.20-3.05 (m, 2H), 3.09 (t, 2H), 2.70-2.60 (m, 1H), 2.45-2.35 (m, 1H), 2.05-1.95 (m, 1H), 1.80-1.70 (m, 1H), 1.45 (s, 9H), 1.40-1.30 (m, 1H)
- [712] Preparation A3-15: tert-butyl (S)-3-(3-(4-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-6-chloropyridin-3-yl)-1H-pyrazol-1-yl)azetidin-1-carboxylate
- [713] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl 3-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)azetidin-1-carboxylate. ¹H NMR (CDCl₃, 400MHz) δ 8.31 (s, 1H), 7.65 (s, 1H), 6.86 (s, 1H), 6.60 (s, 1H), 5.25-5.15 (m, 1H), 5.75-5.65 (m, 1H), 4.43 (t, 2H), 4.40-4.20 (m, 2H), 3.75-3.65 (m, 1H), 3.30-3.20 (m, 1H), 3.10-3.00 (m, 1H), 2.80-2.70 (m, 1H), 2.65-2.55 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.65 (m, 1H), 1.47 (s, 9H), 1.44 (s, 9H), 1.40-1.30 (m, 1H)
- [714] Preparation A3-16: tert-butyl (S)-(1-(6-chloro-6'-(dimethylamino)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [715] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 6-dimethylaminopyridin-3-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.23 (d, 1H), 8.00 (s, 1H), 7.65 (d, 1H), 6.84 (s, 1H), 6.59 (d, 1H), 4.55-4.45 (m, 1H), 3.80-3.65 (m, 1H), 3.40-3.30 (m, 1H), 3.15 (s, 6H), 3.10-3.00 (m, 1H), 2.70-2.55 (m, 2H), 1.90-1.80 (m, 1H), 1.60-1.48 (m, 1H), 1.45 (s, 9H), 1.35-1.30 (m, 1H)
- [716] Preparation A3-17: tert-butyl (S)-(1-(6-chloro-6'-(pyrrolidin-1-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [717] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 2-pyrrolidin-1-yl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine. ¹H NMR (CDCl₃, 400MHz) δ 8.22 (d, 1H), 8.00 (s, 1H), 7.64 (d, 1H), 6.84 (s, 1H), 6.44 (d, 1H), 4.55-4.45 (m, 1H), 3.80-3.65 (m, 1H), 3.51 (t, 4H), 3.40-3.30 (m, 1H), 3.10-3.00 (m, 1H), 2.70-2.55 (m, 2H), 2.05 (t, 4H), 1.90-1.80 (m, 1H), 1.60-1.48 (m, 1H), 1.45 (s, 9H), 1.35-1.30 (m, 1H)
- [718] Preparation A3-18: tert-butyl (S)-(1-(6-chloro-6'-(piperidin-1-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate

- [719] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 6-(piperidin-1-yl)pyridin-3-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.23 (d, 1H), 8.00 (s, 1H), 7.65 (d, 1H), 6.85 (s, 1H), 6.72 (d, 1H), 4.55-4.45 (m, 1H), 3.80-3.65 (m, 1H), 4.65-4.55 (m, 4H), 3.45-3.30 (m, 3H), 3.10-3.00 (m, 1H), 2.70-2.55 (m, 2H), 2.05 (t, 4H), 1.70-1.50 (m, 5H), 1.60-1.48 (m, 1H), 1.46 (s, 9H), 1.35-1.30 (m, 1H)
- [720] Preparation A3-19: tert-butyl (S)-(1-(6-chloro-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [721] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 6-(morpholin-4-yl)pyridin-3-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.28 (d, 1H), 8.00 (s, 1H), 7.71 (d, 1H), 6.86 (s, 1H), 6.72 (d, 1H), 4.55-4.45 (m, 1H), 3.87-3.83 (m, 4H), 3.80-3.65 (m, 1H), 3.59-3.54 (m, 4H), 3.40-3.30 (m, 1H), 3.10-3.00 (m, 1H), 2.70-2.50 (m, 2H), 1.95-1.80 (m, 1H), 1.60-1.50 (m, 1H), 1.45 (s, 9H), 1.35-1.30 (m, 1H)
- [722] Preparation A3-20: tert-butyl (S)-(1-(2-chloro-5-(4-(4-methylpiperazin-1-carbonyl)phenyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [723] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to (4-methylpiperazin-1-yl)-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]methanone. ¹H NMR (CD₃OD, 400MHz) δ 7.96 (s, 1H), 7.65 (dd, 2H), 7.56 (dd, 2H), 7.07 (s, 1H), 3.90-3.75 (m, 2H), 3.70-3.50 (m, 2H), 3.50-3.40 (m, 2H), 3.40-3.35 (m, 1H), 3.20-3.10 (m, 1H), 2.75-2.60 (m, 2H), 2.60-2.40 (m, 4H), 2.36 (s, 3H), 1.95-1.85 (m, 1H), 1.65-1.55 (m, 1H), 1.45 (s, 9H), 1.40-1.30 (m, 1H)
- [724] Preparation A3-21: tert-butyl (S)-(1-(2-chloro-5-(1-(2-methoxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl) carbamate
- [725] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(2-methoxy-2-methylpropyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CD₃OD, 400MHz) δ 8.18 (s, 1H), 7.84 (s, 1H), 7.76 (s, 1H), 6.91 (s, 1H), 4.66-4.54 (m, 1H), 4.25-4.15 (m, 2H), 3.88-3.76 (m, 1H), 3.75-3.65 (m, 1H), 3.44-3.35 (m, 1H), 3.31 (s, 3H), 3.09-2.98 (m, 1H), 2.71-2.58 (m, 2H), 1.98-1.86 (m, 1H), 1.71-1.52 (m, 1H), 1.51 (s, 9H), 1.43-1.33 (m, 1H), 1.23 (s, 6H)
- [726] Preparation A3-22: tert-butyl (S)-(1-(6-chloro-6'-(2-methoxyethoxy)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [727] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 2-(2-methoxyethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine. ¹H NMR (CD₃OD, 400MHz) δ

- 8.26 (s, 1H), 8.06 (s, 1H), 7.82-7.74 (m, 1H), 6.91-6.86 (m, 2H), 4.57-4.52 (m, 2H), 4.52-4.45 (m, 1H), 3.85-3.78 (m, 2H), 3.78-3.63 (m, 2H), 3.52-3.45 (m, 3H), 3.42-3.33 (m, 1H), 3.06-2.94 (m, 1H), 2.73-2.52 (m, 2H), 1.94-1.82 (m, 1H), 1.51 (s, 9H)
- [728] Preparation A3-23: tert-butyl (S)-(1-(2-chloro-5-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl) carbamate
- [729] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to [1-(2-hydroxy-2-methyl-propyl)pyrazol-4-yl]boronic acid pinacol ester. ¹H NMR (CD₃OD, 400MHz) δ 8.24 (s, 1H), 7.99 (s, 1H), 7.84 (s, 1H), 6.94 (s, 1H), 4.48-4.38 (m, 1H), 4.23-4.16 (m, 1H), 4.16 (s, 2H), 3.80-3.63 (m, 1H), 3.62-3.48 (m, 1H), 3.24-3.06 (m, 1H), 2.75-2.62 (m, 1H), 2.29-2.14 (m, 1H), 2.07-1.96 (m, 1H), 1.87-1.77 (m, 1H), 1.77-1.62 (m, 1H), 1.49 (s, 9H)
- [730] Preparation A3-24: tert-butyl (S)-(1-(2-chloro-5-(1-(3-(dimethylamino)propyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [731] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to N,N-dimethyl-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-1-yl]propan-1-amine. ¹H NMR (CD₃OD, 400MHz) δ 8.18 (s, 1H), 7.84 (s, 2H), 6.91 (s, 1H), 4.57-4.46 (m, 1H), 4.34 (t, 2H), 3.82-3.67 (m, 1H), 3.47-3.36 (m, 1H), 3.15-3.05 (m, 1H), 2.63-2.57 (m, 2H), 2.57-2.51 (m, 1H), 2.47 (s, 6H), 2.32-2.21 (m, 2H), 2.03-1.91 (m, 1H), 1.78-1.68 (m, 1H), 1.67-1.54 (m, 1H), 1.51 (s, 9H)
- [732] Preparation A3-25: tert-butyl (S)-3-((4-(4-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-6-chloropyridin-3-yl)-1H-pyrazol-1-yl)methyl)azetidin-1-carboxylate
- [733] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl 3-[[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-1-yl]methyl]azetidin-1-carboxylate. ¹H NMR (CD₃OD, 400MHz) δ 8.17 (s, 1H), 7.81 (s, 1H), 7.76 (s, 1H), 6.91 (s, 1H), 4.55-4.45 (m, 1H), 4.45 (d, 2H), 4.15-4.03 (m, 2H), 3.85-3.76 (m, 2H), 3.76-3.66 (m, 1H), 3.52-3.36 (m, 1H), 3.20-3.02 (m, 2H), 2.67-2.54 (m, 1H), 2.54-2.40 (m, 1H), 2.03-1.89 (m, 1H), 1.78-1.67 (m, 1H), 1.65-1.52 (m, 1H), 1.51 (s, 18H)
- [734] Preparation A3-26: tert-butyl (R)-3-(4-(4-((S)-3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-6-chloropyridin-3-yl)-1H-pyrazol-1-yl)pyrrolidin-1-carboxylate
- [735] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl (R)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pyrrolidin-1-carboxylate. ¹H NMR (CD₃OD, 400MHz) δ 8.18 (s, 1H), 7.83-7.74 (m, 2H), 6.91 (s, 1H), 5.02-4.90 (m, 1H), 4.55-4.42 (m, 1H), 3.93-3.88 (m, 1H), 3.86-3.77 (m, 1H), 3.77-3.62 (m, 2H),

- 3.62-3.52 (m, 1H), 3.52-3.41 (m, 1H), 3.16-3.04 (m, 1H), 2.68-2.55 (m, 1H), 2.56-2.39 (m, 3H), 2.04-1.91 (m, 1H), 1.79-1.66 (m, 1H), 1.52 (s, 9H), 1.47 (s, 9H)
- [736] Preparation A3-27: tert-butyl (S)-3-(4-(4-((S)-3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-6-chloropyridin-3-yl)-1H-pyrazol-1-yl)pyrrolidin-1-carboxylate
- [737] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl (S)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pyrrolidin-1-carboxylate. ¹H NMR (CD₃OD, 400MHz) δ 8.18 (s, 1H), 7.85-7.72 (m, 2H), 6.92 (s, 1H), 5.02-4.91 (m, 1H), 4.56-4.43 (m, 1H), 3.99-3.89 (m, 1H), 3.89-3.77 (m, 1H), 3.77-3.65 (m, 2H), 3.65-3.52 (m, 2H), 3.52-3.39 (m, 1H), 3.17-3.03 (m, 1H), 2.69-2.54 (m, 1H), 2.52-2.38 (m, 3H), 2.02-1.90 (m, 1H), 1.78-1.67 (m, 1H), 1.52 (s, 9H), 1.49 (s, 9H)
- [738] Preparation A3-28: tert-butyl (S)-(1-(6-chloro-6'-((2-(dimethylamino)ethyl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [739] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to N',N'-dimethyl-N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]ethan-1,2-diamine. ¹H NMR (CD₃OD, 400MHz) δ 8.21 (s, 1H), 8.04 (s, 1H), 7.67 (d, 1H), 6.90 (s, 1H), 6.55 (d, 1H), 5.33-5.18 (m, 1H), 4.64-4.51 (m, 1H), 3.80-3.64 (m, 1H), 3.48-3.38 (m, 2H), 3.38-3.30 (m, 1H), 3.08-2.98 (m, 1H), 2.36 (s, 6H), 1.91-1.85 (m, 1H), 1.52 (s, 9H)
- [740] Preparation A3-29: tert-butyl (S)-4-(4'-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-6'-chloro-[3,3'-bipyridin]-6-yl)piperazin-1-carboxylate
- [741] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl 4-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]piperazin-1-carboxylate. ¹H NMR (CD₃OD, 400MHz) δ 8.30 (s, 1H), 8.04 (s, 1H), 7.76 (d, 1H), 6.91 (s, 1H), 6.74 (d, 1H), 4.54-4.42 (m, 1H), 3.79-3.66 (m, 2H), 3.65-3.51 (m, 8H), 3.43-3.33 (m, 3H), 3.11-3.02 (m, 1H), 2.68-2.52 (m, 2H), 1.49 (s, 9H), 1.30 (s, 9H)
- [742] Preparation A3-30: tert-butyl (S)-(1-(2-chloro-5-(1-(1-methoxy-2-methylpropan-2-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [743] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(2-methoxy-1,1-dimethylethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CD₃OD, 400MHz) δ 8.19 (s, 1H), 7.95 (s, 1H), 7.80 (s, 1H), 6.87 (s, 1H), 4.67-4.54 (m, 1H), 3.87-3.77 (m, 1H), 3.77-3.68 (m, 1H), 3.68 (s, 2H), 3.43-3.35 (m, 1H), 3.34 (s, 3H), 3.04-2.93 (m, 1H), 2.71-2.60 (m, 2H), 2.05-1.97 (m, 1H), 1.84-1.76 (m, 1H), 1.69 (s, 6H), 1.52 (s, 9H)

- [744] Preparation A3-31: tert-butyl (S)-(1-(2-chloro-5-(1-((3,3-difluorocyclobutyl)methyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [745] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-[(3,3-difluorocyclobutyl)methyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CD₃OD, 400MHz) δ 8.17 (s, 1H), 7.82 (s, 1H), 7.76 (s, 1H), 6.92 (s, 1H), 4.55-4.45 (m, 1H), 4.35 (d, 2H), 3.81-3.70 (m, 2H), 3.18-3.07 (m, 1H), 2.83-2.70 (m, 3H), 2.66-2.55 (m, 1H), 2.54-2.39 (m, 3H), 2.04-1.95 (m, 1H), 1.75-1.66 (m, 1H), 1.50 (s, 9H)
- [746] Preparation A3-32: tert-butyl (S)-(1-(2-chloro-5-(1-(2-(dimethylamino)ethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [747] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to N,N-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-ethanamine. ¹H NMR (CD₃OD, 400MHz) δ 8.19 (s, 1H), 7.87 (s, 1H), 7.79 (s, 1H), 6.91 (s, 1H), 4.66-4.51 (m, 1H), 4.37 (t, 2H), 3.88-3.70 (m, 1H), 3.47-3.32 (m, 1H), 3.09-2.98 (m, 1H), 2.88-2.76 (m, 2H), 2.72-2.57 (m, 2H), 2.37 (s, 6H), 2.00-1.87 (m, 1H), 1.77-1.65 (m, 1H), 1.52 (s, 9H), 1.43-1.37 (m, 1H)
- [748] Preparation A3-33: tert-butyl (S)-(1-(2-chloro-5-(1-(fluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [749] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(fluoromethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CD₃OD, 400MHz) δ 8.20 (s, 1H), 8.02 (s, 1H), 7.95 (s, 1H), 6.93 (s, 1H), 6.22 (s, 1H), 6.09 (s, 1H), 4.54-4.42 (m, 1H), 3.80-3.66 (m, 2H), 3.50-3.40 (m, 1H), 3.19-3.05 (m, 1H), 2.70-2.56 (m, 1H), 2.55-2.42 (m, 1H), 2.03-1.87 (m, 1H), 1.77-1.67 (m, 1H), 1.52 (s, 9H)
- [750] Preparation A3-34: tert-butyl (S)-4-(4'-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-6'-chloro-[3,3'-bipyridin]-6-yl)piperidin-1-carboxylate
- [751] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl 4-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl]piperidin-1-carboxylate. ¹H NMR (CD₃OD, 400MHz) δ 8.70 (s, 1H), 8.09 (s, 1H), 7.86 (d, 1H), 7.28 (d, 1H), 6.95 (s, 1H), 4.49-4.37 (m, 1H), 4.37-4.21 (m, 2H), 3.72-3.55 (m, 1H), 3.43-3.32 (m, 1H), 3.06-2.95 (m, 1H), 2.95-2.79 (m, 3H), 2.67-2.59 (m, 1H), 2.59-2.47 (m, 1H), 2.05-1.94 (m, 2H), 1.94-1.85 (m, 1H), 1.85-1.71 (m, 2H), 1.53 (s, 9H), 1.47 (s, 9H)
- [752] Preparation A3-35: tert-butyl (S)-(1-(6-chloro-6'-(2-(dimethylamino)ethoxy)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate

- [753] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to N,N-dimethyl-2-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl]oxyethanamine. ¹H NMR (CD₃OD, 400MHz) δ 8.26 (s, 1H), 8.06 (s, 1H), 7.80-7.72 (m, 1H), 6.94-6.83 (m, 2H), 4.56 (t, 2H), 3.75-3.62 (m, 1H), 3.40-3.29 (m, 1H), 3.04-2.96 (m, 1H), 2.83 (t, 2H), 2.43 (s, 6H), 1.92-1.83 (m, 1H), 1.80-1.63 (m, 3H), 1.63-1.52 (m, 1H), 1.52 (s, 9H)
- [754] Preparation A3-36: tert-butyl (S)-(1-(6-chloro-6'-(3-ethylureido)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [755] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-ethyl-3-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl]urea. ¹H NMR (CD₃OD, 400MHz) δ 9.32 (s, 1H), 8.33 (s, 1H), 8.07 (s, 1H), 7.84 (d, 1H), 6.95 (s, 1H), 4.52-4.39 (m, 1H), 3.76-3.60 (m, 1H), 3.53 (q, 2H), 3.45-3.37 (m, 1H), 3.12-2.96 (m, 1H), 2.66-2.51 (m, 2H), 2.00-1.86 (m, 1H), 1.64-1.57 (m, 2H), 1.54 (s, 9H), 0.92 (t, 3H)
- [756] Preparation A3-37: tert-butyl N-[(3S)-1-[2-chloro-5-[4-(morpholin-4-carbonyl)phenyl]-4-pyridyl]-3-piperidyl]carbamate
- [757] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(morpholin-4-carbonyl)phenyl boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.59-7.56 (m, 2H), 7.54-7.51 (m, 2H), 6.91 (s, 1H), 3.90-3.55 (m, 10H), 3.45-3.35 (m, 1H), 3.05-2.95 (m, 1H), 2.65-2.55 (m, 2H), 1.95-1.85 (m, 1H), 1.46 (s, 9H), 1.46-1.40 (m, 2H)
- [758] Preparation A3-38: tert-butyl N-[(3S)-1-[2-chloro-5-(4-methyl-2,3-dihydropyrido[3,2-b][1,4]oxazin-7-yl)-4-pyridyl]-3-piperidyl]carbamate
- [759] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydropyrido[3,2-b][1,4]oxazine. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 7.83 (s, 1H), 7.14 (s, 1H), 6.84 (s, 1H), 4.55-4.40 (m, 1H), 4.40-4.25 (m, 2H), 3.75-3.65 (m, 1H), 3.55-3.45 (m, 2H), 3.41 (d, 1H), 3.19 (s, 3H), 3.15-3.05 (m, 1H), 2.70-2.50 (m, 2H), 1.95-1.85 (m, 1H), 1.55-1.48 (m, 1H), 1.46 (s, 9H), 1.35-1.25 (m, 1H)
- [760] Preparation A3-39: tert-butyl N-[(3S)-1-[2-chloro-5-(4-methyl-2,3-dihydro-1,4-benzoxazin-7-yl)-4-pyridyl]-3-piperidyl]carbamate
- [761] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydro-2H-1,4-benzoxazine. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 6.97 (d, 1H), 6.92 (s, 1H), 6.82 (s, 1H), 6.72 (d, 1H),

- 4.60-4.50 (m, 1H), 4.40-4.30 (m, 2H), 3.80-3.70 (m, 1H), 3.40-3.25 (m, 3H), 3.05-2.96 (m, 1H), 2.95 (s, 3H), 2.70-2.60 (m, 2H), 1.90-1.80 (m, 1H), 1.55-1.40 (m, 10H), 1.40-1.35 (m, 1H)
- [762] Preparation A3-40: tert-butyl N-[(3S)-1-[2-chloro-5-(2-oxo-1,4-dihydro-3,1-benzoxazin-6-yl)-4-pyridyl]-3-piperidyl]carbamate
- [763] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one. ¹H NMR (CDCl₃, 400MHz) δ 8.00 (s, 1H), 7.41 (d, 1H), 7.13 (s, 1H), 6.90-6.85 (m, 1H), 6.67 (d, 1H), 5.45-5.35 (m, 2H), 4.45-4.35 (m, 1H), 3.70-3.60 (m, 1H), 3.35-3.30 (m, 1H), 3.10-3.00 (m, 1H), 2.64 (t, 1H), 2.51 (t, 1H), 1.95-1.85 (m, 1H), 1.45 (s, 9H), 1.45-1.35 (m, 1H), 1.35-1.30 (m, 1H)
- [764] Preparation A3-41: tert-butyl N-[(3S)-1-[2-chloro-5-[4-(2-oxopyrrolidin-1-yl)phenyl]-4-pyridyl]-3-piperidyl]carbamate
- [765] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(2-oxo-1-pyrrolidinyl)phenyl boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.75 (d, 2H), 7.50 (d, 2H), 6.87 (s, 1H), 4.55-4.45 (m, 1H), 3.95 (t, 2H), 3.75-3.65 (m, 1H), 3.35-3.25 (m, 1H), 3.05-2.95 (m, 1H), 2.70-2.60 (m, 3H), 2.30-2.10 (m, 3H), 1.90-1.80 (m, 1H), 1.46 (s, 9H), 1.46-1.30 (m, 2H)
- [766] Preparation A3-42: tert-butyl N-[(3S)-1-[2-chloro-5-(3-oxo-4H-1,4-benzoxazin-7-yl)-4-pyridyl]-3-piperidyl]carbamate
- [767] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 7.68 (s, 1H), 7.16 (s, 1H), 7.10-7.05 (m, 1H), 6.90-6.80 (m, 2H), 4.73 (q, 2H), 4.45-4.35 (m, 1H), 3.70-3.60 (m, 1H), 3.40-3.30 (m, 1H), 3.15-3.05 (m, 1H), 2.65 (t, 1H), 2.47 (t, 1H), 1.95-1.85 (m, 1H), 1.70-1.60 (m, 1H), 1.44 (s, 9H), 1.35-1.30 (m, 1H)
- [768] Preparation A3-43: tert-butyl N-[(3S)-1-[2-chloro-5-(4-methyl-3-oxo-1,4-benzoxazin-7-yl)-4-pyridyl]-3-piperidyl]carbamate
- [769] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.20-7.15 (m, 2H), 7.10-7.05 (m, 1H), 6.86 (s, 1H), 4.72 (q, 2H), 4.45-4.35 (m, 1H), 3.70-3.60 (m, 1H), 3.43 (s, 3H), 3.40-3.30 (m, 1H), 3.15-3.05 (m,

- 1H), 2.65 (t, 1H), 2.47 (t, 1H), 1.95-1.85 (m, 1H), 1.70-1.60 (m, 1H), 1.42 (s, 9H), 1.30-1.20 (m, 1H)
- [770] Preparation A3-44: tert-butyl (S)-(1-(2-chloro-5-(8-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [771] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 8-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinolin-2(1H)-one. ¹H NMR (CDCl₃, 400MHz) δ 7.99 (s, 1H), 7.15 (s, 1H), 6.83 (s, 1H), 6.54 (s, 1H), 4.55-4.45 (m, 1H), 3.75-3.60 (m, 1H), 3.35-3.25 (m, 1H), 3.10-2.95 (m, 3H), 2.90 (t, 1H), 2.80-2.50 (m, 3H), 2.28 (s, 3H), 1.90-1.80 (m, 1H), 1.50-1.40 (m, 10H), 1.40-1.30 (m, 1H)
- [772] Preparation A3-45: tert-butyl (S)-(1-(2-chloro-5-(1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [773] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinolin-2(1H)-one. ¹H NMR (CDCl₃, 400MHz) δ 8.01 (s, 1H), 7.30 (s, 1H), 6.90-6.80 (m, 2H), 6.80-6.70 (m, 1H), 4.50-4.40 (m, 1H), 3.70-3.60 (m, 1H), 3.40 (s, 3H), 3.35-3.30 (m, 1H), 3.10-2.95 (m, 3H), 2.85 (t, 1H), 2.80-2.60 (m, 3H), 1.90-1.80 (m, 1H), 1.50-1.40 (m, 10H), 1.40-1.30 (m, 1H)
- [774] Preparation A3-46: tert-butyl 4-[4-[6-chloro-4-[(3S)-3-(tert-butoxycarbonylamino)-1-piperidyl]-3-pyridyl]benzoyl]piperazin-1-carboxylate
- [775] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl 4-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoyl]piperazin-1-carboxylate. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.60-7.55 (m, 2H), 7.55-7.50 (m, 2H), 6.90 (s, 1H), 4.55-4.45 (m, 1H), 3.75-3.60 (m, 4H), 3.60-3.40 (m, 5H), 3.05-2.95 (m, 1H), 2.70-2.50 (m, 2H), 1.95-1.85 (m, 1H), 1.55-1.45 (m, 10H), 1.45-1.40 (m, 2H)
- [776] Preparation A3-47: tert-butyl N-[(3S)-1-[2-chloro-5-[1-(2,2,6,6-tetramethyltetrahydropyran-4-yl)pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate
- [777] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,6,6-tetramethyltetrahydropyran-4-yl)pyrazole. ¹H NMR (MeOD, 400MHz) δ 8.13 (s, 1H), 8.09 (s, 1H), 7.84 (s, 1H), 7.03 (s, 1H), 4.90-4.80 (m, 1H), 3.65-3.50 (m, 1H), 3.50-3.40 (m, 1H), 3.30-3.20 (m, 1H), 2.64 (t, 1H), 2.41 (t, 1H), 2.25-2.10 (m, 2H), 2.00-1.85 (m, 2H), 1.85-1.70 (m, 1H), 1.70-1.55 (m, 1H), 1.50-1.35 (m, 15H), 1.31 (s, 6H), 1.25-1.15 (m, 2H)
- [778] Preparation A3-48: tert-butyl N-[(3S)-1-[2-chloro-5-(2-methyl-3-oxo-4H-1,4-benzoxazin-6-yl)-4-pyridyl]-3-piperidyl]carbamate

- [779] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3,4-dihydro-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4-benzoxazine. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.15-7.05 (m, 2H), 7.05-6.95 (m, 1H), 6.87 (s, 1H), 3.75-3.60 (m, 1H), 3.35-3.25 (m, 1H), 3.05-2.90 (m, 1H), 2.70-2.50 (m, 2H), 1.90-1.80 (m, 1H), 1.70-1.65 (m, 1H), 1.61 (s, 3H), 1.60-1.50 (m, 2H), 1.46 (s, 9H)
- [780] Preparation A3-49: tert-butyl N-[(3S)-1-[2-chloro-5-(4-methyl-3-oxo-pyrido[3,2-b][1,4]oxazin-7-yl)-4-pyridyl]-3-piperidyl]carbamate
- [781] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrido[3,2-b][1,4]oxazin-3-one. ¹H NMR (CDCl₃, 400MHz) δ 8.05-8.00 (m, 2H), 6.88 (s, 1H), 6.69 (s, 1H), 4.95-4.85 (m, 1H), 4.80-4.70 (m, 1H), 4.35-4.25 (m, 1H), 3.53 (s, 3H), 3.25-3.05 (m, 3H), 2.70-2.60 (m, 1H), 2.30-2.20 (m, 1H), 2.00-1.90 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.65 (m, 1H), 1.60-1.50 (m, 1H), 1.48 (s, 9H)
- [782] Preparation A3-50: tert-butyl N-[(3S)-1-[2-chloro-5-(3-oxo-4H-pyrido[3,2-b][1,4]oxazin-7-yl)-4-pyridyl]-3-piperidyl]carbamate
- [783] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4H-pyrido[3,2-b][1,4]oxazin-3-one. ¹H NMR (CDCl₃, 400MHz) δ 9.41 (s, 1H), 8.15-8.05 (m, 2H), 7.48 (s, 1H), 6.89 (s, 1H), 4.95-4.85 (m, 1H), 4.80-4.70 (m, 1H), 4.40-4.30 (m, 1H), 3.60-3.50 (m, 1H), 3.45-3.30 (m, 1H), 3.25-3.15 (m, 1H), 2.67 (t, 1H), 2.29 (t, 1H), 2.00-1.90 (m, 1H), 1.85-1.70 (m, 1H), 1.70-1.60 (m, 1H), 1.38 (s, 9H)
- [784] Preparation A3-51: tert-butyl N-[(3S)-1-[2-chloro-5-(7-oxo-6,8-dihydro-5H-1,8-naphthyridin-3-yl)-4-pyridyl]-3-piperidyl]carbamate
- [785] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydro-1H-1,8-naphthyridin-2-one. ¹H NMR (CDCl₃, 400MHz) δ 8.27 (s, 1H), 8.20 (s, 1H), 8.04 (s, 1H), 7.70 (s, 1H), 6.90 (s, 1H), 4.45-4.35 (m, 1H), 3.60-3.50 (m, 1H), 3.45-3.35 (m, 1H), 3.20-3.10 (m, 1H), 3.10-3.00 (m, 2H), 2.90-2.70 (m, 2H), 2.67 (t, 1H), 2.40 (t, 1H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.60-1.50 (m, 1H), 1.42 (s, 9H)
- [786] Preparation A3-52: tert-butyl N-[(3S)-1-[2-chloro-5-[1-(oxetan-3-yl)pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate
- [787] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-(oxetan-3-yl)-4-(4,4,5,5-

tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 7.93 (s, 1H), 7.88 (s, 1H), 6.89 (s, 1H), 5.60-5.50 (m, 1H), 5.20-5.05 (m, 4H), 4.50-4.40 (m, 1H), 3.75-3.65 (m, 1H), 3.50-3.40 (m, 1H), 3.20-3.10 (m, 1H), 2.65 (t, 1H), 2.39 (t, 1H), 2.00-1.90 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.60 (m, 1H), 1.44 (s, 9H)

[788] Preparation A3-53: methyl 2-[4-[6-chloro-4-[(3S)-3-(tert-butoxycarbonylamino)-1-piperidyl]-3-pyridyl]pyrazol-1-yl]-2-methyl-propanoate

[789] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to methyl 2-methyl-2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-1-yl]propanoate. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 7.93 (s, 1H), 7.81 (s, 1H), 6.87 (s, 1H), 4.65-4.55 (m, 1H), 3.75 (s, 3H), 3.45-3.35 (m, 1H), 3.10-3.00 (m, 1H), 2.70-2.55 (m, 2H), 2.00-1.90 (m, 6H), 1.70-1.60 (m, 1H), 1.60-1.50 (m, 1H), 1.46 (s, 9H), 1.46-1.25 (m, 2H)

[790] Preparation A3-54: tert-butyl N-[(3S)-1-[5-(4-acetamidophenyl)-2-chloro-4-pyridyl]-3-piperidyl]carbamate

[791] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-acetamidobenzeneboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.65-7.60 (m, 2H), 7.50-7.40 (m, 2H), 7.24 (s, 1H), 6.87 (s, 1H), 4.65-4.55 (m, 1H), 3.75-3.65 (m, 1H), 3.35-3.25 (m, 1H), 3.00-2.90 (m, 1H), 2.70-2.55 (m, 2H), 2.23 (s, 3H), 1.90-1.80 (m, 1H), 1.47 (s, 9H), 1.45-1.30 (m, 2H)

[792] Preparation A3-55: tert-butyl N-[(3S)-1-[2-chloro-5-[3-(dimethylcarbamoyl)phenyl]-4-pyridyl]-3-piperidyl]carbamate

[793] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3-(dimethylcarbamoyl)phenyl boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.06 (s, 1H), 7.67 (s, 1H), 7.60-7.45 (m, 2H), 7.45-7.35 (m, 1H), 6.89 (s, 1H), 4.95-4.85 (m, 1H), 3.80-3.70 (m, 1H), 3.35-3.25 (m, 1H), 3.15 (s, 3H), 3.13 (s, 3H), 2.90-2.80 (m, 1H), 2.80-2.70 (m, 1H), 2.70-2.60 (m, 1H), 1.85-1.75 (m, 1H), 1.50-1.30 (m, 11H)

[794] Preparation A3-56: tert-butyl N-[(3S)-1-[2-chloro-5-[3-methyl-4-(trifluoromethoxy)phenyl]-4-pyridyl]-3-piperidyl]carbamate

[795] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3-methyl-4-trifluoromethoxy phenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.39 (s, 1H), 7.35-7.30 (m, 2H), 6.88 (s, 1H), 4.55-4.45 (m, 1H), 3.80-3.65 (m, 1H), 3.35-3.25 (m, 1H), 2.95-2.85 (m, 1H), 2.70-2.60 (m, 2H), 2.40 (s, 3H), 1.90-1.80 (m, 1H), 1.47 (s, 9H), 1.47-1.30 (m, 2H)

- [796] Preparation A3-57: tert-butyl N-[(3S)-1-[2-chloro-5-(4-fluoro-3-methyl-phenyl)-4-pyridyl]-3-piperidyl]carbamate
- [797] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-fluoro-3-methylphenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.01 (s, 1H), 7.35-7.25 (m, 2H), 7.10 (t, 1H), 6.87 (s, 1H), 4.60-4.45 (m, 1H), 3.75-3.65 (m, 1H), 3.25-3.15 (m, 1H), 2.95-2.85 (m, 1H), 2.75-2.65 (m, 2H), 2.36 (s, 3H), 1.85-1.75 (m, 1H), 1.47 (s, 9H), 1.47-1.35 (m, 2H)
- [798] Preparation A3-58: tert-butyl 4-[4-[6-chloro-4-[(3S)-3-(tert-butoxycarbonylamino)-1-piperidyl]-3-pyridyl]pyrazol-1-yl]piperidin-1-carboxylate
- [799] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to tert-butyl 4-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazol-1-yl]piperidin-1-carboxylate. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.85-7.75 (m, 2H), 6.87 (s, 1H), 4.55-4.45 (m, 1H), 4.40-4.20 (m, 2H), 3.80-3.65 (m, 1H), 3.50-3.40 (m, 1H), 3.15-3.05 (m, 1H), 3.00-2.95 (m, 2H), 2.65-2.50 (m, 1H), 2.50-2.45 (m, 1H), 2.30-2.15 (m, 2H), 2.05-1.90 (m, 2H), 1.75-1.65 (m, 1H), 1.65-1.55 (m, 1H), 1.49 (s, 9H), 1.46 (s, 9H), 1.46-1.25 (m, 2H)
- [800] Preparation A3-59: tert-butyl N-[(3S)-1-[2-chloro-5-(4-isopropoxy-3,5-dimethyl-phenyl)-4-pyridyl]-3-piperidyl]carbamate
- [801] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3,5-dimethyl-4-isopropoxyphenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.12 (s, 2H), 6.82 (s, 1H), 4.70-4.55 (m, 1H), 4.35-4.20 (m, 1H), 3.85-3.70 (m, 1H), 3.30-3.20 (m, 1H), 3.10-3.00 (m, 1H), 2.90-2.80 (m, 1H), 2.34 (s, 6H), 2.00-1.85 (m, 1H), 1.85-1.70 (m, 1H), 1.48 (s, 9H), 1.35 (d, 6H), 1.35-1.25 (m, 2H)
- [802] Preparation A3-60: tert-butyl N-[(3S)-1-[2-chloro-5-(4-methoxy-3,5-dimethyl-phenyl)-4-pyridyl]-3-piperidyl]carbamate
- [803] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-methoxy-3,5-dimethylphenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 7.13 (s, 2H), 6.83 (s, 1H), 4.65-4.55 (m, 1H), 3.79 (s, 3H), 3.79-3.70 (m, 1H), 3.30-3.20 (m, 1H), 2.90-2.80 (m, 1H), 2.80-2.70 (m, 1H), 2.70-2.60 (m, 1H), 2.36 (s, 6H), 1.80-1.70 (m, 1H), 1.47 (s, 9H), 1.47-1.35 (m, 2H)
- [804] Preparation A3-61: tert-butyl N-[(3S)-1-[2-chloro-5-(4-morpholinophenyl)-4-pyridyl]-3-piperidyl]carbamate
- [805] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to (4-morpholinophenyl)boronic

- acid. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 7.41 (d, 2H), 6.99 (d, 2H), 6.85 (s, 1H), 4.60-4.50 (m, 1H), 3.95-3.90 (m, 4H), 3.90-3.85 (m, 1H), 3.80-3.70 (m, 1H), 3.35-3.30 (m, 1H), 3.30-3.20 (m, 4H), 3.10-3.00 (m, 1H), 3.00-2.90 (m, 1H), 2.70-2.60 (m, 2H), 1.90-1.80 (m, 1H), 1.60-1.55 (m, 1H), 1.48 (s, 9H), 1.48-1.30 (m, 1H)
- [806] Preparation A3-62: tert-butyl N-[(3S)-1-[2-chloro-5-(3-methyl-4-morpholino-phenyl)-4-pyridyl]-3-piperidyl]carbamate
- [807] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3-methyl-4-morpholinophenyl boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 7.35-7.25 (m, 2H), 7.10 (d, 2H), 6.84 (s, 1H), 4.60-4.50 (m, 1H), 3.95-3.85 (m, 4H), 3.75-3.65 (m, 1H), 3.30-3.20 (m, 1H), 3.05-2.95 (m, 4H), 2.95-2.90 (m, 1H), 2.75-2.60 (m, 2H), 2.39 (s, 3H), 1.85-1.75 (m, 1H), 1.60-1.50 (m, 1H), 1.46 (s, 9H), 1.46-1.35 (m, 1H)
- [808] Preparation A3-63: tert-butyl N-[(3S)-1-[2-chloro-5-[4-[4-(2-hydroxyethyl)piperazin-1-carbonyl]phenyl]-4-pyridyl]-3-piperidyl]carbamate
- [809] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to [4-[4-(2-hydroxyethyl)piperazin-1-carbonyl]phenyl]boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.04 (s, 1H), 7.60-7.55 (m, 2H), 7.55-7.50 (m, 2H), 6.90 (s, 1H), 4.55-4.45 (m, 1H), 3.90-3.45 (m, 9H), 3.45-3.35 (m, 1H), 3.05-2.95 (m, 1H), 2.70-2.60 (m, 4H), 2.60-2.40 (m, 6H), 1.95-1.80 (m, 1H), 1.47 (s, 9H), 1.47-1.30 (m, 2H)
- [810] Preparation A3-64: tert-butyl N-[(3S)-1-[2-chloro-5-[4-[(trans)4-hydroxycyclohexyl]carbamoyl]phenyl]-4-pyridyl]-3-piperidyl]carbamate
- [811] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(trans-4-hydroxycyclohexylcarbamoyl)phenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.90-7.80 (m, 2H), 7.60-7.50 (m, 2H), 6.90 (s, 1H), 6.15-6.05 (m, 1H), 4.50-4.40 (m, 1H), 4.10-3.90 (m, 2H), 3.75-3.60 (m, 2H), 3.35-3.25 (m, 1H), 3.05-2.95 (m, 1H), 2.70-2.60 (m, 1H), 2.60-2.50 (m, 1H), 2.25-2.15 (m, 3H), 2.15-2.00 (m, 3H), 1.95-1.80 (m, 1H), 1.60-1.50 (m, 1H), 1.44 (s, 9H), 1.44-1.30 (m, 2H)
- [812] Preparation A3-65: tert-butyl N-[(3S)-1-[2-chloro-5-[4-(dimethylcarbamoyl)-3-fluorophenyl]-4-pyridyl]-3-piperidyl]carbamate
- [813] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-(dimethylcarbamoyl)-3-fluorophenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.51 (t, 1H), 7.40-7.35 (m, 1H), 7.35-7.25 (m, 1H), 6.91 (s, 1H), 4.55-4.45 (m, 1H), 3.75-3.65 (m, 1H), 3.50-3.40 (m, 1H), 3.18 (s, 3H), 3.05-2.95 (m, 4H), 2.65-2.55 (m, 2H), 1.95-1.85 (m, 1H), 1.55-1.50 (m, 1H), 1.46 (s, 9H), 1.46-1.30 (m, 1H)

- [814] Preparation A3-66: tert-butyl N-[(3S)-1-[5-(3-acetylphenyl)-2-chloro-4-pyridyl]-3-piperidyl]carbamate
- [815] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3-acetylphenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 8.07 (s, 1H), 7.97 (d, 1H), 7.70 (d, 1H), 7.58 (t, 1H), 6.91 (s, 1H), 4.65-4.55 (m, 1H), 3.75-3.65 (m, 1H), 3.30-3.20 (m, 1H), 2.95-2.85 (m, 1H), 2.75-2.65 (m, 2H), 2.67 (s, 3H), 1.81 (t, 1H), 1.60-1.50 (m, 1H), 1.45 (s, 9H), 1.45-1.35 (m, 1H)
- [816] Preparation A3-67: tert-butyl N-[(3S)-1-[2-chloro-5-(3-chloro-4-fluoro-phenyl)-4-pyridyl]-3-piperidyl]carbamate
- [817] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3-chloro-4-fluorophenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.02 (s, 1H), 7.57 (d, 1H), 7.45-7.35 (m, 1H), 7.25-7.15 (m, 1H), 6.89 (s, 1H), 4.55-4.45 (m, 1H), 3.75-3.65 (m, 1H), 3.35-3.25 (m, 1H), 3.00-2.90 (m, 1H), 2.70-2.60 (m, 2H), 1.90-1.80 (m, 1H), 1.55-1.50 (m, 1H), 1.47 (s, 9H), 1.47-1.35 (m, 1H)
- [818] Preparation A3-68: tert-butyl N-[(3S)-1-[2-chloro-5-[4-fluoro-3-(trifluoromethyl)phenyl]-4-pyridyl]-3-piperidyl]carbamate
- [819] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 4-fluoro-3-(trifluoromethyl)phenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.79 (d, 1H), 7.75-7.65 (m, 1H), 7.33 (t, 1H), 6.91 (s, 1H), 4.55-4.40 (m, 1H), 3.75-3.60 (m, 1H), 3.35-3.25 (m, 1H), 3.00-2.90 (m, 1H), 2.70-2.55 (m, 2H), 1.90-1.80 (m, 1H), 1.60-1.50 (m, 1H), 1.46 (s, 9H), 1.46-1.30 (m, 1H)
- [820] Preparation A3-69: tert-butyl N-[(3S)-1-[2-chloro-5-(3,4-difluorophenyl)-4-pyridyl]-3-piperidyl]carbamate
- [821] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 3,4-difluorophenylboronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.01 (s, 1H), 7.40-7.30 (m, 1H), 7.25-7.20 (m, 1H), 7.20-7.15 (m, 1H), 6.90 (s, 1H), 4.50-4.40 (m, 1H), 3.75-3.60 (m, 1H), 3.35-3.25 (m, 1H), 3.05-2.95 (m, 1H), 2.75-2.60 (m, 2H), 1.95-1.80 (m, 1H), 1.65-1.55 (m, 1H), 1.47 (s, 9H), 1.47-1.30 (m, 1H)
- [822] Preparation A3-70: tert-butyl N-[(3S)-1-[2-chloro-5-[3-(dimethylamino)-4-fluorophenyl]-4-pyridyl]-3-piperidyl]carbamate
- [823] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to (3-(dimethylamino)-4-fluorophenyl)boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.15-7.05 (m, 1H),

7.00-6.95 (m, 1H), 6.95-6.85 (m, 1H), 6.86 (s, 1H), 4.65-4.55 (m, 1H), 3.75-3.65 (m, 1H), 3.30-3.20 (m, 1H), 2.91 (s, 6H), 2.91-2.85 (m, 1H), 2.75-2.65 (m, 2H), 1.85-1.75 (m, 1H), 1.60-1.50 (m, 1H), 1.47 (s, 9H), 1.47-1.35 (m, 1H)

[824] Preparation A3-71: tert-butyl N-[(3S)-1-[2-chloro-5-[1-[(3S)-tetrahydrofuran-3-yl]pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate

[825] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to (S)-1-(tetrahydrofuran-3-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 7.86 (s, 1H), 7.79 (s, 1H), 6.88 (s, 1H), 5.15-5.05 (m, 1H), 4.55-4.45 (m, 1H), 4.25-4.15 (m, 2H), 4.15-4.05 (m, 1H), 3.98 (q, 1H), 3.80-3.70 (m, 1H), 3.45-3.35 (m, 1H), 3.15-3.00 (m, 1H), 2.70-2.60 (m, 1H), 2.60-2.45 (m, 2H), 2.45-2.35 (m, 1H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.46 (s, 9H), 1.46-1.30 (m, 1H)

[826] Preparation A3-72: tert-butyl N-[(3S)-1-[2-chloro-5-[1-[(3R)-tetrahydrofuran-3-yl]pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate

[827] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to (R)-1-(tetrahydrofuran-3-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.85 (s, 1H), 7.78 (s, 1H), 6.87 (s, 1H), 5.10-5.00 (m, 1H), 4.60-4.50 (m, 1H), 4.25-4.15 (m, 2H), 4.15-4.00 (m, 1H), 3.97 (q, 1H), 3.80-3.70 (m, 1H), 3.45-3.35 (m, 1H), 3.15-3.00 (m, 1H), 2.70-2.60 (m, 1H), 2.60-2.45 (m, 2H), 2.45-2.35 (m, 1H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.46 (s, 9H), 1.46-1.35 (m, 1H)

[828] Preparation A3-73: tert-butyl (S)-(1-(2-chloro-5-(1-ethyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[829] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-ethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.19 (s, 1H), 7.81-7.68 (m, 2H), 6.91 (s, 1H), 4.67-4.42 (m, 1H), 4.37 (q, 2H), 3.87-3.64 (m, 1H), 3.52-3.26 (m, 1H), 3.15-2.99 (m, 1H), 2.75-2.45 (m, 2H), 2.05-1.89 (m, 1H), 1.78-1.65 (m, 1H), 1.62 (t, 3H), 1.53 (s, 9H), 1.41-1.32 (m, 1H)

[830] Preparation A3-74: tert-butyl (S)-(1-(2-chloro-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[831] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-isopropylpyrazol-4-boronic acid. ¹H NMR (CDCl₃, 400MHz) δ 8.23 (s, 1H), 7.84-7.67 (m, 2H), 6.91 (s, 1H), 4.65-4.46 (m, 1H), 3.86-3.62 (m, 1H), 3.48-3.32 (m, 1H), 3.14-2.99 (m, 1H), 2.71-2.47

- (m, 2H), 2.02-1.88 (m, 1H), 1.74-1.65 (m, 1H), 1.61 (s, 6H), 1.51 (s, 9H), 1.41-1.34 (m, 1H)
- [832] Preparation A3-75: tert-butyl (S)-(1-(2-chloro-5-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [833] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.18 (s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 6.90 (s, 1H), 4.62-4.43 (m, 1H), 3.84-3.63 (m, 2H), 3.49-3.37 (m, 1H), 3.14-3.01 (m, 1H), 2.70-2.45 (m, 2H), 2.04-1.89 (m, 1H), 1.76-1.65 (m, 1H), 1.59-1.52 (m, 1H), 1.52 (s, 9H), 1.41-1.33 (m, 1H), 1.33-1.25 (m, 2H), 1.24-1.21 (m, 1H), 1.14-1.01 (m, 2H)
- [834] Preparation A3-76: tert-butyl (S)-(1-(2-chloro-5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [835] The titled compound was prepared in accordance with the same procedures as in Preparation A3-1, changing the boronic acid reagent to 1-cyclopropylmethyl-1H-pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.19 (s, 1H), 7.91 (s, 1H), 7.79 (s, 1H), 6.89 (s, 1H), 4.66 (s, 1H), 4.10 (d, 2H), 3.85-3.68 (m, 1H), 3.46-3.31 (m, 1H), 3.11-2.99 (m, 1H), 2.72-2.50 (m, 2H), 1.98-1.89 (m, 1H), 1.78-1.64 (m, 1H), 1.64-1.50 (m, 1H), 1.42-1.33 (m, 2H), 1.33 (s, 9H), 0.76-0.66 (m, 2H), 0.50-0.35 (m, 2H)
- [836] Preparation A4-1: (S)-1-(6-chloro-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [837] Step 1: (S)-1-(2-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-4-yl)piperidin-3-ol (A4)
- [838] 2-Chloro-4-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (3.0 g, 11.65 mmol) was dissolved in anhydrous isopropyl alcohol (58.2 mL) and then (S)-3-hydroxypiperidine hydrochloride (1.8 g, 12.82 mmol) and diisopropylethylamine (4.8 mL, 34.95 mmol) were added dropwise thereto. The reaction mixture was stirred at 50°C for 7 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated to prepare the titled compound, which was used in the subsequent step without further purification.
- [839] Step 2: (S)-1-(6-chloro-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol (A4-1)
- [840] (S)-1-(2-Chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-4-yl)piperidin-3-ol (100.0 mg, 0.30 mmol) was dissolved in anhydrous 1,4-dioxane (2.0 mL) and then 5-bromo-2-tetrahydropyran-4-yl-pyridine (85.8 mg, 0.35 mmol), [1,1'-

bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (24.1 mg, 0.03 mmol), and 2.0M sodium carbonate solution (0.71 mL, 1.43 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (20.1 mg). (Yield: 18.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.69 (s, 1H), 8.03 (s, 1H), 7.78 (d, 1H), 7.28 (d, 1H), 6.90 (s, 1H), 4.14-4.11 (m, 2H), 3.61-3.60 (m, 1H), 3.59-3.55 (m, 2H), 3.21-3.20 (m, 1H), 3.17-3.04 (m, 2H), 2.72-2.67 (m, 2H), 1.96-1.91 (m, 5H), 1.66-1.64 (m, 1H), 1.46-1.44 (m, 2H), 1.42-1.41 (m, 1H)

[841] Preparation A4-2: (S)-1-(6-chloro-6'-((4-methylpiperazin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol

[842] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to 1-((5-bromopyridin-2-yl)methyl)-4-methylpiperazine. ¹H NMR (CDCl₃, 400MHz) δ 8.73 (s, 1H), 8.05 (s, 1H), 7.79-7.77 (m, 1H), 7.46 (d, 1H), 6.90 (s, 1H), 3.81 (s, 2H), 3.65-3.57 (m, 1H), 3.06-3.02 (m, 2H), 2.75-2.71 (m, 1H), 2.61-2.51 (m, 9H), 2.32-2.28 (m, 4H), 1.89-1.83 (m, 2H), 1.52-1.35 (m, 2H)

[843] Preparation A4-3: (S)-1-(6-chloro-6'-(morpholinomethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol

[844] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to 4-((5-bromopyridin-2-yl)methyl)morpholine. ¹H NMR (CDCl₃, 400MHz) δ 8.73 (s, 1H), 8.04 (s, 1H), 7.81 (d, 1H), 7.53-7.51 (m, 1H), 6.91 (s, 1H), 3.78-3.76 (m, 4H), 3.73-3.72 (m, 3H), 3.20-3.17 (m, 1H), 2.98-2.93 (m, 1H), 2.76-2.66 (m, 2H), 2.67-2.53 (m, 4H), 1.88-1.86 (m, 1H), 1.67-1.63 (m, 1H), 1.49-1.41 (m, 2H)

[845] Preparation A4-4: (S)-1-(6-chloro-6'-((4-hydroxypiperidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol

[846] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to 1-[(5-bromo-2-pyridyl)methyl]piperidin-4-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.71 (s, 1H), 8.05 (s, 1H), 7.80 (d, 1H), 7.53-7.51 (m, 1H), 6.91 (s, 1H), 3.84-3.66 (m, 4H), 3.18-3.16 (m, 1H), 3.00-2.97 (m, 1H), 2.82-2.63 (m, 4H), 2.35-2.26 (m, 2H), 1.93-1.86 (m, 3H), 1.76-1.65 (m, 3H), 1.47-1.43 (m, 3H)

- [847] Preparation A4-5: (S)-(6'-chloro-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-methylpiperazin-1-yl)methanone
- [848] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to (5-bromopyridin-2-yl)(4-methylpiperazin-1-yl)methanone. ¹H NMR (CDCl₃, 400MHz) δ 8.76 (s, 1H), 8.38 (s, 1H), 8.05-7.95 (m, 2H), 6.93 (s, 1H), 3.87-3.86 (m, 2H), 3.69-3.68 (m, 2H), 3.63-3.61 (m, 1H), 3.19-3.16 (m, 1H), 3.04-2.99 (m, 1H), 2.70-2.65 (m, 2H), 2.56-2.54 (m, 2H), 2.49-2.46 (m, 2H), 2.35 (s, 3H), 1.90-1.81 (m, 2H), 1.73-1.70 (m, 1H), 1.45-1.42 (m, 2H)
- [849] Preparation A4-6: (S)-(6'-chloro-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(morpholino)methanone
- [850] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to (5-bromopyridin-2-yl)(morpholino)methanone. ¹H NMR (CDCl₃, 400MHz) δ 8.75 (s, 1H), 8.05 (s, 1H), 8.00-7.97 (m, 1H), 7.86-7.81 (m, 1H), 6.94 (s, 1H), 3.85 (s, 4H), 3.74 (s, 4H), 3.19-3.16 (m, 1H), 3.03-2.96 (m, 1H), 2.80-2.69 (m, 2H), 1.92-1.85 (m, 1H), 1.74-1.68 (m, 2H), 1.47-1.43 (m, 2H)
- [851] Preparation A4-7: (S)-(6'-chloro-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone
- [852] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to (5-bromopyridin-2-yl)(4-hydroxypiperidin-1-yl)methanone. ¹H NMR (CDCl₃, 400MHz) δ 8.76 (s, 1H), 8.06 (s, 1H), 7.96 (d, 1H), 7.54 (d, 1H), 6.93 (s, 1H), 4.26-4.23 (m, 1H), 4.04-4.03 (m, 1H), 3.91-3.87 (m, 1H), 3.75-3.67 (m, 1H), 3.51-3.46 (m, 1H), 3.40-3.35 (m, 1H), 3.19-3.16 (m, 1H), 3.02-2.98 (m, 1H), 2.78-2.65 (m, 2H), 2.08-2.03 (m, 1H), 2.01-1.89 (m, 3H), 1.71-1.64 (m, 2H), 1.47-1.44 (m, 2H)
- [853] Preparation A4-8: (S)-6'-chloro-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-carbaldehyde
- [854] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to 5-bromo-2-pyridinecarboxaldehyde. ¹H NMR (CDCl₃, 400MHz) δ 10.13 (s, 1H), 8.97 (s, 1H), 8.07 (d, 3H), 6.96 (s, 1H), 3.77-3.76 (m, 1H), 3.23-3.19 (m, 1H), 2.99-2.96 (m, 1H), 2.78-2.71 (m, 2H), 1.95-1.92 (m, 1H), 1.71-1.68 (m, 1H), 1.52-1.50 (m, 1H), 1.47-1.43 (m, 2H)
- [855] Preparation A4-9: (S)-1-(6'-chloro-5-((1-methylpiperidin-4-yl)oxy)-[2,3'-bipyridin]-4'-yl)piperidin-3-ol
- [856] The titled compound was prepared in accordance with the same procedures as in Preparation A4-1, changing the bromine reagent to 2-bromo-5-[(1-methyl-4-piperidyl

-)oxy]pyridine. ¹H NMR (CD₃OD, 400MHz) δ 8.43 (s, 1H), 8.08 (s, 1H), 7.75 (d, 1H), 7.62 (d, 1H), 7.05 (s, 1H), 3.70-3.60 (m, 2H), 3.55-3.40 (m, 3H), 3.30-3.20 (m, 1H), 3.15-3.05 (m, 1H), 2.93 (s, 3H), 2.74 (t, 1H), 2.61 (t, 1H), 2.35-2.10 (m, 3H), 2.10-2.00 (m, 1H), 2.00-1.90 (m, 1H), 1.80-1.65 (m, 1H), 1.50-1.25 (m, 3H)
- [857] Preparation A5-1: tert-butyl (S)-(1-(6-chloro-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate
- [858] Step 1: tert-butyl (S)-(1-(2-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [859] 2-Chloro-4-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (2.0 g, 7.77 mmol) was dissolved in anhydrous isopropyl alcohol (38.8 mL) and then (S)-3-(tert-butoxycarbonylamino)piperidine (2.33 g, 11.65 mmol) and diisopropylethylamine (3.2 mL, 23.30 mmol) were added dropwise thereto. The reaction mixture was stirred at 50°C for 8 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (1.0 g). (Yield: 29.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.48 (s, 1H), 6.73 (s, 1H), 5.37-5.36 (m, 1H), 3.92-3.89 (m, 1H), 3.19-3.12 (m, 3H), 3.04-3.01 (m, 1H), 1.96-1.95 (m, 1H), 1.82-1.79 (m, 1H), 1.72-1.68 (m, 2H), 1.46 (s, 6H), 1.38 (s, 6H)
- [860] Step 2: tert-butyl (S)-(1-(6-chloro-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-yl)carbamate (A5-1)
- [861] tert-Butyl (S)-(1-(2-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-4-yl)piperidin-3-yl)carbamate (150.0 mg, 0.34 mmol) was dissolved in anhydrous 1,4-dioxane (3.40 mL) and then 5-bromo-2-tetrahydropyran-4-yl-pyridine (99.5 mg, 0.41 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (27.9 mg, 0.034 mmol), and 2.0M sodium carbonate solution (0.69 mL, 1.37 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (51.0 mg). (Yield: 31.5%) ¹H NMR (CDCl₃, 400MHz) δ 8.65 (s, 1H), 8.03 (s, 1H), 7.82 (d, 1H), 7.28 (s, 1H), 6.89 (s, 1H), 4.51-4.41 (m, 1H), 4.14-4.11 (m, 2H), 3.61-3.55 (m, 3H), 3.37-3.34 (m, 1H), 3.04-2.98 (m, 2H), 2.64-2.54 (m, 2H), 1.94-1.82 (m, 4H), 1.54-1.53 (m, 1H), 1.43 (s, 9H), 1.29-1.27 (m, 1H)

- [862] Preparation A5-2: tert-butyl N-[(3S)-1-[2-chloro-5-[6-(1-methyl-4-piperidyl)-3-pyridyl]-4-pyridyl]-3-piperidyl]carbamate
- [863] The titled compound was prepared in accordance with the same procedures as in Preparation A5-1, changing the bromine reagent to 5-bromo-2-(1-methyl-4-piperidyl)pyridine. ¹H NMR (CDCl₃, 400MHz) δ 8.63 (s, 1H), 8.02 (s, 1H), 7.79 (d, 1H), 7.29 (d, 1H), 6.88 (s, 1H), 4.52-4.44 (m, 1H), 3.72-3.65 (m, 1H), 3.37-3.34 (m, 1H), 3.04-2.94 (m, 4H), 2.79-2.72 (m, 2H), 2.63-2.55 (m, 2H), 2.35 (s, 3H), 2.14-2.12 (m, 2H), 2.09-2.05 (m, 2H), 2.01-1.87 (m, 4H), 1.45 (s, 9H)
- [864] Preparation A5-3: tert-butyl (S)-(1-(2-chloro-5-(2-(1-methylpiperidin-4-yl)thiazol-5-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [865] The titled compound was prepared in accordance with the same procedures as in Preparation A5-1, changing the bromine reagent to 5-bromo-2-(1-methyl-4-piperidyl)thiazole. ¹H NMR (CD₃OD, 400MHz) δ 8.46 (s, 1H), 8.18 (s, 1H), 7.93 (s, 1H), 3.89-3.56 (m, 3H), 3.44 (t, 1H), 3.35 (d, 1H), 3.20-3.14 (m, 3H), 2.88 (s, 3H), 2.71 (t, 1H), 2.41 (d, 3H), 2.24-2.17 (m, 2H), 1.93 (d, 1H), 1.78 (brs, 1H), 1.70-1.66 (m, 1H), 1.40 (s, 9H), 1.39-1.25 (m, 1H)
- [866] Preparation A6-1: (S)-1-(2-chloro-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [867] (S)-1-(2-Chloro-5-iodopyridin-4-yl)piperidin-3-ol (A2, 500.0 mg, 1.48 mmol) was dissolved in anhydrous 1,4-dioxane (10.0 mL) and then 4-ethynyl-1-(trifluoromethyl)-1H-pyrazole (354.6 mg, 2.21 mmol), bis(triphenylphosphine)palladium(II) dichloride (51.8 mg, 0.074 mmol), copper(I) iodide (16.9 mg, 0.089 mmol), and triethylamine (0.41 mL, 2.95 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (491.7 mg). (Yield: 89.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.30 (s, 1H), 8.11 (s, 1H), 7.93 (s, 1H), 6.80 (s, 1H), 4.02-4.01 (m, 1H), 3.55-3.51 (m, 2H), 3.36-3.34 (m, 2H), 2.12-1.89 (m, 2H), 1.77-1.72 (m, 2H)
- [868] Preparation A6-2: (S)-1-(2-chloro-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [869] The titled compound was prepared in accordance with the same procedures as in Preparation A6-1, changing the ethyne reagent to 4-ethynyl-tetrahydro-2H-pyran. ¹H NMR (CDCl₃, 400MHz) δ 8.19 (s, 1H), 6.74 (s, 1H), 3.99-3.94 (m, 3H), 3.61-3.52 (m,

- 3H), 3.40-3.37 (m, 1H), 3.33-3.28 (m, 1H), 3.24-3.22 (m, 1H), 3.80 (s, 1H), 2.20-2.19 (m, 1H), 1.98-1.92 (m, 4H), 1.85-1.82 (m, 2H)
- [870] Preparation A6-3: (S)-1-(2-chloro-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [871] The titled compound was prepared in accordance with the same procedures as in Preparation A6-1, changing the ethyne reagent to 1-(difluoromethyl)-4-ethynyl-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.33 (s, 1H), 8.13 (s, 1H), 7.88 (s, 1H), 7.38-7.35 (m, 0.2H), 7.23-7.19 (m, 0.6H), 7.08-7.04 (m, 0.2H), 6.84 (s, 1H), 4.07-3.97 (m, 1H), 3.50-3.44 (m, 1H), 3.43-3.33 (m, 1H), 3.33-3.26 (m, 1H), 2.23-2.12 (m, 1H), 2.06-1.85 (m, 1H), 1.83-1.69 (m, 2H)
- [872] Preparation A6-4: (S)-1-(2-chloro-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [873] The titled compound was prepared in accordance with the same procedures as in Preparation A6-1, changing the ethyne reagent to 1-(2,2-difluoroethyl)-4-ethynyl-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.33-8.34 (s, 1H), 7.81 (s, 2H), 6.83 (s, 1H), 6.30-6.24 (m, 0.2H), 6.16-6.10 (m, 0.6H), 6.01-5.97 (m, 0.2H), 4.56-4.44 (m, 2H), 4.07-3.97 (m, 1H), 3.59-3.47 (m, 2H), 3.41-3.27 (m, 2H), 2.07-1.95 (m, 1H), 1.95-1.86 (m, 1H), 1.80-1.70 (m, 2H)
- [874] Preparation A6-5: (S)-1-(2-chloro-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [875] The titled compound was prepared in accordance with the same procedures as in Preparation A6-1, changing the ethyne reagent to 4-ethynyl-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.33 (s, 1H), 7.84 (s, 1H), 7.81 (s, 1H), 6.82 (s, 1H), 4.07-3.97 (m, 1H), 3.59-3.46 (m, 2H), 3.40-3.25 (m, 2H), 2.19-2.14 (m, 1H), 1.95-1.84 (m, 1H), 1.81-1.69 (m, 2H)
- [876] Preparation A7-1: tert-butyl (S)-1-(2-chloro-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [877] tert-Butyl (S)-1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-yl)carbamate (300.0 mg, 0.68 mmol) was dissolved in anhydrous 1,4-dioxane (8.0 mL) and then 4-ethynyl-tetrahydro-2H-pyran (150.9 mg, 1.37 mmol), bis(triphenylphosphine)palladium(II) dichloride (22.9 mg, 0.033 mmol), copper(I) iodide (7.8 mg, 0.041 mmol), and triethylamine (0.19 mL, 1.37 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound

- (120.4 mg). (Yield: 41.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.19 (s, 1H), 7.27 (s, 1H), 4.89-4.88 (m, 1H), 3.97-3.95 (m, 2H), 3.93-3.91 (m, 1H), 3.57-3.52 (m, 3H), 3.39-3.37 (m, 1H), 3.20-3.19 (m, 2H), 2.96-2.92 (m, 1H), 1.94-1.92 (m, 2H), 1.86-1.63 (m, 6H), 1.43 (s, 9H)
- [878] Preparation A7-2: tert-butyl (S)-(1-(2-chloro-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [879] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 4-ethynyl-1-(trifluoromethyl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.29-8.28 (m, 2H), 7.92 (s, 1H), 6.79 (s, 1H), 4.74-4.73 (m, 1H), 3.89-3.74 (m, 2H), 3.39-3.21 (m, 1H), 3.08-2.99 (m, 1H), 1.92-1.87 (m, 2H), 1.77-1.75 (m, 1H), 1.58-1.55 (m, 1H), 1.42 (s, 9H)
- [880] Preparation A7-3: tert-butyl (S)-(1-(2-chloro-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [881] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 1-(difluoromethyl)-4-ethynyl-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.28 (s, 1H), 8.19 (s, 1H), 7.82 (s, 1H), 7.33-7.03 (m, 1H), 6.77 (s, 1H), 4.80-4.78 (m, 1H), 3.88 (brs, 1H), 3.80-3.77 (m, 1H), 3.41-3.38 (m, 1H), 3.12-3.11 (m, 2H), 1.92-1.88 (m, 2H), 1.76-1.75 (m, 1H), 1.74-1.73 (m, 1H), 1.42 (s, 9H)
- [882] Preparation A7-4: tert-butyl (S)-(1-(2-chloro-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [883] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 1-(2,2-difluoroethyl)-4-ethynyl-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.26 (s, 1H), 7.81 (s, 1H), 7.74 (s, 1H), 6.76 (s, 1H), 6.25-5.95 (m, 1H), 4.82-4.80 (m, 1H), 4.50-4.42 (m, 2H), 3.87-3.86 (m, 1H), 3.72-3.69 (m, 1H), 3.43-3.40 (m, 1H), 3.17-3.15 (m, 2H), 1.92-1.88 (m, 2H), 1.75-1.74 (m, 1H), 1.73-1.71 (m, 1H), 1.43 (s, 9H)
- [884] Preparation A7-5: tert-butyl (S)-(1-(2-chloro-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [885] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 4-ethynyl-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.27 (s, 1H), 7.86 (s, 1H), 7.76 (s, 1H), 6.76 (s, 1H), 4.80-4.78 (m, 1H), 4.73-4.67 (q, 2H), 3.87-3.86 (m, 1H), 3.75-3.72 (m, 1H), 3.44-3.41 (m, 1H), 3.16-3.11 (m, 2H), 1.92-1.88 (m, 2H), 1.76-1.74 (m, 1H), 1.72-1.70 (m, 1H), 1.42 (s, 9H)
- [886] Preparation A7-6: tert-butyl (S)-(1-(2-chloro-5-((4-methyltetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate

- [887] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 4-ethynyl-4-methyltetrahydro-2H-pyran. ¹H NMR (CDCl₃, 400MHz) δ 8.66 (s, 1H), 6.86 (s, 1H), 5.03-4.84 (m, 1H), 3.96 (s, 1H), 3.88-3.82 (m, 3H), 3.24-3.19 (m, 1H), 3.10-2.94 (m, 2H), 2.88-2.78 (m, 1H), 2.10-2.02 (m, 2H), 1.38 (s, 9H)
- [888] Preparation A7-7: tert-butyl (S)-(1-(2-chloro-5-((4-hydroxytetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-yl)carbamate
- [889] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 4-ethynyltetrahydro-2H-pyran-4-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.29 (s, 1H), 6.80 (s, 1H), 4.65-4.50 (m, 2H), 4.03-3.92 (m, 2H), 3.90-3.80 (m, 1H), 3.80-3.70 (m, 2H), 3.40-3.29 (m, 1H), 2.86-2.73 (m, 1H), 2.37-2.26 (m, 1H), 2.15-2.09 (m, 2H), 2.03-1.93 (m, 3H), 1.87-1.75 (m, 1H), 1.55 (s, 9H)
- [890] Preparation A7-8: tert-butyl (S)-(1-(2-chloro-5-(3-hydroxy-3-methylbut-1-yn-1-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [891] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 2-methylbut-3-yn-2-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.26 (s, 1H), 6.80 (s, 1H), 4.64-4.53 (m, 1H), 4.53-4.42 (m, 1H), 3.98-3.78 (m, 1H), 3.36-3.25 (m, 1H), 2.91-2.74 (m, 1H), 2.47-2.32 (m, 1H), 2.11-2.00 (m, 1H), 2.00-1.87 (m, 1H), 1.87-1.78 (m, 1H), 1.70 (s, 6H), 1.52 (s, 9H)
- [892] Preparation A7-9: tert-butyl (S)-(1-(2-chloro-5-(4-hydroxybut-1-yn-1-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [893] The titled compound was prepared in accordance with the same procedures as in Preparation A7-1, changing the ethyne reagent to 3-butyne-1-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.27 (s, 1H), 6.80 (s, 1H), 4.90-4.80 (m, 1H), 4.20 (q, 2H), 3.82-3.74 (m, 1H), 3.35-3.22 (m, 1H), 3.12-3.04 (m, 2H), 1.99-1.85 (m, 2H), 1.82-1.71 (m, 1H), 1.54 (s, 9H), 1.33 (t, 2H)
- [894] Preparation A8-1: (S)-1-(6-chloro-6'-(((S)-3-fluoropyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [895] (S)-6'-chloro-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-carbaldehyde (A4-8, 40 mg, 0.13 mmol) was dissolved in dichloromethane (1.0 mL) and then (S)-(+)-3-fluoropyrrolidine hydrochloride (13.0 mg, 0.10 mmol) and triethylamine (0.03 mL, 0.19 mmol) were added dropwise thereto. Then, the mixed solution was stirred at room temperature for 10 minutes. The reaction mixture was cooled to 0°C with ice water and then sodium borohydride (60.0 mg, 0.28 mmol) was added dropwise thereto. The reaction mixture was stirred at room temperature for 2 hours. After completion of the reaction, dichloromethane was added to the reaction mixture and then a saturated

sodium hydrogen carbonate solution was added thereto. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated to prepare the titled compound (22.5 mg), without further purification. (Yield: 61.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.67 (s, 1H), 8.03-7.99 (m, 2H), 7.64 (d, 1H), 7.06 (s, 1H), 3.87 (s, 2H), 3.60-3.57 (m, 1H), 3.28-3.25 (m, 2H), 3.12-3.08 (m, 1H), 3.02-2.92 (m, 2H), 2.79-2.71 (m, 1H), 2.59-2.53 (m, 2H), 2.25-2.10 (m, 1H), 2.07-1.91 (m, 2H), 1.70-1.66 (m, 1H), 1.44-1.25 (m, 3H)

[896] Preparation A8-2: (3S)-1-[2-chloro-5-[6-[(3-hydroxypyrrolidin-1-yl)methyl]-3-pyridyl]-4-pyridyl]piperidin-3-ol

[897] The titled compound was prepared in accordance with the same procedures as in Preparation A8-1, changing the amine reagent to pyrrolidin-3-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.70 (s, 1H), 8.02-7.99 (m, 2H), 7.64 (d, 1H), 7.07 (s, 1H), 4.41 (brs, 1H), 4.01-3.99 (m, 2H), 3.60-3.56 (m, 1H), 3.28-3.25 (m, 1H), 3.12-3.09 (m, 1H), 2.99-2.98 (m, 2H), 2.79-2.69 (m, 3H), 2.57 (t, 1H), 2.23-2.16 (m, 1H), 2.02-1.91 (m, 1H), 1.83-1.80 (m, 1H), 1.70-1.67 (m, 1H), 1.44-1.25 (m, 3H)

[898] Preparation A8-3: (3S)-1-[2-chloro-5-[6-[[3-(dimethylamino)pyrrolidin-1-yl]methyl]-3-pyridyl]-4-pyridyl]piperidin-3-ol

[899] The titled compound was prepared in accordance with the same procedures as in Preparation A8-1, changing the amine reagent to 3-(dimethylamino)pyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.70 (s, 1H), 8.05 (s, 1H), 7.80-7.75 (m, 1H), 7.46 (d, 1H), 6.90 (s, 1H), 7.38 (d, 1H), 6.89 (d, 1H), 3.98 (s, 2H), 3.55-3.52 (m, 1H), 3.08-3.04 (m, 2H), 2.85-2.78 (m, 6H), 2.49-2.47 (m, 1H), 2.38-2.34 (m, 4H), 2.22 (s, 6H), 2.03-1.99 (m, 1H), 2.22 (s, 1H), 1.79-1.72 (m, 1H)

[900] Preparation A8-4: 1-((6'-chloro-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)methyl)piperidin-3-ol

[901] The titled compound was prepared in accordance with the same procedures as in Preparation A8-1, changing the amine reagent to 3-hydroxypiperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.80-8.70 (m, 1H), 8.05 (s, 1H), 7.84-7.78 (m, 1H), 7.51-7.45 (m, 1H), 6.90 (d, 1H), 3.85-3.82 (m, 2H), 3.61-3.58 (m, 1H), 3.14-3.03 (m, 3H), 2.76-2.71 (m, 2H), 2.56-2.38 (m, 7H), 1.95-1.87 (m, 5H), 1.48-1.39 (m, 2H)

[902] Preparation A8-5: tert-butyl (S)-((1-((6'-chloro-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)methyl)piperidin-4-yl)carbamate

[903] The titled compound was prepared in accordance with the same procedures as in Preparation A8-1, changing the amine reagent to 4-(tert-butoxycarbonylamino)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.68 (s, 1H), 8.00 (s, 2H), 7.63 (d, 1H), 7.07 (s, 1H), 3.75 (s, 2H), 3.60-3.58 (m, 1H), 3.60-3.56 (m, 1H), 3.38-3.23 (m, 2H), 3.14-3.08 (m, 1H), 2.94-2.91 (m, 2H), 2.73-2.68 (m, 1H), 2.57 (t, 1H), 2.30-2.20 (m, 2H),

- 1.94-1.85 (m, 3H), 1.72-1.65 (m, 1H), 1.57-1.52 (m, 2H), 1.44 (s, 9H), 1.36-1.34 (m, 1H)
- [904] Preparation A9-1: (S)-1-(2-chloro-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-4-yl)piperidin-3-ol
- [905] Step 1: (S)-1-(2-chloro-5-iodopyrimidin-4-yl)piperidin-3-ol (A9)
- [906] 2,4-Dichloro-5-iodo-pyrimidine (500 mg, 1.82 mmol) was dissolved in anhydrous acetonitrile (10.0 mL) and the (S)-3-hydroxypiperidine hydrochloride (275.3 mg, 2.00 mmol) and diisopropylethylamine (1.6 mL, 11.65 mmol) were added dropwise thereto. The reaction mixture was stirred 50°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (290 mg). (Yield: 46.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.48 (s, 1H), 3.99 (s, 1H), 3.85 (d, 1H), 3.71/3.67 (m, 1H), 3.62-3.52 (m, 2H), 2.29-2.28 (m, 1H), 1.95-1.93 (m, 2H), 1.74-1.61 (m, 2H)
- [907] Step 2: (S)-1-(2-chloro-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-4-yl)piperidin-3-ol (A9-1)
- [908] (S)-1-(2-Chloro-5-iodopyrimidin-4-yl)piperidin-3-ol (200 mg, 0.59 mmol) was dissolved in anhydrous 1,4-dioxane (6.0 mL) and then 1-methyl-4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)piperidine (205.8 mg, 0.71 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (48.2 mg, 0.06 mmol), and 2.0M sodium carbonate solution (1.48 mL, 2.95 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 6 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (50.0 mg). (Yield: 22.5%) ¹H NMR (CDCl₃, 400MHz) δ 8.03 (s, 1H), 7.60 (s, 1H), 7.59 (s, 1H), 4.19-4.15 (m, 1H), 3.90-3.88 (m, 1H), 3.59-3.58 (m, 1H), 3.56-3.55 (m, 1H), 3.48-3.44 (m, 1H), 3.32-3.29 (m, 1H), 3.22-3.02 (m, 2H), 2.34 (s, 3H), 2.22-2.03 (m, 6H), 1.85-1.82 (m, 1H), 1.78-1.75 (m, 1H), 1.66-1.63 (m, 1H), 1.45-1.44 (m, 1H)
- [909] Preparation A10-1: tert-butyl (S)-1-(6-chloro-3-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridazin-4-yl)piperidin-3-yl carbamate
- [910] Step 1: tert-butyl (S)-1-(3-bromo-6-chloropyridazin-4-yl)piperidin-3-yl carbamate (A10)

- [911] 3-Bromo-4,6-dichloropyridazine (500.0 mg, 2.19 mmol) was dissolved in anhydrous dimethylacetamide (5.0 mL) and then (S)-3-(tert-butoxycarbonylamino)piperidine (659.1 mg, 3.29 mmol) and diisopropylethylamine (1.15 mL, 6.58 mmol) were added dropwise thereto. The reaction mixture was stirred at 90°C for 3 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (700.0 mg). (Yield: 81.6%) ¹H NMR (CDCl₃, 400MHz) δ 6.88 (s, 1H), 4.83 (s, 1H), 3.91 (s, 1H), 3.51-3.48 (m, 1H), 3.39-3.34 (m, 1H), 3.14-3.11 (m, 1H), 3.09-3.00 (m, 1H), 1.97-1.90 (m, 2H), 1.89-1.85 (m, 1H), 1.72 (s, 9H), 1.70-1.68 (m, 1H)
- [912] Step 2: tert-butyl (S)-(1-(6-chloro-3-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridazin-4-yl)piperidin-3-yl) carbamate (A10-1)
- [913] tert-Butyl (S)-(1-(6-chloro-3-bromopyridazin-4-yl)piperidin-3-yl)carbamate (100 mg, 0.25 mmol) was dissolved in anhydrous 1,4-dioxane (3.0 mL) and then 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole (70.5 mg, 0.25 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (10.4 mg, 0.013 mmol), and 2.0M sodium carbonate solution (0.38 mL, 0.76 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 90°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (75.4 mg). (Yield: 64.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.25 (s, 1H), 8.24 (s, 1H), 7.00 (s, 1H), 4.89-4.81 (m, 2H), 4.52-4.51 (m, 1H), 3.80 (s, 1H), 3.56-3.53 (m, 1H), 3.24-3.21 (m, 1H), 2.68-2.67 (m, 1H), 2.50-2.49 (m, 1H), 2.04-2.03 (m, 1H), 1.85-1.82 (m, 1H), 1.81-1.80 (m, 1H), 1.73 (s, 9H), 1.40-1.39 (m, 1H)
- [914] Preparation A11-1: methyl (S)-6-chloro-4-(3-hydroxypiperidin-1-yl)nicotinate
- [915] Methyl-4,6-dichloronicotinate (1.0 g, 4.85 mmol) was dissolved in anhydrous dimethylformamide (20.0 mL) and then (S)-3-hydroxypiperidine hydrochloride (734.7 mg, 5.34 mmol) and diisopropylethylamine (1.7 mL, 9.71 mmol) were added dropwise thereto. The reaction mixture was stirred at 50°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature. Water was added to the reaction mixture and the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography

to prepare the titled compound (1.13 g, Yield: 86.0%). ¹H NMR (CDCl₃, 400MHz) δ 8.60 (s, 1H), 6.86 (s, 1H), 4.00-3.97 (m, 1H), 3.94 (s, 3H), 3.24-3.18 (m, 3H), 3.14-3.09 (m, 1H), 2.90 -2.87 (m, 1H), 2.07-2.03 (m, 1H), 1.83-1.75 (m, 2H), 1.70-1.63 (m, 1H)

[916] Preparation A11-2: (S)-6-chloro-4-(3-hydroxypiperidin-1-yl)nicotinamide

[917] The titled compound was prepared in accordance with the same procedures as in Preparation A11-1, changing the dichloro reagent to 4,6-dichloronicotinamide. ¹H NMR (CD₃OD, 400MHz) δ 8.20 (s, 1H), 7.00 (s, 1H), 3.86-3.82 (m, 1H), 3.54-3.50 (m, 1H), 3.39-3.36 (m, 1H), 3.11-3.05 (m, 1H), 2.97-2.92 (m, 1H), 2.03-1.89 (m, 2H), 1.69-1.65 (m, 1H), 1.57-1.2 (m, 1H)

[918] Preparation B1-1: tert-butyl (S)-(1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)(methyl)carbamate

[919] Step 1: 2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-fluoropyridine (B1)

[920] 2-Chloro-4-fluoro-5-iodo-pyridine (5.0 g, 19.42 mmol) was dissolved in anhydrous 1,4-dioxane (97.1 mL) and then 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester (5.7 g, 23.30 mmol), bis(triphenylphosphine)palladium(II) dichloride (1.36 g, 1.94 mmol), and 2.0M sodium carbonate solution (29.1 mL, 58.3 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 2 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (3.7 g). (Yield: 76.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.63 (d, 1H), 8.23 (s, 1H), 8.04 (s, 1H), 7.41-7.11 (m, 2H)

[921] Step 2: tert-butyl (S)-(1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)(methyl)carbamate (B1-1)

[922] 2-Chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-fluoropyridine (200 mg, 0.81 mmol) was dissolved in anhydrous dimethylformamide (8.0 mL) and then tert-butyl N-methyl-N-[(3S)-3-piperidyl]carbamate (173.1 mg, 0.81 mmol) and diisopropylethylamine (0.33 mL, 2.42 mmol) were added dropwise thereto. The reaction mixture was stirred at 80°C overnight. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (208.6 mg). (Yield: 58.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 2H), 7.97 (s, 1H), 7.41-7.11 (m, 1H), 6.91 (s, 1H), 3.28-3.22 (m, 2H), 2.79

- (s, 3H), 2.75-2.71 (m, 1H), 2.43-2.31 (m, 1H), 1.89-1.88 (m, 1H), 1.74-1.73 (m, 1H), 1.63-1.59 (m, 2H), 1.48 (s, 9H)
- [923] Preparation B1-2: tert-butyl (R)-(1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)(methyl)carbamate
- [924] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-methyl-N-[(3R)-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 2H), 7.97 (s, 1H), 7.42-7.11 (m, 1H), 6.91 (s, 1H), 3.29-3.25 (m, 2H), 2.79 (s, 3H), 2.74-2.71 (m, 1H), 2.45-2.43 (m, 1H), 1.90-1.89 (m, 1H), 1.88-1.74 (m, 1H), 1.72-1.64 (m, 2H), 1.48 (s, 9H)
- [925] Preparation B1-3: tert-butyl((3S,4R)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-methylpiperidin-3-yl)carbamate
- [926] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3S,4R)-4-methyl-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 8.12 (s, 1H), 7.96 (s, 1H), 7.27 (t, 1H), 6.91 (s, 1H), 4.36-4.33 (m, 1H), 3.53 (d, 1H), 3.40-3.31 (m, 1H), 3.23 (d, 1H), 2.52 (t, 1H), 2.38 (t, 1H), 1.73-1.70 (m, 1H), 1.46 (s, 9H), 1.40-1.30 (m, 2H), 1.07 (d, 3H)
- [927] Preparation B1-4: tert-butyl ((3S,5S)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-5-methylpiperidin-3-yl)carbamate
- [928] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3S,5S)-5-methyl-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 8.06 (s, 1H), 7.91 (s, 1H), 7.28 (t, 1H), 6.91 (s, 1H), 7.44 (brs, 1H), 3.97-3.89 (m, 1H), 3.19-3.09 (m, 2H), 2.97-2.93 (m, 1H), 2.27-2.22 (m, 1H), 1.86-1.83 (m, 2H), 1.46 (s, 9H), 1.35-1.27 (m, 1H), 0.82 (d, 3H)
- [929] Preparation B1-5: tert-butyl (S)-(1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-3-methylpiperidin-3-yl)carbamate
- [930] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3S)-3-methyl-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.19 (s, 1H), 8.16 (s, 1H), 7.94 (s, 1H), 7.27 (t, 1H), 6.90 (s, 1H), 4.59 (brs, 1H), 3.50 (d, 1H), 3.11 (d, 1H), 2.55-2.49 (m, 1H), 2.17-2.14 (m, 1H), 1.69-1.60 (m, 1H), 1.50-1.39 (m, 13H), 1.35-1.31 (m, 2H)
- [931] Preparation B1-6: tert-butyl ((3R,4S)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-fluoropiperidin-3-yl)carbamate
- [932] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3R,4S)-4-fluoro-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.17 (s, 1H), 8.13 (s, 1H), 7.95

- (s, 1H), 7.27 (t, 1H), 6.95 (s, 1H), 4.95 (brs, 1H), 4.89 (d, 1H), 3.94-3.87 (m, 1H), 3.34-3.30 (m, 1H), 3.10-3.05 (m, 1H), 2.85-2.80 (m, 2H), 2.07-2.01 (m, 1H), 1.90-1.73 (m, 1H), 1.47 (s, 9H)
- [933] Preparation B1-7: tert-butyl ((3R,4R)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-fluoropiperidin-3-yl)carbamate
- [934] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3R,4R)-4-fluoro-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.18 (s, 1H), 8.11 (s, 1H), 7.95 (s, 1H), 7.28 (t, 1H), 6.95 (s, 1H), 4.70 (brs, 1H), 4.63-4.47 (m, 1H), 3.90-3.82 (m, 1H), 3.57-3.54 (m, 1H), 3.14-3.07 (m, 1H), 2.80-2.77 (m, 2H), 2.09-1.99 (m, 1H), 1.88-1.83 (m, 1H), 1.47 (s, 9H)
- [935] Preparation B1-8: tert-butyl ((3R,4R)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-hydroxypiperidin-3-yl)carbamate
- [936] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3R,4R)-4-hydroxy-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.17 (s, 1H), 8.14 (s, 1H), 7.96 (s, 1H), 7.27 (t, 1H), 6.93 (s, 1H), 4.68-4.67 (m, 1H), 3.61-3.54 (m, 3H), 3.25 (d, 1H), 2.73-2.64 (m, 2H), 2.56 (t, 1H), 2.03-1.99 (m, 1H), 1.47 (s, 9H)
- [937] Preparation B1-9: tert-butyl N-[(3R,4R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-hydroxy-4-piperidyl]carbamate
- [938] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3R,4R)-3-hydroxy-4-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.17 (s, 1H), 8.11 (s, 1H), 7.96 (s, 1H), 7.45-7.10 (m, 1H), 6.95 (s, 1H), 4.75-4.60 (m, 1H), 4.05-3.95 (m, 1H), 3.60-3.40 (m, 3H), 3.30-3.20 (m, 1H), 2.67 (t, 1H), 2.57 (t, 1H), 2.00-1.90 (m, 1H), 1.49 (s, 9H)
- [939] Preparation B1-10: tert-butyl N-[(3R,4S)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-methyl-4-piperidyl]carbamate
- [940] The titled compound was prepared in accordance with the same procedures as in Preparation B1-1, changing the amine reagent to tert-butyl N-[(3R,4S)-3-methyl-4-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 8.12 (s, 1H), 7.95 (s, 1H), 7.45-7.10 (m, 1H), 6.92 (s, 1H), 4.65-4.55 (m, 1H), 3.90-3.80 (m, 1H), 3.05-2.90 (m, 2H), 2.90-2.75 (m, 2H), 2.25-2.15 (m, 1H), 1.75-1.65 (m, 1H), 1.46 (s, 9H), 0.94 (d, 3H)
- [941] Preparation B2-1: 1-(2-chloro-5-iodopyridin-4-yl)-N,N-dimethylpyrrolidin-3-amine
- [942] 2-chloro-4-fluoro-5-iodopyridine (200 mg, 0.78 mmol) was dissolved in anhydrous dimethylformamide (5.0 mL) and then 3-(dimethylamino)pyrrolidine (88.7 mg, 0.77 mmol) and diisopropylethylamine (0.32 mL, 2.33 mmol) were added dropwise thereto.

The reaction mixture was stirred at 50°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (800 mg). (Yield: 60.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.42 (s, 1H), 6.44 (s, 1H), 3.80-3.70 (m, 1H), 3.70-3.65 (m, 2H), 3.60 (t, 1H), 2.76-2.68 (m, 1H), 2.32 (s, 6H), 2.24-2.18 (m, 1H), 1.90-1.79 (m, 1H)

[943] Preparation B2-2: (1-(2-chloro-5-iodopyridin-4-yl)-3-methylpyrrolidin-3-yl)methanol

[944] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (3-methylpyrrolidin-3-yl)methanol. ¹H NMR (CDCl₃, 400MHz) δ 8.42 (s, 1H), 6.45 (s, 1H), 3.79-3.69 (m, 2H), 3.63 (d, 1H), 3.57 (d, 2H), 3.30 (d, 1H), 2.02-1.95 (m, 1H), 1.75-1.68 (m, 1H), 1.18 (s, 3H)

[945] Preparation B2-3: 1-(1-(2-chloro-5-iodopyridin-4-yl)-4-fluoropiperidin-4-yl)-N,N-dimethylmethanamine

[946] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 1-(4-fluoro-4-piperidyl)-N,N-dimethyl-methanamine. ¹H NMR (CDCl₃, 400MHz) δ 8.56 (s, 1H), 6.88 (s, 1H), 3.37 (d, 2H), 3.07 (t, 2H), 2.55 (s, 1H), 2.49 (s, 1H), 2.35 (s, 6H), 2.10 (t, 2H), 1.95-1.75 (m, 2H)

[947] Preparation B2-4: (1-(2-chloro-5-iodopyridin-4-yl)-4-(2,2-difluoroethyl)piperidin-4-yl)methanol

[948] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to [4-(2,2-difluoroethyl)-4-piperidyl]methanol. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.86 (s, 1H), 6.29-5.98 (m, 1H), 3.69 (d, 2H), 3.21-3.09 (m, 4H), 2.12-2.01 (m, 2H), 1.83-1.74 (m, 4H), 1.60 (t, 1H)

[949] Preparation B2-5: (S)-1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-carboxamide

[950] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (3S)-piperidin-3-carboxamide. ¹H NMR (CDCl₃, 400MHz) δ 8.57 (s, 1H), 6.90 (s, 1H), 5.99 (s, 1H), 5.49 (s, 1H), 3.60-3.50 (m, 1H), 3.30-3.20 (m, 1H), 3.05-2.85 (m, 2H), 2.80-2.65 (m, 1H), 2.10-1.90 (m, 2H), 1.90-1.75 (m, 2H)

[951] Preparation B2-6: (R)-1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-carboxamide

[952] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (3R)-piperidin-3-carboxamide. ¹H NMR (CDCl₃, 400MHz) δ 8.58 (s, 1H), 6.90 (s, 1H), 5.98 (s, 1H), 5.43 (s, 1H),

- 3.60-3.50 (m, 1H), 3.30-3.20 (m, 1H), 3.05-2.85 (m, 2H), 2.75-2.65 (m, 1H), 2.10-1.90 (m, 2H), 1.90-1.75 (m, 2H)
- [953] Preparation B2-7: tert-butyl (R)-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-yl) carbamate
- [954] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (R)-3-(tert-butoxycarbonylamino)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.56 (s, 1H), 6.84 (s, 1H), 4.92 (s, 1H), 3.93 (s, 1H), 3.40-3.25 (m, 1H), 3.15-2.95 (m, 2H), 2.95-2.80 (m, 1H), 2.00-1.70 (m, 3H), 1.65-1.50 (m, 1H), 1.46 (s, 9H)
- [955] Preparation B2-8: 2-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-4-yl)-N,N-dimethylethan-1-amine
- [956] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to dimethyl[2-(piperidin-4-yl)ethyl]amine. ¹H NMR (CDCl₃, 400MHz) δ 8.53 (s, 1H), 6.81 (s, 1H), 3.53 (d, 2H), 2.71 (t, 2H), 2.33 (t, 2H), 2.24 (s, 6H), 1.84 (d, 2H), 1.51-1.43 (m, 5H)
- [957] Preparation B2-9: 1-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-4-yl)cyclopropan-1-ol
- [958] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 1-(piperidin-4-yl)cyclopropan-1-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.83 (s, 1H), 3.64 (d, 2H), 2.69 (t, 2H), 1.90-1.70 (m, 5H), 1.25-1.15 (m, 1H), 0.80 (t, 2H), 0.55 (t, 2H)
- [959] Preparation B2-10: 1-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-4-yl)ethan-1-ol
- [960] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 1-(piperidin-4-yl)ethan-1-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.54 (s, 1H), 6.83 (s, 1H), 3.71 (s, 1H), 3.70-3.64 (m, 1H), 3.61 (d, 2H), 2.69 (t, 2H), 2.02 (d, 1H), 1.78 (d, 1H), 1.65-1.40 (m, 2H), 1.39 (d, 1H), 1.26 (d, 3H)
- [961] Preparation B2-11: 2-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-4-yl)-2-methylpropan-1-ol
- [962] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 2-methyl-2-(piperidin-4-yl)propan-1-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.53 (s, 1H), 6.81 (s, 1H), 3.63 (d, 2H), 3.46 (d, 2H), 2.67 (t, 2H), 1.80 (d, 2H), 1.65-1.45 (m, 2H), 1.33 (t, 1H), 0.92 (s, 6H)
- [963] Preparation B2-12: 1-(2-chloro-5-iodopyridin-4-yl)-4-methylpiperazine
- [964] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 1-methylpiperazine. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.84 (s, 1H), 3.21 (s, 4H), 2.64 (s, 4H), 2.38 (s, 3H)
- [965] Preparation B2-13: 2-chloro-5-iodo-4-(3-(2,2,2-trifluoroethyl)piperidin-1-yl)pyridine

- [966] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 3-(2,2,2-trifluoroethyl)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.56 (s, 1H), 6.83 (s, 1H), 3.56 (d, 1H), 3.34 (d, 1H), 2.80 (t, 1H), 2.50 (t, 1H), 2.30-2.20 (m, 1H), 2.20-2.05 (m, 2H), 1.99 (d, 1H), 1.90-1.70 (m, 2H), 1.40-1.20 (m, 1H)
- [967] Preparation B2-14: 2-chloro-4-(3-(fluoromethyl)piperidin-1-yl)-5-iodopyridine
- [968] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 3-(fluoromethyl)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.56 (s, 1H), 6.85 (s, 1H), 4.55-4.25 (m, 2H), 3.56 (d, 1H), 3.42 (d, 1H), 2.77 (t, 1H), 2.64 (t, 1H), 2.35-2.15 (m, 1H), 1.95-1.75 (m, 3H), 1.40-1.20 (m, 1H)
- [969] Preparation B2-15: N-(1-(2-chloro-5-iodopyridin-4-yl)piperidin-3-yl)acetamide
- [970] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 3-acetamidopiperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.59 (s, 1H), 6.87 (s, 1H), 6.04 (s, 1H), 4.35-4.25 (m, 1H), 3.25 (d, 1H), 3.20-3.10 (m, 1H), 3.05-2.95 (m, 2H), 2.03 (s, 3H), 2.00-1.85 (m, 1H), 1.85-1.65 (m, 3H)
- [971] Preparation B2-16: 2-chloro-5-iodo-4-(4-(trifluoromethyl)piperidin-1-yl)pyridine
- [972] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 4-(trifluoromethyl)piperidine. ¹H NMR (CDCl₃, 400MHz) δ 8.58 (s, 1H), 6.85 (s, 1H), 3.63 (d, 2H), 2.73 (t, 2H), 2.35-2.20 (m, 1H), 2.10-2.00 (m, 2H), 1.95-1.80 (m, 2H)
- [973] Preparation B2-17: tert-butyl 8-(2-chloro-5-iodopyridin-4-yl)-2,8-diazaspiro[4.5]decan-2-carboxylate
- [974] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl 2,8-diazaspiro[4.5]decan-2-carboxylate. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.85 (d, 1H), 3.50-3.40 (m, 2H), 3.40-3.10 (m, 4H), 3.10-2.95 (m, 2H), 1.90-1.70 (m, 6H), 1.48 (s, 9H)
- [975] Preparation B2-18: tert-butyl 2-(2-chloro-5-iodopyridin-4-yl)-2,8-diazaspiro[4.5]decan-8-carboxylate
- [976] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl 2,8-diazaspiro[4.5]decan-8-carboxylate. ¹H NMR (CDCl₃, 400MHz) δ 8.42 (s, 1H), 6.44 (s, 1H), 3.72 (t, 2H), 3.55-3.45 (m, 4H), 3.45-3.35 (m, 2H), 1.87 (t, 2H), 1.65-1.50 (m, 4H), 1.48 (s, 9H)
- [977] Preparation B2-19: (3R,4R)-1-(2-chloro-5-iodopyridin-4-yl)-4-fluoropiperidin-3-ol
- [978] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl (3R,4R)-4-fluoropiperid

- in-3-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.60 (s, 1H), 6.92 (s, 1H), 4.70-4.50 (m, 1H), 4.10-4.00 (m, 1H), 3.51 (d, 1H), 3.35-3.20 (m, 1H), 3.10-3.00 (m, 2H), 2.60 (d, 1H), 2.40-2.25 (m, 1H), 2.10-2.00 (m, 1H)
- [979] Preparation B2-20: (3R,4R)-1-(2-chloro-5-iodopyridin-4-yl)-4-(hydroxymethyl)piperidin-3-ol
- [980] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to trans-4-(hydroxymethyl)-3-piperidinol hydrochloride. ¹H NMR (CDCl₃, 400MHz) δ 8.56 (s, 1H), 6.86 (s, 1H), 3.95-3.85 (m, 2H), 3.85-3.75 (m, 1H), 3.68 (d, 1H), 3.51 (d, 1H), 3.32 (s, 1H), 2.74 (t, 1H), 2.59 (t, 1H), 2.24 (t, 1H), 1.85-1.70 (m, 2H), 1.55-1.40 (m, 1H)
- [981] Preparation B2-21: tert-butyl (R)-(1-(2-chloro-5-iodopyridin-4-yl)pyrrolidin-3-yl)carbamate
- [982] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (R)-3-(tert-butoxycarbonylamino)pyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.43 (s, 1H), 6.46 (s, 1H), 4.70 (s, 1H), 4.32 (s, 1H), 3.90-3.80 (m, 1H), 3.80 (q, 1H), 3.62 (q, 1H), 3.55-3.50 (m, 1H), 2.28-2.19 (m, 1H), 2.00-1.90 (m, 1H), 1.47 (s, 9H)
- [983] Preparation B2-22: tert-butyl (S)-(1-(2-chloro-5-iodopyridin-4-yl)pyrrolidin-3-yl)carbamate
- [984] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (S)-3-(tert-butoxycarbonylamino)pyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.43 (s, 1H), 6.46 (s, 1H), 4.71 (s, 1H), 4.32 (s, 1H), 3.90-3.85 (m, 1H), 3.78 (q, 1H), 3.62 (q, 1H), 3.55-3.50 (m, 1H), 2.28-2.19 (m, 1H), 2.00-1.90 (m, 1H), 1.47 (s, 9H)
- [985] Preparation B2-23: 8-(2-chloro-5-iodopyridin-4-yl)-2-methyl-2,8-diazaspiro[4.5]decane
- [986] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to 2-methyl-2,8-diazaspiro[4.5]decane. ¹H NMR (CD₃OD, 400MHz) δ 8.50 (s, 1H), 7.02 (d, 1H), 3.20-3.10 (m, 4H), 2.68 (t, 2H), 2.55 (s, 2H), 2.39 (s, 3H), 1.90-1.75 (m, 6H)
- [987] Preparation B2-24: (3S)-1-(2-chloro-5-iodo-4-pyridyl)-N-methyl-pyrrolidin-3-amine
- [988] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (S)-3-(methylamino)pyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.42 (s, 1H), 6.45 (s, 1H), 3.86-3.81 (m, 1H), 3.73 (q, 1H), 3.62 (q, 1H), 3.51-3.47 (m, 1H), 3.40-3.30 (m, 1H), 2.48 (s, 3H), 2.19-2.11 (m, 1H), 1.90-1.82 (m, 1H)
- [989] Preparation B2-25: (3S)-1-(2-chloro-5-iodo-4-pyridyl)-N-ethyl-pyrrolidin-3-amine

- [990] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (S)-3-(ethylamino)pyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.41 (s, 1H), 6.44 (s, 1H), 3.86-3.81 (m, 1H), 3.73-3.50 (m, 2H), 3.50-3.40 (m, 2H), 2.80-2.65 (m, 2H), 2.22-2.14 (m, 1H), 1.87-1.79 (m, 1H), 1.27 (t, 3H)
- [991] Preparation B2-26: (R)-N-(1-(2-chloro-5-iodopyridin-4-yl)pyrrolidin-3-yl)acetamide
- [992] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (R)-3-acetamidopyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.41 (s, 1H), 6.45 (s, 1H), 6.05-5.95 (m, 1H), 4.65-4.55 (m, 1H), 3.96-3.91 (m, 1H), 3.78 (q, 1H), 3.59-3.53 (m, 2H), 2.30-2.20 (m, 1H), 2.10-2.00 (m, 1H), 2.03 (s, 3H)
- [993] Preparation B2-27: (S)-N-(1-(2-chloro-5-iodopyridin-4-yl)pyrrolidin-3-yl)acetamide
- [994] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (S)-3-acetamidopyrrolidine. ¹H NMR (CDCl₃, 400MHz) δ 8.41 (s, 1H), 6.45 (s, 1H), 6.00-5.90 (m, 1H), 4.65-4.55 (m, 1H), 4.14-3.91 (m, 1H), 3.78 (q, 1H), 3.58-3.53 (m, 2H), 2.30-2.20 (m, 1H), 2.10-1.98 (m, 4H)
- [995] Preparation B2-28: 1-(2-chloro-5-iodo-4-pyridyl)piperidin-3-carboxamide
- [996] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to piperidin-3-carboxamide. ¹H NMR (CDCl₃, 400MHz) δ 8.58 (s, 1H), 6.90 (s, 1H), 5.98 (s, 1H), 5.41 (s, 1H), 3.56 (d, 1H), 3.30-3.20 (m, 1H), 3.10-2.90 (m, 2H), 2.75-2.65 (m, 1H), 2.10-1.90 (m, 2H), 1.90-1.75 (m, 2H)
- [997] Preparation B2-29: (1S,4S)-4-((2-chloro-5-iodopyridin-4-yl)(methyl)amino)cyclohexan-1-ol
- [998] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to cis-4-(methylamino)cyclohexanol. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.82 (s, 1H), 4.08 (brs, 1H), 3.59-3.53 (m, 1H), 2.80 (s, 3H), 2.05-2.00 (m, 2H), 1.92-1.88 (m, 2H), 1.65-1.57 (m, 4H), 1.27-1.27 (m, 1H)
- [999] Preparation B2-30: tert-butyl N-[(3S,6R)-1-(2-chloro-5-iodo-4-pyridyl)-6-methyl-3-piperidyl]carbamate
- [1000] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,6R)-6-methyl-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.71 (s, 1H), 7.00 (s, 1H), 5.20 (s, 1H), 3.94 (s, 1H), 3.73 (s, 1H), 3.11-2.89 (m, 2H), 2.04-1.87 (m, 1H), 1.87-1.63 (m, 3H), 1.54 (s, 9H), 1.08 (d, 3H)

- [1001] Preparation B2-31: tert-butyl N-[(3R,4S)-1-(2-chloro-5-iodo-4-pyridyl)-4-methoxy-3-piperidyl]carbamate
- [1002] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3R,4S)-4-methoxy-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.62 (s, 1H), 6.92 (s, 1H), 5.27 (d, 1H), 4.11-3.98 (m, 1H), 3.64-3.52 (m, 1H), 3.48 (s, 3H), 3.34-3.25 (m, 1H), 3.23-3.12 (m, 1H), 3.07-2.93 (m, 2H), 2.19-2.08 (m, 1H), 1.97-1.81 (m, 1H), 1.56 (s, 9H)
- [1003] Preparation B2-32: tert-butyl N-[(3R,4R)-1-(2-chloro-5-iodo-4-pyridyl)-4-methoxy-3-piperidyl]carbamate
- [1004] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3R,4R)-4-methoxypiperidin-3-yl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.66 (s, 1H), 6.96 (s, 1H), 5.38 (s, 1H), 4.05 (s, 1H), 3.50 (s, 3H), 3.45-3.38 (m, 2H), 3.16-3.02 (m, 3H), 2.25-2.08 (m, 1H), 1.95-1.83 (m, 1H), 1.55 (s, 9H)
- [1005] Preparation B2-33: tert-butyl N-methyl-N-[(3R)-1-(2-chloro-5-iodo-4-pyridyl)-3-piperidyl]methyl]carbamate
- [1006] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-methyl-N-[(3R)-piperidin-3-yl]methyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.82 (s, 1H), 3.55-3.45 (m, 1H), 3.45-3.35 (m, 1H), 3.35-3.15 (m, 1H), 3.15-3.05 (m, 1H), 2.91 (s, 3H), 2.80-2.65 (m, 1H), 2.55-2.40 (m, 1H), 2.25-2.10 (m, 1H), 1.95-1.70 (m, 3H), 1.48 (s, 9H), 1.25-1.10 (m, 1H)
- [1007] Preparation B2-34: tert-butyl N-methyl-N-[(3S)-1-(2-chloro-5-iodo-4-pyridyl)-3-piperidyl]methyl]carbamate
- [1008] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-methyl-N-[(3S)-piperidin-3-yl]methyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.54 (s, 1H), 6.82 (s, 1H), 3.55-3.45 (m, 1H), 3.45-3.35 (m, 1H), 3.35-3.20 (m, 1H), 3.20-3.05 (m, 1H), 2.90 (s, 3H), 2.85-2.65 (m, 1H), 2.50-2.40 (m, 1H), 2.25-2.10 (m, 1H), 1.95-1.70 (m, 3H), 1.48 (s, 9H), 1.25-1.10 (m, 1H)
- [1009] Preparation B2-35: tert-butyl N-[(3R,4R)-1-(2-chloro-5-iodo-4-pyridyl)-3-methyl-4-piperidyl]carbamate
- [1010] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3R,4R)-3-methyl-4-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.55 (s, 1H), 6.84 (s, 1H), 4.50-4.40 (m, 1H), 3.60-3.50 (m, 2H), 2.85-2.75 (m, 1H), 2.55-2.45 (m, 1H), 2.20-2.10 (m, 1H), 1.85-1.70 (m, 1H), 1.49 (s, 9H), 1.04 (d, 3H)

- [1011] Preparation B2-36: 2-chloro-5-iodo-4-[(3S)-3-methyl-1-piperidyl]pyridine
- [1012] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (3S)-3-methylpiperidine. ¹H NMR (CDCl₃, 400MHz) δ 12.40 (s, 1H), 10.90 (s, 1H), 7.50-7.40 (m, 2H), 6.69 (t, 1H), 6.33 (t, 1H), 5.90-5.70 (m, 4H), 5.20-5.10 (m, 1H), 4.92 (d, 3H)
- [1013] Preparation B2-37: 2-chloro-5-iodo-4-[(3S)-3-(fluoromethyl)-1-piperidyl]pyridine
- [1014] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (3S)-3-(fluoromethyl)piperidine hydrochloride. ¹H NMR (CDCl₃, 400MHz) δ 12.50 (s, 1H), 11.00 (s, 1H), 8.45-8.35 (m, 1H), 8.35-8.20 (m, 1H), 7.60-7.50 (m, 1H), 7.45-7.35 (m, 1H), 6.78 (t, 1H), 6.60 (t, 1H), 6.25-6.10 (m, 1H), 5.90-5.70 (m, 3H), 5.35-5.20 (m, 1H)
- [1015] Preparation B2-38: 2-chloro-5-iodo-4-[(3R)-3-(difluoromethyl)-1-piperidyl]pyridine
- [1016] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to (3R)-3-(difluoromethyl)piperidine hydrochloride. ¹H NMR (CDCl₃, 400MHz) δ 12.50 (s, 1H), 11.00 (s, 1H), 10.00-9.60 (m, 1H), 7.65-7.50 (m, 1H), 7.40-7.30 (m, 1H), 6.78 (t, 1H), 6.68 (t, 1H), 6.30-6.15 (m, 1H), 6.00-5.80 (m, 2H), 5.80-5.65 (m, 1H), 5.50-5.35 (m, 1H)
- [1017] Preparation B2-39: tert-butyl N-[(3S,4S)-1-(2-chloro-5-iodo-4-pyridyl)-3-fluoro-4-piperidyl]carbamate
- [1018] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,4S)-3-fluoro-4-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.34 (s, 1H), 6.60 (s, 1H), 4.85-4.70 (m, 1H), 4.50-4.30 (m, 1H), 4.05-3.90 (m, 1H), 3.70-3.60 (m, 1H), 3.20-3.05 (m, 1H), 2.20-2.10 (m, 1H), 1.65-1.55 (m, 1H), 1.51 (s, 9H), 1.30-1.20 (m, 1H)
- [1019] Preparation B2-40: tert-butyl N-[(3R,4S)-1-(2-chloro-5-iodo-4-pyridyl)-3-fluoro-4-piperidyl]carbamate
- [1020] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3R,4S)-3-fluoro-4-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.58 (s, 1H), 6.88 (s, 1H), 5.00-4.90 (m, 1H), 4.90-4.70 (m, 1H), 3.95-3.75 (m, 1H), 3.75-3.65 (m, 1H), 3.20-3.00 (m, 1H), 2.87 (t, 1H), 2.20-2.00 (m, 1H), 1.95-1.85 (m, 1H), 1.49 (s, 9H)
- [1021] Preparation B2-41: tert-butyl N-[(3S,4R)-1-(2-chloro-5-iodo-4-pyridyl)-3-fluoro-4-piperidyl]carbamate
- [1022] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,4R)-3-fluoro-4-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.58 (s, 1H), 6.88 (s, 1H), 5.00-4.90

- (m, 1H), 4.90-4.75 (m, 1H), 3.95-3.75 (m, 1H), 3.75-3.60 (m, 1H), 3.20-3.00 (m, 1H), 2.87 (t, 1H), 2.20-2.00 (m, 1H), 1.95-1.85 (m, 1H), 1.49 (s, 9H)
- [1023] Preparation B2-42: tert-butyl N-[(3S,5R)-1-(2-chloro-5-iodo-4-pyridyl)-5-fluoro-3-piperidyl]carbamate
- [1024] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,5R)-5-fluoro-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.68 (s, 1H), 6.98 (s, 1H), 5.28-5.08 (m, 1H), 5.07-4.84 (m, 1H), 4.16-3.98 (m, 1H), 3.45-3.28 (m, 2H), 3.28-3.11 (m, 2H), 2.32-2.13 (m, 1H), 2.07-1.87 (m, 1H), 1.64-1.54 (m, 1H), 1.54 (s, 9H)
- [1025] Preparation B2-43: tert-butyl N-[(3S,5S)-1-(2-chloro-5-iodo-4-pyridyl)-5-fluoro-3-piperidyl]carbamate
- [1026] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,5S)-5-fluoro-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.65 (s, 1H), 6.98 (s, 1H), 5.10-5.00 (m, 1H), 4.98-4.90 (m, 1H), 4.90-4.80 (m, 1H), 4.31-4.18 (m, 1H), 3.49-3.35 (m, 2H), 3.30-3.15 (m, 1H), 3.05-2.92 (m, 1H), 2.15-2.01 (m, 2H), 1.54 (s, 9H)
- [1027] Preparation B2-44: tert-butyl N-[(3S,5R)-1-(2-chloro-5-iodo-4-pyridyl)-5-(trifluoromethyl)-3-piperidyl]carbamate
- [1028] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,5R)-5-(trifluoromethyl)-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.66 (s, 1H), 6.93 (s, 1H), 4.59-4.39 (m, 1H), 4.04-3.85 (m, 1H), 3.81-3.65 (m, 2H), 2.86-2.69 (m, 1H), 2.69-2.56 (m, 1H), 2.52-2.33 (m, 2H), 1.54 (s, 9H)
- [1029] Preparation B2-45: tert-butyl N-[(3S,5S)-1-(2-chloro-5-iodo-4-pyridyl)-5-hydroxy-3-piperidyl]carbamate
- [1030] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3S,5S)-5-hydroxy-3-piperidyl]carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.65 (s, 1H), 6.96 (s, 1H), 5.33-5.13 (m, 1H), 4.22-4.07 (m, 1H), 4.05-3.89 (m, 1H), 3.43-3.27 (m, 2H), 3.07-2.95 (m, 2H), 2.24-2.14 (m, 1H), 2.14-2.06 (m, 1H), 1.70-1.61 (m, 1H), 1.53 (s, 9H)
- [1031] Preparation B2-46: tert-butyl N-[(3R,4R)-1-(2-chloro-5-iodo-4-pyridyl)-3-hydroxy-4-piperidyl]carbamate
- [1032] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl ((3R,4R)-3-hydroxypiperidin-4-yl)carbamate. ¹H NMR (CDCl₃, 400MHz) δ 8.58 (s, 1H), 6.89 (s, 1H), 4.80-4.65 (m, 1H), 4.10-3.95 (m, 1H), 3.80-3.65 (m, 2H), 3.60-3.45 (m, 2H), 2.82 (t, 1H), 2.66 (t, 1H), 2.20-2.05 (m, 1H), 1.80-1.65 (m, 1H), 1.50 (s, 9H)

- [1033] Preparation B2-47: tert-butyl ((3R,4R)-1-(2-chloro-5-iodopyridin-4-yl)-4-fluoropiperidin-3-yl)carbamate
- [1034] The titled compound was prepared in accordance with the same procedures as in Preparation B2-1, changing the amine reagent to tert-butyl N-[(3R,4R)-4-fluoropiperidin-3-yl]carbamate. ¹H NMR (CDCl₃, 400MHz) 8.68 (s, 1H), 7.00 (s, 1H), 5.31-5.03 (m, 1H), 4.86-4.72 (m, 0.5H), 4.74-4.59 (m, 0.5H), 4.20-3.87 (m, 1H), 3.52-3.32 (m, 1H), 3.25-3.02 (m, 3H), 2.41-2.16 (m, 1H), 2.16-1.96 (m, 1H), 1.48 (s, 9H)
- [1035] Preparation B3-1: 1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-N,N-dimethylpyrrolidin-3-amine
- [1036] 1-(2-chloro-5-iodopyridin-4-yl)-N,N-dimethylpyrrolidin-3-amine (the B2-1 intermediate, 44.2 mg, 0.13 mmol) was dissolved in anhydrous 1,4-dioxane (1.5 mL) and then 1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-boronic acid pinacol ester (35.0 mg, 0.13 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)-dichloromethane complex (5.1 mg, 0.006 mmol), and 2.0M sodium carbonate solution (0.3 mL, 0.6 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (24.4 mg). (Yield: 51.6%) ¹H NMR (CDCl₃, 400MHz) δ 7.87 (s, 1H), 7.52 (s, 1H), 7.43 (s, 1H), 6.53 (s, 1H), 4.42-4.33 (m, 1H), 4.13 (d, 2H), 3.57 (t, 2H), 3.26-3.14 (m, 3H), 2.95 (t, 1H), 2.64-3.32 (m, 1H), 2.19 (s, 6H), 2.15-2.00 (m, 5H), 1.80-1.65 (m, 1H)
- [1037] Preparation B3-2: (1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-3-methylpyrrolidin-3-yl)methanol
- [1038] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-2 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.87 (s, 1H), 7.51 (s, 1H), 7.44 (s, 1H), 6.55 (s, 1H), 4.43-4.35 (m, 1H), 4.14 (d, 2H), 3.58 (t, 2H), 3.46 (d, 2H), 3.15 (t, 2H), 3.11 (d, 1H), 2.79 (d, 1H), 2.20-2.00 (m, 4H), 1.88-1.80 (m, 1H), 1.62-1.55 (m, 2H), 1.55-1.50 (m, 1H), 1.08 (s, 3H)
- [1039] Preparation B3-3: 1-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-fluoropiperidin-4-yl)-N,N-dimethylmethanamine
- [1040] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-3 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.85 (s, 1H), 7.74 (s, 1H), 6.90 (s, 1H), 4.44-4.38 (m, 1H), 4.15 (d, 2H), 3.56 (t, 2H), 3.15 (d, 2H), 2.95 (t, 2H), 2.50 (s, 1H), 2.44 (s, 1H), 2.32 (s, 6H), 2.30-2.24 (m, 1H), 2.20-2.10 (m, 4H), 2.00-1.90 (m, 2H), 1.70-1.60 (m, 1H)

- [1041] Preparation B3-4: (1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-(2,2-difluoroethyl)piperidin-4-yl)methanol
- [1042] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-4 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.84 (s, 1H), 7.76 (s, 1H), 6.88 (s, 1H), 6.24-5.93 (m, 1H), 4.44-4.37 (m, 1H), 4.15 (d, 2H), 3.64 (d, 2H), 3.58 (t, 2H), 3.05-2.90 (m, 4H), 2.20-1.95 (m, 7H), 1.65-1.55 (m, 4H), 1.27 (t, 1H)
- [1043] Preparation B3-5: (S)-1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide
- [1044] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-5 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.83 (s, 1H), 7.75 (s, 1H), 6.88 (s, 1H), 5.45-5.40 (m, 1H), 5.25-5.15 (m, 1H), 4.45-4.40 (m, 1H), 4.15 (d, 2H), 3.58 (t, 2H), 3.43 (d, 1H), 3.21 (d, 1H), 2.79 (t, 1H), 2.65 (t, 1H), 2.55-2.40 (m, 1H), 2.37 (t, 1H), 2.20-2.05 (m, 4H), 2.05-1.90 (m, 3H)
- [1045] Preparation B3-6: (R)-1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide
- [1046] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-6 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.83 (s, 1H), 7.75 (s, 1H), 6.89 (s, 1H), 5.45-5.35 (m, 1H), 5.25-5.15 (m, 1H), 4.50-4.30 (m, 1H), 4.15 (d, 2H), 3.58 (t, 2H), 3.43 (d, 1H), 3.22 (d, 1H), 2.79 (t, 1H), 2.66 (t, 1H), 2.50-2.40 (m, 1H), 2.20-2.05 (m, 4H), 2.05-1.90 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.60 (m, 1H)
- [1047] Preparation B3-7: tert-butyl(R)-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [1048] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-7 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.81 (s, 1H), 7.77 (s, 1H), 6.86 (s, 1H), 4.55-4.45 (m, 1H), 4.45-4.35 (m, 1H), 4.15 (d, 2H), 3.80-3.70 (m, 1H), 3.58 (t, 2H), 3.43 (d, 1H), 3.07 (d, 1H), 2.65-2.55 (m, 1H), 2.55-2.45 (m, 1H), 2.25-2.05 (m, 4H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.45 (s, 9H), 1.40-1.30 (m, 1H)
- [1049] Preparation B3-8: 2-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-N,N-dimethylethan-1-amine
- [1050] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-8 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.11 (s, 1H), 7.84 (s, 1H), 7.78 (s, 1H), 6.84 (s, 1H), 4.44-4.38 (m, 1H), 4.15 (d, 2H), 3.59 (t, 2H), 3.32 (d, 2H), 2.57 (t, 2H), 2.40-2.30 (m, 2H), 2.27 (s, 6H), 2.20-2.00 (m, 4H), 1.73 (d, 2H), 1.50-1.40 (m, 4H), 1.30-1.20 (m, 1H)

- [1051] Preparation B3-9: 1-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)cyclopropan-1-ol
- [1052] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-9 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (s, 1H), 7.85 (s, 1H), 7.82 (s, 1H), 6.89 (s, 1H), 4.50-4.35 (m, 1H), 4.13 (d, 2H), 3.58 (t, 2H), 3.42 (d, 2H), 2.55 (t, 2H), 2.20-2.05 (m, 4H), 1.90-1.70 (m, 5H), 1.20-1.05 (m, 1H), 0.79 (t, 2H), 0.50 (t, 2H)
- [1053] Preparation B3-10: 1-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)ethan-1-ol
- [1054] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-10 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.84 (s, 1H), 7.79 (s, 1H), 6.86 (s, 1H), 4.44-4.35 (m, 1H), 4.14 (d, 2H), 3.65-3.50 (m, 4H), 3.45-3.35 (m, 2H), 2.56 (t, 2H), 2.20-2.05 (m, 4H), 1.90 (d, 1H), 1.65 (d, 1H), 1.45-1.35 (m, 2H), 1.35-1.25 (m, 1H), 1.21 (d, 3H)
- [1055] Preparation B3-11: 2-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-2-methylpropan-1-ol
- [1056] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-11 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.83 (s, 1H), 7.81 (s, 1H), 6.84 (s, 1H), 4.50-4.35 (m, 1H), 4.14 (d, 2H), 3.58 (t, 2H), 3.45-3.35 (m, 4H), 2.54 (t, 2H), 2.20-2.15 (m, 2H), 2.15-2.05 (m, 2H), 1.68 (d, 2H), 1.50-1.30 (m, 2H), 1.30-1.20 (m, 2H), 0.86 (s, 6H)
- [1057] Preparation B3-12: 1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-methylpiperazine
- [1058] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-12 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (s, 1H), 7.84 (s, 1H), 7.78 (s, 1H), 6.86 (s, 1H), 4.45-4.35 (m, 1H), 4.16 (d, 2H), 3.59 (t, 2H), 3.01 (s, 4H), 2.47 (s, 4H), 2.33 (s, 3H), 2.20-2.05 (m, 4H)
- [1059] Preparation B3-13: 2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(3-(2,2,2-trifluoroethyl)piperidin-1-yl)pyridine
- [1060] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-13 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.80 (s, 1H), 7.75 (s, 1H), 6.85 (s, 1H), 4.44-4.35 (m, 1H), 4.15 (d, 2H), 3.58 (t, 2H), 3.41 (d, 1H), 3.26 (d, 1H), 2.60 (t, 1H), 2.25 (t, 1H), 2.20-2.05 (m, 4H), 2.05-1.80 (m, 4H), 1.80-1.70 (m, 1H), 1.70-1.65 (m, 1H), 1.20-1.05 (m, 1H)
- [1061] Preparation B3-14: 2-chloro-4-(3-(fluoromethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridine

- [1062] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-14 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (s, 1H), 7.80 (s, 1H), 7.76 (s, 1H), 6.87 (s, 1H), 4.45-4.35 (m, 2H), 4.28-4.23 (m, 1H), 4.20-4.10 (m, 3H), 3.58 (t, 2H), 3.42 (d, 1H), 3.27 (d, 1H), 2.56 (t, 1H), 2.43 (t, 1H), 2.20-2.00 (m, 4H), 1.78 (t, 2H), 1.75-1.60 (m, 1H), 1.25-1.10 (m, 1H)
- [1063] Preparation B3-15: N-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)acetamide
- [1064] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-15 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.14 (s, 1H), 7.82-7.75 (m, 2H), 6.88 (s, 1H), 5.45-5.35 (m, 1H), 4.50-4.35 (m, 1H), 4.15 (d, 2H), 4.10-4.00 (m, 1H), 3.59 (t, 2H), 3.34 (d, 1H), 3.08 (d, 1H), 2.65 (t, 1H), 2.58 (t, 1H), 2.25-2.10 (m, 5H), 2.10-2.05 (m, 1H), 1.99 (s, 3H), 1.95-1.85 (m, 1H), 1.75-1.65 (m, 1H), 1.45-1.35 (m, 1H)
- [1065] Preparation B3-16: 2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(4-(trifluoromethyl)piperidin-1-yl)pyridine
- [1066] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-16 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.83 (s, 1H), 7.78 (s, 1H), 6.87 (s, 1H), 4.50-4.35 (m, 1H), 4.15 (d, 2H), 3.59 (t, 2H), 3.43 (d, 2H), 2.67 (t, 2H), 2.20-2.05 (m, 5H), 1.91 (d, 2H), 1.70-1.55 (m, 2H)
- [1067] Preparation B3-17: tert-butyl 8-[2-chloro-5-(1-tetrahydropyran-4-ylpyrazol-4-yl)-4-pyridyl]-2,8-diazaspiro[4.5]decan-2-carboxylate
- [1068] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-17 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.86 (d, 1H), 7.76 (s, 1H), 6.87 (d, 1H), 4.45-4.35 (m, 1H), 4.15 (d, 2H), 3.59 (t, 2H), 3.45-3.30 (m, 2H), 3.25 (s, 1H), 3.17 (s, 1H), 3.05-2.95 (m, 2H), 2.95-2.80 (m, 2H), 2.16-2.05 (m, 4H), 1.80-1.70 (m, 2H), 1.65-1.50 (m, 4H), 1.47 (s, 9H)
- [1069] Preparation B3-18: tert-butyl 2-[2-chloro-5-(1-tetrahydropyran-4-ylpyrazol-4-yl)-4-pyridyl]-2,8-diazaspiro[4.5]decan-8-carboxylate
- [1070] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-18 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.87 (s, 1H), 7.50 (s, 1H), 7.44 (s, 1H), 6.54 (s, 1H), 4.45-4.35 (m, 1H), 4.14 (d, 2H), 3.58 (t, 2H), 3.45-3.39 (m, 2H), 3.31-3.24 (m, 2H), 3.15 (t, 2H), 2.95 (s, 2H), 2.20-2.00 (m, 4H), 1.73 (t, 2H), 1.46 (s, 9H)
- [1071] Preparation B3-19: (3R,4R)-1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-fluoropiperidin-3-ol
- [1072] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-19 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.15

- (s, 1H), 7.79 (s, 1H), 7.76 (s, 1H), 6.90 (s, 1H), 4.60-4.35 (m, 2H), 4.15 (d, 2H), 3.95-3.80 (m, 1H), 3.58 (t, 2H), 3.45-3.35 (m, 1H), 3.25-3.15 (m, 1H), 2.81-2.70 (m, 2H), 2.25-2.00 (m, 6H), 1.85-1.70 (m, 1H)
- [1073] Preparation B3-20: (3R,4R)-1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-(hydroxymethyl)piperidin-3-ol
- [1074] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-20 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.13 (s, 1H), 7.81 (s, 1H), 7.72 (s, 1H), 6.89 (s, 1H), 4.45-4.35 (m, 1H), 4.15 (d, 2H), 3.90-3.80 (m, 1H), 3.80-3.65 (m, 2H), 3.58 (t, 2H), 3.48 (d, 1H), 3.32 (d, 1H), 3.19 (s, 1H), 2.59 (t, 1H), 2.45 (t, 1H), 2.25-2.00 (m, 5H), 1.75-1.60 (m, 2H), 1.35-1.20 (m, 1H)
- [1075] Preparation B3-21: tert-butyl (R)-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)carbamate
- [1076] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-21 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.88 (s, 1H), 7.51 (s, 1H), 7.45 (s, 1H), 6.56 (s, 1H), 4.60-4.45 (m, 1H), 4.45-4.30 (m, 1H), 4.20-4.05 (m, 3H), 3.58 (t, 2H), 3.40-3.30 (m, 1H), 3.30-3.20 (m, 1H), 3.20-3.12 (m, 1H), 2.93-2.88 (m, 1H), 2.20-2.05 (m, 5H), 1.85-1.75 (m, 1H), 1.44 (s, 9H)
- [1077] Preparation B3-22: tert-butyl (S)-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)carbamate
- [1078] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-22 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.88 (s, 1H), 7.51 (s, 1H), 7.45 (s, 1H), 6.56 (s, 1H), 4.60-4.45 (m, 1H), 4.45-4.30 (m, 1H), 4.20-4.05 (m, 3H), 3.58 (t, 2H), 3.40-3.30 (m, 1H), 3.27-3.20 (m, 1H), 3.20-3.12 (m, 1H), 2.93-2.89 (m, 1H), 2.20-2.05 (m, 5H), 1.85-1.75 (m, 1H), 1.44 (s, 9H)
- [1079] Preparation B3-23: 8-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-2-methyl-2,8-diazaspiro[4.5]decane
- [1080] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-23 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 8.11 (s, 1H), 8.08 (s, 1H), 7.89 (s, 1H), 7.02 (s, 1H), 4.55-4.45 (m, 1H), 4.09 (d, 2H), 3.60 (t, 2H), 3.55-3.40 (m, 2H), 3.05-2.95 (m, 2H), 2.70-2.65 (m, 2H), 2.57 (s, 1H), 2.45-2.35 (m, 4H), 2.20-2.00 (m, 4H), 1.85-1.75 (m, 2H), 1.75-1.60 (m, 4H)
- [1081] Preparation B3-24: (3S)-1-[2-chloro-5-(1-tetrahydropyran-4-yl)pyrazol-4-yl]-4-pyridyl]-N-methyl-pyrrolidin-3-amine
- [1082] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-24 intermediate. ¹H NMR (CD₃OD, 400MHz) δ 7.81 (s, 1H), 7.76 (s, 1H), 7.56 (s, 1H), 6.69 (s, 1H), 4.50-4.40 (m, 1H), 4.08 (d, 2H),

- 3.59 (t, 2H), 3.35-3.25 (m, 2H), 3.25-3.10 (m, 2H), 2.99-2.94 (m, 1H), 2.39 (s, 3H), 2.20-2.00 (m, 6H), 1.80-1.70 (m, 1H)
- [1083] Preparation B3-25: (3S)-1-[2-chloro-5-(1-tetrahydropyran-4-yl)pyrazol-4-yl]-4-pyridyl]-N-ethyl-pyrrolidin-3-amine
- [1084] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-25 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.86 (s, 1H), 7.52 (s, 1H), 7.45 (s, 1H), 6.54 (s, 1H), 4.45-4.30 (m, 1H), 4.14 (d, 2H), 3.57 (t, 2H), 3.40-3.30 (m, 1H), 3.30-3.20 (m, 2H), 3.20-3.10 (m, 1H), 2.90-2.80 (m, 1H), 2.70-2.50 (m, 2H), 2.20-2.00 (m, 6H), 1.80-1.65 (m, 1H), 1.10 (t, 3H)
- [1085] Preparation B3-26: (R)-N-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide
- [1086] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-26 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.88 (s, 1H), 7.51 (s, 1H), 7.46 (s, 1H), 6.56 (s, 1H), 5.65-5.55 (m, 1H), 4.50-4.35 (m, 2H), 4.14 (d, 2H), 3.58 (t, 2H), 3.40-3.30 (m, 1H), 3.30-3.15 (m, 2H), 2.95-2.85 (m, 1H), 2.20-2.00 (m, 5H), 1.98 (s, 3H), 1.90-1.80 (m, 1H)
- [1087] Preparation B3-27: (S)-N-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide
- [1088] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-27 intermediate. ¹H NMR (CDCl₃, 400MHz) δ 7.87 (s, 1H), 7.51 (s, 1H), 7.46 (s, 1H), 6.56 (s, 1H), 5.65-5.55 (m, 1H), 4.50-4.30 (m, 2H), 4.15 (d, 2H), 3.58 (t, 2H), 3.40-3.30 (m, 1H), 3.30-3.10 (m, 2H), 2.95-2.85 (m, 1H), 2.20-2.00 (m, 5H), 1.97 (s, 3H), 1.90-1.80 (m, 1H)
- [1089] Preparation B3-28: 8-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-2-methyl-2,8-diazaspiro[4.5]decane
- [1090] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-23 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.17 (s, 1H), 8.15 (s, 1H), 8.03 (s, 1H), 7.45-7.05 (m, 1H), 6.91 (s, 1H), 2.93 (t, 4H), 2.57 (t, 2H), 2.41 (s, 2H), 2.32 (s, 3H), 1.71 (t, 4H), 1.69-1.62 (m, 2H)
- [1091] Preparation B3-29: 8-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-2-methyl-2,8-diazaspiro[4.5]decane
- [1092] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-23 intermediate and changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.93 (s, 1H), 7.87 (s, 1H), 6.89 (s, 1H), 4.78

- (q, 2H), 2.93 (t, 4H), 2.60 (t, 2H), 2.43 (s, 2H), 2.36 (s, 3H), 1.70 (t, 2H), 1.70-1.60 (m, 4H)
- [1093] Preparation B3-30: 4-(6'-chloro-4'-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-[3,3'-bipyridin]-6-yl)morpholine
- [1094] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-23 intermediate and changing the boronic acid reagent to 6-(morpholin-4-yl)pyridin-3-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.35 (s, 1H), 7.99 (s, 1H), 7.76 (d, 1H), 6.85 (s, 1H), 6.72 (d, 1H), 3.88 (t, 4H), 3.58 (t, 4H), 2.94 (t, 4H), 2.57 (t, 2H), 2.44 (s, 2H), 2.33 (s, 3H), 1.65 (t, 2H), 1.65-1.45 (m, 4H)
- [1095] Preparation B3-31: 2-(1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-N,N-dimethylethan-1-amine
- [1096] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-8 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 8.15 (s, 1H), 8.02 (s, 1H), 7.45-7.05 (m, 1H), 6.89 (s, 1H), 3.29 (d, 2H), 2.62 (t, 2H), 2.31 (t, 2H), 2.26 (s, 1H), 2.24 (s, 6H), 1.75 (d, 2H), 1.48 (t, 2H), 1.35-1.20 (m, 2H)
- [1097] Preparation B3-32: 2-(1-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-N,N-dimethylethan-1-amine
- [1098] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-8 intermediate and changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.92 (s, 1H), 7.87 (s, 1H), 6.88 (s, 1H), 4.78 (q, 2H), 3.31 (d, 2H), 2.59 (t, 2H), 2.31 (t, 2H), 2.27 (s, 1H), 2.25 (s, 6H), 1.73 (d, 2H), 1.47 (t, 2H), 1.30-1.20 (m, 2H)
- [1099] Preparation B3-33: 2-(1-(6-chloro-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-4-yl)-N,N-dimethylethan-1-amine
- [1100] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-8 intermediate and changing the boronic acid reagent to 6-(morpholin-4-yl)pyridin-3-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.34 (s, 1H), 7.98 (s, 1H), 7.76 (d, 1H), 6.84 (s, 1H), 6.72 (d, 1H), 3.88 (t, 4H), 3.59 (t, 4H), 3.34 (d, 2H), 2.59 (t, 2H), 2.30-2.25 (m, 3H), 2.23 (s, 6H), 1.66 (d, 2H), 1.43 (t, 2H), 1.25-1.10 (m, 2H)
- [1101] Preparation B3-34: tert-butyl (R)-(1-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

- [1102] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-7 intermediate and changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.15 (s, 1H), 7.88 (s, 1H), 7.82 (s, 1H), 6.88 (s, 1H), 4.83-4.80 (m, 2H), 4.47-4.45 (m, 1H), 3.76-3.68 (m, 1H), 3.44-3.41 (m, 1H), 3.12-3.09 (m, 1H), 2.63-2.58 (m, 1H), 2.43-2.41 (m, 1H), 1.97-1.94 (m, 1H), 1.75-1.69 (m, 1H), 1.44 (s, 10H)
- [1103] Preparation B3-35: (1S,4S)-4-((2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)(methylamino)cyclohexan-1-ol
- [1104] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-29 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.04 (d, 2H), 7.86 (s, 1H), 7.26 (t, 1H), 6.86 (s, 1H), 3.96 (brs, 1H), 3.22-3.14 (m, 1H), 2.72 (s, 3H), 1.98-1.88 (m, 2H), 1.80 (d, 2H), 1.36-1.25 (m, 5H)
- [1105] Preparation B3-36: tert-butyl N-[(3S,6R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-6-methyl-3-piperidyl]carbamate
- [1106] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-30 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.19 (s, 2H), 8.00 (s, 1H), 7.42-7.38 (m, 0.2H), 7.27-7.22 (m, 0.5H), 7.12-7.07 (m, 0.3H), 6.92-6.82 (m, 1H), 4.59-4.44 (m, 1H), 3.83-3.63 (m, 1H), 3.59-3.43 (m, 1H), 3.38-3.23 (m, 1H), 2.89-2.75 (m, 1H), 1.93-1.82 (m, 1H), 1.82-1.68 (m, 1H), 1.53 (s, 9H), 1.33-1.26 (m, 1H), 0.95 (d, 3H)
- [1107] Preparation B3-37: tert-butyl N-[(3R,4S)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-4-methoxy-3-piperidyl]carbamate
- [1108] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-31 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.18-8.09 (m, 2H), 7.99 (s, 1H), 7.44-7.40 (m, 0.2H), 7.28-7.26 (m, 0.6H), 7.13-7.11 (m, 0.2H), 6.97 (s, 1H), 5.12-5.01 (m, 1H), 3.91-3.76 (m, 1H), 3.59-3.51 (m, 1H), 3.41 (s, 3H), 3.25-3.14 (m, 1H), 3.00-2.85 (m, 2H), 2.85-2.74 (m, 1H), 2.01-1.89 (m, 1H), 1.52 (s, 9H)
- [1109] Preparation B3-38: tert-butyl N-[(3R,4R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-4-methoxy-3-piperidyl]carbamate
- [1110] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-32 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz)

δ 8.15 (s, 1H), 8.10 (s, 1H), 7.94 (s, 1H), 7.41-7.39 (m, 0.2H), 7.26-7.24 (m, 0.6H), 7.11-7.00 (m, 0.2H), 4.73-4.69 (m, 1H), 3.71-3.69 (m, 1H), 3.67-3.58 (m, 1H), 3.40 (s, 3H), 3.29-3.22 (m, 1H), 3.11-3.08 (m, 2H), 2.76-2.72 (m, 1H), 1.98-1.96 (m, 1H), 1.26 (s, 9H)

[1111] Preparation B3-39: tert-butyl (R)-((1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)methyl)(methyl)carbamate

[1112] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-33 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.20-8.05 (m, 2H), 8.00 (s, 1H), 7.45-7.10 (m, 1H), 6.89 (s, 1H), 3.30-3.10 (m, 3H), 3.10-2.90 (m, 1H), 2.80-2.70 (m, 3H), 2.59 (t, 1H), 2.45-2.25 (m, 1H), 2.00-1.85 (m, 1H), 1.85-1.70 (m, 2H), 1.65-1.50 (m, 1H), 1.48 (s, 9H), 1.15-1.00 (m, 1H)

[1113] Preparation B3-40: tert-butyl (S)-((1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)methyl)(methyl)carbamate

[1114] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-34 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.20-8.05 (m, 2H), 8.00 (s, 1H), 7.45-7.10 (m, 1H), 6.89 (s, 1H), 3.30-3.05 (m, 3H), 3.05-2.90 (m, 1H), 2.85-2.70 (m, 3H), 2.59 (t, 1H), 2.45-2.25 (m, 1H), 2.00-1.80 (m, 1H), 1.80-1.70 (m, 2H), 1.65-1.55 (m, 1H), 1.45 (s, 9H), 1.20-1.00 (m, 1H)

[1115] Preparation B3-41: tert-butyl ((3R,4R)-1-(2-chloro-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-3-methylpiperidin-4-yl)carbamate

[1116] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-35 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.20-8.10 (m, 2H), 7.98 (s, 1H), 7.45-7.10 (m, 1H), 7.11 (s, 1H), 4.45-4.35 (m, 1H), 3.35-3.20 (m, 3H), 2.69 (t, 1H), 2.40 (t, 1H), 2.05-1.95 (m, 1H), 1.55-1.50 (m, 1H), 1.47 (s, 9H), 0.93 (d, 3H)

[1117] Preparation B3-42: 2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-[(3S)-3-methyl-1-piperidyl]pyridine

[1118] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-36 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.17 (s, 1H), 8.15 (s, 1H), 7.99 (s, 1H), 7.45-7.10 (m, 1H), 6.90 (s, 1H), 3.30-3.15 (m, 2H), 2.60-2.50 (m, 1H), 2.30-2.20 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.65 (m, 2H), 1.65-1.50 (m, 1H), 1.10-1.00 (m, 1H), 0.87 (d, 3H)

- [1119] Preparation B3-43: 2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-[(3S)-3-(fluoromethyl)-1-piperidyl]pyridine
- [1120] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-37 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 8.15 (s, 1H), 7.98 (s, 1H), 7.45-7.10 (m, 1H), 6.93 (s, 1H), 4.45-4.10 (m, 2H), 3.45-3.35 (m, 1H), 3.30-3.15 (m, 1H), 2.59 (t, 1H), 2.52 (t, 1H), 2.15-2.00 (m, 1H), 1.85-1.70 (m, 2H), 1.70-1.55 (m, 1H), 1.30-1.10 (m, 1H)
- [1121] Preparation B3-44: 2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-[(3R)-3-(difluoromethyl)-1-piperidyl]pyridine
- [1122] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-38 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.18 (s, 1H), 8.14 (s, 1H), 7.97 (s, 1H), 7.45-7.10 (m, 1H), 6.93 (s, 1H), 5.80-5.45 (m, 1H), 3.45-3.35 (m, 1H), 3.30-3.20 (m, 1H), 2.65-2.55 (m, 2H), 2.20-2.00 (m, 1H), 2.00-1.90 (m, 1H), 1.85-1.75 (m, 1H), 1.65-1.50 (m, 1H), 1.45-1.30 (m, 1H)
- [1123] Preparation B3-45: tert-butyl N-[(3S,4S)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-fluoro-4-piperidyl]carbamate
- [1124] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-39 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 7.95 (s, 1H), 7.94 (s, 1H), 7.78 (s, 1H), 7.43-7.12 (m, 1H), 6.70 (s, 1H), 4.45-4.35 (m, 1H), 4.35-4.20 (m, 1H), 4.05-3.90 (m, 1H), 3.70-3.55 (m, 1H), 3.15-3.00 (m, 1H), 3.00-2.95 (m, 1H), 2.20-2.10 (m, 1H), 1.46 (s, 9H), 1.45-1.35 (m, 1H)
- [1125] Preparation B3-46: tert-butyl N-[(3R,4S)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-fluoro-4-piperidyl]carbamate
- [1126] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-40 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.25 (s, 1H), 8.21 (s, 1H), 8.00 (s, 1H), 7.41-7.10 (m, 1H), 6.93 (s, 1H), 4.95-4.85 (m, 1H), 4.85-4.70 (m, 1H), 3.87-3.70 (m, 1H), 3.70-3.60 (m, 1H), 3.35-3.25 (m, 1H), 3.00-2.80 (m, 1H), 2.80-2.70 (m, 1H), 1.90-1.80 (m, 1H), 1.48 (s, 9H)
- [1127] Preparation B3-47: tert-butyl N-[(3S,4R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-fluoro-4-piperidyl]carbamate
- [1128] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-41 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz)

- δ 8.25 (s, 1H), 8.21 (s, 1H), 8.07 (s, 1H), 7.41-7.02 (m, 1H), 6.93 (s, 1H), 4.95-4.85 (m, 1H), 4.85-4.70 (m, 1H), 3.85-3.70 (m, 1H), 3.70-3.60 (m, 1H), 3.40-3.25 (m, 1H), 3.00-2.80 (m, 1H), 2.80-2.70 (m, 1H), 1.85-1.75 (m, 1H), 1.48 (s, 9H)
- [1129] Preparation B3-48: tert-butyl N-[(3S,5R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-5-fluoro-3-piperidyl]carbamate
- [1130] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-42 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.23 (s, 1H), 8.15 (s, 1H), 7.94 (s, 1H), 7.43-7.39 (m, 0.2H), 7.28-7.25 (m, 0.6H), 7.13-7.10 (m, 0.2H), 7.03 (s, 1H), 5.12-4.97 (m, 1H), 4.84-4.74 (m, 0.5H), 4.72-4.62 (m, 0.5H), 4.03-3.87 (m, 1H), 3.31-3.19 (m, 1H), 3.19-3.10 (m, 2H), 3.07-2.91 (m, 1H), 2.20-2.10 (m, 0.5H), 2.10-2.03 (m, 0.5H), 2.03-1.88 (m, 1H), 1.51 (s, 9H)
- [1131] Preparation B3-49: tert-butyl N-[(3S,5S)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-5-fluoro-3-piperidyl]carbamate
- [1132] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-43 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.25 (s, 2H), 7.97 (s, 1H), 7.44-7.40 (m, 0.2H), 7.27-7.25 (m, 0.6H), 7.13-7.09 (m, 0.2H), 7.02 (s, 1H), 4.95-4.86 (m, 0.5H), 4.83-4.75 (m, 0.5H), 4.47-4.32 (m, 1H), 4.12-3.98 (m, 1H), 3.63-3.53 (m, 1H), 3.53-3.43 (m, 1H), 2.84-2.76 (m, 0.5H), 2.76-2.68 (m, 0.5H), 2.60-2.49 (m, 1H), 2.42-2.29 (m, 1H), 1.50 (s, 9H)
- [1133] Preparation B3-50: tert-butyl N-[(3S,5R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-5-(trifluoromethyl)-3-piperidyl]carbamate
- [1134] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-44 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) 8.64 (s, 1H), 8.12 (s, 1H), 7.99 (s, 1H), 7.28-7.26 (m, 0.2H), 7.26-7.20 (m, 0.6H), 7.02-7.01 (m, 0.2H), 6.93-6.93 (m, 1H), 4.43-4.41 (m, 1H), 3.73-3.71 (m, 2H), 3.63-3.60 (m, 1H), 3.45-3.42 (m, 1H), 2.66-2.52 (m, 1H), 2.49-2.33 (m, 2H), 1.47 (s, 9H)
- [1135] Preparation B3-51: tert-butyl N-[(3S,5S)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-5-hydroxy-3-piperidyl]carbamate
- [1136] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-45 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.17-8.15 (m, 2H), 7.93 (s, 1H), 7.41-7.40 (m, 0.2H), 7.28-7.20 (m, 0.6H), 7.11-7.09 (m, 0.2H), 6.98 (s, 1H), 5.15-5.10 (m, 1H), 3.92-3.90 (m, 1H), 3.89-3.82 (m, 1H),

- 3.33-3.30 (m, 1H), 3.12-3.09 (m, 1H), 2.81-2.76 (m, 2H), 2.16-2.13 (m, 1H), 1.55-1.52 (m, 1H), 1.45 (s, 9H)
- [1137] Preparation B3-52: tert-butyl N-[(3R,4R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-hydroxy-4-piperidyl]carbamate
- [1138] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-46 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.17 (s, 1H), 8.11 (s, 1H), 7.96 (s, 1H), 7.41-7.10 (m, 1H), 6.95 (s, 1H), 4.75-4.65 (m, 1H), 4.10-4.00 (m, 1H), 3.60-3.40 (m, 2H), 3.30-3.20 (m, 1H), 2.75-2.60 (m, 1H), 2.60-2.55 (m, 1H), 2.00-1.90 (m, 1H), 1.48 (s, 9H)
- [1139] Preparation B3-53: (3R,4R)-1-[2-chloro-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-4-fluoro-piperidin-3-ol
- [1140] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-19 intermediate and changing the boronic acid reagent to 1-(difluoromethyl)pyrazol-4-boronic acid pinacol ester. ¹H NMR (CDCl₃, 400MHz) δ 8.20 (s, 1H), 8.18 (s, 1H), 7.98 (s, 1H), 7.42-7.12 (m, 1H), 6.96 (s, 1H), 4.60-4.40 (m, 1H), 3.95-3.85 (m, 1H), 3.45-3.35 (m, 1H), 3.25-3.15 (m, 1H), 2.85-2.75 (m, 1H), 2.30-2.20 (m, 1H), 2.20-2.10 (m, 1H), 1.90-1.75 (m, 1H)
- [1141] Preparation B3-54: tert-butyl ((3S,5R)-1-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-5-fluoropiperidin-3-yl)carbamate
- [1142] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-42 intermediate and changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.24 (s, 1H), 7.91 (s, 1H), 7.84 (s, 1H), 7.02 (s, 1H), 5.03-4.93 (m, 1H), 4.87-4.75 (m, 3H), 3.99-3.87 (m, 1H), 3.27-3.11 (m, 2H), 3.11-2.95 (m, 2H), 2.21-2.04 (m, 1H), 1.94-1.84 (m, 1H), 1.50 (s, 9H)
- [1143] Preparation B3-55: tert-butyl ((3S,5S)-1-(2-chloro-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)-5-fluoropiperidin-3-yl)carbamate
- [1144] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-43 intermediate and changing the boronic acid reagent to 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.24 (s, 1H), 8.03 (s, 1H), 7.84 (s, 1H), 6.97 (s, 1H), 4.91-4.70 (m, 4H), 4.47-4.32 (m, 1H), 4.13-3.98 (m, 1H), 3.61-3.40 (m, 2H), 2.88-2.69 (m, 1H), 2.51-2.29 (m, 2H), 1.51 (s, 9H)
- [1145] Preparation B3-56: tert-butyl N-[(3S,5R)-1-[2-chloro-5-(1-isopropylpyrazol-4-yl)-4-pyridyl]-5-fluoro-3-piperidyl]carbamate

- [1146] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-42 intermediate and changing the boronic acid reagent to 1-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.25 (s, 1H), 7.83 (s, 1H), 7.75 (s, 1H), 6.98 (s, 1H), 5.14-4.99 (m, 1H), 4.81-4.72 (m, 0.5H), 4.69-4.63 (m, 0.5H), 4.63-4.51 (m, 1H), 4.05-3.92 (m, 1H), 3.33-3.23 (m, 1H), 3.23-3.14 (m, 1H), 3.14-3.05 (m, 1H), 3.01-2.80 (m, 1H), 2.19-2.06 (m, 0.5H), 2.06-1.89 (m, 1.5H), 1.60 (d, 6H), 1.51 (s, 9H)
- [1147] Preparation B3-57: tert-butyl N-[(3S,5S)-1-[2-chloro-5-(1-isopropylpyrazol-4-yl)-4-pyridyl]-5-fluoro-3-piperidyl]carbamate
- [1148] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-43 intermediate and changing the boronic acid reagent to 1-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.23 (s, 1H), 7.94 (s, 1H), 7.74 (s, 1H), 6.94 (s, 1H), 4.90-4.81 (m, 1H), 4.77-4.70 (m, 1H), 4.64-4.58 (m, 1H), 4.58-4.47 (m, 1H), 4.15-4.01 (m, 1H), 3.58-3.39 (m, 2H), 2.79-2.59 (m, 1H), 2.59-2.48 (m, 1H), 2.39-2.26 (m, 1H), 1.57 (d, 6H), 1.48 (s, 9H)
- [1149] Preparation B3-58: tert-butyl N-[(3R,4R)-1-[2-chloro-5-(1-isopropylpyrazol-4-yl)-4-pyridyl]-4-fluoro-3-piperidyl]carbamate
- [1150] The titled compound was prepared in accordance with the same procedures as in Preparation B3-1, using the B2-47 intermediate and changing the boronic acid reagent to 1-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.16 (s, 1H), 7.76 (s, 1H), 7.73 (s, 1H), 6.90 (s, 1H), 4.80-4.70 (m, 1H), 4.65-4.55 (m, 1H), 4.55-4.40 (m, 1H), 4.00-3.85 (m, 1H), 3.55-3.45 (m, 1H), 3.10-3.00 (m, 1H), 2.85-2.75 (m, 1H), 2.05-1.95 (m, 1H), 1.85-1.75 (m, 1H), 1.59 (d, 6H), 1.47 (s, 9H)
- [1151] Preparation B4-1: 2-chloro-4-fluoro-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridine
- [1152] 2-Chloro-4-fluoro-5-iodopyridine (1.0 g, 3.88 mmol) was dissolved in anhydrous 1,4-dioxane (10.00 mL) and then 4-ethynyl-tetrahydro-2H-pyran (470.7 mg, 4.27 mmol), bis(triphenylphosphine)palladium(II) dichloride (129.8 mg, 0.18 mmol), copper(I) iodide (44.4 mg, 0.23 mmol), and triethylamine (1.0 mL, 7.77 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 80°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (799.6 mg). (Yield: 85.9%) ¹H NMR (CDCl₃, 400MHz)

- δ 8.41 (d, 1H), 7.11 (d, 1H), 3.95-3.92 (m, 2H), 3.58-3.53 (m, 2H), 2.93-2.89 (m, 1H), 1.95-1.91 (m, 2H), 1.81-1.74 (m, 2H)
- [1153] Preparation B4-2: 2-chloro-4-fluoro-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridine
- [1154] The titled compound was prepared in accordance with the same procedures as in Preparation B4-1, changing the ethyne reagent to 4-ethynyl-1-(trifluoromethyl)-1H-pyrazole. ¹H NMR (CDCl₃, 400MHz) δ 8.52 (d, 1H), 8.07 (s, 1H), 7.92 (s, 1H), 7.18 (d, 1H)
- [1155] Preparation B5-1: 1-(2-chloro-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)azetidin-3-ol
- [1156] 2-Chloro-4-fluoro-5-(2-tetrahydropyran-4-ylethynyl)pyridine (the B4-1 intermediate, 100 mg, 0.42 mmol) was dissolved in anhydrous dimethylformamide (2.0 mL) and then 3-hydroxyazetidine hydrochloride (50.3 mg, 0.46 mmol) and diisopropylethylamine (0.17 mL, 1.25 mmol) were added dropwise thereto. Then, the mixed solution was stirred at room temperature overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (83.3 mg). (Yield: 68.2%) ¹H NMR (CDCl₃, 400MHz) δ 7.99 (s, 1H), 6.16 (s, 1H), 4.77-4.75 (m, 1H), 4.53-4.49 (m, 2H), 4.09-4.08 (m, 2H), 4.06-3.91 (m, 2H), 3.55-3.49 (m, 2H), 2.93-2.81 (m, 1H), 2.51-2.49 (m, 1H), 1.91-1.87 (m, 2H), 1.79-1.72 (m, 2H)
- [1157] Preparation B5-2: (R)-1-(2-chloro-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [1158] The titled compound was prepared in accordance with the same procedures as in Preparation B5-1, using the B4-2 intermediate and changing the amine reagent to (R)-piperidin-3-ol. ¹H NMR (CDCl₃, 400MHz) δ 8.27 (s, 1H), 8.16 (s, 1H), 7.92 (s, 1H), 6.83 (s, 1H), 4.01-4.13 (m, 1H), 3.60-3.71 (m, 1H), 3.46-3.20 (m, 2H), 3.17-3.15 (m, 1H), 1.98-1.81 (m, 2H), 1.61-1.56 (m, 2H)
- [1159] Preparation C1-1: 2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1160] 2-bromo-4-pyrimidinamine (3.0 g, 17.24 mmol) was dissolved in anhydrous acetonitrile (86.2 mL) and then 2-fluoro-6-methoxyphenylboronic acid (4.4 g, 25.86 mmol), bis(triphenylphosphine)palladium(II) dichloride (605.0 mg, 0.86 mmol), and 2.0M sodium carbonate solution (25.8 mL, 51.72 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted

organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (1.2 g). (Yield: 31.7%) ¹H NMR (CDCl₃, 400MHz) δ 8.39 (d, 1H), 7.34-7.28 (m, 1H), 6.81-6.76 (m, 2H), 6.43 (d, 1H), 4.97 (brs, 2H), 3.81 (s, 3H)

[1161] Preparation C1-2: 5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-amine

[1162] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the amine reagent to 6-chloro-5-fluoropyridin-2-amine. ¹H NMR (CDCl₃, 400MHz) δ 7.37-7.30 (m, 2H), 6.82-6.77 (m, 2H), 6.54-6.51 (m, 1H), 4.41 (brs, 2H), 3.81 (s, 3H)

[1163] Preparation C1-3: 5-chloro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-amine

[1164] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the amine reagent to 6-bromo-5-chloro-pyridin-2-amine. ¹H NMR (CDCl₃, 400MHz) δ 7.52 (d, 1H), 7.37-7.33 (m, 1H), 6.82-6.77 (m, 2H), 6.50 (d, 1H), 4.52 (brs, 2H), 3.81 (s, 3H)

[1165] Preparation C1-4: 6-(2-fluoro-6-methoxyphenyl)-5-methylpyridin-2-amine

[1166] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the amine reagent to 6-bromo-5-methyl-pyridin-2-amine. ¹H NMR (CDCl₃, 400MHz) δ 7.37 (d, 1H), 7.35-7.31 (m, 1H), 6.81-6.76 (m, 2H), 6.49 (d, 1H), 4.35 (brs, 2H), 3.78 (s, 3H), 1.99 (s, 3H)

[1167] Preparation C1-5: 6-(2-fluoro-6-methoxy-phenyl)-5-methylsulfonyl-pyridin-2-amine

[1168] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the amine reagent to 6-bromo-5-(methylsulfonyl)pyridin-2-amine. ¹H NMR (CDCl₃, 400MHz) 8.17 (d, 1H), 7.40 (q, 1H), 6.85-6.79 (m, 2H), 6.61 (d, 1H), 5.06 (s, 2H), 3.81 (s, 3H), 2.84 (s, 3H)

[1169] Preparation C1-6: 2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine

[1170] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the boronic acid reagent to (7-fluoroquinoxalin-6-yl)boronic acid. ¹H NMR (CD₃OD, 400MHz) 8.94-9.92 (m, 2H), 8.54 (d, 1H), 8.24 (d, 1H), 7.89 (d, 1H), 6.59 (d, 1H)

[1171] Preparation C1-7: 2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine

[1172] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the boronic acid reagent to (2,4-difluoro-6-methoxy-phenyl)boronic acid. ¹H NMR (CD₃OD, 400MHz) 8.38 (d, 1H), 6.53-6.50 (m, 2H), 6.43 (d, 1H), 5.00 (brs, 2H), 3.78 (s, 3H)

[1173] Preparation C1-8: 6-(2-fluoro-6-methoxyphenyl)pyridin-2-amine

- [1174] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the amine reagent to 6-bromopyridin-2-amine. ¹H NMR (CDCl₃, 400MHz) δ 7.52 (t, 1H), 7.34-7.28 (m, 1H), 6.80-6.74 (m, 3H), 6.51 (d, 1H), 4.48 (brs, 2H), 3.79 (s, 3H)
- [1175] Preparation C1-9: 2-(2-methoxypyridin-3-yl)pyrimidin-4-amine
- [1176] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the boronic acid reagent to 2-methoxy-3-pyridylboronic acid reagent. ¹H NMR (CDCl₃, 400MHz) 8.39 (d, 1H), 8.25 (s, 1H), 8.01 (d, 1H), 6.99 (t, 1H), 6.40 (d, 1H), 4.97 (s, 2H), 4.03 (s, 3H)
- [1177] Preparation C1-10: methyl 4-(4-aminopyrimidin-2-yl)-3-fluoro-5-methoxybenzoate
- [1178] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the boronic acid reagent to (methyl 3-fluoro-5-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate. ¹H NMR (CD₃OD, 400MHz) 8.17 (d, 1H), 7.55 (s, 1H), 7.46 (d, 1H), 6.56 (d, 1H), 3.96 (s, 3H), 3.87 (s, 3H)
- [1179] Preparation C1-11: [2-(4-aminopyrimidin-2-yl)-3-fluoro-phenyl]methanol
- [1180] The titled compound was prepared in accordance with the same procedures as in Preparation C1-1, changing the boronic acid reagent to [2-fluoro-6-(hydroxymethyl)phenyl]boronic acid. ¹H NMR (CD₃OD, 400MHz) δ 8.22 (d, 1H), 7.53-7.43 (m, 1H), 7.43-7.38 (m, 1H), 7.18-7.11 (m, 1H), 6.60 (d, 1H), 4.54 (s, 2H)
- [1181] Preparation C2-1: methyl 6-amino-2-(2-fluoro-6-methoxyphenyl)nicotinate
- [1182] Methyl 6-amino-2-chloronicotinate (1.0 g, 5.36 mmol) was dissolved in anhydrous acetonitrile (30.0 mL) and then 2-fluoro-6-methoxyphenylboronic acid (1.82 g, 10.72 mmol), tetrakis(triphenylphosphine)palladium(0) (400.0 mg, 0.35 mmol), and potassium carbonate (2.22 g, 16.08 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C for 2 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (1.1 g). (Yield: 78.5%) ¹H NMR (CDCl₃, 400MHz) δ 8.15 (d, 1H), 7.34-7.32 (m, 1H), 6.81-6.75 (m, 2H), 6.51 (d, 1H), 4.94 (brs, 2H), 3.76 (s, 3H), 3.66 (s, 3H)
- [1183] Preparation C3-1: 6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-amine
- [1184] 6-Chloro-5-nitro-pyridin-2-amine (1.0 g, 5.76 mmol) was dissolved in anhydrous acetonitrile (30.0 mL) and then 2-fluoro-6-methoxyphenylboronic acid (1.82 g, 10.72 mmol), tetrakis(triphenylphosphine)palladium(0) (400.0 mg, 0.35 mmol), and potassium carbonate (2.22 g, 16.08 mmol) were added dropwise thereto. Then, the

mixed solution was stirred at 100°C for 2 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (1.17 g). (Yield: 82.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.30 (d, 1H), 7.39-7.35 (m, 1H), 6.83 (t, 1H), 6.77 (d, 1H), 6.54 (d, 1H), 5.22 (brs, 2H), 3.76 (s, 3H)

[1185] Preparation C3-2: 6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-amine

[1186] The titled compound was prepared in accordance with the same procedures as in Preparation C3-1, changing the boronic acid reagent to (2,4-difluoro-6-methoxy-phenyl)boronic acid. ¹H NMR (CD₃OD, 400MHz) δ 8.26 (d, 1H), 6.75 (d, 1H), 6.66-6.61 (m, 2H), 3.74 (s, 3H)

[1187] Preparation C4-1: 4-(4-aminopyrimidin-2-yl)-3-fluoro-5-methoxybenzaldehyde

[1188] 2-Bromopyrimidin-4-amine (1.9 g, 11.11 mmol) was dissolved in anhydrous acetonitrile (44.9 mL) and water (12.5 mL) and then (2-fluoro-4-formyl-6-methoxy-phenyl)boronic acid (2.0 g, 10.1 mmol), XPhos Pd G2 (794.9 mg, 1.01 mmol), and potassium phosphate tribasic (6.4 g, 30.31 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C for 4 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (414.6 mg). (Yield: 16.6%) ¹H NMR (CDCl₃, 400MHz) δ 9.97 (s, 1H), 8.40 (d, 1H), 7.33-7.27 (m, 2H), 6.46 (d, 1H), 5.02 (brs, 2H), 3.88 (s, 3H)

[1189] Preparation C4-2: 5-(4-aminopyrimidin-2-yl)thiophen-3-carbaldehyde

[1190] The titled compound was prepared in accordance with the same procedures as in Preparation C4-1, changing the boronic acid reagent to (4-formylthiophen-2-yl)boronic acid. ¹H NMR (CD₃OD, 400MHz) δ 9.86 (s, 1H), 8.45 (s, 1H), 8.19 (s, 1H), 8.08 (d, 1H), 6.41 (d, 1H)

[1191] Preparation C5-1: (4-(4-aminopyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol

[1192] 4-(4-Aminopyrimidin-2-yl)-3-fluoro-5-methoxybenzaldehyde (the C4-1 intermediate, 100.0 mg, 0.40 mmol) was dissolved in anhydrous tetrahydrofuran (6.0 mL) and then sodium borohydride (15.3 mg, 0.40 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 1 hour. After completion of the reaction, the reaction mixture was diluted with dichloromethane and then water was slowly added thereto. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated to prepare the titled

compound (69.0 mg), without further purification. (Yield: 68.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.14 (d, 1H), 6.91 (s, 1H), 6.81 (d, 1H), 6.53 (d, 1H), 4.67 (s, 2H), 3.8 (s, 3H)

[1193] Preparation C5-2: (5-(4-aminopyrimidin-2-yl)thiophen-3-yl)methanol

[1194] The titled compound was prepared in accordance with the same procedures as in Preparation C5-1, using the C4-2 intermediate. ¹H NMR (CD₃OD, 400MHz) 8.04 (d, 1H), 7.82 (s, 1H), 7.38 (s, 1H), 6.36 (d, 1H), 4.60 (s, 2H)

[1195] Preparation C6-1: 2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine

[1196] 4-(4-Aminopyrimidin-2-yl)-3-fluoro-5-methoxybenzaldehyde (the C4-1 intermediate, 100 mg, 0.4 mmol) was dissolved in methanol (2.0 mL) and then 2.0M dimethylamine dissolved in tetrahydrofuran (0.4 mL, 0.8 mmol) and sodium acetate (33.2 mg, 0.40 mmol) were added dropwise thereto. Then, the mixed solution was stirred at room temperature overnight. Sodium borohydride (15.3 mg, 0.40 mmol) was added at room temperature to the reaction mixture, which was then stirred for 1 hour. After completion of the reaction, dichloromethane was added to the reaction mixture and then a saturated sodium hydrogen carbonate solution was added thereto. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated to prepare the titled compound (96.0 mg), without further purification. (Yield: 85.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.14 (d, 1H), 6.92 (s, 1H), 6.81 (d, 1H), 6.53 (d, 1H), 3.8 (s, 3H), 3.54 (s, 2H), 2.30-2.28 (m, 6H)

[1197] Preparation C6-2: 1-((5-(4-aminopyrimidin-2-yl)thiophen-3-yl)methyl)azetidin-3-ol

[1198] The titled compound was prepared in accordance with the same procedures as in Preparation C6-1, using the C4-2 intermediate and changing the amine reagent to 3-hydroxyazetidine hydrochloride. The product was used in the subsequent reaction without further purification.

[1199] Preparation C7: 3-(6-amino-2-pyridyl)oxazolidin-2-one

[1200] 6-Bromopyridin-2-amine (300.0 mg, 1.734 mmol) was dissolved in anhydrous 1,4-dioxane (3.0 mL) and then oxazolidin-2-one (151.0 mg, 1.734 mmol), palladium(II) acetate (38.9 mg, 0.173 mmol), XantPhos (150.5 mg, 0.26 mmol), and cesium carbonate (1.41 g, 4.335 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (63.4 mg). (Yield:

20.4%) ¹H NMR (CDCl₃, 400MHz) δ 7.55 (d, 1H), 7.47 (t, 1H), 6.25 (d, 1H), 4.45 (t, 2H), 4.40-4.30 (s, 2H), 4.22 (t, 2H)

[1201] Preparation C8-1: 6-amino-2-(2-fluoro-6-methoxy-phenyl)pyridin-3-carbonitrile

[1202] 6-Amino-2-chloro-pyridin-3-carbonitrile (500.0 mg, 3.26 mmol) was dissolved in anhydrous 1,4-dioxane (5.0 mL) and water (1.0 mL) and then 2-fluoro-6-methoxyphenylboronic acid (608.7 mg, 3.58 mmol), tetrakis(triphenylphosphine)palladium(0) (376.2 mg, 0.33 mmol), and potassium carbonate (899.9mg, 6.51mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C for 17 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (355.8 mg, Yield: 44.9%). ¹H NMR (CDCl₃, 400MHz) δ 7.72 (d, 1H), 7.39 (q, 1H), 6.86-6.80 (m, 2H), 6.51 (d, 1H), 5.11 (s, 2H), 3.85 (s, 3H)

[1203] Preparation C8-2: 6-amino-2-(2,4-difluoro-6-methoxy-phenyl)pyridin-3-carbonitrile

[1204] The titled compound was prepared in accordance with the same procedures as in Preparation C8-1, changing the boronic acid reagent to (2,4-difluoro-6-methoxyphenyl)boronic acid. ¹H NMR (CDCl₃, 400MHz) 7.73 (d, 1H), 6.62-6.51 (m, 3H), 5.04 (s, 2H), 3.84 (s, 3H)

[1205] Example 1: (S)-cyclopropyl(4-(3-hydroxypiperidin-1-yl)-6-((2-(5-methylpyridin-3-yl)pyrimidin-4-yl)amino)pyridin-3-yl)methanone

[1206] (S)-(6-((2-Chloropyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone (Intermediate A1-1, 15.0 mg, 0.04 mmol) was dissolved in anhydrous 1,4-dioxane (0.4 mL) and then (5-methylpyridin-3-yl)boronic acid (10.9 mg, 0.08 mmol), bis(triphenylphosphine)palladium(II) dichloride (1.4 mg, 0.002 mmol), and 2.0M sodium carbonate solution (0.1 mL, 0.20 mmol) were added dropwise thereto. Then, the mixed solution was stirred in a microwave reactor for 1 hour. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (3.7 mg). (Yield: 21.4%) ¹H NMR (CDCl₃, 400MHz) δ 9.59 (s, 1H), 8.52-8.49 (m, 3H), 8.34-8.32 (m, 2H), 7.94 (s, 1H), 6.78 (d, 1H), 5.82-5.52 (brs, 1H), 4.13-4.05 (m, 2H), 3.31-3.28 (m, 1H), 3.14-3.11 (m, 2H), 2.54-2.51 (m, 1H), 2.46 (s, 3H), 2.18-2.15 (m, 1H), 1.80-1.79 (m, 1H), 1.65-1.63 (m, 2H), 1.28-1.25 (m, 2H), 1.09-1.07 (m, 1H), 1.06-1.01 (m, 1H) MS m/z= 431.1 (M +H)+

- [1207] Example 2: (S)-(6-((2-(5-aminopyridin-3-yl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone
- [1208] The titled compound (6.8 mg) was prepared in accordance with the same procedures as in Example 1, changing the boronic acid reagent to 3-aminopyridin-5-boronic acid pinacol ester. (Yield: 38.9%) ¹H NMR (CDCl₃, 400MHz) δ 9.17 (s, 1H), 8.50-8.49 (d, 1H), 8.36 (s, 1H), 8.3 (s, 1H), 8.13 (s, 1H), 8 (s, 1H), 7.89 (brs, 1H), 6.74 (d, 1H), 4.12-4.10 (m, 1H), 4.07 (brs, 2H), 3.32-3.27 (m, 1H), 3.12-3.06 (m, 2H), 2.54-2.52 (m, 1H), 2.15-2.12 (m, 1H), 1.81-1.79 (m, 1H), 1.54-1.51 (m, 2H), 1.28-1.26 (m, 2H), 1.26-1.25 (m, 1H), 1.07-1.06 (m, 1H) MS m/z= 432.0 (M+H)+
- [1209] Example 3: (S)-cyclopropyl(4-(3-hydroxypiperidin-1-yl)-6-((2-(5-methoxypyridin-3-yl)pyrimidin-4-yl)amino)pyridin-3-yl)methanone
- [1210] The titled compound (4.4 mg) was prepared in accordance with the same procedures as in Example 1, changing the boronic acid reagent to 3-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine. (Yield: 24.5%) ¹H NMR (CDCl₃, 400MHz) δ 9.38 (s, 1H), 8.52 (d, 1H), 8.37 (s, 1H), 8.36 (s, 1H), 8.32 (s, 1H), 8.29 (s, 1H), 8.23 (s, 1H), 8.22 (s, 1H), 6.8 (d, 1H), 5.41-5.31 (brs, 1H), 4.13-4.10 (m, 2H), 4.05 (s, 3H), 3.31-3.28 (m, 1H), 3.13-3.10 (m, 2H), 2.55-2.52 (m, 1H), 2.18-2.15 (m, 1H), 1.81-1.80 (m, 1H), 1.60-1.56 (m, 2H), 1.28-1.25 (m, 2H), 1.09-1.07 (m, 1H), 1.06-1.02 (m, 1H) MS m/z= 447.0 (M+H)+
- [1211] Example 4: (S)-cyclopropyl(6-((2-(3-hydroxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)methanone
- [1212] The titled compound (1.4 mg) was prepared in accordance with the same procedures as in Example 1, changing the boronic acid reagent to 3-hydroxyphenylboronic acid. (Yield: 8.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.46 (d, 1H), 8.24 (s, 1H), 7.99 (s, 1H), 7.85-7.81 (m, 2H), 7.35-7.28 (m, 2H), 6.96-6.93 (m, 1H), 3.90-3.88 (m, 1H), 3.57-3.54 (m, 1H), 3.46-3.43 (m, 1H), 3.02-2.91 (m, 1H), 2.89-2.83 (m, 2H), 2.03-1.96 (m, 1H), 1.82-1.62 (m, 1H), 1.50-1.45 (m, 1H), 1.29-1.20 (m, 2H), 1.19-1.12 (m, 2H) MS m/z= 432.1 (M+H)+
- [1213] Example 5: (S)-cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)methanone
- [1214] The titled compound (1.4 mg) was prepared in accordance with the same procedures as in Example 1, changing the boronic acid reagent to 2-fluoro-6-methoxyphenylboronic acid. (Yield: 7.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.62 (d, 1H), 8.40 (s, 1H), 7.82 (s, 1H), 7.54 (s, 1H), 7.39-7.30 (m, 2H), 6.84-6.80 (m, 2H), 3.88-3.86 (m, 1H), 3.82 (s, 3H), 3.34-3.30 (m, 1H), 3.13-3.07 (m, 1H), 3.04-3.02 (m, 1H), 3.01-2.99 (m, 2H), 2.62-2.58 (m, 1H), 2.24-2.21 (m, 1H), 1.90-1.84 (m, 2H), 1.31-1.26 (m, 2H), 1.04-1.02 (m, 2H) MS m/z= 464.1 (M+H)+

- [1215] Example 6: cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxyazetidin-1-yl)pyridin-3-yl)methanone
- [1216] Step 1: (6-chloro-4-(3-hydroxyazetidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone
- [1217] Cyclopropyl(4,6-dichloropyridin-3-yl)methanone (1.0 g, 4.62 mmol) was dissolved in anhydrous dimethylformamide (23.1 mL) and then 3-hydroxyazetidine hydrochloride (0.61 g, 5.55 mmol) and diisopropylethylamine (1.26 mL, 9.25 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature overnight. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (0.94 g). (Yield: 80.5%) ¹H NMR (CDCl₃, 400MHz) δ 8.46 (s, 1H), 6.31 (s, 1H), 4.75-4.70 (m, 1H), 4.23-4.19 (m, 2H), 3.81-3.77 (m, 2H), 3.03-3.02 (m, 1H), 2.44-2.38 (m, 1H), 1.24-1.21 (m, 2H), 1.11-1.08 (m, 2H)
- [1218] Step 2: cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxyazetidin-1-yl)pyridin-3-yl)methanone
- [1219] (6-Chloro-4-(3-hydroxyazetidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone (63.4 mg, 0.25 mmol) was dissolved in anhydrous toluene (2.0 mL) and then 2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine (Intermediate C1-1, 50.0 mg, 0.23 mmol), tris(dibenzylideneacetone)dipalladium(0) (20.8 mg, 0.02 mmol), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (21.7 mg, 0.04 mmol), and cesium carbonate (111.4 mg, 0.34 mmol) were added dropwise thereto. Then, the mixed solution was refluxed under stirring at 110°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (10 mg). (Yield: 8.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.52 (s, 1H), 8.45 (d, 1H), 7.45-7.41 (m, 2H), 7.25 (s, 1H), 6.97 (dd, 1H), 6.87 (dd, 1H), 4.57-4.54 (m, 1H), 4.08-4.04 (m, 2H), 3.81 (s, 3H), 3.66-3.62 (m, 2H), 2.58-2.55 (m, 1H), 1.13-1.05 (m, 4H) MS m/z= 436.0 (M+H)+
- [1220] Example 7: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1221] (S)-1-(2-Chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol (Intermediate A2-1, 40.0 mg, 0.12 mmol) was dissolved in anhydrous 1,4-dioxane (0.5 mL) and then 2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine (Intermediate C1-1, 20.9 mg, 0.09 mmol), tris(dibenzylideneacetone)dipalladium(0) (10.9 mg, 0.012 mmol), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (11.39

mg, 0.024 mmol), and cesium carbonate (77.8 mg, 0.24 mmol) were added dropwise thereto. Then, the mixed solution was stirred at 100°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (10.6 mg). (Yield: 16.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.4 (d, 1H), 8.09-8.08 (m, 2H), 7.83 (s, 1H), 7.60 (s, 1H), 7.51-7.50 (m, 1H), 7.44-7.42 (m, 1H), 6.96 (d, 1H), 6.84 (dd, 1H), 4.49-4.46 (m, 1H), 4.10-4.07 (m, 2H), 3.81 (s, 3H), 3.70-3.61 (m, 1H), 3.59-3.56 (m, 2H), 3.31-3.30 (m, 1H), 3.29-3.27 (m, 1H), 2.72-2.60 (m, 1H), 2.45-2.40 (m, 1H), 2.14-2.08 (m, 4H), 1.98-1.97 (m, 1H), 1.33-1.31 (m, 1H), 1.30-1.29 (m, 1H) MS m/z= 546.2 (M+H)+

[1222] Example 8: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol

[1223] The titled compound (2.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-1 and C1-1. (Yield: 7.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.60 (d, 1H), 8.23 (s, 1H), 8.06 (s, 1H), 7.90 (s, 1H), 7.78 (s, 1H), 7.45 (s, 1H), 7.37-7.31 (m, 2H), 6.83-6.80 (m, 2H), 3.96-3.95 (m, 1H), 3.82 (s, 3H), 3.45-3.44 (m, 2H), 3.30-3.24 (m, 2H), 1.92-1.83 (m, 4H) MS m/z= 554.1 (M+H)+

[1224] Example 9: (R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol

[1225] The titled compound (2.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B5-2 and C1-1. (Yield: 7.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.60 (d, 1H), 8.22 (s, 1H), 8.06 (s, 1H), 7.97 (s, 1H), 7.90 (s, 1H), 7.49 (s, 1H), 7.37-7.31 (m, 1H), 7.29-7.27 (m, 1H), 6.83-6.80 (m, 2H), 3.95-3.94 (m, 1H), 3.84 (s, 3H), 3.45-3.42 (m, 2H), 3.33-3.28 (m, 1H), 3.24-3.21 (m, 1H), 1.92-1.83 (m, 4H) MS m/z= 554.1 (M+H)+

[1226] Example 10: 1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)azetidin-3-ol

[1227] The titled compound (7.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediate B5-1 and C1-1. (Yield: 15.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.39 (d, 1H), 7.89 (s, 1H), 7.44-7.40 (m, 1H), 7.37 (d, 1H), 6.99 (s, 1H), 6.96 (d, 1H), 6.85 (dd, 1H), 4.59-4.57 (m, 1H), 4.41-4.39 (m, 2H), 3.93-3.88 (m, 4H), 3.81 (s, 3H), 3.56-3.50 (m, 2H), 2.97-2.87 (m, 1H), 1.92-1.87 (m, 2H), 1.74-1.68 (m, 2H) MS m/z= 476.1 (M+H)+

[1228] Example 11: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol

- [1229] The titled compound (6.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-2 and C1-1. (Yield: 11.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.06 (s, 1H), 7.51 (s, 1H), 7.46-7.42 (m, 2H), 6.96 (d, 1H), 6.85 (dd, 1H), 3.95-3.94 (m, 1H), 3.93-3.90 (m, 2H), 3.81 (s, 3H), 3.58-3.55 (m, 1H), 3.54-3.52 (m, 3H), 3.01-2.98 (m, 1H), 2.98-2.94 (m, 1H), 2.69-2.63 (m, 1H), 1.96-1.95 (m, 1H), 1.93-1.91 (m, 2H), 1.79-1.73 (m, 3H), 1.62-1.58 (m, 1H), 1.33-1.29 (m, 1H) MS m/z= 504.2 (M+H)+
- [1230] Example 12: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1231] The titled compound (17.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-2 and C1-1. (Yield: 32.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.39 (d, 1H), 8.07 (s, 1H), 7.93 (s, 1H), 7.8 (s, 1H), 7.58 (s, 1H), 7.51-7.50 (m, 1H), 7.46-7.40 (m, 1H), 6.93 (d, 1H), 6.81 (dd, 1H), 3.81 (s, 3H), 3.7 (s, 3H), 3.69-3.68 (m, 1H), 3.32-3.31 (m, 1H), 3.28-3.27 (m, 1H), 3.06-3.03 (m, 1H), 2.62-2.58 (m, 1H), 2.42-2.37 (m, 1H), 1.97-1.96 (m, 1H), 1.70-1.69 (m, 1H), 1.59-1.58 (m, 1H), 1.34-1.32 (m, 1H) MS m/z= 476.1 (M+H)+
- [1232] Example 13: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1233] The titled compound (2.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-3 and C1-1. (Yield: 2.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.1 (s, 1H), 8.05 (s, 1H), 7.81 (s, 1H), 7.61 (s, 1H), 7.51-7.50 (m, 1H), 7.44-7.42 (m, 1H), 6.96 (d, 1H), 6.86 (dd, 1H), 4.60-4.56 (m, 1H), 3.82 (s, 3H), 3.79-3.69 (m, 1H), 3.29-3.28 (m, 1H), 3.06-3.03 (m, 1H), 2.63-2.60 (m, 1H), 2.45-2.40 (m, 1H), 1.96-1.93 (m, 1H), 1.55-1.53 (m, 1H), 1.36-1.33 (m, 1H), 1.29 (d, 6H), 0.92-0.88 (m, 2H) MS m/z= 504.2 (M+H)+
- [1234] Example 14: (3S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1235] The titled compound (9.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-4 and C1-1. (Yield: 12.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.09 (s, 1H), 8.06 (s, 1H), 7.83 (s, 1H), 7.6 (s, 1H), 7.51-7.50 (m, 1H), 7.44-7.42 (m, 1H), 6.96 (d, 1H), 6.86 (dd, 1H), 5.08-5.07 (m, 1H), 4.15-4.11 (m, 1H), 4.09-4.04 (m, 2H), 3.95-3.91 (m, 1H), 3.81 (s, 3H), 3.70-3.68 (m, 1H), 3.31-3.27 (m, 1H), 3.06-3.03 (m, 1H), 2.59-2.49 (m, 2H), 2.40-2.35 (m, 2H), 1.97-1.93 (m, 1H), 1.88-1.71 (m, 1H), 1.59-1.57 (m, 1H), 1.34-1.29 (m, 1H) MS m/z= 532.2 (M+H)+
- [1236] Example 15: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

- [1237] The titled compound (6.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-5 and C1-1. (Yield: 8.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.1 (d, 2H), 7.82 (s, 1H), 7.61 (s, 1H), 7.51-7.50 (m, 1H), 7.44-7.42 (m, 1H), 6.96 (d, 1H), 6.86 (dd, 1H), 4.25-4.22 (m, 1H), 3.82 (s, 3H), 3.72-3.70 (m, 1H), 3.04-3.02 (m, 3H), 2.62-2.59 (m, 1H), 2.57-2.41 (m, 1H), 2.39 (s, 3H), 2.35-2.27 (m, 2H), 2.24-2.12 (m, 4H), 1.95-1.93 (m, 1H), 1.74-1.71 (m, 1H), 1.58-1.55 (m, 1H), 1.35-1.33 (m, 1H) MS m/z= 559.3 (M+H)+
- [1238] Example 16: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1239] The titled compound (6.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-6 and C1-1. (Yield: 8.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.13 (d, 2H), 7.94 (s, 1H), 7.63 (s, 1H), 7.53-7.52 (m, 1H), 7.44-7.43 (m, 1H), 6.96 (d, 1H), 6.86 (dd, 1H), 5.02 (q, 2H), 3.82 (s, 3H), 3.79-3.70 (m, 1H), 3.31-3.26 (m, 1H), 3.05-3.02 (m, 1H), 2.62-2.57 (m, 1H), 2.48-2.43 (m, 1H), 1.95-1.93 (m, 1H), 1.72-1.60 (m, 1H), 1.57-1.54 (m, 1H), 1.35-1.29 (m, 1H) MS m/z= 544.2 (M+H)+
- [1240] Example 17: (S)-1-(5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1241] The titled compound (2.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-7 and C1-1. (Yield: 3.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.10 (d, 2H), 7.81 (s, 1H), 7.61 (s, 1H), 7.51-7.50 (m, 1H), 7.44-7.43 (m, 1H), 6.96 (d, 1H), 6.86 (dd, 1H), 4.06 (d, 2H), 3.84 (s, 3H), 3.74-3.70 (m, 1H), 3.07-3.04 (m, 1H), 2.63-2.58 (m, 1H), 2.45-2.40 (m, 1H), 1.97-1.93 (m, 1H), 1.75-1.71 (m, 1H), 1.62-1.56 (m, 2H), 1.35-1.33 (m, 1H), 0.95-0.92 (m, 1H), 0.62-0.51 (m, 2H), 0.42-0.32 (m, 2H) MS m/z= 516.2 (M+H)+
- [1242] Example 18: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(tetrahydro-2H-pyran-4-yl)phenyl)pyridin-4-yl)piperidin-3-ol
- [1243] The titled compound (14.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-12 and C1-1. (Yield: 18.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 7.90 (s, 1H), 7.56 (s, 1H), 7.52-7.40 (m, 5H), 7.33-7.31 (m, 2H), 6.96 (d, 1H), 6.86 (dd, 1H), 4.07-4.04 (m, 2H), 3.82 (s, 3H), 3.79-3.31 (m, 3H), 3.27-3.26 (m, 1H), 3.09-3.06 (m, 1H), 2.84-2.81 (m, 1H), 2.56-2.53 (m, 1H), 2.40-2.35 (m, 1H), 1.90-1.79 (m, 5H), 1.57-1.53 (m, 1H), 1.42-1.24 (m, 4H) MS m/z= 556.2 (M+H)+
- [1244] Example 19: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(4-methylpiperazin-1-yl)phenyl)pyridin-4-yl)piperidin-3-ol

- [1245] The titled compound (8.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-13 and C1-1. (Yield: 10.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 7.88 (s, 1H), 7.52-7.50 (m, 2H), 7.43-7.40 (m, 3H), 7.03 (d, 2H), 6.95 (d, 1H), 6.86 (dd, 1H), 3.81 (s, 3H), 3.56-3.54 (m, 1H), 3.31-3.24 (m, 5H), 3.10-3.07 (m, 1H), 2.65-2.64 (m, 4H), 2.55-2.51 (m, 1H), 2.37 (s, 3H), 2.34-2.32 (m, 1H), 1.92-1.55 (m, 1H), 1.62-1.55 (m, 1H), 1.29-1.26 (m, 1H) MS m/z= 570.3 (M+H)+
- [1246] Example 20: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1247] The titled compound (8.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-14 and C1-1. (Yield: 11.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.29 (s, 1H), 7.92 (s, 1H), 7.83-7.81 (m, 1H), 7.59 (s, 1H), 7.54-7.52 (m, 1H), 7.46-7.40 (m, 1H), 6.96 (d, 1H), 6.91 (d, 1H), 6.86 (dd, 1H), 3.82-8.80 (m, 7H), 3.56-3.55 (m, 1H), 3.54-3.50 (m, 4H), 3.31-3.28 (m, 1H), 3.10-3.07 (m, 1H), 2.59-2.53 (m, 1H), 2.40-2.35 (m, 1H), 1.93-1.90 (m, 1H), 1.64-1.61 (m, 1H), 1.48-1.45 (m, 1H), 1.33-1.29 (m, 1H) MS m/z= 558.2 (M+H)+
- [1248] Example 21: (S)-1-(2-((2-(4-(hydroxymethyl)thiophen-2-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1249] The titled compound (6.7 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C5-2. (Yield: 15.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.41-8.40 (m, 1H), 8.29-8.06 (m, 3H), 7.85 (d, 2H), 7.48-7.47 (m, 1H), 7.31 (s, 1H), 6.62-6.61 (m, 1H), 4.71 (s, 2H), 4.45-4.41 (m, 1H), 4.17-4.15 (m, 2H), 3.62-3.61 (m, 1H), 3.59-3.57 (m, 3H), 3.18-3.15 (m, 1H), 2.89-2.86 (m, 1H), 2.47-2.44 (m, 1H), 2.20-2.05 (m, 6H), 1.71-1.67 (m, 1H), 1.49-1.43 (m, 1H) MS m/z= 534.2 (M+H)+
- [1250] Example 22: (S)-1-(2-((2-(2,6-difluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1251] (3S)-1-[2-[(2-Chloropyrimidin-4-yl)amino]-5-(1-tetrahydropyran-4-ylpyrazol-4-yl)-4-pyridyl]piperidin-3-ol (Intermediate A1-2, 20.0 mg, 0.04 mmol) was dissolved in anhydrous 1,4-dioxane (0.6 mL) and water (0.2 mL) and then 2-(2,6-difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (21.0 mg, 0.08 mmol), XPhos Pd G2 (3.45 mg, 0.004 mmol), and K₃PO₄ (27.9 mL, 0.130 mmol) were added thereto. Then, the mixed solution was stirred in a microwave reactor for 1 hour. After completion of the reaction, the reaction mixture was cooled to room temperature and water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to

prepare the titled compound (3.1 mg). (Yield: 13.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.58 (s, 1H), 8.25 (s, 1H), 7.95 (d, 1H), 7.88 (s, 1H), 7.35-7.33 (m, 1H), 7.12 (s, 2H), 7.03-6.98 (m, 1H), 6.04 (d, 1H), 5.09-5.07 (m, 1H), 5.03 (s, 1H), 4.47-4.37 (m, 2H), 4.19-4.12 (m, 3H), 3.71-3.55 (m, 1H), 3.07-3.05 (m, 2H), 2.96-2.91 (m, 1H), 2.52-2.40 (m, 3H), 2.16-2.03 (m, 1H), 1.92-1.91 (m, 1H), 1.81-1.78 (m, 1H), 1.64-1.58 (m, 1H) MS m/z= 534.2 (M+H)+

[1252] Example 23: (S)-1-(2-((2-(3,6-difluoro-2-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1253] The titled compound (8.2 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to 2-(3,6-difluoro-2-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (Yield: 33.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.56 (s, 1H), 8.26 (s, 1H), 7.95 (d, 1H), 7.89 (s, 1H), 7.08-7.06 (m, 2H), 6.87-6.84 (m, 1H), 6.04 (d, 1H), 5.09-5.07 (m, 1H), 4.57-4.47 (m, 1H), 4.19-4.12 (m, 2H), 3.89 (s, 3H), 3.61-3.55 (m, 3H), 3.04-2.95 (m, 1H), 2.93-2.88 (m, 2H), 2.62-2.51 (m, 1H), 2.17-2.05 (m, 5H), 1.90-1.81 (m, 1H), 1.79-1.63 (m, 1H) MS m/z= 564.2 (M+H)+

[1254] Example 24: (S)-1-(2-((2-(2,3-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1255] The titled compound (4.7 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to (2,3-difluoro-6-methoxyphenyl)boronic acid. (Yield: 19.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.56 (s, 1H), 8.24 (s, 1H), 7.95 (d, 1H), 7.88 (s, 1H), 7.15-7.13 (m, 1H), 7.05 (s, 1H), 6.69-6.66 (m, 1H), 6.04 (d, 1H), 5.08-5.05 (m, 1H), 5.02 (s, 1H), 4.47-4.45 (m, 1H), 4.19-4.12 (m, 2H), 3.8 (s, 3H), 3.78-3.55 (m, 3H), 3.15-3.04 (m, 1H), 2.94-2.87 (m, 2H), 2.42-2.38 (m, 1H), 2.16-2.05 (m, 5H), 1.91-1.90 (m, 1H), 1.80-1.77 (m, 1H) MS m/z= 564.2 (M+H)+

[1256] Example 25: (S)-1-(2-((2-(2-ethoxy-6-fluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1257] The titled compound (4.9 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to 2-(2-ethoxy-6-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (Yield: 19.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.56 (s, 1H), 8.26 (s, 1H), 7.95 (d, 1H), 7.89 (s, 1H), 7.12 (s, 1H), 6.81-6.75 (m, 2H), 6.03 (d, 1H), 5.08-5.06 (m, 1H), 5.01 (s, 1H), 4.47-4.45 (m, 1H), 4.19-4.12 (m, 2H), 4.05 (q, 2H), 3.71-3.56 (m, 3H), 3.06-3.03 (m, 1H), 2.88-2.84 (m, 2H), 2.25-2.47 (m, 1H), 2.17-2.05 (m, 5H), 1.89-1.77 (m, 1H), 1.64-1.63 (m, 1H), 1.31 (t, 3H) MS m/z= 560.3 (M+H)+

[1258] Example 26: (S)-1-(2-((2-([1,2,4]triazolo[1,5-a]pyridin-7-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

- [1259] The titled compound (11.6 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,2,4]triazolo[1,5-a]pyridine. (Yield: 49.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.66 (d, 1H), 8.64 (s, 1H), 8.57-8.41 (m, 2H), 8.21 (s, 1H), 8.04 (d, 1H), 7.94-7.85 (m, 2H), 7.63 (s, 1H), 6.10-6.09 (d, 1H), 5.18 (brs, 2H), 4.49-4.46 (m, 1H), 4.18-4.13 (m, 2H), 3.69-3.56 (m, 3H), 3.15-3.08 (m, 2H), 3.00-2.98 (m, 1H), 2.40-2.37 (m, 1H), 2.17-2.05 (m, 5H), 1.94-1.89 (m, 1H), 1.63-1.62 (m, 1H) MS m/z= 539.2 (M+H)+
- [1260] Example 27: (S)-1-(2-((2-(pyrazolo[1,5-a]pyridin-3-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1261] The titled compound (4.1 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to 3-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)pyrazolo[1,5-a]pyridine. (Yield: 17.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.66 (d, 1H), 8.64 (s, 1H), 8.57-8.41 (m, 2H), 8.21 (s, 1H), 8.04 (d, 1H), 7.94-7.85 (m, 2H), 7.63 (s, 1H), 6.10-6.09 (d, 1H), 5.18 (brs, 2H), 4.49-4.46 (m, 1H), 4.18-4.13 (m, 2H), 3.69-3.56 (m, 3H), 3.15-3.08 (m, 2H), 3.00-2.98 (m, 1H), 2.40-2.37 (m, 1H), 2.17-2.05 (m, 5H), 1.94-1.89 (m, 1H), 1.63-1.62 (m, 1H) MS m/z= 538.2 (M+H)+
- [1262] Example 28: (S)-1-(2-((2-(quinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1263] The titled compound (6.9 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to quinoxalin-6-ylboronic acid reagent. (Yield: 28.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.89 (d, 2H), 8.66 (s, 1H), 8.62 (s, 1H), 8.58-8.56 (m, 1H), 8.26 (s, 1H), 8.19 (d, 1H), 8.03 (d, 1H), 7.91 (s, 1H), 7.65 (s, 1H), 6.07 (d, 1H), 5.17-5.16 (m, 1H), 5.06 (s, 1H), 4.52-4.48 (m, 1H), 4.19-4.13 (m, 2H), 3.71-3.68 (m, 1H), 3.63-3.57 (m, 2H), 3.12-3.11 (m, 1H), 3.07-3.05 (m, 1H), 3.04-2.96 (m, 1H), 2.43-2.39 (m, 1H), 2.18-2.09 (m, 5H), 1.93-1.90 (m, 1H), 1.88-1.85 (m, 1H) MS m/z= 550.2 (M+H)+
- [1264] Example 29: (S)-1-(2-((2-(8-fluoroquinolin-7-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1265] The titled compound (6.6 mg) was prepared in accordance with the same procedures as in Example 22, changing the boronic acid reagent to 8-fluoro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline. (Yield: 26.5%) ¹H NMR (CD₃OD, 400MHz) δ 9.02-9.01 (m, 1H), 8.63 (s, 1H), 8.3 (s, 1H), 8.22-8.20 (m, 2H), 7.98 (d, 1H), 7.9 (s, 1H), 7.72-7.70 (m, 2H), 7.52-7.51 (m, 1H), 6.04 (d, 1H), 5.13-5.11 (m, 1H), 5.05 (s, 1H), 4.52-4.48 (m, 1H), 4.19-4.13 (m, 2H), 3.65-3.56 (m, 3H), 3.10-3.00 (m, 1H), 2.99-2.96 (m, 2H), 2.52-2.47 (m, 1H), 2.18-2.04 (m, 4H), 1.85-1.83 (m, 1H), 1.67-1.66 (m, 1H), 1.64-1.61 (m, 2H) MS m/z= 567.3 (M+H)+

- [1266] Example 30: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((4-methylpiperazin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1267] The titled compound (7.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-2 and C1-1. (Yield: 20.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.74 (s, 1H), 8.61 (d, 1H), 8.01 (s, 1H), 7.80 (d, 1H), 7.56 (s, 1H), 7.45-7.43 (m, 2H), 7.39-7.36 (m, 2H), 6.84-6.80 (m, 2H), 3.89 (s, 3H), 3.71 (s, 2H), 3.66-3.61 (m, 1H), 3.06 (d, 1H), 3.01-2.97 (m, 1H), 2.68-2.50 (m, 9H), 2.01 (s, 3H), 1.83-1.62 (m, 9H) MS m/z= 586.3 (M+H)+
- [1268] Example 31: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1269] The titled compound (8.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-1 and C1-1. (Yield: 19.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.71 (s, 1H), 8.58 (d, 1H), 7.99 (s, 2H), 7.81 (d, 1H), 7.43 (s, 1H), 7.38-7.31 (m, 2H), 7.27-7.23 (m, 2H), 6.83-6.79 (m, 2H), 4.14-4.11 (m, 2H), 3.82 (s, 3H), 3.70-3.69 (m, 1H), 3.60-3.55 (m, 2H), 3.19-3.16 (m, 1H), 3.10-3.00 (m, 1H), 2.98-2.82 (m, 1H), 2.67-2.62 (m, 2H), 1.95-1.93 (m, 4H), 1.92-1.91 (m, 1H), 1.41-1.39 (m, 1H), 1.31-1.27 (m, 2H) MS m/z= 557.2 (M+H)+
- [1270] Example 32: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(morpholinomethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1271] The titled compound (1.7 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-3 and C1-1. (Yield: 5.01%) ¹H NMR (CDCl₃, 400MHz) δ 8.74 (s, 1H), 8.61 (d, 1H), 8.00 (s, 1H), 7.83 (d, 1H), 7.55-7.53 (m, 1H), 7.49 (d, 1H), 7.43-7.35 (m, 3H), 6.84-6.80 (m, 2H), 3.83 (s, 3H), 3.78-3.76 (m, 4H), 3.72 (s, 3H), 3.18-3.15 (m, 1H), 2.95-2.92 (m, 1H), 2.75-2.65 (m, 3H), 2.01 (s, 4H), 1.86-1.85 (m, 1H), 1.41-1.40 (m, 1H) MS m/z= 573.3 (M+H)+
- [1272] Example 33: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((4-hydroxypiperidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1273] The titled compound (1.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-4 and C1-1. (Yield: 3.17%) ¹H NMR (CDCl₃, 400MHz) δ 8.74 (s, 1H), 8.61 (d, 1H), 8.00 (s, 1H), 7.84-7.81 (m, 1H), 7.53-7.35 (m, 5H), 6.82-6.80 (m, 2H), 3.83 (s, 3H), 3.74-3.73 (m, 4H), 3.18-3.12 (m, 1H), 2.97-2.94 (m, 1H), 2.88-2.83 (m, 1H), 2.73-2.60 (m, 4H), 2.38-2.30 (m, 2H), 1.94-1.86 (m, 4H), 1.49-1.40 (m, 3H). MS m/z= 587.3 (M+H)+
- [1274] Example 34: 1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide
- [1275] The titled compound (8.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-6 and C1-1. (Yield: 32.6%) ¹H NMR (CD₃

OD, 400MHz) δ 8.41 (d, 1H), 8.09 (s, 1H), 8.04 (s, 1H), 7.84 (s, 1H), 7.60 (s, 1H), 7.51 (d, 1H), 7.44 (q, 1H), 6.96 (d, 1H), 6.85 (t, 1H), 4.49-4.44 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.60 (t, 2H), 3.32-3.20 (m, 2H), 2.69 (t, 1H), 2.57-2.52 (m, 2H), 2.15-2.09 (m, 4H), 2.09-1.94 (m, 1H), 1.66-1.55 (m, 3H) MS m/z = 573.3 (M+H)+

[1276] Example 35: (S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1277] The titled compound (4.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C1-8. (Yield: 22.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.05 (s, 1H), 7.74 (s, 2H), 7.68-7.66 (m, 1H), 7.57-7.53 (m, 1H), 7.34-7.33 (m, 1H), 7.01 (s, 1H), 6.85-6.80 (m, 2H), 4.41-4.37 (m, 1H), 3.83 (d, 2H), 3.81 (s, 3H), 3.58 (t, 2H), 3.24-3.21 (m, 1H), 2.98-2.95 (m, 1H), 2.73-2.70 (m, 2H), 2.16-2.06 (m, 5H), 1.94-1.88 (m, 1H), 1.78-1.74 (m, 1H), 1.52-1.49 (m, 2H). MS m/z = 545.4 (M+H)+

[1278] Example 36: (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-methylpiperazin-1-yl)methanone

[1279] The titled compound (2.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-5 and C1-1. (Yield: 7.63%) ¹H NMR (CDCl₃, 400MHz) δ 8.78 (s, 1H), 8.62 (d, 1H), 8.00-7.96 (m, 2H), 7.75 (d, 1H), 7.61-7.59 (m, 1H), 7.53-7.50 (m, 1H), 7.40-7.34 (m, 2H), 6.85-6.81 (m, 2H), 3.90-3.88 (m, 2H), 3.81 (s, 3H), 3.75-3.72 (m, 3H), 3.03-3.02 (m, 2H), 2.68-2.65 (m, 2H), 2.58-2.56 (m, 2H), 2.52-2.49 (m, 2H), 2.20 (s, 3H), 2.06-2.01 (m, 2H), 1.43-1.41 (m, 2H). MS m/z = 599.2 (M+H)+

[1280] Example 37: (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(morpholino)methanone

[1281] The titled compound (1.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-6 and C1-1. (Yield: 5.93%) ¹H NMR (CDCl₃, 400MHz) δ 8.78 (s, 1H), 8.62 (d, 1H), 8.00-7.98 (m, 2H), 7.75 (d, 1H), 7.53-7.49 (m, 2H), 7.40-7.34 (m, 2H), 6.85-6.81 (m, 2H), 3.86-3.82 (m, 7H), 3.79-3.70 (m, 6H), 3.18-3.16 (m, 1H), 2.98-2.94 (m, 1H), 2.68-2.63 (m, 2H), 2.03-2.00 (m, 1H), 1.91-1.88 (m, 1H), 1.43-1.41 (m, 2H). MS m/z = 586.2 (M+H)+

[1282] Example 38: (S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone

[1283] The titled compound (2.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-7 and C1-1. (Yield: 7.31%) ¹H NMR (CD₃OD, 400MHz) δ 8.81 (s, 1H), 8.45 (d, 1H), 8.16 (d, 1H), 8.05 (s, 1H), 7.70-7.66 (m, 2H), 7.57 (d, 1H), 7.46-7.42 (m, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 4.21-4.19 (m, 1H), 3.83 (s, 3H), 3.74-3.71 (m, 1H), 3.60-3.56 (m, 1H), 3.55-3.53 (m, 1H), 3.49-3.40 (m,

- 1H), 3.19-3.16 (m, 1H), 3.08-3.05 (m, 1H), 2.65-2.60 (m, 1H), 2.46-2.41 (m, 1H), 2.06-1.98 (m, 3H), 1.95-1.89 (m, 2H), 1.63-1.50 (m, 4H). MS m/z= 600.3 (M+H)+
- [1284] Example 39: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(((S)-3-fluoropyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1285] The titled compound (2.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A8-1 and C1-1. (Yield: 7.13%) ¹H NMR (CD₃OD, 400MHz) δ 8.74 (s, 1H), 8.61 (d, 1H), 8.00 (s, 1H), 7.83 (d, 1H), 7.55-7.53 (m, 1H), 7.49 (d, 1H), 7.43-7.35 (m, 3H), 6.84-6.80 (m, 2H), 3.83 (s, 3H), 3.78-3.76 (m, 4H), 3.72 (s, 3H), 3.18-3.15 (m, 1H), 2.95-2.92 (m, 1H), 2.75-2.65 (m, 3H), 2.01 (s, 4H), 1.86-1.85 (m, 1H), 1.41-1.40 (m, 8H). MS m/z= 574.3 (M+H)+
- [1286] Example 40: (3S)-1-(2-((5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1287] The titled compound (8.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C1-2. (Yield: 28.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.69 (s, 1H), 8.44 (d, 1H), 8.04 (d, 1H), 8.00 (s, 1H), 7.67-7.55 (m, 3H), 7.57 (d, 1H), 6.97 (d, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 3.87 (s, 2H), 3.83 (s, 3H), 3.54-3.49 (m, 2H), 3.22-3.14 (m, 1H), 3.07-3.02 (m, 1H), 2.99-2.93 (m, 2H), 2.87-2.75 (m, 1H), 2.62-2.53 (m, 2H), 2.44-2.39 (m, 1H), 2.08-2.02 (m, 2H), 1.93-1.90 (m, 1H), 1.61-1.58 (m, 2H), 1.45-1.42 (m, 1H). MS m/z= 563.4 (M+H)+
- [1288] Example 41: (3S)-1-(2-(((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1289] The titled compound (6.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C3-1. (Yield: 20.7%) ¹H NMR (CDCl₃, 400MHz) δ 8.38 (d, 1H), 8.11 (s, 1H), 7.78 (s, 2H), 7.69-7.68 (m, 1H), 7.53-7.45 (m, 2H), 7.41-7.36 (m, 1H), 6.89-6.84 (m, 1H), 6.77 (d, 1H), 4.44-4.37 (m, 1H), 4.16-4.11 (m, 3H), 3.85-3.79 (m, 1H), 3.75 (s, 3H), 3.61-3.56 (m, 3H), 3.20-3.14 (m, 1H), 2.97-2.89 (m, 1H), 2.20 (s, 2H), 2.16-2.04 (m, 4H), 1.90-1.87 (m, 1H), 1.75-1.70 (m, 1H). MS m/z= 590.2 (M+H)+
- [1290] Example 42: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1291] The titled compound (2.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-15 and C1-1. (Yield: 4.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.78 (s, 1H), 8.60-8.57 (m, 2H), 7.99 (s, 1H), 7.87-7.85 (m, 1H), 7.81 (s, 1H), 7.45 (s, 1H), 7.40-7.27 (m, 2H), 6.84-6.80 (m, 2H), 3.83 (s, 3H), 3.70-3.62 (m, 1H), 3.19-3.16 (m, 1H), 2.95-2.92 (m, 1H), 2.67-2.62 (m, 2H), 1.85-1.74 (m, 2H), 1.60-1.52 (m, 1H), 1.44-1.31 (m, 2H) MS m/z= 473.2 (M+H)+

- [1292] Example 43: (3S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((3-hydroxypyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1293] The titled compound (6.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A8-2 and C1-1. (Yield: 15.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (s, 1H), 8.44 (d, 1H), 8.03 (d, 1H), 8.00 (s, 1H), 7.67-7.55 (m, 3H), 7.46-7.42 (m, 1H), 6.97 (d, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 3.82 (s, 3H), 3.54-3.49 (m, 1H), 3.22-3.19 (m, 1H), 3.07-3.04 (m, 1H), 2.89-2.85 (m, 2H), 2.62-2.56 (m, 3H), 2.44-2.39 (m, 1H), 2.21-2.14 (m, 2H), 2.04-2.02 (m, 1H), 1.92-1.90 (m, 2H), 1.77-1.72 (m, 1H), 1.62-1.60 (m, 1H), 1.46-1.43 (m, 1H). MS m/z= 572.2 (M+H)+
- [1294] Example 44: N-(4-(3-(dimethylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1295] The titled compound (6.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-1 and C1-1. (Yield: 17.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.39 (d, 1H), 7.79 (s, 1H), 7.76 (s, 1H), 7.53 (s, 1H), 7.46-7.35 (m, 3H), 6.96 (d, 1H), 6.83 (t, 1H), 4.48-4.41 (m, 1H), 4.08 (d, 2H), 3.81 (s, 3H), 3.59 (t, 2H), 3.19-3.13 (m, 3H), 2.91 (t, 1H), 2.72-2.63 (m, 1H), 2.16 (s, 6H), 2.14-2.02 (m, 4H), 1.73-1.65 (m, 1H), 1.41-1.29 (m, 1H) MS m/z= 559.2 (M+H)+
- [1296] Example 45: (1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-3-methylpyrrolidin-3-yl)methanol
- [1297] The titled compound (12.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-2 and C1-1. (Yield: 34.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 7.77 (s, 1H), 7.75 (s, 1H), 7.51 (s, 1H), 7.43 (q, 1H), 7.39 (s, 1H), 7.34 (d, 1H), 6.96 (d, 1H), 6.84 (t, 1H), 4.46-4.43 (m, 1H), 4.08 (d, 2H), 3.82 (s, 3H), 3.59 (t, 2H), 3.35-3.31 (m, 2H), 3.14-3.08 (m, 2H), 3.03 (dd, 1H), 2.74 (dd, 1H), 2.13-2.07 (m, 4H), 1.81-1.77 (m, 1H), 1.56-1.51 (m, 1H) MS m/z= 560.2 (M+H)+
- [1298] Example 46: N-(4-(4-((dimethylamino)methyl)-4-fluoropiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1299] The titled compound (2.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-3 and C1-1. (Yield: 7.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.09 (s, 1H), 8.06 (s, 1H), 7.86 (s, 1H), 7.77 (s, 1H), 7.48-7.42 (m, 2H), 6.96 (d, 1H), 6.85 (t, 1H), 4.50-4.44 (m, 1H), 4.09 (d, 2H), 3.83 (s, 3H), 3.60 (t, 2H), 3.13 (d, 2H), 2.85 (t, 2H), 2.54 (s, 1H), 2.48 (s, 1H), 2.31 (s, 6H), 2.15-2.06 (m, 4H), 1.87-1.77 (m, 1H), 1.75-1.69 (m, 1H) MS m/z= 606.3 (M+H)+

- [1300] Example 47: (4-(2,2-difluoroethyl)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)methanol
- [1301] The titled compound (14.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-4 and C1-1. (Yield: 53.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.08 (s, 1H), 8.07 (s, 1H), 7.85 (s, 1H), 7.74 (s, 1H), 7.47-7.41 (m, 2H), 6.96 (d, 1H), 6.84 (t, 1H), 6.12 (t, 1H), 4.50-4.45 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.60 (t, 2H), 3.50 (s, 2H), 2.99-2.94 (m, 2H), 2.90-2.84 (m, 2H), 2.15-2.09 (m, 4H), 2.00-1.89 (m, 2H), 1.62-1.46 (m, 4H) MS m/z= 624.3 (M+H)+
- [1302] Example 48: (3S)-1-(6'-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1303] The titled compound (5.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A8-3 and C1-1. (Yield: 16.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (s, 1H), 8.44 (d, 1H), 8.03 (d, 1H), 8.00 (s, 1H), 7.67 (s, 1H), 7.60-7.55 (m, 2H), 7.46-7.42 (m, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 3.89-3.77 (m, 5H), 3.53-3.49 (m, 1H), 3.21-3.18 (m, 1H), 3.07-3.04 (m, 1H), 2.95-2.91 (m, 2H), 2.83-2.79 (m, 1H), 2.68-2.56 (m, 2H), 2.47-2.40 (m, 2H), 2.25 (s, 6H), 2.08-2.02 (m, 1H), 1.92-1.90 (m, 1H), 1.78-1.73 (m, 1H), 1.63-1.60 (m, 1H), 1.46-1.42 (m, 1H). MS m/z= 599.3 (M+H)+
- [1304] Example 49: 1-((6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)methyl)piperidin-3-ol
- [1305] The titled compound (2.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A8-4 and C1-1. (Yield: 6.91%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (s, 1H), 8.44 (d, 1H), 8.04-8.00 (m, 2H), 7.67-7.55 (m, 3H), 7.48-7.42 (m, 1H), 7.57 (d, 1H), 6.85 (t, 1H), 3.83 (s, 3H), 3.74-3.67 (m, 4H), 3.60-3.49 (m, 2H), 3.21-3.18 (m, 1H), 3.07-3.03 (m, 1H), 2.92-2.87 (m, 1H), 2.72-2.71 (m, 1H), 2.61-2.56 (m, 1H), 2.44-2.39 (m, 1H), 2.19-2.16 (m, 1H), 2.25 (s, 1H), 1.96-1.91 (m, 2H), 1.81-1.76 (m, 1H), 1.61-1.54 (m, 2H), 1.43-1.41 (m, 1H). MS m/z= 586.2 (M+H)+
- [1306] Example 50: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide
- [1307] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-5 and C1-1. (Yield: 12.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.09 (s, 1H), 8.04 (s, 1H), 7.84 (s, 1H), 7.60 (s, 1H), 7.52-7.43 (m, 2H), 6.96 (d, 1H), 6.86 (t, 1H), 4.54-4.40 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.63 (t, 2H), 3.32-3.14 (m, 2H), 2.69 (t, 1H), 2.55-2.53 (m, 2H), 2.15-2.09 (m, 4H), 2.09-1.94 (m, 1H), 1.66-1.56 (m, 3H) MS m/z= 573.3 (M+H)+

- [1308] Example 51: (R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide
- [1309] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-6 and C1-1. (Yield: 10.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.09 (s, 1H), 8.04 (s, 1H), 7.84 (s, 1H), 7.60 (s, 1H), 7.52-7.41 (m, 2H), 6.96 (d, 1H), 6.85 (t, 1H), 4.56-4.40 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.63 (t, 2H), 3.32-3.20 (m, 2H), 2.69 (t, 1H), 2.60-2.48 (m, 2H), 2.15-2.02 (m, 4H), 2.02-1.95 (m, 1H), 1.66-1.55 (m, 3H) MS m/z= 573.3 (M+H)+
- [1310] Example 52: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1311] Step 1: tert-butyl (S)-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [1312] tert-Butyl (S)-(1-(2-chloro-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate (intermediate A3-1, 100 mg, 0.21 mmol) was dissolved in anhydrous 1,4-dioxane (4.0 mL) and then 2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine (C1-1, 47.4 mg, 0.21 mmol), tris(dibenzylideneacetone)dipalladium(0) (59.4 mg, 0.065 mmol), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (61.9 mg, 0.13 mmol), and cesium carbonate (211.6 mg, 0.65 mmol) were added dropwise thereto. Then, the mixed solution was refluxed under stirring at 100°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and water was added thereto. The aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (75.8 mg). (Yield: 54.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.58 (d, 1H), 8.11 (s, 1H), 7.79-7.76 (m, 2H), 7.41 (s, 1H), 7.38-7.33 (m, 3H), 6.85-6.80 (m, 2H), 4.48-4.38 (m, 2H), 4.16-4.13 (m, 2H), 3.82 (s, 3H), 3.74-3.73 (m, 1H), 3.71-3.55 (m, 2H), 3.37-3.35 (m, 1H), 3.05-3.03 (m, 1H), 2.56-2.47 (m, 2H), 2.16-2.11 (m, 4H), 1.95-1.93 (m, 1H), 1.57-1.54 (m, 1H), 1.52 (s, 9H), 1.45-1.32 (m, 1H)
- [1313] Step 2: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1314] tert-Butyl (S)-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate (75.0 mg, 0.12 mmol) was dissolved in dichloromethane (5.0 ml) and then 4.0M hydrochloric acid solution dissolved in 1,4-dioxane (1.5 ml, 7.69 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 4 hours. After completion of the reaction, the reaction mixture was concentrated and the

resulting solid was dried to prepare the titled compound (60.0 mg). (Yield: 82.3%)
1H NMR (CD₃OD, 400MHz) δ 8.72 (d, 1H), 8.16 (s, 1H), 8.13 (s, 1H), 7.85 (s, 1H), 7.65-7.40 (m, 2H), 7.14-7.09 (m, 2H), 6.97 (t, 1H), 4.54-4.50 (m, 1H), 4.10 (d, 2H), 3.92 (s, 3H), 3.81 (d, 1H), 3.60 (t, 2H), 3.58-3.32 (m, 2H), 2.95-2.85 (m, 2H), 2.21-2.11 (m, 5H), 1.86-1.58 (m, 3H) MS m/z= 545.4 (M+H)+

[1315] Example 53: (R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine

[1316] The titled compound (4.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-7 and C1-1. (Yield: 70.0%) 1H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.20-8.10 (m, 2H), 7.45 (s, 1H), 7.66 (q, 1H), 7.54 (s, 1H), 7.22 (s, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 4.54-4.51 (m, 1H), 4.09 (d, 2H), 3.95 (s, 3H), 3.88 (d, 1H), 3.66-3.57 (m, 3H), 3.57-3.32 (m, 1H), 3.04-2.90 (m, 2H), 2.22-2.11 (m, 5H), 1.85-1.58 (m, 3H) MS m/z= 545.4 (M+H)+

[1317] Example 54: (6'-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone

[1318] The titled compound (2.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-7 and C3-1. (Yield: 6.48%) 1H NMR (CD₃OD, 400MHz) δ 8.74 (s, 1H), 8.57 (d, 1H), 8.09-8.08 (m, 1H), 7.99 (s, 1H), 7.71 (d, 1H), 7.55-7.49 (m, 1H), 7.28 (d, 1H), 4.18-4.20 (m, 1H), 3.94-3.91 (m, 1H), 3.79 (s, 3H), 3.69-3.67 (m, 3H), 3.49-3.41 (m, 2H), 3.14-3.12 (m, 1H), 2.97-2.91 (m, 1H), 1.89-1.80 (m, 3H), 1.51-1.47 (m, 6H) MS m/z= 644.3 (M+H)+

[1319] Example 55: (S)-1-(6'-((4-aminopiperidin-1-yl)methyl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol hydrochloride

[1320] The titled compound (1.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A8-5 and C1-1. (Yield: 13.5%) 1H NMR (CD₃OD, 400MHz) δ 8.85 (s, 1H), 8.72 (d, 1H), 8.09-8.06 (m, 2H), 7.71 (d, 1H), 7.62-7.56 (m, 1H), 7.38-7.30 (m, 1H), 7.10-7.07 (m, 2H), 6.95 (t, 1H), 3.90 (s, 3H), 3.79-3.76 (m, 2H), 3.68-3.65 (m, 1H), 3.75 (s, 1H), 3.40-3.38 (m, 3H), 3.18-3.05 (m, 1H), 2.92-2.86 (m, 1H), 2.20 (s, 2H), 2.16-2.11 (m, 3H), 1.93-1.83 (m, 2H), 1.55-1.50 (m, 3H). MS m/z= 585.3 (M+H)+

[1321] Example 56: (S)-1-(6'-ethoxy-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol

[1322] The titled compound (1.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-16 and C1-1. (Yield: 2.4%) 1H NMR (CDCl₃, 400MHz) δ 8.43 (d, 1H), 8.26 (s, 1H), 7.94 (s, 1H), 7.93 (d, 1H), 7.62 (s, 1H), 7.55-7.53 (m, 1H), 7.45-7.43 (m, 1H), 6.97 (d, 1H), 6.87-6.82 (m, 2H), 4.38 (q, 2H), 3.82 (s, 3H), 3.57-3.53 (m, 1H), 3.27-3.24 (m, 1H), 3.09-3.06 (m, 1H), 2.60-2.55 (m,

- 1H), 2.42-2.37 (m, 1H), 1.64-1.61 (m, 1H), 1.47-1.42 (m, 1H), 1.39 (t, 3H) MS m/z= 503.1 (M+H)+
- [1323] Example 57: (S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(tri fluoromethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol
- [1324] The titled compound (9.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-17 and C1-1. (Yield: 14.9%) ¹H NMR (CD₃ OD, 400MHz) δ 8.93 (s, 1H), 8.45 (d, 1H), 8.27 (d, 1H), 8.05 (s, 1H), 7.89 (d, 1H), 7.7 (s, 1H), 7.58-7.56 (m, 1H), 7.45-7.43 (m, 1H), 6.97 (d, 1H), 6.85 (dd, 1H), 3.82 (s, 3H), 3.56-3.31 (m, 1H), 3.18-3.17 (m, 1H), 3.04-3.01 (m, 1H), 2.64-2.62 (m, 1H), 2.48-2.43 (m, 1H), 1.92-1.88 (m, 1H), 1.65-1.60 (m, 1H), 1.44-1.41 (m, 1H), 1.31-1.28 (m, 1H) MS m/z= 541.2 (M+H)+
- [1325] Example 58: (3S)-1-(2-(((6-(2-fluoro-6-methoxyphenyl)-5-methylpyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1326] The titled compound (7.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C1-4. (Yield: 23.6%) ¹H NMR (CDCl₃, 400MHz) δ 7.75-7.55 (m, 3H), 7.53-7.35 (m, 3H), 7.22-7.15 (m, 1H), 6.87-6.82 (m, 2H), 4.42-4.36 (m, 1H), 4.15-4.12 (m, 2H), 3.93-3.87 (m, 1H), 3.80 (s, 3H), 3.60-3.54 (m, 3H), 3.17-2.87 (m, 2H), 2.28-1.96 (m, 7H), 1.89-1.86 (m, 2H). MS m/z= 559.2 (M +H)+
- [1327] Example 59: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile
- [1328] The titled compound (1.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C8-1. (Yield: 4.55%) ¹H NMR (CDCl₃, 400MHz) δ 8.07-8.03 (m, 1H), 7.83 (d, 1H), 7.75 (s, 2H), 7.63-7.53 (m, 1H), 7.45-7.40 (m, 2H), 6.88-6.84 (m, 2H), 4.43-4.38 (m, 1H), 4.15 (d, 2H), 3.88 (s, 3H), 3.84-3.76 (m, 1H), 3.58 (t, 3H), 3.20-3.18 (m, 1H), 2.72-2.70 (m, 1H), 2.18-2.03 (m, 5H), 1.90-1.88 (m, 1H), 1.78-1.73 (m, 1H), 1.52-1.49 (m, 1H) MS m/z= 570.2 (M+H)+
- [1329] Example 60: methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate
- [1330] The titled compound (1.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C2-1. (Yield: 4.52%) ¹H NMR (CDCl₃, 400MHz) δ 8.27 (d, 1H), 8.10-8.05 (m, 1H), 7.74 (s, 2H), 7.64-7.53 (m, 1H), 7.45-7.34 (m, 2H), 6.85-6.76 (m, 2H), 4.43-4.36 (m, 1H), 4.15 (d, 2H), 3.81-3.80 (m, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 3.58 (t, 2H), 3.17-3.10 (m, 1H), 2.97-2.90 (m, 1H), 2.74-2.67 (m, 1H), 2.14-2.03 (m, 5H), 1.89-1.85 (m, 1H), 1.74-1.70 (m, 1H), 1.50-1.46 (m, 2H) MS m/z= 603.2 (M+H)+

- [1331] Example 61: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(imidazo[1,2-a]pyridin-6-yl)pyridin-4-yl)piperidin-3-ol
- [1332] The titled compound (2.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-18 and C1-1. (Yield: 5.6%) ¹H NMR (CDCl₃, 400MHz) δ 8.61 (d, 1H), 8.27 (s, 1H), 8.03 (s, 1H), 7.66 (d, 3H), 7.62-7.53 (m, 1H), 7.45-7.33 (m, 4H), 6.85-6.80 (m, 2H), 3.83 (s, 3H), 3.82-3.75 (m, 1H), 3.28-3.25 (m, 1H), 3.04-3.01 (m, 1H), 2.76-2.69 (m, 2H), 1.92-1.87 (m, 1H), 1.71-1.70 (m, 2H), 1.65-1.58 (m, 2H) MS m/z= 512.2 (M+H)+
- [1333] Example 62: (S)-1-(5-([1,2,4]triazolo[4,3-a]pyridin-6-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1334] The titled compound (2.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-19 and C1-1. (Yield: 4.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.84 (s, 1H), 8.62 (d, 1H), 8.26 (s, 1H), 8.02 (s, 1H), 7.81-7.79 (m, 1H), 7.56-7.54 (m, 2H), 7.40-7.34 (m, 2H), 6.85-6.81 (m, 2H), 3.83 (s, 3H), 3.75-3.62 (m, 1H), 3.28-3.25 (m, 1H), 3.12-3.02 (m, 1H), 2.79-2.70 (m, 2H), 2.05-2.03 (m, 1H), 1.90-1.87 (m, 2H), 1.69-1.59 (m, 2H) MS m/z= 513.2 (M+H)+
- [1335] Example 63: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-yl)amino)nicotinonitrile
- [1336] The titled compound (7.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A9-1 and C8-1. (Yield: 22.9%) ¹H NMR (CDCl₃, 400MHz) 8.57 (d, 1H), 8.08 (s, 1H), 8.04 (s, 1H), 7.99 (d, 1H), 7.61 (d, 2H), 7.41-7.39 (m, 1H), 6.86-6.82 (m, 2H), 4.21-4.16 (m, 1H), 3.85 (s, 3H), 3.59-3.55 (m, 1H), 3.34-3.32 (m, 2H), 3.15-3.12 (m, 1H), 3.02-2.99 (m, 2H), 2.35 (s, 3H), 2.23-2.05 (m, 6H), 1.87-1.85 (m, 1H), 1.77-1.76 (m, 1H), 1.62-1.58 (m, 1H), 1.47-1.45 (m, 1H) MS m/z= 564.3 (M+H)+
- [1337] Example 64: N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1338] The titled compound (6.7 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-8 and C1-1. (Yield: 43.6%) ¹H NMR (CDCl₃, 400MHz) δ 8.70 (d, 1H), 7.96-7.84 (m, 1H), 7.63 (s, 1H), 7.62 (s, 1H), 7.53-7.50 (m, 2H), 7.43 (q, 1H), 7.01-6.84 (m, 2H), 4.45-4.40 (m, 1H), 4.16 (d, 2H), 3.86 (s, 3H), 3.69 (d, 2H), 3.59 (t, 2H), 3.10-2.98 (m, 2H), 2.81 (t, 2H), 2.81 (s, 6H), 2.14-2.01 (m, 5H), 1.88-1.85 (m, 2H), 1.75-1.72 (m, 2H), 1.38-1.11 (m, 2H) MS m/z= 601.3 (M+H)+
- [1339] Example 65: 1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)cyclopropan-1-ol

- [1340] The titled compound (1.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-9 and C1-1. (Yield: 8.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 8.08 (s, 1H), 8.05 (s, 1H), 7.83 (s, 1H), 7.60 (s, 1H), 7.47-7.44 (m, 2H), 6.98 (d, 1H), 6.86 (t, 1H), 4.49-4.46 (m, 1H), 4.09 (d, 2H), 3.83 (s, 3H), 3.63-3.57 (m, 6H), 3.38-3.31 (m, 2H), 2.63 (t, 2H), 2.58-2.52 (m, 2H), 2.17-2.02 (m, 5H), 1.80-1.76 (m, 2H), 1.67-1.57 (m, 2H), 1.03 (t, 2H) MS m/z= 586.3 (M+H)+
- [1341] Example 66: 1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)ethan-1-ol
- [1342] The titled compound (8.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-10 and C1-1. (Yield: 35.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.58 (d, 1H), 8.07 (s, 1H), 7.81 (s, 1H), 7.77 (s, 1H), 7.52 (d, 1H), 7.35 (q, 1H), 7.23 (s, 1H), 6.83-6.79 (m, 2H), 4.44-4.37 (m, 1H), 4.13 (d, 2H), 3.82 (s, 3H), 3.61-3.55 (m, 3H), 3.45-3.32 (m, 2H), 2.53 (t, 2H), 2.19-2.03 (m, 4H), 1.84-1.81 (m, 1H), 1.80-1.43 (m, 4H), 1.20 (d, 3H) MS m/z= 574.2 (M+H)+
- [1343] Example 67: 2-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-2-methylpropan-1-ol
- [1344] The titled compound (7.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-11 and C1-1. (Yield: 28.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.58 (d, 1H), 8.08 (s, 1H), 7.81 (s, 1H), 7.79 (s, 1H), 7.59 (d, 1H), 7.35 (q, 1H), 7.14 (s, 1H), 6.83-6.79 (m, 2H), 4.45-4.38 (m, 1H), 4.14 (d, 2H), 3.82 (s, 3H), 3.58 (t, 2H), 3.42-3.39 (m, 4H), 2.52 (t, 2H), 2.20-2.03 (m, 5H), 1.64-1.60 (m, 2H), 1.44-1.26 (m, 2H), 0.86 (s, 6H) MS m/z= 602.3 (M+H)+
- [1345] Example 68: 2-(2-fluoro-6-methoxyphenyl)-N-(4-(4-methylpiperazin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine
- [1346] The titled compound (14.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-12 and C1-1. (Yield: 37.1%) ¹H NMR (CDCl₃, 400MHz) δ 8.58 (d, 1H), 8.06 (s, 1H), 7.80 (s, 1H), 7.74 (s, 1H), 7.65 (s, 1H), 7.64-7.32 (m, 2H), 6.83-6.79 (m, 2H), 4.44-4.38 (m, 1H), 4.15 (d, 2H), 3.82 (s, 3H), 3.59 (t, 2H), 3.20-3.02 (m, 4H), 2.58-2.42 (m, 4H), 2.37 (s, 3H), 2.19-2.03 (m, 4H) MS m/z= 545.3 (M+H)+
- [1347] Example 69: (S)-1-(2-((2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1348] The titled compound (7.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C1-6. (Yield: 22.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.97 (d, 1H), 8.93 (s, 1H), 8.85 (s, 1H), 8.6 (d, 1H), 8.13 (s, 2H), 8.07 (s, 1H), 7.93 (d, 1H), 7.82 (d, 2H), 6.91-6.90 (m, 1H), 4.45-4.44 (m, 1H), 4.43-4.39

- (m, 2H), 4.16-4.13 (m, 1H), 3.94-3.71 (m, 1H), 3.69-3.55 (m, 2H), 3.20-3.16 (m, 1H), 2.98-2.94 (m, 1H), 2.54-2.49 (m, 1H), 2.16-2.03 (m, 5H), 1.71-1.70 (m, 1H), 1.68-1.54 (m, 1H), 1.51-1.48 (m, 1H) MS m/z = 568.3 (M+H)+
- [1349] Example 70: 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-amine hydrochloride
- [1350] The titled compound (5.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-1 and C3-1. (Yield: 20.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.58 (d, 1H), 8.09 (s, 1H), 8.02 (s, 1H), 7.82 (s, 1H), 7.55-7.51 (m, 1H), 7.32 (d, 1H), 7.01-6.94 (m, 3H), 4.53-4.49 (m, 1H), 4.09 (d, 2H), 3.83-3.78 (m, 4H), 3.64-3.57 (m, 3H), 3.50-3.48 (m, 1H), 2.94-2.85 (m, 2H), 2.22-2.17 (m, 1H), 2.15-2.05 (m, 3H), 1.83-1.73 (m, 2H), 1.64-1.59 (m, 1H) MS m/z = 589.3 (M+H)+
- [1351] Example 71: methyl 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinate hydrochloride
- [1352] The titled compound (3.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-1 and C2-1. (Yield: 15.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.58 (d, 1H), 8.08 (s, 1H), 8.00 (s, 1H), 7.82 (s, 1H), 7.49-7.47 (m, 1H), 7.24 (d, 1H), 6.99-6.88 (m, 3H), 4.54-4.50 (m, 1H), 4.09 (d, 2H), 3.79-3.78 (m, 4H), 3.71 (s, 3H), 3.64-3.60 (m, 2H), 3.57-3.49 (m, 2H), 2.90-2.84 (m, 2H), 2.20-2.04 (m, 5H), 1.85-1.82 (m, 1H), 1.79-1.75 (m, 1H), 1.62-1.57 (m, 1H) MS m/z = 602.3 (M+H)+
- [1353] Example 72: (S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1354] The titled compound (3.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-8 and C1-1. (Yield: 11.6%) ¹H NMR (CDCl₃, 400MHz) δ 8.60-8.58 (m, 1H), 8.13-8.11 (m, 2H), 7.95 (s, 1H), 7.68 (s, 1H), 7.42-7.32 (m, 3H), 7.25-7.24 (m, 1H), 6.84-6.80 (m, 2H), 4.88 (s, 1H), 3.82 (s, 3H), 3.23-3.20 (m, 1H), 3.00-2.96 (m, 1H), 2.70-2.64 (m, 2H), 1.93-1.91 (m, 1H), 1.86-1.74 (m, 5H) MS m/z = 512.2 (M+H)+
- [1355] Example 73: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1356] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-1. (Yield: 24.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (d, 1H), 8.50 (s, 1H), 8.24 (s, 1H), 8.10 (s, 1H), 7.62-7.59 (m, 2H), 7.19 (s, 1H), 7.10 (d, 1H), 6.97 (t, 1H), 3.92 (s, 3H), 3.71 (d, 1H), 3.49-3.39 (m,

- 2H), 2.91-2.86 (m, 2H), 2.20-2.17 (m, 1H), 1.86-1.70 (m, 2H), 1.63-1.55 (m, 1H) MS $m/z = 511.1$ (M+H)+
- [1357] Example 74: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1358] The titled compound (4.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-3 and C1-1. (Yield: 47.9%) ^1H NMR (CD_3OD , 400MHz) δ 8.68 (d, 1H), 8.20-8.13 (m, 2H), 7.89 (s, 1H), 7.63-7.57 (m, 1H), 7.10-7.08 (m, 1H), 6.96 (t, 1H), 6.99-6.88 (m, 2H), 4.12-4.07 (m, 1H), 3.90 (s, 3H), 3.72-3.69 (m, 2H), 3.60-3.44 (m, 3H), 2.96 (s, 3H), 2.91-2.82 (m, 2H), 2.44-2.36 (m, 4H), 2.21-2.17 (m, 2H), 1.81-1.66 (m, 3H), 1.60-1.54 (m, 1H) MS $m/z = 558.3$ (M+H)+
- [1359] Example 75: (3S)-1-(2-((5-chloro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1360] The titled compound (8.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C1-3. (Yield: 24.4%) ^1H NMR (CDCl_3 , 400MHz) δ 8.06 (s, 1H), 7.75 (s, 2H), 7.69 (d, 1H), 7.53-7.51 (m, 1H), 7.40-7.37 (m, 1H), 7.21 (s, 1H), 6.99-6.88 (m, 2H), 4.43-4.37 (m, 1H), 3.90 (d, 2H), 3.82-3.80 (m, 4H), 3.58 (t, 2H), 3.17-3.14 (m, 1H), 2.94-2.90 (m, 1H), 2.70-2.64 (m, 1H), 2.18-2.02 (m, 5H), 1.90-1.86 (m, 1H), 1.77-1.72 (m, 1H), 1.50-1.48 (m, 2H) MS $m/z = 579.2$ (M+H)+
- [1361] Example 76: 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine hydrochloride
- [1362] The titled compound (6.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-2. (Yield: 53.9%) ^1H NMR (CD_3OD , 400MHz) δ 8.46 (s, 1H), 8.03 (d, 2H), 7.87 (t, 1H), 7.58 (t, 1H), 7.57-7.51 (m, 1H), 7.29 (d, 1H), 7.05 (d, 1H), 6.94-6.88 (m, 2H), 3.87 (s, 3H), 3.76 (d, 1H), 3.50-3.47 (m, 1H), 3.41-3.39 (m, 1H), 2.97-2.85 (m, 2H), 2.21-2.18 (m, 1H), 1.85-1.82 (m, 1H), 1.74-1.71 (m, 1H), 1.64-1.58 (m, 1H) MS $m/z = 528.2$ (M+H)+
- [1363] Example 77: (R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1364] The titled compound (3.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-34 and C1-1. (Yield: 27.0%) ^1H NMR (CD_3OD , 400MHz) δ 8.69 (d, 1H), 8.20 (d, 2H), 7.95 (s, 1H), 7.62-7.58 (m, 1H), 7.15 (s, 1H), 7.19 (d, 1H), 6.97 (t, 1H), 5.09-5.03 (m, 2H), 3.91 (s, 3H), 3.76-3.73 (m, 1H), 3.48-3.38 (m, 2H), 2.91-2.83 (m, 2H), 2.20-2.17 (m, 1H), 1.84-1.73 (m, 2H), 1.60-1.58 (m, 1H) MS $m/z = 543.2$ (M+H)+

- [1365] Example 78: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1366] The titled compound (6.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C1-1. (Yield: 57.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (d, 1H), 8.20 (d, 2H), 7.95 (s, 1H), 7.62-7.60 (m, 1H), 7.15 (s, 1H), 7.19 (d, 1H), 6.97 (t, 1H), 5.09-5.02 (m, 2H), 3.91 (s, 3H), 3.75-3.73 (m, 1H), 3.48-3.36 (m, 2H), 2.91-2.83 (m, 2H), 2.20-2.17 (m, 1H), 1.81-1.70 (m, 2H), 1.62-1.55 (m, 1H) MS m/z= 543.2 (M+H)+
- [1367] Example 79: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1368] The titled compound (8.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-1 and C1-1. (Yield: 16.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.73 (d, 1H), 8.28 (s, 1H), 7.68-7.64 (m, 2H), 7.14-7.11 (m, 2H), 7.03 (dd, 1H), 4.31-4.29 (m, 2H), 3.95 (s, 3H), 3.91-3.90 (m, 2H), 3.58-3.50 (m, 1H), 3.48-3.47 (m, 1H), 3.35-3.31 (m, 1H), 3.00-2.99 (m, 1H), 1.97-1.94 (m, 1H), 1.80-1.74 (m, 3H), 1.20-1.18 (m, 4H) MS m/z= 503.0 (M+H)+
- [1369] Example 80: (S)-3-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)pyridin-2-ol hydrochloride
- [1370] The titled compound (11.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-1 and C1-9. (Yield: 84.9%) ¹H NMR (CD₃OD, 400MHz) δ 9.00 (d, 1H), 8.67 (d, 1H), 8.27 (s, 1H), 8.20 (s, 1H), 7.93 (d, 1H), 7.89 (s, 1H), 7.50-7.20 (m, 1H), 7.13 (s, 1H), 6.76 (t, 1H), 4.57-4.54 (m, 1H), 4.11 (d, 2H), 3.62 (t, 2H), 3.49-3.31 (m, 1H), 2.25-2.18 (m, 2H), 2.18-2.14 (m, 4H), 1.90-1.57 (m, 4H), 0.92-0.89 (m, 2H) MS m/z= 514.2 (M+H)+
- [1371] Example 81: (S)-1-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-methylpiperidin-4-yl)oxy)-[2,3'-bipyridin]-4'-yl)piperidin-3-ol
- [1372] The titled compound (8.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A4-9 and C1-1. (Yield: 30.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.34 (s, 1H), 8.12 (s, 1H), 7.76 (d, 1H), 7.66 (s, 1H), 7.56-7.51 (m, 2H), 7.45 (q, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 4.75-4.60 (m, 1H), 3.83 (s, 3H), 3.68-3.48 (m, 1H), 3.10-2.95 (m, 2H), 2.88-2.70 (m, 2H), 2.57 (s, 3H), 2.20-2.05 (m, 2H), 2.05-1.85 (m, 4H), 1.64-1.38 (m, 4H), 0.98-0.80 (m, 2H) MS m/z= 586.3 (M+H)+
- [1373] Example 82: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-6-amine hydrochloride

- [1374] The titled compound (9.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A5-1 and C1-1. (Yield: 44.7%) ¹H NMR (CD₃OD, 400MHz) δ 9.03-9.01 (m, 1H), 8.86-8.84 (m, 1H), 8.68-8.66 (m, 1H), 8.32 (s, 1H), 8.12-8.10 (m, 1H), 7.70-7.64 (m, 1H), 7.14-7.12 (m, 1H), 7.03 (d, 1H), 6.99 (dd, 1H), 4.15-4.12 (m, 2H), 3.94 (s, 3H), 3.67-3.61 (m, 3H), 3.48-3.40 (m, 2H), 2.83-2.77 (m, 2H), 2.15-1.99 (m, 5H), 1.82-1.79 (m, 1H), 1.66-1.64 (m, 1H), 1.55-1.53 (m, 1H) MS m/z= 556.2 (M+H)+
- [1375] Example 83: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(1-methylpiperidin-4-yl)-[3,3'-bipyridin]-6-amine hydrochloride
- [1376] The titled compound (6.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A5-2 and C1-1. (Yield: 30.6%) ¹H NMR (CD₃OD, 400MHz) δ 9.07 (s, 1H), 8.81 (s, 1H), 8.76-8.74 (m, 1H), 8.34 (s, 1H), 8.16-8.14 (m, 1H), 7.72-7.67 (m, 1H), 7.44 (s, 1H), 7.16 (d, 1H), 7.05 (dd, 1H), 3.96 (s, 3H), 3.75-3.73 (m, 2H), 3.66-3.45 (m, 2H), 3.1 (s, 3H), 2.97-2.92 (m, 1H), 2.49-2.47 (m, 2H), 2.46-2.43 (m, 2H), 2.33-2.30 (m, 1H), 2.26-2.17 (m, 1H), 2.14-2.04 (m, 2H), 2.02-1.83 (m, 1H), 1.72-1.58 (m, 2H), 1.56-1.40 (m, 2H) MS m/z= 569.3 (M+H)+
- [1377] Example 84: 2-(2-fluoro-6-methoxyphenyl)-N-(5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(3-(2,2,2-trifluoroethyl)piperidin-1-yl)pyridin-2-yl)pyrimidin-4-amine
- [1378] The titled compound (23.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-13 and C1-1. (Yield: 67.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.08 (s, 1H), 8.03 (s, 1H), 7.82 (s, 1H), 7.71 (s, 1H), 7.47-7.41 (m, 2H), 6.97 (d, 1H), 6.84 (t, 1H), 4.49-4.43 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.63-3.56 (m, 3H), 3.32 (d, 1H), 3.22 (d, 1H), 2.19 (t, 1H), 2.15-2.09 (m, 5H), 2.09-1.83 (m, 3H), 1.72-1.60 (m, 2H), 1.16-1.12 (m, 1H) MS m/z= 612.2 (M+H)+
- [1379] Example 85: 2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(fluoromethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine
- [1380] The titled compound (20.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-14 and C1-1. (Yield: 66.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.08 (s, 1H), 8.03 (s, 1H), 7.82 (s, 1H), 7.71 (s, 1H), 7.47-7.41 (m, 2H), 6.96 (d, 1H), 6.85 (t, 1H), 4.50-4.45 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.63-3.56 (m, 3H), 3.33 (d, 1H), 3.23 (d, 1H), 2.50 (t, 1H), 2.33 (t, 1H), 2.15-1.95 (m, 6H), 1.76 (d, 1H), 1.76-1.60 (m, 2H), 1.20-1.12 (m, 1H) MS m/z= 562.3 (M+H)+
- [1381] Example 86: N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)acetamide

- [1382] The titled compound (11.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-15 and C1-1. (Yield: 38.0%)
1H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.10 (s, 1H), 8.08 (s, 1H), 7.81 (s, 1H), 7.64 (s, 1H), 7.50-7.41 (m, 2H), 6.96 (d, 1H), 6.85 (t, 1H), 4.59-4.44 (m, 1H), 4.09 (d, 2H), 3.87 (t, 1H), 3.82 (s, 3H), 3.60 (t, 2H), 3.14 (d, 1H), 2.56 (t, 1H), 2.41 (t, 1H), 2.16-2.05 (m, 4H), 1.95-1.82 (m, 1H), 1.91 (s, 3H), 1.67-1.61 (m, 2H), 1.38-1.33 (m, 2H) MS m/z= 587.3 (M+H)+
- [1383] Example 87: 2-(2-fluoro-6-methoxyphenyl)-N-(5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(4-(trifluoromethyl)piperidin-1-yl)pyridin-2-yl)pyrimidin-4-amine
- [1384] The titled compound (23.7 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-16 and C1-1. (Yield: 69.0%)
1H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.10 (s, 1H), 8.05 (s, 1H), 7.91 (s, 1H), 7.84 (s, 1H), 7.70-7.42 (m, 2H), 6.97 (d, 1H), 6.85 (t, 1H), 4.58-4.44 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.79-3.57 (m, 3H), 3.41 (d, 1H), 2.58 (t, 2H), 2.35-2.20 (m, 1H), 2.20-1.98 (m, 4H), 1.87-1.76 (m, 2H), 1.65-1.56 (m, 2H) MS m/z= 598.2 (M+H)+
- [1385] Example 88: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine hydrochloride
- [1386] The titled compound (9.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-6. (Yield: 46.6%) 1H NMR (CD₃OD, 400MHz) δ 9.12 (d, 1H), 9 (d, 2H), 8.9 (d, 1H), 8.56 (s, 1H), 8.27 (s, 1H), 8.12 (s, 1H), 8.06 (d, 1H), 7.77-7.47 (m, 1H), 7.28 (s, 1H), 7.06 (s, 1H), 3.85-3.83 (m, 1H), 3.60-3.57 (m, 1H), 3.48-3.43 (m, 1H), 3.03-2.94 (m, 2H), 2.22-2.20 (m, 1H), 1.88-1.85 (m, 1H), 1.77-1.74 (m, 1H), 1.64-1.61 (m, 1H) MS m/z= 533.1 (M+H)+
- [1387] Example 89: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine hydrochloride
- [1388] The titled compound (1.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C1-6. (Yield: 6.3%) 1H NMR (CD₃OD, 400MHz) δ 9.11 (d, 1H), 9 (d, 2H), 8.9 (d, 1H), 8.25 (s, 1H), 8.2 (s, 1H), 8.06 (d, 1H), 7.97 (s, 1H), 7.26 (d, 1H), 7.05 (s, 1H), 5.10-5.08 (m, 2H), 3.89-3.86 (m, 1H), 3.60-3.57 (m, 1H), 3.48-3.45 (m, 1H), 3.04-2.90 (m, 2H), 2.22-2.20 (m, 1H), 1.76-1.73 (m, 1H), 1.66-1.63 (m, 1H), 1.40-1.30 (m, 1H) MS m/z= 565.1 (M+H)+
- [1389] Example 90: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine hydrochloride
- [1390] The titled compound (7.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-1 and C1-6. (Yield: 31.5%) 1H NMR (CD₃OD, 400MHz) δ 9.08 (d, 1H), 9 (d, 2H), 8.86 (d, 1H), 8.33 (s, 1H), 8.07 (d, 1H), 7.26-7.25 (m, 1H), 6.93 (s, 1H), 4.33-4.26 (m, 2H), 3.96-3.93 (m, 2H), 3.59-3.49 (m,

- 3H), 3.40-3.35 (m, 2H), 3.03-3.01 (m, 1H), 2.27-2.25 (m, 1H), 2.01-1.95 (m, 2H), 1.89-1.81 (m, 2H), 1.79-1.77 (m, 4H) MS m/z = 578.2 (M+H)+
- [1391] Example 91: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1392] The titled compound (7.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-5 and C1-1. (Yield: 34.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.74-8.70 (m, 1H), 8.14 (s, 1H), 8.06 (s, 1H), 7.83 (s, 1H), 7.62-7.50 (m, 1H), 7.17-7.10 (m, 2H), 6.98-6.96 (m, 1H), 4.40-4.39 (m, 2H), 3.92-3.91 (m, 3H), 3.84-3.81 (m, 3H), 3.53-3.49 (m, 1H), 3.42-3.37 (m, 4H), 2.90-2.85 (m, 2H), 2.21-2.18 (m, 1H), 1.88-1.79 (m, 2H), 1.61-1.60 (m, 1H) MS m/z = 519.3 (M+H)+
- [1393] Example 92: N-(4-(2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1394] The titled compound (29.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-17 and C1-1. (Yield: 84.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.09 (s, 1H), 8.04 (s, 1H), 7.80 (s, 1H), 7.62 (q, 1H), 7.36 (s, 1H), 7.15-7.10 (m, 2H), 6.98 (t, 1H), 4.60-4.45 (m, 1H), 4.09 (d, 2H), 3.92 (s, 3H), 3.60 (t, 2H), 3.43-3.31 (m, 6H), 3.19 (s, 2H), 2.18-2.05 (m, 4H), 2.02 (t, 2H), 1.85-1.65 (m, 4H) MS m/z = 585.3 (M+H)+
- [1395] Example 93: N-(4-(2,8-diazaspiro[4.5]decan-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1396] The titled compound (36.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-18 and C1-1. (Yield: 98.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 7.94 (s, 1H), 7.85 (s, 1H), 7.66-7.60 (m, 1H), 7.31 (d, 1H), 7.11 (d, 1H), 6.98 (t, 1H), 6.79 (s, 1H), 4.52-4.47 (m, 1H), 4.08 (d, 2H), 3.92 (s, 3H), 3.60 (t, 2H), 3.57-3.31 (m, 2H), 3.31-3.16 (m, 6H), 2.20-2.02 (m, 4H), 1.96 (t, 2H), 1.86-1.70 (m, 4H) MS m/z = 585.3 (M+H)+
- [1397] Example 94: (3R,4R)-4-fluoro-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1398] The titled compound (20.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-19 and C1-1. (Yield: 39.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.11 (s, 1H), 8.10 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.50-7.41 (m, 2H), 6.96 (d, 1H), 6.85 (t, 1H), 4.50-4.48 (m, 1H), 4.48-4.20 (m, 1H), 4.10 (d, 2H), 3.83 (s, 3H), 3.80-3.65 (m, 1H), 3.60 (t, 2H), 3.35-3.17 (m, 2H), 2.72 (t, 1H), 2.52 (t, 1H), 2.15-2.05 (m, 4H), 2.05-1.96 (m, 1H), 1.30-1.22 (m, 1H) MS m/z = 564.2 (M+H)+

- [1399] Example 95: (3R,4R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-(hydroxymethyl)piperidin-3-ol
- [1400] The titled compound (11.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-20 and C1-1. (Yield: 26.7%)
1H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.11 (s, 1H), 8.05 (s, 1H), 7.83 (s, 1H), 7.61 (s, 1H), 7.52 (d, 1H), 7.44 (q, 1H), 6.96 (d, 1H), 6.85 (t, 1H), 4.52-4.40 (m, 1H), 4.09 (d, 2H), 3.83 (s, 3H), 3.83-3.74 (m, 1H), 3.68-3.55 (m, 3H), 3.55-3.45 (m, 1H), 3.45-3.36 (m, 1H), 3.36 (s, 2H), 2.53 (t, 1H), 2.29 (t, 1H), 2.20-2.04 (m, 4H), 1.80-1.68 (m, 1H), 1.50-1.34 (m, 1H) MS m/z= 576.2 (M+H)+
- [1401] Example 96: (R)-N-(4-(3-aminopyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1402] The titled compound (23.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-21 and C1-1. (Yield: 80.8%)
1H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 7.96 (s, 1H), 7.89 (s, 1H), 7.65 (s, 1H), 7.60 (q, 1H), 7.26 (d, 1H), 7.09 (d, 1H), 6.95 (t, 1H), 6.73 (s, 1H), 4.53-4.44 (m, 1H), 4.08 (d, 2H), 4.04-3.94 (m, 1H), 3.91 (s, 3H), 3.75-3.50 (m, 5H), 3.45-3.35 (m, 1H), 2.48-2.32 (m, 1H), 2.20-2.00 (m, 5H) MS m/z= 531.2 (M+H)+
- [1403] Example 97: (S)-N-(4-(3-aminopyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1404] The titled compound (23.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-22 and C1-1. (Yield: 79.6%)
1H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 7.97 (s, 1H), 7.89 (s, 1H), 7.65 (s, 1H), 7.61 (q, 1H), 7.29 (d, 1H), 7.09 (d, 1H), 6.96 (t, 1H), 6.76 (s, 1H), 4.53-4.44 (m, 1H), 4.08 (d, 2H), 4.00-3.92 (m, 1H), 3.92 (s, 3H), 3.73-3.60 (m, 2H), 3.60-3.56 (m, 3H), 3.50-3.35 (m, 1H), 2.43-2.37 (m, 1H), 2.20-2.00 (m, 5H) MS m/z= 531.2 (M+H)+
- [1405] Example 98: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(2-(1-methylpiperidin-4-yl)thiazol-5-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1406] The titled compound (10.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A5-3 and C1-1. (Yield: 96.6%)
1H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 8.18 (s, 1H), 7.75 (s, 1H), 7.55 (s, 1H), 7.45 (q, 1H), 6.97 (d, 1H), 6.87 (t, 1H), 3.82 (s, 3H), 3.64 (brs, 1H), 3.12-3.05 (m, 5H), 2.56 (brs, 1H), 2.40 (s, 3H), 2.38 (t, 3H), 2.22 (d, 2H), 1.98-1.88 (m, 4H), 1.66 (s, 2H), 1.42 (s, 9H) MS m/z= 575.2 (M+H)+

- [1407] Example 99: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-6-amine hydrochloride
- [1408] The titled compound (7.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A5-1 and C1-6. (Yield: 31.5%) ¹H NMR (CD₃OD, 400MHz) δ 9.10-9.07 (m, 2H), 9 (s, 2H), 8.98 (d, 1H), 8.89 (d, 1H), 8.82 (s, 1H), 8.37 (d, 1H), 8.15 (d, 1H), 7.39 (s, 1H), 7.2 (s, 1H), 4.15-4.13 (m, 2H), 3.86-3.83 (m, 1H), 3.68-3.62 (m, 2H), 3.51-3.41 (m, 3H), 3.07-3.01 (m, 2H), 2.19-2.17 (m, 1H), 2.06-2.01 (m, 4H), 1.85-1.82 (m, 1H), 1.70-1.59 (m, 2H) MS m/z= 578.2 (M+H)+
- [1409] Example 100: 4-((S)-3-aminopiperidin-1-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine hydrochloride
- [1410] The titled compound (6.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C1-2. (Yield: 60.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.17 (s, 1H), 7.98 (s, 1H), 7.89-7.86 (m, 2H), 7.54-7.52 (m, 1H), 7.30 (d, 1H), 7.06-7.03 (m, 1H), 6.93-6.91 (m, 1H), 6.90-6.88 (m, 2H), 5.06 (q, 2H), 3.87 (s, 3H), 3.80-3.78 (m, 1H), 3.47-3.41 (m, 2H), 2.94-2.91 (m, 1H), 2.87-2.81 (m, 1H), 2.20-2.17 (m, 1H), 1.73-1.70 (m, 1H), 1.66-1.64 (m, 1H), 1.61-1.58 (m, 1H) MS m/z= 560.2 (M+H)+
- [1411] Example 101: (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol hydrochloride
- [1412] The titled compound (5.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C5-1. (Yield: 80.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.71 (d, 1H), 8.52 (s, 1H), 8.23 (s, 1H), 8.10 (s, 1H), 7.75-7.45 (m, 1H), 7.25 (s, 1H), 7.10 (s, 1H), 7.00 (d, 1H), 4.72 (s, 2H), 3.94 (s, 3H), 3.77-3.74 (m, 1H), 3.48-3.39 (m, 2H), 2.97-2.87 (m, 2H), 2.20-2.17 (m, 1H), 1.86-1.82 (m, 1H), 1.75-1.72 (m, 1H), 1.62-1.59 (m, 1H) MS m/z= 541.2 (M+H)+
- [1413] Example 102: (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol hydrochloride
- [1414] The titled compound (2.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C5-1. (Yield: 28.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (d, 1H), 8.22-8.19 (m, 2H), 7.95 (s, 1H), 7.18 (s, 1H), 7.08 (s, 1H), 6.98 (d, 1H), 5.07 (q, 2H), 4.72 (s, 2H), 3.92 (s, 3H), 3.76-3.74 (m, 1H), 3.47-3.39 (m, 2H), 2.92-2.85 (m, 2H), 2.19-2.17 (m, 1H), 1.75-1.72 (m, 2H), 1.60-1.58 (m, 1H) MS m/z= 573.2 (M+H)+

- [1415] Example 103: (S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol hydrochloride
- [1416] The titled compound (2.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-1 and C5-1. (Yield: 37.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.64 (d, 1H), 8.26 (s, 1H), 7.09 (s, 2H), 6.99 (d, 1H), 4.72 (s, 2H), 4.17-4.15 (m, 1H), 4.01-4.00 (m, 1H), 3.94 (s, 3H), 3.93-3.91 (m, 2H), 3.58-3.53 (m, 2H), 3.48-3.46 (m, 1H), 3.23-3.20 (m, 2H), 2.99-2.98 (m, 1H), 2.24-2.21 (m, 1H), 1.97-1.94 (m, 3H), 1.77-1.75 (m, 4H) MS m/z= 533.3 (M+H)+
- [1417] Example 104: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1418] The titled compound (10.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C6-1. (Yield: 55.7%) ¹H NMR (CDCl₃, 400MHz) δ 8.8 (d, 1H), 8.54 (s, 1H), 8.25 (s, 1H), 8.08 (s, 1H), 7.61 (s, 1H), 7.51 (s, 1H), 7.24-7.23 (m, 2H), 4.47 (s, 2H), 4.01 (s, 3H), 3.89-3.87 (m, 1H), 3.58-3.56 (m, 1H), 3.44-3.42 (m, 1H), 3.12-3.07 (m, 2H), 2.96 (s, 6H), 2.22-2.19 (m, 1H), 1.83-1.81 (m, 1H), 1.69-1.67 (m, 2H) MS m/z= 568.2 (M+H)+
- [1419] Example 105: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1420] The titled compound (15.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C6-1. (Yield: 74.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.81-8.80 (m, 1H), 8.26 (s, 1H), 8.2 (s, 1H), 7.93 (s, 1H), 7.49-7.48 (m, 1H), 7.41 (s, 1H), 7.23-7.22 (m, 2H), 5.09 (q, 2H), 4.47 (s, 2H), 4 (s, 3H), 3.92-3.89 (m, 1H), 3.60-3.57 (m, 1H), 3.48-3.46 (m, 1H), 3.35-3.31 (m, 1H), 3.07 (s, 6H), 2.21-2.19 (m, 1H), 1.80-1.69 (m, 3H) MS m/z= 600.3 (M+H)+
- [1421] Example 106: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1422] The titled compound (9.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-1 and C6-1. (Yield: 47.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.74-8.72 (m, 1H), 8.27 (s, 1H), 7.47 (s, 1H), 7.36 (s, 1H), 7.2 (d, 1H), 6.98 (s, 1H), 4.45 (s, 2H), 4.30-4.27 (m, 2H), 3.97 (s, 3H), 3.93-3.90 (m, 2H), 3.57-3.48 (m, 3H), 3.12-3.00 (m, 1H), 2.96 (s, 6H), 2.26-2.23 (m, 1H), 2.04-1.96 (m, 3H), 1.93-1.74 (m, 4H) MS m/z= 560.3 (M+H)+

- [1423] Example 107: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1424] The titled compound (30.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-11 and C1-1. (Yield: 66.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.83 (d, 1H), 8.68 (s, 1H), 8.25 (d, 2H), 7.74-7.69 (m, 1H), 7.63-7.61 (m, 1H), 7.37 (s, 1H), 7.18 (d, 1H), 7.06 (dd, 1H), 3.99 (s, 3H), 3.94-3.91 (m, 1H), 3.62-3.59 (m, 1H), 3.48-3.44 (m, 1H), 3.16-3.10 (m, 1H), 3.07-3.02 (m, 1H), 2.22-2.20 (m, 1H), 1.74-1.71 (m, 1H), 1.68-1.66 (m, 2H) MS m/z= 529.1 (M+H)+
- [1425] Example 108: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1426] The titled compound (29.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-7. (Yield: 89.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.83-8.82 (d, 1H), 8.57 (s, 1H), 8.23 (s, 1H), 8.09 (s, 1H), 7.63-7.57 (m, 2H), 7.35 (s, 1H), 7.06 (d, 1H), 6.92 (dd, 1H), 3.99 (s, 3H), 3.96-3.93 (m, 1H), 3.64-3.61 (m, 1H), 3.48-3.46 (m, 1H), 3.17-3.16 (m, 1H), 3.14-3.04 (m, 1H), 2.22-2.20 (m, 1H), 1.83-1.69 (m, 3H) MS m/z= 529.2 (M+H)+
- [1427] Example 109: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1428] The titled compound (56.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C1-7. (Yield: 72.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.11 (s, 2H), 7.92 (s, 1H), 7.57 (s, 2H), 6.83 (d, 1H), 6.7 (dd, 1H), 5.02 (q, 2H), 3.82 (s, 3H), 3.17-3.13 (m, 1H), 2.87-2.84 (m, 1H), 2.58-2.53 (m, 1H), 2.35-2.30 (m, 1H), 2.04-2.02 (m, 1H), 1.97-1.94 (m, 1H), 1.26-1.20 (m, 2H) MS m/z= 560.9 (M+H)+
- [1429] Example 110: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1430] The titled compound (5.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-1 and C1-7. (Yield: 40.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.09 (s, 1H), 7.53-7.51 (m, 1H), 7.46 (s, 1H), 6.82 (d, 1H), 6.72 (dd, 1H), 3.95-3.92 (m, 2H), 3.89 (s, 3H), 3.72-3.69 (m, 1H), 3.58-3.55 (m, 2H), 2.95-2.83 (m, 3H), 2.64-2.59 (m, 1H), 2.21-2.18 (m, 2H), 2.04-1.93 (m, 2H), 1.80-1.70 (m, 3H), 1.66-1.61 (m, 1H), 1.25-1.23 (m, 1H)
- [1431] Example 111: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1432] The titled compound (28.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-2 and C1-1. (Yield: 84.5%)

- 1H NMR (CD₃OD, 400MHz) δ 8.73-8.72 (m, 1H), 8.62-8.60 (m, 1H), 8.42 (s, 1H), 8.06 (s, 1H), 7.70-7.67 (m, 1H), 7.21 (s, 1H), 7.16-7.14 (m, 1H), 7.04-7.00 (m, 1H), 4.32-4.29 (m, 1H), 4.13-4.10 (m, 1H), 3.96 (s, 3H), 3.52-3.48 (m, 2H), 2.32-2.22 (m, 1H), 2.12-2.02 (m, 1H), 1.89-1.86 (m, 1H), 1.76-1.64 (m, 1H)
- [1433] Example 112: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide
- [1434] Step 1: methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate
- [1435] The titled compound (105.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C2-1. (Yield: 48.2%)
1H NMR (CDCl₃, 400MHz) δ 8.25 (d, 1H), 8.07 (s, 1H), 7.76 (s, 2H), 7.62 (s, 1H), 7.55 (s, 1H), 7.37-7.31 (m, 2H), 6.84-6.76 (m, 2H), 4.41-4.39 (m, 1H), 4.16-4.12 (m, 2H), 3.84-3.77 (m, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.58 (t, 2H), 3.15-3.12 (m, 1H), 2.95-2.87 (m, 1H), 2.73-2.61 (m, 2H), 2.18-2.06 (m, 4H), 1.87-1.85 (m, 1H), 1.78-1.70 (m, 1H), 1.49-1.40 (m, 2H)
- [1436] Step 2: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinic acid
- [1437] Methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate (48.9 mg, 0.08 mmol) was dissolved in tetrahydrofuran (1.5 ml) and methanol (0.5 ml) and then 1.0M sodium hydroxide solution (0.24 mL, 0.24 mmol) was added dropwise thereto. Then, the mixed solution was stirred at 60°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then neutralized with 1.0N hydrochloric acid solution. The aqueous layer was extracted with dichloromethane. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then dried to prepare the titled compound (33.0 mg), without further purification. (Yield: 69.0%)
1H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.03 (s, 1H), 7.88 (s, 1H), 7.74 (s, 1H), 7.46-7.44 (m, 1H), 7.15 (d, 1H), 6.96 (d, 1H), 6.87 (t, 1H), 6.78 (s, 1H), 4.49-4.46 (m, 1H), 4.09 (d, 2H), 3.80 (s, 4H), 3.63-3.56 (m, 2H), 3.48 (d, 1H), 3.14-3.07 (m, 1H), 2.94-2.89 (m, 1H), 2.16-2.06 (m, 4H), 2.02-1.98 (m, 1H), 1.88-1.84 (m, 1H), 1.62-1.49 (m, 2H)
- [1438] Step 3: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide
- [1439] 2-(2-Fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinic acid (10.0 mg, 0.017 mmol) was dissolved in anhydrous dimethylformamide (1.0 mL) and then 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide

hexafluorophosphate (HATU, 12.92 mg, 0.034 mmol) and diisopropylethylamine (0.01 mL, 0.051 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature for 15 minutes and then 0.4M ammonia solution dissolved in 1,4-dioxane (0.05 mL, 0.02 mmol) was dropwise thereto. The reaction mixture was stirred at room temperature overnight. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (2.3 mg). (Yield: 23.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.08 (s, 1H), 8.03 (s, 1H), 7.96 (d, 1H), 7.85 (d, 1H), 7.82 (s, 1H), 7.41-7.33 (m, 2H), 6.91-6.83 (m, 2H), 4.49-4.45 (m, 1H), 4.09 (d, 2H), 3.80 (s, 3H), 3.70-3.57 (m, 3H), 3.00-2.94 (m, 1H), 2.64-2.55 (m, 1H), 2.41-2.37 (m, 1H), 2.20-2.04 (m, 4H), 1.97-1.92 (m, 1H), 1.79-1.72 (m, 1H), 1.55-1.50 (m, 1H), 1.35-1.30 (m, 1H) MS m/z= 588.3 (M+H)+

[1440] Example 113: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-N,N-dimethylnicotinamide

[1441] The titled compound (4.3 mg) was prepared in accordance with the same procedures as in Example 112, using Intermediates A2-1 and C2-1 and changing the amine reagent to 2.0M dimethylamine dissolved in tetrahydrofuran (0.01 mL, 0.02 mmol). (Yield: 41.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.08 (s, 1H), 8.02 (s, 1H), 7.85 (d, 1H), 7.82 (s, 1H), 7.71 (d, 1H), 7.42-7.37 (m, 2H), 6.91 (d, 1H), 6.87-4.45 (m, 1H), 4.48-4.46 (m, 1H), 4.09 (d, 2H), 3.78 (s, 3H), 3.72-3.70 (m, 1H), 3.60 (t, 2H), 3.05-3.00 (m, 1H), 2.89 (s, 3H), 2.85 (s, 3H), 2.62-2.58 (m, 1H), 2.40 (t, 1H), 2.14-2.02 (m, 4H), 1.95-1.92 (m, 1H), 1.73-1.72 (m, 1H), 1.60-1.50 (m, 1H), 1.34-1.30 (m, 2H) MS m/z= 616.3 (M+H)+

[1442] Example 114: 4-((S)-3-aminopiperidin-1-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-amine hydrochloride

[1443] The titled compound (18.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-2 and C1-2. (Yield: 52.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.6 (s, 1H), 8.25 (s, 1H), 8.04 (s, 1H), 7.88-7.84 (m, 1H), 7.55-7.53 (m, 1H), 7.31 (d, 1H), 7.07 (d, 1H), 6.94 (dd, 1H), 6.75 (s, 1H), 4.33-4.30 (m, 1H), 4.19-4.16 (m, 1H), 3.88 (s, 3H), 3.51-3.49 (m, 1H), 3.39-3.37 (m, 2H), 2.27-2.24 (m, 1H), 2.05-2.02 (m, 1H), 1.89-1.81 (m, 1H), 1.78-1.76 (m, 1H)

[1444] Example 115: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine hydrochloride

- [1445] The titled compound (5.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-2 and C1-6. (Yield: 14.6%) ¹H NMR (CD₃OD, 400MHz) δ 9.08 (d, 1H), 8.99-8.98 (m, 2H), 8.85 (d, 1H), 8.64 (s, 1H), 8.45 (s, 1H), 8.08 (s, 1H), 8.05 (d, 1H), 7.30 (s, 1H), 6.98 (s, 1H), 4.40-4.37 (m, 1H), 4.25-4.22 (m, 1H), 3.57-3.52 (m, 1H), 3.48-3.37 (m, 2H), 2.28-2.26 (m, 1H), 2.08-2.07 (m, 1H), 2.05-2.02 (m, 1H), 1.88-1.76 (m, 1H)
- [1446] Example 116: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-methoxypropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1447] The titled compound (8.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-6 and C1-1. (Yield: 96.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.82 (d, 1H), 8.14 (d, 2H), 7.86 (s, 1H), 7.74 (dd, 1H), 7.57 (d, 1H), 7.35 (s, 1H), 7.18 (d, 1H), 7.05 (t, 1H), 4.34 (t, 2H), 3.99 (s, 3H), 3.96 (s, 1H), 3.67 (d, 1H), 3.42 (t, 3H), 3.35-3.32 (m, 3H), 3.10 (t, 1H), 3.02 (t, 1H), 2.22-2.14 (m, 3H), 1.82 (brs, 1H), 1.75-1.65 (m, 2H). MS m/z= 533.3 (M+H)+
- [1448] Example 117: 2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine
- [1449] The titled compound (22.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-23 and C1-1. (Yield: 40.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 8.08 (s, 1H), 8.06 (s, 1H), 7.86 (s, 1H), 7.77 (s, 1H), 7.48-7.40 (m, 2H), 6.97 (d, 1H), 6.86 (t, 1H), 4.54-4.42 (m, 1H), 4.09 (d, 2H), 3.82 (s, 3H), 3.60 (t, 2H), 2.92-2.82 (m, 4H), 2.80-2.66 (m, 2H), 2.56-2.50 (m, 2H), 2.53 (s, 3H), 2.14-2.02 (m, 4H), 1.72 (t, 2H), 1.72-1.61 (m, 4H) MS m/z= 599.3 (M+H)+
- [1450] Example 118: (S)-4-(3-aminopiperidin-1-yl)-N⁶-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-N⁶,N⁶-dimethyl-[3,3'-bipyridin]-6,6'-diamine hydrochloride
- [1451] The titled compound (30.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-16 and C1-1. (Yield: 97.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.68 (d, 1H), 8.26 (d, 1H), 8.21 (s, 1H), 8.17 (s, 1H), 7.63 (q, 1H), 7.38 (d, 1H), 7.29 (s, 1H), 7.11 (d, 1H), 6.89 (t, 1H), 3.93 (s, 3H), 3.73 (d, 1H), 3.48-3.30 (m, 2H), 3.39 (s, 6H), 2.98-2.80 (m, 2H), 2.22-2.10 (m, 1H), 1.92-1.80 (m, 1H), 1.80-1.65 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 515.1 (M+H)+
- [1452] Example 119: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(pyrrolidin-1-yl)-[3,3'-bipyridin]-6-amine hydrochloride

- [1453] The titled compound (20.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-17 and C1-1. (Yield: 97.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.56 (d, 1H), 8.17 (d, 1H), 8.11 (s, 1H), 8.10 (s, 1H), 7.66 (s, 1H), 7.55-7.45 (m, 2H), 7.13 (d, 1H), 7.03 (d, 1H), 6.91 (t, 1H), 3.87 (s, 3H), 3.76-3.65 (m, 4H), 3.65-3.55 (m, 1H), 3.40-3.20 (m, 2H), 2.88-2.65 (m, 2H), 2.26-2.15 (m, 4H), 2.15-2.00 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.65 (m, 1H), 1.65-1.45 (m, 1H) MS m/z= 540.9 (M+H)+
- [1454] Example 120: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperidin-1-yl)-[3,3'-bipyridin]-6-amine hydrochloride
- [1455] The titled compound (29.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-18 and C1-1. (Yield: 96.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.68 (d, 1H), 8.23 (d, 1H), 8.20 (s, 1H), 8.16 (s, 1H), 7.63 (q, 1H), 7.49 (d, 1H), 7.28 (s, 1H), 7.11 (d, 1H), 6.98 (t, 1H), 3.80 (s, 3H), 3.84-3.75 (m, 4H), 3.75-3.70 (m, 1H), 3.44 (d, 1H), 3.42-3.32 (m, 1H), 2.88 (q, 2H), 2.18 (d, 1H), 1.90-1.78 (m, 7H), 1.74 (q, 1H), 1.57 (q, 1H) MS m/z= 556.0 (M+H)+
- [1456] Example 121: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine hydrochloride
- [1457] The titled compound (24.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-19 and C1-1. (Yield: 96.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (d, 1H), 8.25 (s, 1H), 8.25-8.18 (m, 2H), 7.62 (q, 1H), 7.42 (d, 1H), 7.26 (s, 1H), 7.11 (d, 1H), 6.98 (t, 1H), 3.93 (s, 3H), 3.93-3.84 (m, 4H), 3.80-3.68 (m, 5H), 3.52-3.30 (m, 2H), 2.87 (q, 2H), 2.17 (d, 1H), 1.90-1.80 (m, 1H), 1.73 (q, 1H), 1.57 (q, 1H) MS m/z= 557.9 (M+H)+
- [1458] Example 122: (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(methylamino)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1459] The titled compound (7.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-1 and C1-1. (Yield: 97.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.77 (d, 1H), 8.54 (s, 1H), 8.23 (s, 1H), 8.1 (s, 1H), 7.78-7.49 (m, 2H), 7.29 (s, 1H), 7.15 (d, 1H), 7.03-6.99 (m, 1H), 3.95 (s, 3H), 3.91-3.89 (m, 1H), 3.55-3.52 (m, 1H), 3.33-3.32 (m, 1H), 3.04-2.94 (m, 2H), 2.61 (s, 3H), 2.30-2.27 (m, 1H), 1.92-1.89 (m, 1H), 1.85-1.77 (m, 1H), 1.64-1.61 (m, 1H) MS m/z= 524.9 (M+H)+
- [1460] Example 123: (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(methylamino)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

- [1461] The titled compound (15.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-2 and C1-1. (Yield: 81.2%)
1H NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.55 (s, 1H), 8.23 (s, 1H), 8.11 (s, 1H), 7.79-7.49 (m, 2H), 7.32 (s, 1H), 7.17 (d, 1H), 7.14 (dd, 1H), 3.97 (s, 3H), 3.93-3.92 (m, 1H), 3.59-3.56 (m, 1H), 3.33-3.32 (m, 1H), 3.05-2.97 (m, 2H), 2.62 (s, 3H), 2.30-2.27 (m, 1H), 1.92-1.89 (m, 1H), 1.77-1.74 (m, 1H), 1.68-1.63 (m, 1H) MS m/z= 524.9 (M+H)+
- [1462] Example 124: (S)-2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(methy
lamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-
yl)pyrimidin-4-amine
- [1463] The titled compound (5.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-24 and C1-1. (Yield: 21.3%) 1H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 7.81 (s, 1H), 7.79 (s, 1H), 7.57 (s, 1H), 7.50-7.34 (m, 3H), 6.97 (d, 1H), 6.85 (t, 1H), 4.52-4.40 (m, 1H), 4.10 (d, 2H), 3.83 (s, 3H), 3.61 (t, 2H), 3.30-3.18 (m, 3H), 3.10 (q, 1H), 3.00-2.90 (m, 1H), 2.32 (s, 3H), 2.20-2.00 (m, 5H), 1.80-1.68 (m, 1H) MS m/z= 545.9 (M+H)+
- [1464] Example 125: (S)-N-(4-(3-(ethylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1465] The titled compound (11.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-25 and C1-1. (Yield: 18.6%)
1H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 7.79 (s, 1H), 7.78 (s, 1H), 7.56 (s, 1H), 7.50-7.35 (m, 3H), 6.97 (d, 1H), 6.85 (t, 1H), 4.52-4.40 (m, 1H), 4.10 (d, 2H), 3.83 (s, 3H), 3.61 (t, 2H), 3.29-3.18 (m, 3H), 3.10 (q, 1H), 2.94-2.84 (m, 1H), 2.60-2.42 (m, 2H), 2.20-2.00 (m, 5H), 1.80-1.64 (m, 1H), 1.10 (t, 3H) MS m/z= 559.9 (M+H)+
- [1466] Example 126: (R)-N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide
- [1467] The titled compound (13.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-26 and C1-1. (Yield: 39.0%)
1H NMR (CD₃OD, 400MHz) δ 8.41 (d, 1H), 7.81 (s, 1H), 7.78 (s, 1H), 7.55 (s, 1H), 7.50-7.40 (m, 2H), 7.39 (d, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 4.52-4.40 (m, 1H), 4.34-4.24 (m, 1H), 4.10 (d, 2H), 3.83 (s, 3H), 3.61 (t, 2H), 3.31-3.28 (m, 1H), 3.28-3.19 (m, 1H), 3.19-3.10 (m, 1H), 2.96-2.85 (m, 1H), 2.20-2.00 (m, 5H), 1.92 (s, 3H), 1.88-1.74 (m, 1H) MS m/z= 573.9 (M+H)+
- [1468] Example 127: (S)-3-(6-((4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyridin-2-yl)oxazolidin-2-one hydrochloride
- [1469] The titled compound (20.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-1 and C7. (Yield: 64.8%)

¹H NMR (CD₃OD, 400MHz) δ 8.13 (s, 1H), 7.99 (s, 1H), 7.78 (s, 1H), 7.55 (s, 1H), 7.50-7.40 (m, 2H), 7.39 (d, 1H), 6.97 (d, 1H), 6.85 (t, 1H), 4.52-4.40 (m, 1H), 4.34-4.24 (m, 1H), 4.10 (d, 2H), 3.83 (s, 3H), 3.61 (t, 2H), 3.31-3.28 (m, 1H), 3.28-3.18 (m, 1H), 3.18-3.08 (m, 1H), 2.96-2.86 (m, 1H), 2.20-2.00 (m, 5H), 1.92 (s, 3H), 1.88-1.76 (m, 1H) MS m/z= 505.9 (M+H)+

[1470] Example 128: (S)-N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide

[1471] The titled compound (4.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-27 and C1-1. (Yield: 14.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 7.81 (s, 1H), 7.96-7.80 (m, 2H), 7.00-6.84 (m, 2H), 4.68-4.58 (m, 3H), 4.58-4.48 (m, 1H), 4.26 (t, 2H), 4.11 (d, 2H), 3.80-3.70 (m, 1H), 3.62 (t, 2H), 3.50-3.35 (m, 2H), 2.95-2.78 (m, 2H), 2.28-2.09 (m, 4H), 1.90-1.78 (m, 2H), 1.78-1.50 (m, 1H) MS m/z= 573.9 (M+H)+

[1472] Example 129: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide hydrochloride

[1473] Step 1: methyl 6-((4-((S)-3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinate

[1474] The titled compound (58.3 mg) was prepared in accordance with the same procedures as in Step 1 of Example 52, using Intermediates A3-1 and C2-1. (Yield: 32.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.28-8.25 (m, 1H), 8.10 (d, 1H), 7.80 (s, 1H), 7.77 (s, 1H), 7.62-7.60 (m, 2H), 7.37-7.34 (m, 2H), 6.88-6.77 (m, 2H), 4.54-4.39 (m, 2H), 4.17-4.14 (m, 2H), 3.76-3.72 (m, 6H), 3.63-3.56 (m, 2H), 3.31-3.22 (m, 1H), 3.01-2.94 (m, 1H), 2.54-2.48 (m, 1H), 2.43-2.39 (m, 1H), 2.24-2.07 (m, 4H), 1.97-1.90 (m, 1H), 1.48 (s, 9H).

[1475] Step 2: 6-((4-((S)-3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinic acid

[1476] Methyl 6-((4-((S)-3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinate (68.0 mg, 0.09 mmol) was dissolved in tetrahydrofuran (1.5 ml) and methanol (0.5 ml) and then 1.0M sodium hydroxide solution (0.29 mL, 0.24 mmol) was added dropwise thereto. Then, the mixed solution was stirred at 60°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then neutralized with 1.0N hydrochloric acid solution. The aqueous layer was extracted with dichloromethane. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then dried to

prepare the titled compound (57.1 mg), without further purification. (Yield: 85.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.44-8.41 (m, 1H), 8.01 (d, 1H), 7.90 (s, 1H), 7.73 (s, 1H), 7.46-7.44 (m, 1H), 7.17 (d, 1H), 6.88 (t, 2H), 4.49-4.45 (m, 1H), 4.09 (d, 2H), 3.81 (s, 3H), 3.75-3.71 (m, 1H), 3.65-3.57 (m, 3H), 3.52-3.48 (m, 1H), 2.96-2.86 (m, 1H), 2.72-2.65 (m, 1H), 2.18-2.10 (m, 4H), 2.03-1.98 (m, 1H), 1.76-1.72 (m, 1H), 1.62-1.55 (m, 1H), 1.46 (s, 9H)

[1477] Step 3: tert-butyl ((3S)-1-(2-((5-carbamoyl-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate

[1478] 6-((4-((S)-3-((tert-Butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinic acid (27.0 mg, 0.039 mmol) was dissolved in anhydrous dimethylformamide (1.0 mL) and then 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide hexafluorophosphate (HATU, 29.8 mg, 0.079 mmol) and diisopropylethylamine (0.02 mL, 0.12 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature for 15 minutes and then 0.4M ammonia solution dissolved in 1,4-dioxane (0.12 mL, 0.047 mmol) was added dropwise thereto. The reaction mixture was stirred at room temperature overnight. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (12.3 mg). (Yield: 45.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.21-8.19 (m, 1H), 8.09 (d, 1H), 7.79-7.77 (m, 2H), 7.59-7.54 (m, 2H), 7.46-7.34 (m, 2H), 6.93-6.83 (m, 2H), 5.64 (brs, 1H), 5.32 (brs, 1H), 4.50-4.39 (m, 2H), 4.17-4.14 (m, 2H), 3.82 (s, 3H), 3.76-3.71 (m, 1H), 3.63-3.56 (m, 2H), 3.33-3.19 (m, 2H), 2.98-2.91 (m, 1H), 2.64-2.53 (m, 1H), 2.45-2.40 (m, 1H), 2.24-2.11 (m, 4H), 1.98-1.90 (m, 1H), 1.48 (s, 9H)

[1479] Step 4: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide hydrochloride

[1480] tert-Butyl ((3S)-1-(2-((5-carbamoyl-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate (12.3 mg, 0.02 mmol) was dissolved in dichloromethane (1 ml) and then 4.0M hydrogen chloride solution dissolved in 1,4-dioxane (0.5 ml, 7.69 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 4 hours. After completion of the reaction, the reaction mixture was concentrated and then filtered. The resulting solid was dried to prepare the titled compound (3.3 mg). (Yield: 27.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.20 (d, 1H), 8.10 (s, 1H), 8.00 (s, 1H), 7.83 (s,

- 1H), 7.50-7.48 (m, 1H), 7.25-7.23 (m, 1H), 6.99 (d, 1H), 6.94-6.85 (m, 2H), 4.09 (d, 1H), 4.12-4.09 (m, 2H), 3.85 (s, 3H), 3.83-3.81 (m, 1H), 3.65-3.50 (m, 3H), 3.49-3.42 (m, 1H), 2.93-2.88 (m, 2H), 2.22-2.20 (m, 1H), 2.15-2.10 (m, 3H), 1.90-1.70 (m, 2H), 1.65-1.59 (m, 2H) MS m/z= 587.9 (M+H)+
- [1481] Example 130: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-N,N-dimethylnicotinamide hydrochloride
- [1482] The titled compound (3.3 mg) was prepared in accordance with the same procedures as in Example 129, using Intermediates A3-1 and C2-1 and changing the amine reagent to 2.0M dimethylamine dissolved in tetrahydrofuran (0.02 mL, 0.05 mmol). (Yield: 27.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.10 (s, 1H), 8.09-8.00 (m, 2H), 7.82 (s, 1H), 7.83 (s, 1H), 7.52-7.48 (m, 1H), 7.29-7.25 (m, 1H), 7.01 (d, 1H), 6.93-6.88 (m, 2H), 4.58-4.52 (m, 1H), 4.12-4.09 (m, 2H), 3.85-3.82 (m, 4H), 3.64-3.54 (m, 4H), 3.50-3.43 (m, 1H), 2.95-2.91 (m, 4H), 2.88-2.85 (m, 4H), 2.24-2.20 (m, 1H), 2.15-2.09 (m, 4H), 1.90-1.72 (m, 2H), 1.66-1.60 (m, 1H) MS m/z= 615.9 (M+H)+
- [1483] Example 131: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1484] The titled compound (19.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-7 and C1-1. (Yield: 67.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.70 (d, 1H), 8.05 (s, 1H), 8.03 (s, 1H), 7.60 (q, 1H), 7.18-7.06 (m, 2H), 6.96 (t, 1H), 4.06 (s, 3H), 3.91 (s, 3H), 3.80-3.68 (m, 1H), 3.52-3.40 (m, 1H), 3.30-3.20 (m, 1H), 2.86 (q, 1H), 2.22-2.10 (m, 1H), 2.10-2.00 (m, 1H), 1.84-1.75 (m, 1H), 1.80-1.50 (m, 1H), 1.00-0.82 (m, 1H) MS m/z= 543.9 (M+H)+
- [1485] Example 132: (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-N,N-dimethylacetamide hydrochloride
- [1486] The titled compound (7.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-8 and C1-1. (Yield: 54.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.45 (d, 1H), 8.11 (s, 1H), 7.97 (s, 1H), 7.79 (s, 1H), 7.74 (s, 1H), 7.52 (d, 1H), 7.47 (q, 1H), 6.99 (d, 1H), 6.86 (t, 1H), 5.26 (q, 2H), 3.84 (s, 3H), 3.50 (d, 1H), 3.30-3.20 (m, 1H), 3.19 (s, 3H), 3.03 (s, 3H), 2.82 (t, 1H), 2.48 (t, 1H), 2.05 (q, 1H), 1.98-1.85 (m, 1H), 1.85-1.70 (m, 1H), 1.56-1.42 (m, 1H), 1.00-0.82 (m, 1H) MS m/z= 547.0 (M+H)+
- [1487] Example 133: (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)ethan-1-ol hydrochloride
- [1488] The titled compound (21.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-9 and C1-1. (Yield: 52.8%) ¹H

NMR (CD₃OD, 400MHz) δ 8.73 (d, 1H), 8.16 (s, 1H), 8.09 (s, 1H), 7.85 (s, 1H), 7.63 (q, 1H), 7.63-7.40 (m, 1H), 7.16 (s, 1H), 7.11 (d, 1H), 6.98 (t, 1H), 4.33 (t, 2H), 3.96 (t, 2H), 3.83 (s, 3H), 3.82 (d, 1H), 3.55 (d, 1H), 3.46-3.35 (m, 1H), 2.95 (t, 1H), 2.84 (t, 1H), 2.18 (d, 1H), 1.96-1.72 (m, 2H), 1.60 (q, 1H) MS m/z= 506.0 (M+H)+

[1489] Example 134: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1490] The titled compound (10.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-10 and C1-1. (Yield: 38.2%)
1H NMR (CD₃OD, 400MHz) δ 8.84-8.83 (m, 1H), 8.23-8.18 (m, 2H), 7.91 (s, 1H), 7.77-7.71 (m, 1H), 7.59 (s, 1H), 7.36 (s, 1H), 7.20 (d, 1H), 7.08 (dd, 1H), 6.43-6.16 (m, 1H), 4.74-4.70 (m, 2H), 4.00 (s, 3H), 3.92-3.82 (m, 1H), 3.70-3.66 (m, 1H), 3.45-3.36 (m, 1H), 3.09-3.04 (m, 2H), 2.23-2.20 (m, 1H), 1.84-1.68 (m, 3H) MS m/z= 525.2 (M+H)+

[1491] Example 135: N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine

[1492] The titled compound (14.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-28 and C1-1. (Yield: 24.2%)
1H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 8.40 (s, 1H), 8.15 (s, 1H), 8.12 (s, 1H), 7.84 (s, 1H), 7.54 (t, 1H), 7.50-7.40 (m, 2H), 6.99 (d, 1H), 6.87 (t, 1H), 3.84 (s, 3H), 2.92-2.84 (m, 3H), 2.65 (t, 2H), 2.46 (s, 2H), 2.38 (s, 3H), 2.10-2.00 (m, 1H), 1.70 (t, 2H), 1.68-1.52 (m, 4H) MS m/z= 565.9 (M+H)+

[1493] Example 136: 2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine

[1494] The titled compound (13.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-29 and C1-1. (Yield: 21.9%)
1H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.13 (s, 1H), 8.10 (s, 1H), 7.95 (s, 1H), 7.82 (s, 1H), 7.52-7.40 (m, 2H), 6.99 (d, 1H), 6.87 (t, 1H), 5.02 (q, 2H), 3.84 (s, 3H), 2.95-2.80 (m, 3H), 2.65 (t, 2H), 2.46 (s, 2H), 2.38 (s, 3H), 2.10-2.00 (m, 1H), 1.69 (t, 2H), 1.66-1.50 (m, 4H) MS m/z= 567.9 (M+H)+

[1495] Example 137: N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine

[1496] The titled compound (13.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-30 and C1-1. (Yield: 26.5%)
1H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.32 (d, 1H), 7.92 (s, 1H), 7.84 (d, 1H), 7.75 (s, 1H), 7.50-7.42 (m, 2H), 6.99 (d, 1H), 6.92 (d, 1H), 6.87 (t, 1H), 3.88-3.78 (m, 7H), 3.53 (t, 4H), 2.94-2.84 (m, 3H), 2.65 (t, 2H), 2.45 (s, 2H), 2.38 (s, 3H), 2.10-2.00 (m, 1H), 1.67 (t, 2H), 1.60-1.45 (m, 4H) MS m/z= 612.0 (M+H)+

- [1497] Example 138: (S)-3-(6-((4-(3-aminopiperidin-1-yl)-6'-morpholino-[3,3'-bipyridin]-6-yl)amino)pyridin-2-yl)oxazolidin-2-one hydrochloride
- [1498] The titled compound (5.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-19 and C7. (Yield: 63.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.32 (d, 1H), 7.88 (s, 1H), 7.84 (d, 1H), 7.70-7.64 (m, 1H), 7.64-7.58 (m, 1H), 7.43 (s, 1H), 7.16 (d, 1H), 6.94 (d, 1H), 4.55 (t, 2H), 4.39 (t, 2H), 3.84 (t, 4H), 3.54 (t, 4H), 3.45-3.38 (m, 1H), 3.24-3.16 (m, 1H), 3.00-2.90 (m, 1H), 2.65-2.48 (m, 2H), 2.08-1.95 (m, 2H), 1.68-1.50 (m, 2H) MS m/z= 517.9 (M+H)+
- [1499] Example 139: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinic acid
- [1500] Step 1: methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinate
- [1501] The titled compound (20.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-2 and C2-1. (Yield: 33.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.20 (d, 1H), 8.02 (s, 1H), 7.78 (s, 1H), 7.42-7.32 (m, 2H), 6.91-6.83 (m, 2H), 4.07-4.01 (m, 1H), 3.97-3.92 (m, 2H), 3.75 (d, 3H), 3.67 (s, 3H), 3.60-3.54 (m, 2H), 3.45-3.42 (m, 1H), 2.98-2.92 (m, 1H), 2.83-2.73 (m, 1H), 2.65-2.59 (m, 1H), 2.01-1.93 (m, 3H), 1.81-1.72 (m, 3H), 1.66-1.55 (m, 2H), 1.45-1.35 (m, 1H)
- [1502] Step 2: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinic acid
- [1503] Methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinate (20.3 mg, 0.036 mmol) was dissolved in tetrahydrofuran (1.0 ml) and methanol (0.3 ml) and then 1.0M sodium hydroxide solution (0.11 mL, 0.11 mmol) was added dropwise thereto. Then, the mixed solution was stirred at 60°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then neutralized with 1.0N hydrochloric acid solution. The aqueous layer was extracted with dichloromethane. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then dried to prepare the titled compound (19.0 mg), without further purification. (Yield: 96.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.42 (d, 1H), 8.05 (s, 1H), 7.48-7.43 (m, 1H), 7.14 (d, 1H), 6.97 (d, 1H), 6.89 (t, 1H), 6.66 (s, 1H), 4.20-4.14 (m, 1H), 3.95-3.84 (m, 3H), 3.82 (s, 3H), 3.59-3.50 (m, 3H), 3.41-3.39 (m, 1H), 2.99-2.93 (m, 1H), 2.10-1.92 (m, 4H), 1.79-1.66 (m, 4H), 1.40-1.34 (m, 1H) MS m/z= 546.9 (M+H)+
- [1504] Example 140: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinamide
- [1505] The titled compound (7.4 mg) was prepared in accordance with the same procedures as in Step 3 of Example 112, using the compound prepared in Example 139. (Yield:

- 49.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.01 (s, 1H), 7.97 (d, 1H), 7.76 (s, 1H), 7.42-7.37 (m, 1H), 7.34-7.31 (m, 1H), 6.92-6.85 (m, 2H), 4.07-4.02 (m, 1H), 3.97-3.92 (m, 2H), 3.81 (s, 3H), 3.74-3.72 (m, 1H), 3.60-3.50 (m, 3H), 2.97-2.93 (m, 1H), 2.88-2.73 (m, 1H), 2.64-2.62 (m, 1H), 2.03-2.00 (m, 1H), 1.98-1.93 (m, 2H), 1.81-1.74 (m, 2H), 1.62-1.62 (m, 1H), 1.37-1.35 (m, 1H) MS m/z= 546.3 (M+H)+
- [1506] Example 141: 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-N,N-dimethylnicotinamide
- [1507] The titled compound (1.1 mg) was prepared in accordance with the same procedures as in Example 112, using Intermediates A2-8 and C2-1 and changing the amine reagent to 2.0M dimethylamine dissolved in tetrahydrofuran (0.01 mL, 0.02 mmol). (Yield: 5.47%) ¹H NMR (CD₃OD, 400MHz) δ 8.40 (s, 1H), 8.09 (d, 2H), 7.91 (d, 1H), 7.73 (d, 1H), 7.53 (s, 1H), 7.46-7.38 (m, 2H), 6.92 (d, 1H), 6.88-6.86 (m, 1H), 3.80 (s, 3H), 3.73-3.70 (m, 1H), 3.30-3.23 (m, 1H), 3.05-2.98 (m, 1H), 2.90 (s, 3H), 2.87 (s, 3H), 2.63-2.61 (m, 1H), 2.48-2.43 (m, 1H), 1.95-1.94 (m, 1H), 1.75-1.73 (m, 1H), 1.57-1.55 (m, 2H) MS m/z= 582.2 (M+H)+
- [1508] Example 142: 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide
- [1509] The titled compound (1.3 mg) was prepared in accordance with the same procedures as in Example 112, using Intermediates A2-8 and C2-1. (Yield: 10.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (s, 1H), 8.13 (s, 2H), 8.02 (d, 1H), 7.94 (d, 1H), 7.56 (t, 1H), 7.48-7.40 (m, 2H), 6.97-6.88 (m, 2H), 3.84 (s, 3H), 3.76-3.74 (m, 1H), 3.30-3.26 (m, 1H), 3.04-3.02 (m, 1H), 2.71-2.61 (m, 1H), 2.48 (t, 1H), 2.01-1.97 (m, 1H), 1.80-1.77 (m, 1H), 1.59-1.58 (m, 1H), 1.44-1.43 (m, 1H) MS m/z= 554.2 (M+H)+
- [1510] Example 143: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide
- [1511] The titled compound (3.0 mg) was prepared in accordance with the same procedures as in Example 112, using Intermediates A2-6 and C2-1. (Yield: 28.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.13 (s, 1H), 8.05 (s, 2H), 7.98 (d, 1H), 7.94 (s, 1H), 7.86 (s, 1H), 7.44-7.36 (m, 2H), 6.93-6.86 (m, 2H), 5.03-4.97 (m, 2H), 3.81 (s, 3H), 3.74-3.68 (m, 1H), 3.26-3.22 (m, 1H), 3.02-2.96 (m, 1H), 2.64-2.56 (m, 1H), 2.47-2.41 (m, 1H), 1.94-1.93 (m, 1H), 1.77-1.69 (m, 1H), 1.57-1.52 (m, 1H), 1.40-1.33 (m, 1H) MS m/z= 586.2 (M+H)+
- [1512] Example 144: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide
- [1513] The titled compound (7.7 mg) was prepared in accordance with the same procedures as in Example 112, using Intermediates A2-9 and C2-1. (Yield: 51.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.03-8.02 (m, 2H), 7.97 (d, 1H), 7.85 (d, 1H), 7.82 (s, 1H),

7.44-7.35 (m, 2H), 6.93-6.86 (m, 2H), 4.36 (t, 2H), 3.82-3.70 (m, 5H), 3.75-3.70 (m, 1H), 3.36 (s, 3H), 3.29-3.28 (m, 1H), 3.02-2.98 (m, 1H), 2.60-2.56 (m, 1H), 2.38 (t, 1H), 1.97-1.95 (m, 1H), 1.76-1.72 (m, 1H), 1.62-1.58 (m, 1H), 1.40-1.35 (m, 1H) MS m/z = 562.0 (M+H)+

[1514] Example 145: (3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol

[1515] The titled compound (29.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-8 and C3-1. (Yield: 35.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.40 (d, 1H), 8.14 (d, 2H), 7.97 (s, 1H), 7.86 (s, 1H), 7.57 (s, 1H), 7.48-7.37 (m, 2H), 7.26 (t, 1H), 6.88 (t, 1H), 6.79 (d, 1H), 3.85-3.82 (m, 1H), 3.76 (s, 3H), 3.23-3.15 (m, 1H), 3.00-2.93 (m, 1H), 2.72-2.62 (m, 2H), 1.94-1.92 (m, 1H), 1.78-1.74 (m, 1H), 1.52-1.47 (m, 2H). MS m/z = 556.2 (M+H)+

[1516] Example 146: 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine hydrochloride

[1517] The titled compound (5.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C3-1. (Yield: 58.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.60 (d, 1H), 8.49 (s, 1H), 8.16-8.07 (m, 2H), 7.60 (t, 1H), 7.58-7.52 (m, 1H), 7.36 (d, 1H), 7.09 (s, 1H), 7.02-6.95 (m, 1H), 3.79-3.77 (m, 4H), 3.56-3.49 (m, 1H), 3.43-3.37 (m, 1H), 2.97-2.91 (m, 2H), 2.22-2.20 (m, 1H), 1.87-1.74 (m, 2H), 1.64-1.58 (m, 1H) MS m/z = 555.2 (M+H)+

[1518] Example 147: N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine

[1519] The titled compound (13.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-31 and C1-1. (Yield: 18.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 8.38 (s, 1H), 8.14 (s, 1H), 8.10 (s, 1H), 7.72 (s, 1H), 7.54 (t, 1H), 7.58-7.40 (m, 2H), 6.98 (d, 1H), 6.86 (t, 1H), 3.84 (s, 3H), 2.58 (t, 2H), 2.39 (t, 2H), 2.29 (s, 6H), 2.10-2.00 (m, 1H), 1.66 (d, 2H), 1.55-1.44 (m, 2H), 1.44-1.20 (m, 4H) MS m/z = 568.0 (M+H)+

[1520] Example 148: N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine

[1521] The titled compound (6.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-32 and C1-1. (Yield: 17.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.11 (s, 1H), 8.10 (s, 1H), 7.94 (s, 1H), 7.70 (s, 1H), 7.52-7.40 (m, 2H), 6.98 (d, 1H), 6.86 (t, 1H), 5.02 (q, 2H), 3.83 (s, 3H), 2.56 (t, 2H), 2.46-2.32 (m, 2H), 2.29 (s, 6H), 2.10-2.00 (m, 1H), 1.64 (d, 2H), 1.54-1.42 (m, 2H), 1.42-1.20 (m, 4H) MS m/z = 599.9 (M+H)+

- [1522] Example 149: 4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine
- [1523] The titled compound (16.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-33 and C1-1. (Yield: 24.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.30 (d, 1H), 7.91 (s, 1H), 7.83 (d, 1H), 7.67 (s, 1H), 7.52-7.40 (m, 2H), 6.98 (d, 1H), 6.93 (d, 1H), 6.86 (t, 1H), 3.90-3.78 (m, 7H), 3.54 (t, 4H), 2.55 (t, 2H), 2.36 (t, 2H), 2.27 (s, 6H), 2.10-2.00 (m, 1H), 1.57 (d, 2H), 1.50-1.40 (m, 2H), 1.40-1.10 (m, 4H) MS m/z= 614.1 (M+H)+
- [1524] Example 150: (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1525] Step 1: (3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1526] The titled compound (29.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-8 and C3-1. (Yield: 35.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.40 (d, 1H), 8.14 (d, 2H), 7.97 (s, 1H), 7.86 (s, 1H), 7.57 (s, 1H), 7.48-7.37 (m, 2H), 7.26 (t, 1H), 6.88 (t, 1H), 6.79 (d, 1H), 3.85-3.82 (m, 1H), 3.76 (s, 3H), 3.23-3.15 (m, 1H), 3.00-2.93 (m, 1H), 2.72-2.62 (m, 2H), 1.94-1.92 (m, 1H), 1.78-1.74 (m, 1H), 1.52-1.47 (m, 2H)
- [1527] Step 2: (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1528] (3S)-1-(5-(1-(Difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol (15.0 mg, 0.027 mmol) was dissolved in methanol (2.0 mL) and then Pd/C (15 mg, 0.14 mmol) was added dropwise thereto. The reaction mixture was stirred at room temperature for 3 hours under a pressure of a balloon filled with hydrogen gas. After completion of the reaction, the reaction mixture was filtered through a Celite filter. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (5.0 mg). (Yield: 35.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.36 (s, 1H), 8.06 (s, 1H), 7.97 (s, 1H), 7.52 (t, 1H), 7.49-7.37 (m, 1H), 7.31 (d, 2H), 7.25-7.22 (m, 1H), 6.99 (d, 1H), 6.90 (t, 1H), 3.86 (s, 3H), 3.75-3.71 (m, 1H), 3.28-3.25 (m, 1H), 3.11-3.02 (m, 1H), 2.68-2.62 (m, 1H), 2.50-2.46 (m, 1H), 1.98-1.94 (m, 1H), 1.77-1.74 (m, 1H), 1.65-1.52 (m, 1H), 1.38-1.36 (m, 1H) MS m/z= 526.2 (M+H)+
- [1529] Example 151: N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride
- [1530] Step 1: tert-butyl ((3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-yl)carbamate
- [1531] The titled compound (45.7 mg) was prepared in accordance with the same procedures as in Step 1 of Example 52, using Intermediates A3-2 and C3-1. (Yield:

- 45.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.42-8.38 (m, 1H), 8.12-8.11 (m, 2H), 7.96 (s, 1H), 7.85 (s, 1H), 7.45-7.40 (m, 2H), 7.26 (t, 1H), 6.92-6.89 (m, 1H), 6.81-6.78 (m, 1H), 4.47 (brs, 1H), 3.76 (s, 4H), 3.39 (d, 1H), 3.29 (d, 1H), 3.01-2.98 (m, 1H), 2.55-2.42 (m, 2H), 1.97-1.94 (m, 1H), 1.49 (s, 10H)
- [1532] Step 2: tert-butyl ((3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate
- [1533] tert-Butyl ((3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-yl)carbamate (17.7 mg, 0.03 mmol) was dissolved in methanol (2.0 mL) and then Pd/C (18.0 mg, 0.17 mmol) was added dropwise thereto. The reaction mixture was stirred at room temperature for 3 hours under a pressure of a balloon filled with hydrogen gas. After completion of the reaction, the reaction mixture was filtered through a Celite filter. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (9.90 mg). (Yield: 58.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.32 (s, 1H), 8.03 (s, 1H), 7.96 (s, 1H), 7.52 (t, 1H), 7.50-7.44 (m, 1H), 7.32-7.21 (m, 2H), 7.01-6.90 (m, 2H), 3.85 (s, 3H), 3.64-3.54 (m, 1H), 3.11-3.09 (m, 1H), 2.54-2.39 (m, 3H), 1.94-1.90 (m, 1H), 1.65-1.61 (m, 3H), 1.45 (s, 9H)
- [1534] Step 3: N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride
- [1535] tert-Butyl ((3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)carbamate (9.9 mg, 0.02 mmol) was dissolved in dichloromethane (1.0 ml) and then 4.0M hydrogen chloride solution dissolved in 1,4-dioxane (0.02 mL, 0.01 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 2 hours. After completion of the reaction, the reaction mixture was concentrated and then dried to prepare the titled compound (4.6 mg). (Yield: 48.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.47 (s, 1H), 8.05-8.02 (m, 2H), 7.83-7.74 (m, 1H), 7.64-7.59 (m, 2H), 7.33-7.31 (m, 1H), 7.11 (d, 1H), 7.01 (t, 1H), 6.92 (s, 1H), 3.92 (s, 3H), 3.77-3.75 (m, 1H), 3.50-3.44 (m, 2H), 2.97-2.84 (m, 2H), 2.21-2.19 (m, 1H), 1.83-1.71 (m, 2H), 1.61-1.59 (m, 1H) MS m/z= 525.2 (M+H)⁺
- [1536] Example 152: 4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine hydrochloride
- [1537] The titled compound (9.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-10 and C3-1. (Yield: 92.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.59 (d, 1H), 8.13 (s, 1H), 8.05 (s, 1H), 7.89 (s, 1H), 7.58-7.52 (m, 1H), 7.35 (d, 1H), 7.05-6.95 (m, 3H), 6.42-6.92 (m, 1H), 4.73-4.64 (m, 2H), 3.83-3.80

- (m, 4H), 3.58-3.55 (m, 1H), 3.42-3.39 (m, 1H), 2.95-2.88 (m, 2H), 2.22-2.20 (m, 1H), 1.88-1.85 (m, 1H), 1.78-1.75 (m, 1H), 1.65-1.58 (m, 1H). MS m/z = 569.2 (M+H)+
- [1538] Example 153: 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine hydrochloride
- [1539] The titled compound (8.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C3-1. (Yield: 79.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.60 (d, 1H), 8.20-8.18 (m, 1H), 8.06 (s, 1H), 7.92 (s, 1H), 7.58-7.52 (m, 1H), 7.38-7.36 (m, 1H), 7.05-6.95 (m, 3H), 5.10-5.04 (m, 2H), 3.85-3.80 (m, 4H), 3.57-3.54 (m, 1H), 3.50-3.42 (m, 1H), 3.01-2.88 (m, 2H), 2.22-2.19 (m, 1H), 1.82-1.70 (m, 2H), 1.63-1.61 (m, 1H) MS m/z = 587.2 (M+H)+
- [1540] Example 154: 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-amine hydrochloride
- [1541] The titled compound (3.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-11 and C3-1. (Yield: 37.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.62-8.59 (m, 2H), 8.20 (s, 1H), 8.14 (d, 1H), 7.58-7.52 (m, 1H), 7.37 (d, 1H), 7.09 (s, 1H), 7.02-6.95 (m, 2H), 3.80 (s, 4H), 3.56-3.50 (m, 1H), 3.40-3.38 (m, 1H), 3.01-2.93 (m, 2H), 2.22-2.20 (m, 1H), 1.85-1.72 (m, 2H), 1.70-1.60 (m, 1H) MS m/z = 573.2 (M+H)+
- [1542] Example 155: 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-amine hydrochloride
- [1543] The titled compound (4.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-1 and C3-1. (Yield: 43.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.58 (d, 1H), 8.21 (s, 1H), 7.58-7.53 (m, 1H), 7.31 (d, 1H), 7.02-6.96 (m, 2H), 6.85 (s, 1H), 4.37-4.34 (m, 1H), 4.25-4.23 (m, 1H), 3.96-3.91 (m, 2H), 3.80 (s, 3H), 3.59-3.45 (m, 4H), 3.02-2.97 (m, 1H), 2.28-2.25 (m, 1H), 2.05-2.01 (m, 1H), 1.97-1.94 (m, 2H), 1.88-1.85 (m, 1H), 1.81-1.71 (m, 3H) MS m/z = 547.2 (M+H)+
- [1544] Example 156: 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-amine hydrochloride
- [1545] The titled compound (9.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-2 and C3-1. (Yield: 93.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.61-8.56 (m, 2H), 8.34 (s, 1H), 8.06 (s, 1H), 7.57-7.52 (m, 1H), 7.36 (d, 1H), 7.02-6.95 (m, 3H), 4.39-4.35 (m, 1H), 4.11-4.08 (m, 1H), 3.80 (s, 3H), 3.52-3.51 (m, 1H), 3.43-3.37 (m, 1H), 2.27-2.24 (m, 1H), 2.06-2.01 (m, 1H), 1.90-1.72 (m, 3H) MS m/z = 597.2 (M+H)+

- [1546] Example 157: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1547] The titled compound (7.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-11 and C1-7. (Yield: 72.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.66 (s, 1H), 8.25 (d, 2H), 7.62 (s, 1H), 7.27 (s, 1H), 7.02 (d, 1H), 6.91 (dd, 1H), 3.96 (s, 3H), 3.86-3.83 (m, 1H), 3.56-3.52 (m, 1H), 3.44-3.33 (m, 1H), 3.07-2.95 (m, 2H), 2.22-2.20 (m, 1H), 1.87-1.84 (m, 1H), 1.75-1.63 (m, 2H) MS m/z= 547.2 (M+H)+
- [1548] Example 158: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1549] The titled compound (15.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-10 and C1-7. (Yield: 92.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.19 (d, 2H), 7.9 (s, 1H), 7.52-7.50 (m, 1H), 7.23 (s, 1H), 7.01 (d, 1H), 6.89 (dd, 1H), 6.43-6.15 (m, 1H), 4.74-4.66 (m, 2H), 3.95 (s, 3H), 3.91-3.88 (m, 1H), 3.61-3.58 (m, 1H), 3.45-3.33 (m, 1H), 3.05-2.96 (m, 2H), 2.22-2.20 (m, 1H), 1.84-1.77 (m, 1H), 1.66-1.64 (m, 1H) MS m/z= 543.2 (M+H)+
- [1550] Example 159: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1551] The titled compound (3.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-2 and C1-7. (Yield: 85.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.72 (d, 1H), 8.7 (s, 1H), 8.62 (s, 1H), 8.42 (s, 1H), 8.07 (s, 1H), 7.76 (s, 1H), 7.15 (s, 1H), 7.02 (d, 1H), 6.92 (dd, 1H), 4.31-4.28 (m, 1H), 4.09-4.06 (m, 1H), 3.95 (s, 3H), 3.53-3.52 (m, 1H), 3.40-3.33 (m, 2H), 2.26-2.23 (m, 1H), 2.11-2.03 (m, 1H), 1.91-1.88 (m, 1H), 1.76-1.67 (m, 1H) MS m/z= 571.2 (M+H)+
- [1552] Example 160: 6-((5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide
- [1553] The titled compound (3.7 mg) was prepared in accordance with the same procedures as in Example 112, using Intermediates A2-10 and C2-1. (Yield: 35.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.05 (d, 2H), 7.97 (d, 1H), 7.90 (s, 1H), 7.87 (d, 1H), 7.44-7.35 (m, 2H), 6.93-6.85 (m, 2H), 6.37-6.08 (m, 1H), 4.66-3.80 (m, 2H), 3.82 (s, 3H), 3.74-3.70 (m, 1H), 3.26-3.23 (m, 1H), 3.03-2.96 (m, 1H), 2.63-2.54 (m, 1H), 2.41 (t, 1H), 1.96-1.94 (m, 1H), 1.83-1.72 (m, 1H), 1.57-1.56 (m, 1H), 1.39-1.35 (m, 1H). MS m/z= 567.9 (M+H)+

- [1554] Example 161: (S)-1-(2-((2-(2-fluoro-4-(hydroxymethyl)-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1555] The titled compound (6.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C5-1. (Yield: 33.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.55 (d, 1H), 8.3 (s, 1H), 8.14 (s, 1H), 7.79 (s, 1H), 7.66 (s, 1H), 7.42 (s, 1H), 6.77-6.73 (m, 2H), 4.7 (s, 2H), 4.42-4.38 (m, 1H), 4.15-4.12 (m, 2H), 3.77 (s, 3H), 3.75-3.74 (m, 1H), 3.60-3.54 (m, 2H), 3.21-3.18 (m, 1H), 2.99-2.96 (m, 1H), 2.63-2.59 (m, 2H), 2.14-2.05 (m, 2H), 1.91-1.89 (m, 1H), 1.70-1.49 (m, 3H), 1.46-1.41 (m, 2H) MS m/z= 576.2 (M+H)+
- [1556] Example 162: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1557] The titled compound (12.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-12 and C1-1. (Yield: 73.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.60 (d, 1H), 8.22 (s, 1H), 8.19 (s, 1H), 7.57 (s, 1H), 7.65-7.50 (m, 2H), 7.34 (s, 1H), 7.05 (d, 1H), 6.92 (t, 1H), 4.72 (t, 2H), 3.96 (t, 4H), 3.88 (s, 3H), 3.80-3.70 (m, 1H), 3.70-3.58 (m, 2H), 3.52-3.20 (m, 6H), 2.90-2.80 (m, 2H), 2.25-2.00 (m, 3H), 1.94-1.80 (m, 1H) MS m/z= 575.0 (M+H)+
- [1558] Example 163: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1559] The titled compound (11.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-13 and C1-1. (Yield: 85.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.52 (d, 1H), 8.28-8.15 (m, 2H), 7.97 (s, 1H), 7.60 (s, 1H), 7.58-7.42 (m, 2H), 7.02 (d, 1H), 6.90 (t, 1H), 4.70 (t, 2H), 3.86 (s, 3H), 3.83 (t, 2H), 3.72-3.60 (m, 1H), 3.60-3.30 (m, 4H), 3.30-3.20 (m, 2H), 2.85-2.60 (m, 2H), 2.25-2.10 (m, 4H), 2.10-2.00 (m, 2H), 1.90-1.74 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 558.0 (M+H)+
- [1560] Example 164: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1561] The titled compound (16.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-3 and C1-1. (Yield: 48.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.77 (d, 1H), 8.49 (s, 1H), 8.43 (s, 1H), 7.96-7.72 (m, 1H), 7.71-7.42 (m, 1H), 7.23 (s, 1H), 7.18 (d, 1H), 7.07 (t, 1H), 4.42-4.39 (m, 1H), 4.24-4.21 (m, 1H), 3.98 (s, 3H), 3.53-3.51 (m, 1H), 3.47-3.40 (m, 2H), 2.28-2.26 (m, 1H), 2.24-2.05 (m, 1H), 2.04-1.82 (m, 2H), MS m/z= 535.2 (M+H)+

- [1562] Example 165: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1563] The titled compound (19.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-4 and C1-1. (Yield: 57.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.39 (s, 1H), 8.11 (s, 1H), 7.81 (s, 1H), 7.74-7.69 (m, 2H), 7.21 (s, 1H), 7.18 (d, 1H), 7.07 (t, 1H), 6.37-6.10 (m, 1H), 4.68-4.60 (m, 2H), 4.43-4.40 (m, 1H), 4.31-4.26 (m, 1H), 3.98 (s, 3H), 3.53-3.51 (m, 1H), 3.48-3.43 (m, 2H), 2.28-2.26 (m, 1H), 2.25-2.12 (m, 1H), 2.04-1.82 (m, 2H) MS m/z= 549.2 (M+H)+
- [1564] Example 166: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1565] The titled compound (13.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-5 and C1-1. (Yield: 39.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.4 (s, 1H), 8.18 (s, 1H), 7.83 (s, 1H), 7.73-7.67 (m, 2H), 7.2 (s, 1H), 7.17 (d, 1H), 7.06 (t, 1H), 5.06 (q, 2H), 4.39-4.36 (m, 1H), 4.23-4.20 (m, 1H), 3.97 (s, 3H), 3.53-3.51 (m, 1H), 3.50-3.38 (m, 2H), 2.24-2.24 (m, 1H), 2.07-2.04 (m, 1H), 1.92-1.81 (m, 2H), MS m/z= 567.2 (M+H)+
- [1566] Example 167: (S)-3-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)propanamide hydrochloride
- [1567] The titled compound (1.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-14 and C1-1. (Yield: 40.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.60 (d, 1H), 8.22 (s, 1H), 8.19 (s, 1H), 7.57 (s, 1H), 7.65-7.50 (m, 2H), 7.34 (s, 1H), 7.05 (d, 1H), 6.92 (t, 1H), 4.72 (t, 2H), 3.96 (t, 4H), 3.88 (s, 3H), 3.80-3.70 (m, 1H), 3.70-3.58 (m, 2H), 3.52-3.20 (m, 6H), 2.90-2.80 (m, 2H), 2.25-2.00 (m, 3H), 1.94-1.80 (m, 1H) MS m/z= 531.9 (M+H)+
- [1568] Example 168: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(azetidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1569] The titled compound (1.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-15 and C1-1. (Yield: 11.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.47 (d, 1H), 8.43 (s, 1H), 7.84 (d, 1H), 7.67 (s, 1H), 7.61 (d, 1H), 7.47 (q, 1H), 6.99 (d, 1H), 6.88 (t, 1H), 6.75 (d, 1H), 5.55-5.44 (m, 1H), 4.60-4.50 (m, 2H), 4.50-4.40 (m, 2H), 3.84 (s, 3H), 3.36 (d, 1H), 3.35-3.15 (m, 2H), 2.80-2.62 (m, 2H), 2.10-2.00 (m, 2H), 1.80-1.66 (m, 1H), 1.66-1.46 (m, 1H) MS m/z= 515.9 (M+H)+
- [1570] Example 169: N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride

- [1571] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 151, using Intermediates A3-10 and C3-1. (Yield: 48.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.09 (s, 1H), 7.95 (s, 1H), 7.86 (s, 1H), 7.67 (d, 1H), 7.61-7.55 (m, 1H), 7.19 (d, 1H), 7.09 (d, 1H), 6.98 (t, 1H), 6.80 (s, 1H), 6.40-6.13 (m, 1H), 4.71-4.62 (m, 2H), 3.90 (s, 3H), 3.74-3.71 (m, 1H), 3.51-3.37 (m, 2H), 2.87-2.80 (m, 2H), 2.22-2.19 (m, 1H), 1.92-1.74 (m, 2H), 1.63-1.53 (m, 1H) MS m/z= 538.9 (M+H)+
- [1572] Example 170: N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride
- [1573] The titled compound (6.1 mg) was prepared in accordance with the same procedures as in Example 151, using Intermediates A3-4 and C3-1. (Yield: 58.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.16 (s, 1H), 7.97 (s, 1H), 7.90 (s, 1H), 7.71-7.66 (m, 1H), 7.59-7.55 (m, 1H), 7.24-7.18 (m, 1H), 7.09 (d, 1H), 6.99 (t, 1H), 6.84-6.80 (m, 1H), 5.08-5.02 (m, 2H), 3.90 (s, 3H), 3.76-3.73 (m, 1H), 3.50-3.40 (m, 2H), 2.91-2.79 (m, 2H), 2.22-2.19 (m, 1H), 1.81-1.69 (m, 2H), 1.64-1.54 (m, 1H) MS m/z= 556.9 (M+H)+
- [1574] Example 171: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1575] The titled compound (5.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-11 and C1-7. (Yield: 16.8%) ¹H NMR (CDCl₃, 400MHz) δ 8.60 (d, 1H), 8.58 (d, 1H), 8.16 (s, 1H), 7.69 (s, 1H), 7.44-7.43 (m, 1H), 7.39 (s, 1H), 6.60-6.55 (m, 2H), 3.86-3.84 (m, 1H), 3.82 (s, 3H), 3.24-3.23 (m, 1H), 3.20-2.97 (m, 1H), 2.73-2.67 (m, 2H), 1.96-1.94 (m, 1H), 1.79-1.77 (m, 1H), 1.54-1.47 (m, 2H) MS m/z= 547.9 (M+H)+
- [1576] Example 172: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1577] The titled compound (3.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-10 and C1-7. (Yield: 12.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.58 (d, 1H), 8.11 (s, 1H), 7.84 (d, 2H), 7.81 (s, 1H), 7.47 (s, 1H), 7.31-7.28 (m, 1H), 6.60-6.59 (m, 2H), 6.32-6.16 (m, 1H), 4.57-4.49 (m, 2H), 3.84-3.83 (m, 1H), 3.82 (s, 3H), 3.25-3.22 (m, 1H), 2.92-2.71 (m, 1H), 2.68-2.66 (m, 2H), 1.78-1.76 (m, 1H), 1.68-1.56 (m, 1H), 1.53-1.48 (m, 2H) MS m/z= 543.9 (M+H)+
- [1578] Example 173: N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride
- [1579] The titled compound (2.8 mg) was prepared in accordance with the same procedures as in Example 151, using Intermediates A3-11 and C3-1. (Yield: 38.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.56 (s, 1H), 8.19 (s, 1H), 8.03 (s, 1H), 7.72-7.56 (m, 2H), 7.25-7.17

- (m, 1H), 7.09 (d, 1H), 6.98 (t, 1H), 6.85-6.77 (m, 1H), 3.90 (s, 3H), 3.74-3.71 (m, 1H), 3.43-3.38 (m, 2H), 2.93-2.85 (m, 2H), 2.22-2.18 (m, 1H), 1.85-1.83 (m, 1H), 1.73-1.70 (m, 1H), 1.63-1.57 (m, 1H) MS m/z= 542.9 (M+H)+
- [1580] Example 174: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1581] The titled compound (2.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-6 and C1-7. (Yield: 6.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.58 (d, 1H), 8.12 (s, 1H), 7.87 (d, 1H), 7.65 (s, 1H), 7.52-7.47 (m, 1H), 7.31-7.28 (m, 1H), 6.60-6.55 (m, 2H), 4.81 (q, 2H), 3.82 (s, 3H), 3.81-3.80 (m, 1H), 3.26-3.22 MS m/z= 561.9 (M+H)+
- [1582] Example 175: (S)-5-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridazin-3-amine hydrochloride
- [1583] The titled compound (8.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A10-1 and C1-1. (Yield: 48.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.52 (d, 1H), 8.37 (s, 1H), 8.17 (s, 1H), 8.09 (s, 1H), 7.54-7.42 (m, 2H), 7.00 (d, 1H), 6.89 (t, 1H), 5.08 (q, 2H), 3.84 (s, 3H), 3.20 (d, 1H), 3.00-2.86 (m, 1H), 2.70-2.56 (m, 1H), 2.03 (t, 1H), 2.10-2.00 (m, 2H), 1.78-1.68 (m, 1H), 1.30-1.16 (m, 1H) MS m/z= 544.9 (M+H)+
- [1584] Example 176: (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(4-methylpiperazin-1-yl)methanone hydrochloride
- [1585] The titled compound (10.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-20 and C1-1. (Yield: 85.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.53 (d, 1H), 8.08 (s, 1H), 7.74 (dd, 2H), 7.68-7.58 (m, 3H), 7.55 (s, 1H), 7.50 (q, 1H), 7.01 (d, 1H), 6.89 (t, 1H), 3.92-3.80 (m, 1H), 3.85 (s, 3H), 3.50-3.24 (m, 4H), 3.24-3.10 (m, 2H), 2.94 (s, 3H), 2.80-2.60 (m, 2H), 2.15-2.00 (m, 4H), 1.80-1.70 (m, 1H), 1.70-1.56 (m, 2H), 1.56-1.44 (m, 1H) MS m/z= 597.0 (M+H)+
- [1586] Example 177: (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1587] The titled compound (7.3 mg) was prepared in accordance with the same procedures as in Example 150, using Intermediates A2-1 and C3-1. (Yield: 51.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.04 (s, 1H), 7.92 (s, 1H), 7.79 (s, 1H), 7.49-7.43 (m, 1H), 7.33-7.29 (m, 1H), 7.25-7.22 (m, 1H), 6.99 (d, 1H), 6.89 (t, 1H), 4.49-4.45 (m, 1H), 4.13-4.09 (m, 2H), 3.85 (s, 3H), 3.74-3.68 (m, 1H), 3.64-3.58 (m, 2H), 3.28-3.25 (m, 1H),

- 3.03-3.01 (m, 1H), 2.62-2.59 (m, 1H), 2.46-2.40 (m, 1H), 2.15-2.05 (m, 4H), 1.98-1.92 (m, 1H), 1.76-1.73 (m, 1H), 1.57-1.55 (m, 1H), 1.37-1.35 (m, 1H) MS m/z= 559.9 (M+H)+
- [1588] Example 178: (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1589] The titled compound (2.8 mg) was prepared in accordance with the same procedures as in Example 150, using Intermediates A2-11 and C3-1. (Yield: 35.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.48 (s, 1H), 8.20 (s, 1H), 8.00 (s, 1H), 7.49-7.41 (m, 2H), 7.31-7.26 (m, 2H), 6.99 (d, 1H), 6.89 (t, 1H), 3.86 (s, 3H), 3.82 (s, 1H), 3.23-3.20 (m, 1H), 2.99-2.98 (m, 1H), 2.65-2.62 (m, 1H), 2.51-2.46 (m, 1H), 1.97-1.92 (m, 1H), 1.78-1.75 (m, 1H), 1.56-1.54 (m, 1H), 1.38-1.35 (m, 1H) MS m/z= 543.9 (M+H)+
- [1590] Example 179: (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1591] The titled compound (6.6 mg) was prepared in accordance with the same procedures as in Example 150, using Intermediates A2-10 and C3-1. (Yield: 32.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.02 (s, 1H), 7.92 (s, 1H), 7.86 (s, 1H), 7.49-7.43 (m, 1H), 7.31-7.29 (m, 2H), 7.25-7.22 (m, 1H), 6.99 (d, 1H), 6.89 (t, 1H), 6.36-6.08 (m, 1H), 4.66-4.57 (m, 2H), 3.85 (s, 3H), 3.76-3.70 (m, 1H), 3.28-3.25 (m, 1H), 3.06-3.02 (m, 1H), 2.63-2.56 (m, 1H), 2.46-2.41 (m, 1H), 1.98-1.92 (m, 1H), 1.75-1.72 (m, 1H), 1.58-1.55 (m, 1H), 1.37-1.34 (m, 1H). MS m/z= 539.9 (M+H)+
- [1592] Example 180: (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1593] The titled compound (6.9 mg) was prepared in accordance with the same procedures as in Example 150, using Intermediates A2-6 and C3-1. (Yield: 39.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.08 (s, 1H), 7.93 (s, 1H), 7.90 (s, 1H), 7.49-7.43 (m, 1H), 7.33-7.29 (m, 2H), 7.26-7.22 (m, 1H), 6.99 (d, 1H), 6.89 (t, 1H), 5.02-4.98 (m, 2H), 3.86 (s, 3H), 3.75-3.71 (m, 1H), 3.28-3.26 (m, 1H), 3.03-3.01 (m, 1H), 2.62-2.55 (m, 1H), 2.48-2.42 (m, 1H), 1.97-1.92 (m, 1H), 1.74-1.71 (m, 1H), 1.64-1.47 (m, 1H), 1.36-1.34 (m, 1H). MS m/z= 557.9 (M+H)+
- [1594] Example 181: N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride
- [1595] The titled compound (7.5 mg) was prepared in accordance with the same procedures as in Example 151, using Intermediates A3-1 and C3-1. (Yield: 76.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.09 (s, 1H), 7.96 (s, 1H), 7.88-7.84 (m, 1H), 7.81 (s, 1H), 7.63-7.61 (m, 1H), 7.32-7.30 (m, 1H), 7.12 (d, 1H), 7.02 (t, 1H), 6.92-6.89 (m, 1H), 4.52-4.49 (m, 1H), 4.13-4.09 (m, 2H), 3.92 (s, 3H), 3.82-3.79 (m, 1H), 3.64-3.58 (m, 2H),

- 3.54-3.41 (m, 2H), 2.97-2.92 (m, 1H), 2.87-2.81 (m, 1H), 2.22-2.19 (m, 1H), 2.15-2.03 (m, 4H), 1.81-1.76 (m, 1H), 1.74-1.71 (m, 1H), 1.65-1.59 (m, 1H). MS m/z= 559.3 (M+H)+
- [1596] Example 182: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1597] The titled compound (4.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-8 and C1-7. (Yield: 15.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.59 (d, 1H), 8.15 (d, 1H), 7.97 (s, 1H), 7.75 (s, 1H), 7.46-7.44 (m, 1H), 7.41-7.10 (m, 2H), 6.59-6.54 (m, 2H), 3.86-3.84 (m, 1H), 3.82 (s, 3H), 3.25-3.21 (m, 1H), 2.98-2.82 (m, 1H), 2.70-2.65 (m, 2H), 2.06-1.92 (m, 1H), 1.77-1.76 (m, 1H), 1.75-1.74 (m, 1H), 1.56-1.50 (m, 2H), MS m/z= 529.9 (M+H)+
- [1598] Example 183: (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1599] The titled compound (8.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-8 and C3-2. (Yield: 39.2%) ¹H NMR (CDCl₃, 400MHz) δ 8.41 (d, 1H), 8.15 (d, 2H), 7.97 (s, 1H), 7.92 (s, 1H), 7.53-7.48 (m, 2H), 7.41-7.10 (m, 1H), 6.66 (d, 1H), 6.55 (dd, 1H), 3.86-3.84 (m, 1H), 3.75 (s, 3H), 3.21-2.97 (m, 1H), 2.69-2.67 (m, 1H), 2.66-2.62 (m, 2H), 1.93-1.79 (m, 1H), 1.78-1.76 (m, 1H), 1.56-1.51 (m, 2H), MS m/z= 573.9 (M+H)+
- [1600] Example 184: (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1601] The titled compound (1.8 mg) was prepared in accordance with the same procedures as in Step 2 of Example 150, using the compound prepared in Example 183. (Yield: 30.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.35 (s, 1H), 8.06 (s, 1H), 7.97 (s, 1H), 7.66-7.38 (m, 1H), 7.36 (s, 1H), 7.29-7.26 (m, 2H), 6.82 (d, 1H), 6.74 (dd, 1H), 3.85 (s, 3H), 3.73-3.71 (m, 1H), 3.32-3.26 (m, 1H), 3.23-3.00 (m, 1H), 2.58-2.56 (m, 1H), 2.43-2.42 (m, 1H), 1.98-1.96 (m, 1H), 1.74-1.72 (m, 1H), 1.57-1.37 (m, 1H), 1.34-1.31 (m, 1H), MS m/z= 543.9 (M+H)+
- [1602] Example 185: methyl (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate hydrochloride
- [1603] The titled compound (9.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-10. (Yield: 51.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.82 (d, 1H), 8.52 (s, 1H), 8.19 (s, 1H), 8.07 (s, 1H), 7.76-7.46 (m, 4H), 7.21 (s, 1H), 4 (s, 3H), 3.99 (s, 3H), 3.87-3.85 (m, 1H), 3.58-3.54 (m, 1H), 3.50-3.43 (m, 1H), 3.06-2.97 (m, 2H), 2.22-2.20 (m, 1H), 1.76-1.73 (m, 1H), 1.65-1.62 (m, 2H), MS m/z= 568.9 (M+H)+

- [1604] Example 186: (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N-methylbenzamide hydrochloride
- [1605] Step 1: methyl (S)-4-(4-((4-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate
- [1606] The titled compound (151.5 mg) was prepared in accordance with the same procedures as in Step 1 of Example 52, using Intermediates A3-2 and C1-10. (Yield: 32.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.61 (d, 1H), 8.13 (s, 2H), 7.95 (s, 1H), 7.53 (s, 1H), 7.42 (s, 2H), 7.28-7.11 (m, 2H), 4.51-4.50 (m, 1H), 4.15 (s, 3H), 3.98 (s, 3H), 3.72-3.71 (m, 1H), 3.43-3.40 (m, 1H), 3.05-3.02 (m, 1H), 2.59-2.47 (m, 2H), 1.95-1.91 (m, 1H), 1.62-1.59 (m, 2H), 1.46 (s, 9H)
- [1607] Step 2: (S)-4-(4-((4-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoic acid
- [1608] Methyl (S)-4-(4-((4-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate (130.0 mg, 0.19 mmol) was dissolved in methanol (2.0 ml) and then 1.0N sodium hydroxide solution (1.0 mL) was added dropwise thereto. Then, the mixed solution was stirred at 60°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then neutralized with 1.0N hydrochloric acid solution. The aqueous layer was extracted with dichloromethane. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then dried to prepare the titled compound (98.0 mg), without further purification. (Yield: 77.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.37 (s, 1H), 8.05 (s, 1H), 7.95 (s, 1H), 7.65-7.41 (m, 2H), 7.22 (s, 1H), 6.59 (s, 1H), 3.93 (s, 3H), 3.57-3.56 (m, 1H), 3.54-3.50 (m, 2H), 3.02-2.96 (m, 1H), 2.86-2.80 (m, 1H), 1.62-1.61 (m, 1H), 1.51-1.48 (m, 1H), 1.45-1.44 (m, 1H), 1.27-1.25 (m, 1H), 1.24 (s, 9H)
- [1609] Step 3: tert-butyl (S)-(1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxy-4-(methylcarbamoyl)phenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-yl)carbamate
- [1610] (S)-4-(4-((4-(3-((tert-Butoxycarbonyl)amino)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoic acid (20.0 mg, 0.031 mmol) was dissolved in anhydrous dimethylformamide (1.0 mL) and then 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide hexafluorophosphate (HATU, 23.2 mg, 0.061 mmol) and diisopropylethylamine (16 uL, 0.092 mmol) were added dropwise thereto. The reaction mixture was

stirred at room temperature for 15 minutes and then 2.0M methylamine dissolved in tetrahydrofuran (30.5 uL, 0.061 mmol) was added dropwise thereto. The reaction mixture was stirred at 80°C for 4 hours. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (10.6 mg). (Yield: 51.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.6 (d, 1H), 8.11 (s, 2H), 8 (s, 1H), 7.54 (s, 1H), 7.35-7.02 (m, 2H), 4.82-4.77 (m, 1H), 3.9 (s, 3H), 3.85-3.82 (m, 1H), 3.26-3.25 (m, 1H), 3.21-3.16 (m, 1H), 3.06 (s, 3H), 2.98-2.71 (m, 2H), 2.14-2.11 (m, 1H), 2.10-2.09 (m, 1H), 2.07-2.06 (m, 1H), 1.47 (s, 9H)

[1611] Step 4: (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N-methylbenzamide hydrochloride

[1612] tert-Butyl (S)-(1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxy-4-(methylcarbamoyl)phenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-yl)carbamate (10.6 mg, 0.016 mmol) was dissolved in dichloromethane (2.0 ml) and then 4.0M hydrochloric acid solution dissolved in 1,4-dioxane (0.2 ml, 27.9 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 4 hours. After completion of the reaction, the reaction mixture was concentrated and the resulting solid was dried to prepare the titled compound (7.3 mg). (Yield: 71.2%) ¹H NMR (CD₃OD, 400MHz) 8.82 (d, 1H), 8.54 (s, 1H), 8.21 (s, 1H), 8.08 (s, 1H), 7.77-7.46 (m, 3H), 7.43 (s, 1H), 7.28 (s, 1H), 4.01 (s, 3H), 3.89-3.87 (m, 1H), 3.59-3.56 (m, 1H), 3.44-3.33 (m, 1H), 3.08-3.02 (m, 2H), 2.98 (s, 3H), 2.22-2.20 (m, 1H), 1.75-1.72 (m, 1H), 1.69-1.64 (m, 2H) MS m/z= 568.9 (M+H)+

[1613] Example 187: (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N,N-dimethylbenzamide hydrochloride

[1614] The titled compound (9.0 mg) was prepared in accordance with the same procedures as in Step 3 of Example 186, changing the amine reagent to 2.0M dimethylamine dissolved in tetrahydrofuran. (Yield: 49.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.85-8.83 (m, 1H), 8.55 (s, 1H), 8.23 (s, 1H), 8.09 (s, 1H), 7.77-7.48 (m, 2H), 7.33 (s, 1H), 7.19 (s, 1H), 7.1 (d, 1H), 4.03 (s, 3H), 3.93-3.90 (m, 1H), 3.63-3.59 (m, 1H), 3.45-3.33 (m, 1H), 3.16 (s, 3H), 3.13 (s, 3H), 3.08-2.98 (m, 2H), 2.23-2.20 (m, 1H), 1.84-1.78 (m, 1H), 1.76-1.65 (m, 2H) MS m/z= 582.0 (M+H)+

[1615] Example 188: (S)-1-(2-((2-(4-((3-hydroxyazetidin-1-yl)methyl)thiophen-2-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

- [1616] The titled compound (7.4 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C6-2. (Yield: 23.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.31 (d, 1H), 8.13 (d, 1H), 7.91 (s, 1H), 7.87 (s, 1H), 7.77 (s, 1H), 7.46 (s, 1H), 7.2 (d, 1H), 4.48-4.42 (m, 1H), 4.40-4.39 (m, 1H), 4.11-4.08 (m, 2H), 3.84-3.72 (m, 3H), 3.64-3.60 (m, 2H), 3.58-3.48 (m, 1H), 3.22-3.19 (m, 1H), 3.14-3.10 (m, 2H), 2.70-2.66 (m, 2H), 2.16-2.01 (m, 2H), 1.64-1.61 (m, 1H), 1.44-1.41 (m, 1H), 1.33-1.31 (m, 2H), 1.29-1.27 (m, 1H), MS m/z= 589.3 (M+H)+
- [1617] Example 189: (S)-3-fluoro-4-(4-((4-(3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-5-methoxybenzaldehyde
- [1618] The titled compound (95.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C4-1. (Yield: 30.1%) ¹H NMR (CDCl₃, 400MHz) 9.98 (s, 1H), 8.57 (d, 1H), 8.11 (s, 1H), 7.95 (s, 1H), 7.77 (d, 2H), 7.51 (s, 1H), 7.33-7.30 (m, 2H), 7.27-7.23 (m, 1H), 4.41-4.38 (m, 1H), 4.11-4.10 (m, 2H), 3.89 (s, 3H), 3.82-3.80 (m, 1H), 3.60-3.54 (m, 2H), 3.21-3.19 (m, 1H), 3.01-2.95 (m, 1H), 2.67-2.62 (m, 2H), 2.17-2.11 (m, 4H), 1.90-1.87 (m, 1H), 1.73-1.48 (m, 1H), 1.46-1.24 (m, 2H) δ MS m/z= 574.1 (M+H)+
- [1619] Example 190: (S)-1-(2-((2-(2-fluoro-6-methoxy-4-((methylamino)methyl)phenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1620] The compound prepared in Example 189 (20.0 mg, 0.035 mmol) was dissolved in methanol (0.5 mL) and then 2.0M methylamine dissolved in tetrahydrofuran (34.8 uL, 0.07 mmol) and sodium acetate (2.8 mg, 0.035 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature overnight. Then, sodium borohydride (1.3 mg, 0.035 mmol) was added to the reaction mixture, which was then stirred at room temperature for 1 hour. Dichloromethane was added to the reaction mixture and then a saturated sodium hydrogen carbonate solution was added thereto. The organic layer was extracted, dried over anhydrous magnesium sulfate, and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (10.2 mg). (Yield: 49.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.57 (d, 1H), 8.09 (s, 1H), 7.77 (s, 2H), 7.45-7.44 (m, 1H), 7.31 (s, 1H), 7.30-7.28 (m, 1H), 6.80-6.79 (m, 2H), 4.41-4.40 (m, 1H), 4.39-4.13 (m, 2H), 3.83 (s, 3H), 3.78 (s, 3H), 3.60-3.55 (m, 2H), 3.23-3.21 (m, 1H), 3.02-2.99 (m, 1H), 2.62-2.58 (m, 2H), 2.48-2.38 (m, 2H), 2.17-2.10 (m, 4H), 1.92-1.91 (m, 1H), 1.51-1.48 (m, 1H), 1.45-1.42 (m, 1H) MS m/z= 589.3 (M+H)+
- [1621] Example 191: 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

- [1622] The titled compound (5.5 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A11-2 and C3-1. (Yield: 14.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (s, 1H), 8.41 (d, 1H), 7.92 (s, 1H), 7.52-7.44 (m, 2H), 6.94-6.90 (m, 2H), 3.85-3.81 (m, 1H), 3.76 (s, 3H), 3.28-3.23 (m, 1H), 3.09-3.07 (m, 1H), 2.87-2.79 (m, 1H), 2.77-2.72 (m, 1H), 1.91-1.87 (m, 2H), 1.66-1.63 (m, 1H), 1.53-1.47 (m, 1H) MS m/z= 483.2 (M+H)+
- [1623] Example 192: 6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide
- [1624] Step 1: methyl (S)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)nicotinate
- [1625] The titled compound (99.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A11-1 and C1-1. (Yield: 19.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.50-8.45 (m, 2H), 7.69 (s, 1H), 7.49-7.41 (m, 2H), 6.95 (d, 1H), 6.84 (t, 1H), 3.88 (s, 3H), 3.81 (s, 3H), 3.75-3.71 (m, 1H), 3.39-3.36 (m, 1H), 2.86-2.80 (m, 1H), 2.72-2.67 (m, 1H), 2.01-1.96 (m, 1H), 1.77-1.73 (m, 1H), 1.63-1.60 (m, 1H), 1.42-1.39 (m, 1H)
- [1626] Step 2: (S)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)nicotinic acid
- [1627] Methyl (S)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)nicotinate (50.0 mg, 0.11 mmol) was dissolved in methanol (2.0 ml) and then 1.0N sodium hydroxide solution (0.55 mL) was added dropwise thereto. Then, the mixed solution was stirred at 60°C overnight. After completion of the reaction, the reaction mixture was cooled to room temperature and then neutralized with 1.0N hydrochloric acid solution. The aqueous layer was extracted with dichloromethane. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then dried to prepare the titled compound (54.1 mg), without further purification. (Yield: 98.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.53 (s, 1H), 7.70-7.64 (m, 1H), 7.40 (d, 1H), 7.17-7.13 (m, 2H), 7.02 (t, 1H), 3.95-3.92 (m, 4H), 3.73-3.69 (m, 1H), 3.62-3.58 (m, 1H), 3.50-3.45 (m, 1H), 2.09-1.95 (m, 2H), 1.70-1.67 (m, 2H)
- [1628] Step 3: 6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide
- [1629] (S)-6-((2-(2-Fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)nicotinic acid (30.0 mg, 0.06 mmol) was dissolved in anhydrous dimethylformamide (1.0 mL) and then 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide hexafluorophosphate (HATU, 45.7 mg, 0.12 mmol) and diisopropylethylamine (31 uL, 0.18 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature for 15 minutes and then (3R)-1-

methylpyrrolidin-3-amine (9.03 mg, 0.09 mmol) was added dropwise thereto. The reaction mixture was stirred at 60°C overnight. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (2.8 mg). (Yield: 8.94%) ¹H NMR (CD₃OD, 400MHz) δ 8.49-8.42 (m, 3H), 7.79 (s, 1H), 7.52-7.46 (m, 2H), 6.98 (d, 1H), 6.86 (t, 1H), 4.59-4.51 (m, 1H), 3.83 (s, 3H), 3.52-3.42 (m, 2H), 3.24-3.21 (m, 2H), 3.15-3.09 (m, 1H), 2.95-2.82 (m, 4H), 2.60-2.51 (m, 1H), 2.28-2.13 (m, 1H), 1.90-1.88 (m, 2H), 1.65-1.60 (m, 2H) MS m/z= 522.2 (M+H)+

[1630] Example 193: 6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1631] The titled compound (5.5 mg) was prepared in accordance with the same procedures as in Example 150, using Intermediates A11-2 and C3-1. (Yield: 48.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.38 (s, 1H), 7.49-7.43 (m, 2H), 7.30-7.21 (m, 2H), 6.99 (d, 1H), 6.89 (t, 1H), 3.88-3.81 (m, 4H), 3.25-3.21 (m, 1H), 3.10-3.02 (m, 1H), 2.87-2.79 (m, 1H), 2.75-2.70 (m, 1H), 1.96-1.85 (m, 2H), 1.72-1.62 (m, 1H), 1.54-1.46 (m, 1H) MS m/z= 453.2 (M+H)+

[1632] Example 194: 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1633] The titled compound (3.3 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to (1R,3R)-3-aminocyclopentan-1-ol hydrochloride. (Yield: 14.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 8.31 (s, 1H), 7.91 (d, 1H), 7.49-7.42 (m, 2H), 6.94-6.89 (m, 2H), 4.55-4.52 (m, 1H), 4.39-4.37 (m, 1H), 3.83-3.81 (m, 1H), 3.76 (s, 3H), 3.27-3.18 (m, 1H), 3.08-2.96 (m, 1H), 2.90-2.82 (m, 1H), 2.79-2.72 (m, 1H), 2.30-2.22 (m, 1H), 2.11-2.06 (m, 2H), 1.89-1.84 (m, 3H), 1.64-1.53 (m, 4H) MS m/z= 568.2 (M+H)+

[1634] Example 195: 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3S)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1635] The titled compound (4.5 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to (1S,3R)-3-aminocyclopentan-1-ol hydrochloride. (Yield: 19.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 8.40 (d, 1H), 8.37 (s, 1H), 7.92 (s, 1H), 7.51-7.42 (m, 2H), 6.94-6.89 (m, 2H), 4.37-4.31 (m, 2H), 3.88-3.81 (m, 1H), 3.76 (s, 3H), 3.76 (s, 1H), 3.13-3.04 (m, 1H), 2.86-2.77 (m, 1H), 2.75-2.68 (m, 1H), 2.30-2.22 (m, 1H),

2.14-2.07 (m, 1H), 1.95-1.77 (m, 5H), 1.69-1.64 (m, 2H), 1.49-1.42 (m, 1H) MS m/z = 568.2 (M+H)+

[1636] Example 196: 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-(3-hydroxycyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1637] The titled compound (3.6 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to 3-aminocyclobutanol. (Yield: 15.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.42-8.33 (m, 2H), 7.93-7.90 (m, 1H), 7.50-7.43 (m, 2H), 6.94-6.88 (m, 2H), 4.29-4.25 (m, 1H), 4.15-4.09 (m, 1H), 3.87-3.82 (m, 1H), 3.76 (s, 3H), 3.29-3.20 (m, 1H), 3.10-3.02 (m, 1H), 2.96-2.82 (m, 1H), 2.78-2.72 (m, 1H), 2.15-2.10 (m, 2H), 1.97-1.83 (m, 2H), 1.64-1.47 (m, 4H) MS m/z = 552.9 (M+H)+

[1638] Example 197: 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,2R)-2-hydroxycyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1639] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to (1R,2R)-2-aminocyclobutanol hydrochloride. (Yield: 9.19%) ¹H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 8.34-8.32 (m, 1H), 7.92 (d, 1H), 7.50-7.43 (m, 2H), 6.94-6.90 (m, 2H), 4.57-4.43 (m, 1H), 4.06-4.00 (m, 1H), 3.88-3.80 (m, 1H), 3.76 (s, 3H), 3.26-3.18 (m, 1H), 3.07-3.00 (m, 1H), 2.93-2.85 (m, 1H), 2.81-2.73 (m, 2H), 2.46-2.37 (m, 1H), 2.01-1.89 (m, 4H), 1.67-1.49 (m, 2H) MS m/z = 552.9 (M+H)+

[1640] Example 198: N-(3,3-difluorocyclobutyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1641] The titled compound (3.5 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to 3,3-difluorocyclobutanamine hydrochloride. (Yield: 14.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.42-8.37 (m, 2H), 7.95 (d, 1H), 7.50-7.43 (m, 2H), 6.94-6.88 (m, 2H), 4.33-4.31 (m, 1H), 3.85-3.82 (m, 1H), 3.87-3.82 (m, 1H), 3.76 (s, 3H), 3.20-3.12 (m, 1H), 3.06-2.98 (m, 3H), 2.96-2.84 (m, 1H), 2.82-2.71 (m, 3H), 2.91-2.82 (m, 2H), 1.64-1.53 (m, 2H) MS m/z = 573.9 (M+H)+

[1642] Example 199: N-((1R,3R)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide hydrochloride

[1643] Step 1: tert-butyl ((1R,3R)-3-(6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamido)cyclopentyl)carbamate

[1644] The titled compound (11.3 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to tert-butyl N-[(1R,3R)-3-aminocyclopentyl]carbamate. (Yield: 41.0%)

¹H NMR (CD₃OD, 400MHz) δ 8.40 (d, 1H), 8.31 (s, 1H), 7.91 (s, 1H), 7.50-7.44 (m, 2H), 6.94-6.89 (m, 2H), 4.43-4.39 (m, 1H), 4.08-4.03 (m, 1H), 3.84-3.80 (m, 1H), 3.76 (s, 3H), 3.26-3.18 (m, 1H), 3.09-3.00 (m, 1H), 2.91-2.82 (m, 1H), 2.78-2.69 (m, 1H), 2.25-2.18 (m, 1H), 2.16-2.05 (m, 1H), 1.98-1.88 (m, 4H), 1.62-1.51 (m, 4H), 1.46 (s, 9H)

[1645] Step 2: N-((1R,3R)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide hydrochloride

[1646] tert-Butyl ((1R,3R)-3-(6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamido)cyclopentyl)carbamate (11.3 mg, 0.017 mmol) was dissolved in dichloromethane (1 ml) and then 4.0M hydrogen chloride solution dissolved in 1,4-dioxane (20 μl, 0.085 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 4 hours. After completion of the reaction, the reaction mixture was concentrated and the resulting solid was dried to prepare the titled compound (5.5 mg). (Yield: 50.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.57 (d, 1H), 8.07 (s, 1H), 7.54 (q, 1H), 7.25 (d, 1H), 7.01-6.96 (m, 2H), 6.84 (s, 1H), 4.48-4.46 (m, 1H), 3.86-3.81 (m, 2H), 3.79 (s, 3H), 3.67-3.64 (m, 1H), 3.57-3.52 (m, 1H), 3.39-3.37 (m, 1H), 3.26-3.21 (m, 1H), 2.34-2.28 (m, 2H), 2.15 (t, 2H), 2.04-1.96 (m, 2H), 1.78-1.64 (m, 4H) MS m/z= 565.9 (M+H)+

[1647] Example 200: N-((1R,3S)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1648] The titled compound (4.4 mg) was prepared in accordance with the same procedures as in Example 199, changing the amine reagent to tert-butyl N-[(1R,3S)-3-aminocyclopentyl]carbamate. (Yield: 40.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.57 (d, 1H), 8.08 (s, 1H), 7.54 (q, 1H), 7.25 (d, 1H), 7.01-6.94 (m, 2H), 6.86 (s, 1H), 4.29-4.27 (m, 1H), 3.88-3.84 (m, 1H), 3.79 (s, 3H), 3.69-3.64 (m, 2H), 3.56-3.50 (m, 1H), 3.39-3.37 (m, 1H), 3.26-3.21 (m, 1H), 2.65-2.62 (m, 1H), 2.19-2.15 (m, 2H), 2.04-1.90 (m, 4H), 1.76-1.67 (m, 3H) MS m/z= 566.0 (M+H)+

[1649] Example 201: 6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide

[1650] 6-((6-(2-Fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide (Example 194, 7.0 mg, 0.012 mmol) was dissolved in methanol (1.0 mL) and then Pd/C (5.26 mg, 0.05 mmol) was added dropwise thereto. The reaction mixture was stirred at room temperature for 3 hours under a pressure of a balloon filled with hydrogen gas. After completion of the reaction, the reaction mixture was filtered through a Celite filter. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (2.1 mg). (Yield: 31.7%) ¹H NMR (CD₃OD, 400MHz)

- δ 8.28 (s, 1H), 7.49-7.45 (m, 2H), 7.29 (d, 1H), 7.23-7.20 (m, 1H), 6.99 (d, 1H), 6.89 (t, 1H), 4.54-4.50 (m, 1H), 4.42-4.38 (m, 1H), 3.85-3.81 (m, 4H), 3.25-3.19 (m, 1H), 3.03-2.96 (m, 1H), 2.87-2.81 (m, 1H), 2.77-2.69 (m, 1H), 2.30-2.22 (m, 1H), 2.11-2.06 (m, 2H), 1.90-1.85 (m, 3H), 1.64-1.56 (m, 4H) MS m/z = 538.3 (M+H)+
- [1651] Example 202: 6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-N-((1R,3S)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide
- [1652] The titled compound (2.2 mg) was prepared in accordance with the same procedures as in Example 201, using the compound of Example 195. (Yield: 33.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.33 (s, 1H), 7.50-7.42 (m, 2H), 7.29 (d, 1H), 7.24-7.21 (m, 1H), 6.98 (d, 1H), 6.89 (t, 1H), 4.36-4.30 (m, 2H), 4.42-4.38 (m, 1H), 3.85-3.82 (m, 4H), 3.25-3.23 (m, 1H), 3.08-3.02 (m, 1H), 2.83-2.75 (m, 1H), 2.70-2.63 (m, 1H), 2.34-2.28 (m, 1H), 2.11-2.07 (m, 1H), 1.91-1.76 (m, 5H), 1.69-1.64 (m, 2H), 1.52-1.43 (m, 1H) MS m/z = 538.3 (M+H)+
- [1653] Example 203: 6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide
- [1654] The titled compound (2.6 mg) was prepared in accordance with the same procedures as in Example 192, using Intermediates A11-1 and C3-1 and changing the amine reagent to (3R)-1-methylpyrrolidin-3-amine. (Yield: 22.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.44-8.38 (m, 2H), 7.95 (s, 1H), 7.52-7.45 (m, 2H), 6.96-6.92 (m, 2H), 4.57-4.51 (m, 1H), 3.85-3.82 (m, 1H), 3.78 (s, 3H), 3.27-3.20 (m, 1H), 3.09-3.02 (m, 1H), 2.98-2.93 (m, 1H), 2.89-2.82 (m, 1H), 2.80-2.74 (m, 2H), 2.67-2.59 (m, 2H), 2.43-2.38 (m, 4H), 1.92-1.86 (m, 3H), 1.68-1.59 (m, 1H), 1.58-1.49 (m, 1H) MS m/z = 566.2 (M+H)+
- [1655] Example 204: N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1656] The titled compound (7.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-3 and C1-1. (Yield: 62.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.75-8.72 (m, 1H), 8.52 (s, 1H), 8.26 (s, 1H), 8.11 (s, 1H), 7.68-7.65 (m, 2H), 7.61 (t, 1H), 7.28-7.22 (m, 1H), 7.15-7.13 (m, 1H), 7.03-6.99 (m, 1H), 3.96 (s, 3H), 3.91-3.82 (m, 1H), 3.62-3.56 (m, 1H), 3.08-2.74 (m, 3H), 1.87-1.74 (m, 2H), 1.56-1.50 (m, 1H), 1.16 (d, 3H) MS m/z = 525.2 (M+H)+
- [1657] Example 205: N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1658] The titled compound (2.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-4 and C1-1. (Yield: 24.6%) ¹H NMR (CD₃

- OD, 400MHz) δ 8.74-8.68 (m, 1H), 8.52 (s, 1H), 8.25-8.23 (m, 1H), 8.11 (s, 1H), 7.68-7.66 (m, 2H), 7.61 (t, 1H), 7.30-7.23 (m, 1H), 7.14-7.12 (m, 1H), 7.02-6.98 (m, 1H), 3.94 (s, 3H), 3.70-3.64 (m, 1H), 3.50-3.36 (m, 3H), 2.63-2.57 (m, 1H), 2.05-2.01 (m, 1H), 1.97-1.94 (m, 1H), 1.16 (d, 1H), 0.93 (d, 3H) MS m/z = 525.2 (M+H)+
- [1659] Example 206: (S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1660] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-5 and C1-1. (Yield: 17.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.74-8.69 (m, 1H), 8.50 (s, 1H), 8.23 (s, 1H), 8.07 (s, 1H), 7.67-7.64 (m, 2H), 7.62 (t, 1H), 7.38-7.30 (m, 1H), 7.15-7.12 (m, 1H), 7.01-6.98 (m, 1H), 3.95 (s, 3H), 3.49-3.36 (m, 1H), 3.22-3.03 (m, 3H), 1.98-1.72 (m, 4H), 1.39 (s, 3H) MS m/z = 525.2 (M+H)+
- [1661] Example 207: N-(4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1662] The titled compound (7.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-6 and C1-1. (Yield: 58.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.67 (d, 1H), 8.54 (s, 1H), 8.33 (s, 1H), 8.16 (s, 1H), 7.68-7.62 (m, 2H), 7.60 (t, 1H), 7.35-7.26 (m, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 5.22-5.18 (m, 1H), 5.07-5.04 (m, 1H), 3.94 (s, 3H), 3.76-3.60 (m, 2H), 3.54-3.50 (m, 1H), 3.15-3.09 (m, 2H), 2.21-2.17 (m, 1H) MS m/z = 529.2 (M+H)+
- [1663] Example 208: N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1664] The titled compound (1.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-7 and C1-1. (Yield: 12.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.69 (d, 1H), 8.55 (s, 1H), 8.33 (s, 1H), 8.16 (s, 1H), 7.69-7.61 (m, 3H), 7.28-7.23 (m, 1H), 7.13 (d, 1H), 7.01 (t, 1H), 4.68-4.65 (m, 1H), 3.94 (s, 3H), 3.75-3.69 (m, 1H), 3.58-3.49 (m, 2H), 3.06-3.00 (m, 1H), 2.96-2.89 (m, 1H), 2.30-2.27 (m, 1H), 2.05-1.94 (m, 1H) MS m/z = 529.2 (M+H)+
- [1665] Example 209: (3R,4R)-3-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-4-ol hydrochloride
- [1666] The titled compound (4.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-8 and C1-1. (Yield: 34.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.72-8.68 (m, 1H), 8.53 (s, 1H), 8.28 (s, 1H), 8.12 (s, 1H), 7.67-7.61

- (m, 3H), 7.28-7.20 (m, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 3.94 (s, 3H), 3.80-3.74 (m, 1H), 3.74-3.61 (m, 1H), 3.60-3.51 (m, 1H), 3.18-3.11 (m, 1H), 2.98-2.85 (m, 2H), 2.11-2.03 (m, 1H), 1.75-1.69 (m, 1H) MS m/z= 527.2 (M+H)+
- [1667] Example 210: N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1668] The titled compound (4.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-4 and C1-7. (Yield: 45.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.54 (s, 1H), 8.21 (s, 1H), 8.10 (s, 1H), 7.79-7.49 (m, 2H), 7.23 (s, 1H), 7.01 (d, 1H), 6.90-6.85 (m, 1H), 3.95 (s, 3H), 3.75-3.69 (m, 1H), 3.48-3.44 (m, 3H), 2.72-2.67 (m, 1H), 2.06-1.95 (m, 2H), 1.76-1.70 (m, 1H), 0.90 (d, 3H) MS m/z= 543.2 (M+H)+
- [1669] Example 211: N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1670] The titled compound (5.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-3 and C1-7. (Yield: 58.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.53 (s, 1H), 8.24 (s, 1H), 8.10 (s, 1H), 7.77-7.47 (m, 2H), 7.22 (s, 1H), 7.00 (d, 1H), 6.90-6.85 (m, 1H), 3.95 (s, 3H), 3.85 (d, 1H), 3.59 (d, 1H), 3.08-3.04 (m, 1H), 3.00-2.88 (m, 2H), 1.87-1.78 (m, 2H), 1.55-1.47 (m, 1H), 1.17 (d, 3H) MS m/z= 543.2 (M+H)+
- [1671] Example 212: (S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1672] The titled compound (3.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-5 and C1-7. (Yield: 37.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.73 (d, 1H), 8.49 (s, 1H), 8.22 (s, 1H), 8.06 (s, 1H), 7.77-7.47 (m, 2H), 7.26 (s, 1H), 7.00 (d, 1H), 6.90-6.85 (m, 1H), 3.94 (s, 3H), 3.45-3.39 (m, 1H), 3.25-3.22 (m, 2H), 3.20-3.12 (m, 1H), 1.93-1.85 (m, 2H), 1.83-1.76 (m, 2H), 1.40 (s, 3H) MS m/z= 543.2 (M+H)+
- [1673] Example 213: (3R,4R)-3-amino-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-ol hydrochloride
- [1674] The titled compound (2.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-8 and C1-7. (Yield: 21.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.73 (d, 1H), 8.53 (s, 1H), 8.26 (s, 1H), 8.11 (s, 1H), 7.76-7.47 (m, 2H), 7.21 (s, 1H), 6.99 (d, 1H), 6.89-6.84 (m, 1H), 3.94 (s, 3H), 3.80 (d, 1H), 3.69-3.58

(m, 2H), 3.18-3.12 (m, 1H), 3.02-2.91 (m, 2H), 2.13-2.05 (m, 1H), 1.77-1.67 (m, 1H)

MS m/z= 545.2 (M+H)+

[1675] Example 214: (1S,4S)-4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)(methyl)amino)cyclohexan-1-ol

[1676] The titled compound (5.7 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-35 and C1-1. (Yield: 15.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.45 (d, 1H), 8.28 (s, 1H), 8.02 (s, 1H), 7.95 (s, 1H), 7.69-7.39 (m, 4H), 6.98 (d, 1H), 6.86 (t, 1H), 3.83 (s, 3H), 3.79-3.74 (m, 1H), 3.28-3.22 (m, 1H), 2.65 (s, 3H), 1.93-1.85 (m, 2H), 1.70 (d, 2H), 1.35-1.32 (m, 3H) MS m/z= 540.3 (M+H)+

[1677] Example 215: N²-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride

[1678] The titled compound (1.9 mg) was prepared in accordance with the same procedures as in Example 151, using Intermediates B1-3 and C3-2. (Yield: 10.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.46 (s, 1H), 8.05 (s, 2H), 7.82 (d, 1H), 7.60 (t, 1H), 7.31 (d, 1H), 6.97-6.92 (m, 2H), 6.85 (t, 1H), 3.91 (s, 3H), 3.82 (d, 3H), 3.80 (d, 1H), 3.54 (d, 1H), 3.10-3.02 (m, 1H), 2.90 (t, 2H), 1.84-1.76 (m, 2H), 1.50-1.47 (m, 1H), 1.17 (d, 3H) MS m/z= 557.2 (M+H)+

[1679] Example 216: N²-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine hydrochloride

[1680] The titled compound (4.7 mg) was prepared in accordance with the same procedures as in Example 151, using Intermediates B1-7 and C3-2. (Yield: 25.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.50 (s, 1H), 8.07 (s, 2H), 7.80 (d, 1H), 7.60 (t, 1H), 7.30 (d, 1H), 6.97-6.94 (m, 2H), 6.84 (t, 1H), 4.89-4.64 (m, 1H), 3.90-3.84 (m, 4H), 3.68-3.50 (m, 2H), 3.07-2.97 (m, 2H), 2.31-2.17 (m, 1H), 1.96-1.82 (m, 1H), 1.84-1.76 (m, 2H), 1.50-1.47 (m, 1H), 1.17 (d, 3H) MS m/z= 561.2 (M+H)+

[1681] Example 217: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol

[1682] The titled compound (14.8 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-3 and C1-7. (Yield: 31.7%) ¹H NMR (CDCl₃, 400MHz) δ 8.64 (d, 1H), 8.32 (s, 1H), 8.12 (s, 1H), 7.88 (s, 1H), 7.78 (s, 1H), 7.41-7.32 (m, 2H), 7.30-7.28 (m, 0.2H), 7.23-7.18 (m, 0.6H), 7.07-7.04 (m, 0.2H), 6.63-6.51 (m, 2H), 4.05-3.95 (m, 1H), 3.86 (s, 3H), 3.53-3.44 (m, 2H), 3.37-3.19 (m, 2H), 2.35-2.19 (m, 1H), 2.04-1.90 (m, 1H), 1.90-1.82 (m, 1H), 1.79-1.67 (m, 2H) MS m/z= 553.9 (M+H)+

- [1683] Example 218: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [1684] The titled compound (3.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-1 and C1-7. (Yield: 6.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.65 (d, 1H), 8.30 (s, 1H), 8.12 (s, 1H), 7.96 (s, 1H), 7.88 (s, 1H), 7.40-7.32 (m, 2H), 6.60-6.51 (m, 2H), 4.03-3.94 (m, 1H), 3.85 (s, 3H), 3.54-3.44 (m, 2H), 3.34-3.22 (m, 2H), 2.02 (s, 1H), 1.92-1.82 (m, 1H), 1.78-1.64 (m, 2H) MS m/z= 571.9 (M+H)+
- [1685] Example 219: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [1686] The titled compound (15.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-4 and C1-7. (Yield: 31.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.61 (d, 1H), 8.31 (s, 1H), 8.12 (s, 1H), 7.79 (s, 2H), 7.39 (s, 2H), 6.62-6.48 (m, 2H), 6.29-5.96 (m, 1H), 4.56-4.42 (m, 2H), 4.05-3.94 (m, 1H), 3.88 (s, 3H), 3.52-3.43 (m, 2H), 3.37-3.17 (m, 2H), 2.52-2.28 (m, 1H), 2.03-1.90 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.63 (m, 2H) MS m/z= 567.9 (M+H)+
- [1687] Example 220: (S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol
- [1688] The titled compound (9.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-5 and C1-7. (Yield: 19.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.61 (d, 1H), 8.32 (s, 1H), 8.17 (s, 1H), 7.83 (d, 2H), 7.39-7.30 (m, 2H), 6.59-6.50 (m, 2H), 4.80 (q, 2H), 4.05-3.93 (m, 1H), 3.84 (s, 3H), 3.51-3.41 (m, 2H), 3.36-3.19 (m, 2H), 2.02-1.92 (m, 1H), 1.91-1.80 (m, 1H), 1.75-1.65 (m, 2H) MS m/z= 585.9 (M+H)+
- [1689] Example 221: (3S)-1-(5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1690] The titled compound (57.1 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-4 and C3-1. (Yield: 63.3%) ¹H NMR (CDCl₃, 400MHz) δ 8.43 (d, 1H), 8.28 (s, 1H), 8.05 (s, 1H), 7.79 (s, 2H), 7.56-7.49 (m, 1H), 7.46-7.34 (m, 2H), 6.92 (t, 1H), 6.82 (d, 1H), 6.30-5.94 (m, 1H), 4.56-4.42 (m, 2H), 4.04-3.91 (m, 1H), 3.80 (s, 3H), 3.52-3.34 (m, 2H), 3.33-3.14 (m, 2H), 2.34-2.15 (m, 1H), 2.03-1.89 (m, 1H), 1.89-1.77 (m, 1H), 1.77-1.66 (m, 2H) MS m/z= 593.9 (M+H)+
- [1691] Example 222: (3S)-1-(5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1692] The titled compound (81.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-3 and C3-1. (Yield: 92.3%) ¹H

NMR (CDCl₃, 400MHz) δ 8.42 (d, 1H), 8.28 (s, 1H), 8.13 (s, 1H), 8.08 (s, 1H), 7.86 (s, 1H), 7.60-7.53 (m, 1H), 7.44-7.34 (m, 2.2H), 7.23-7.19 (m, 0.6H), 7.08-7.04 (m, 0.2H), 6.91 (t, 1H), 6.82 (d, 1H), 4.02-3.94 (m, 1H), 3.79 (s, 3H), 3.46-3.43 (m, 2H), 3.33-3.19 (m, 2H), 2.34-2.16 (m, 1H), 1.99-1.91 (m, 1H), 1.90-1.79 (m, 1H), 1.76-1.66 (m, 2H) MS m/z= 579.9 (M+H)+

[1693] Example 223: (3S)-1-(2-(((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1694] The titled compound (15.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-10 and C3-2. (Yield: 17.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.46 (d, 1H), 8.18 (s, 1H), 7.90-7.81 (m, 2H), 7.81-7.70 (m, 1H), 7.63-7.51 (m, 1H), 7.45 (s, 1H), 6.69 (t, 1H), 6.58 (d, 1H), 6.33-6.00 (m, 1H), 4.65-4.46 (m, 2H), 3.91-3.79 (m, 1H), 3.79 (s, 3H), 3.26-3.16 (m, 1H), 3.05-2.90 (m, 1H), 2.78-2.58 (m, 2H), 2.00-1.89 (m, 1H), 1.87-1.73 (m, 1H), 1.56-1.43 (m, 2H) MS m/z= 587.9 (M+H)+

[1695] Example 224: (3S)-1-(2-(((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1696] The titled compound (10.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-1 and C3-2. (Yield: 11.6%) ¹H NMR (CDCl₃, 400MHz) δ 8.44 (d, 1H), 8.17 (s, 1H), 7.84 (s, 2H), 7.75 (s, 1H), 7.63-7.52 (m, 1H), 7.40 (s, 1H), 6.69 (t, 1H), 6.58 (d, 1H), 4.50-4.36 (m, 1H), 4.22-4.10 (m, 2H), 3.91-3.80 (m, 1H), 3.80 (s, 3H), 3.67-3.54 (m, 2H), 3.28-3.15 (m, 1H), 3.03-2.90 (m, 1H), 2.81-2.61 (m, 2H), 2.26-2.05 (m, 4H), 1.97-1.87 (m, 1H), 1.83-1.74 (m, 1H), 1.55-1.48 (m, 2H) MS m/z= 607.9 (M+H)+

[1697] Example 225: (3S)-1-(2-(((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol

[1698] The titled compound (8.0 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A6-2 and C3-2. (Yield: 9.9%) ¹H NMR (CDCl₃, 400MHz) δ 8.44 (d, 1H), 8.22 (s, 1H), 7.69 (s, 1H), 7.53-7.46 (m, 1H), 7.35-7.30 (m, 1H), 6.66 (t, 1H), 6.57 (d, 1H), 4.03-3.90 (m, 3H), 3.81 (s, 3H), 3.61-3.51 (m, 2H), 3.50-3.42 (m, 1H), 3.37-3.30 (m, 1H), 3.30-3.23 (m, 1H), 3.20-3.12 (m, 1H), 2.97-2.87 (m, 1H), 2.14-2.05 (m, 1H), 2.01-1.91 (m, 2H), 1.91-1.76 (m, 3H), 1.73-1.63 (m, 2H) MS m/z= 565.9 (M+H)+

[1699] Example 226: (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1700] The titled compound (10.2 mg) was prepared in accordance with the same procedures as in Step 2 of Example 150, using (3S)-1-(2-(((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-

yl)pyridin-4-yl)piperidin-3-ol (Example 223). (Yield: 69.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.05 (s, 1H), 7.95 (s, 1H), 7.90 (s, 1H), 7.33-7.20 (m, 3H), 6.87 (d, 1H), 6.77 (t, 1H), 6.40-6.04 (m, 1H), 4.68-4.55 (m, 2H), 3.88 (s, 3H), 3.78-3.69 (m, 1H), 3.32-3.25 (m, 1H), 3.10-2.99 (m, 1H), 2.64-2.51 (m, 1H), 2.49-2.39 (m, 1H), 2.02-1.92 (m, 1H), 1.80-1.69 (m, 1H), 1.63-1.51 (m, 1H), 1.43-1.31 (m, 2H) MS m/z= 557.9 (M+H)+

[1701] Example 227: (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol

[1702] The titled compound (5.5 mg) was prepared in accordance with the same procedures as in Step 2 of Example 150, using (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol (Example 224). (Yield: 38.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.07 (s, 1H), 7.96 (s, 1H), 7.84 (s, 1H), 7.33-7.17 (m, 3H), 6.87 (d, 1H), 6.77 (t, 1H), 4.53-4.40 (m, 1H), 4.16-4.04 (m, 2H), 3.88 (s, 3H), 3.77-3.68 (m, 1H), 3.65-3.56 (m, 2H), 3.32-3.24 (m, 1H), 3.10-2.98 (m, 1H), 2.66-2.54 (m, 1H), 2.49-2.38 (m, 1H), 2.18-2.04 (m, 4H), 2.03-1.93 (m, 1H), 1.81-1.71 (m, 1H), 1.64-1.52 (m, 1H), 1.43-1.33 (m, 1H) MS m/z= 578.0 (M+H)+

[1703] Example 228: (3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(2-(tetrahydro-2H-pyran-4-yl)ethyl)pyridin-4-yl)piperidin-3-ol

[1704] The titled compound (2.7 mg) was prepared in accordance with the same procedures as in Step 2 of Example 150, using (3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol (Example 225). (Yield: 31.2%) ¹H NMR (CD₃OD, 400MHz) δ 7.85 (s, 1H), 7.33-7.25 (m, 1H), 7.23-7.12 (m, 2H), 6.86 (d, 1H), 6.76 (t, 1H), 3.99-3.89 (m, 2H), 3.87 (s, 3H), 3.83-3.73 (m, 1H), 3.46 (t, 2H), 3.31-3.24 (m, 1H), 3.12-3.02 (m, 1H), 2.71-2.64 (m, 1H), 2.64-2.58 (m, 2H), 2.57-2.48 (m, 1H), 2.11-1.99 (m, 1H), 1.93-1.82 (m, 1H), 1.76-1.66 (m, 3H), 1.65-1.57 (m, 2H), 1.56-1.48 (m, 1H), 1.48-1.38 (m, 1H), 1.37-1.25 (m, 2H) MS m/z= 540.0 (M+H)+

[1705] Example 229: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyridin-4-amine

[1706] The titled compound (10.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-21 and C1-1. (Yield: 27.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.60 (d, 1H), 8.16 (s, 1H), 7.96-7.85 (m, 1H), 7.83-7.72 (m, 2H), 7.50-7.42 (m, 1H), 7.40 (s, 1H), 7.28-7.23 (m, 1H), 6.86-6.73 (m, 2H), 4.22 (s, 2H), 3.85 (s, 3H), 3.35-3.30 (m, 1H), 3.30 (s, 3H), 3.23-3.14 (m, 1H), 2.98-2.85 (m,

- 1H), 2.57-2.46 (m, 1H), 2.35-2.24 (m, 1H), 2.00-1.90 (m, 1H), 1.75-1.56 (m, 2H), 1.23 (s, 6H), 1.17-1.09 (m, 1H) MS m/z= 547.0 (M+H)+
- [1707] Example 230: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(2-methoxyethoxy)-[3,3'-bipyridin]-6-amine
- [1708] The titled compound (7.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-22 and C1-1. (Yield: 27.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.64 (d, 1H), 8.32 (s, 1H), 8.01 (s, 1H), 7.94 (s, 1H), 7.85 (d, 1H), 7.48-7.40 (m, 1H), 7.40-7.31 (m, 2H), 6.92 (d, 1H), 6.85-6.77 (m, 2H), 4.58-4.48 (m, 2H), 3.87 (d, 3H), 3.82-3.77 (m, 2H), 3.53-3.44 (m, 3H), 3.28-3.17 (m, 1H), 3.16-3.05 (m, 1H), 2.86-2.73 (m, 1H), 2.59-2.47 (m, 1H), 2.38-2.24 (m, 1H), 1.96-1.83 (m, 1H), 1.64-1.53 (m, 1H), 1.53-1.38 (m, 1H), 1.19-1.06 (m, 2H) MS m/z= 545.9 (M+H)+
- [1709] Example 231: (S)-(3,3-difluoroazetidin-1-yl)(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanone
- [1710] Step 1: methyl (S)-4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate
- [1711] The titled compound (212.9 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-8 and C1-10. (Yield: 37.5%) ¹H NMR (CDCl₃, 400MHz) δ 8.63 (d, 1H), 8.44 (d, 2H), 8.18-8.12 (m, 2H), 8.01 (s, 1H), 7.73 (s, 1H), 7.42-7.40 (m, 0.2H), 7.27-7.23 (m, 0.6H), 7.13-7.08 (m, 0.2H), 4.00 (s, 3H), 3.91 (s, 3H), 3.26-3.16 (m, 1H), 3.04-2.94 (m, 1H), 2.74-2.61 (m, 2H), 1.99-1.90 (m, 1H), 1.84-1.73 (m, 2H), 1.59-1.41 (m, 2H)
- [1712] Step 2: (S)-4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoic acid
- [1713] Methyl (S)-4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate (212.0 mg, 0.37 mmol) was dissolved in methanol (2.0 ml) and then 1.0N sodium hydroxide solution (1.0 mL) was added dropwise thereto. Then, the mixed solution was stirred at 60°C for 3 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and then neutralized with 1.0N hydrochloric acid solution. The aqueous layer was extracted with dichloromethane. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then dried to prepare the titled compound (200.0 mg), without further purification. (Yield: 96.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.84 (d, 1H), 8.45 (s, 1H), 8.30 (d, 2H), 8.10 (s, 1H), 8.03 (s, 1H), 6.85 (d, 2H), 4.05 (s, 3H), 3.86-3.78 (m, 1H), 3.56-3.46 (m, 1H), 3.18-3.07 (m, 1H), 2.02-1.86 (m, 2H), 1.68-1.50 (m, 2H)

- [1714] Step 3: (S)-(3,3-difluoroazetidin-1-yl)(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanone
- [1715] ((S)-4-(4-((5-(1-(Difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoic acid (30.0 mg, 0.05 mmol) was dissolved in anhydrous dimethylformamide (1.0 mL) and then 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide hexafluorophosphate (HATU, 41.0 mg, 0.11 mmol) and diisopropylethylamine (28.2 μ L, 0.16 mmol) were added dropwise thereto. The reaction mixture was stirred at room temperature for 15 minutes and then 3,3-difluoroazetidine hydrochloride (14.0 mg, 0.11 mmol) was added dropwise thereto. The reaction mixture was stirred at 80°C for 4 hours. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (6.0 mg). (Yield: 17.6%) ¹H NMR (CDCl₃, 400MHz) δ 8.67-8.58 (m, 1H), 8.19 (s, 1H), 8.01 (s, 1H), 7.54-7.46 (m, 1H), 7.43-7.40 (m, 0.2H), 7.35-7.30 (m, 1H), 7.27-7.24 (m, 0.6H), 7.21-7.16 (m, 1H), 7.13-7.10 (m, 0.2H), 7.06 (d, 1H), 4.68-4.49 (m, 4H), 3.93-3.88 (m, 3H), 3.88-3.82 (m, 1H), 3.35-3.22 (m, 1H), 3.10-3.00 (m, 1H), 2.77-2.67 (m, 1H), 2.09-2.03 (m, 1H), 2.01-1.94 (m, 1H), 1.84-1.75 (m, 2H) MS m/z= 630.9 (M+H)+
- [1716] Example 232: (4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((S)-3-fluoropyrrolidin-1-yl)methanone
- [1717] The titled compound (10.0 mg) was prepared in accordance with the same procedures as in Step 3 of Example 231, changing the amine reagent to (S)-3-fluoropyrrolidine hydrochloride. (Yield: 29.6%) ¹H NMR (CDCl₃, 400MHz) δ 8.67-8.58 (m, 1H), 8.17 (s, 1H), 8.10-8.02 (m, 1H), 7.98 (s, 1H), 7.51-7.42 (m, 1H), 7.43-7.40 (m, 0.2H), 7.39-7.33 (m, 1H), 7.26-7.25 (m, 0.6H), 7.12-7.09 (m, 0.2H), 7.05-6.98 (m, 2H), 5.48-5.17 (m, 1H), 4.98-4.84 (m, 1H), 3.88 (s, 3H), 3.79-3.72 (m, 1H), 3.69-3.60 (m, 1H), 3.34-3.21 (m, 1H), 3.10-2.97 (m, 1H), 2.73-2.58 (m, 2H), 2.43-2.29 (m, 1H), 2.05-1.96 (m, 1H), 1.83-1.72 (m, 1H), 1.68-1.58 (m, 2H), 1.57-1.43 (m, 2H) MS m/z= 626.9 (M+H)+
- [1718] Example 233: (4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone
- [1719] The titled compound (11.2 mg) was prepared in accordance with the same procedures as in Step 3 of Example 231, changing the amine reagent to (R)-3-fluoropyrrolidine hydrochloride. (Yield: 33.1%) ¹H NMR (CDCl₃, 400MHz) δ

8.65-8.56 (m, 1H), 8.19 (s, 1H), 8.13-8.05 (m, 1H), 7.99 (s, 1H), 7.53-7.43 (m, 1H), 7.42-7.39 (m, 0.2H), 7.39-7.32 (m, 1H), 7.27-7.24 (m, 0.6H), 7.13-7.09 (m, 0.2H), 7.05-6.97 (m, 2H), 6.97-5.28 (m, 1H), 4.98-4.81 (m, 1H), 3.90 (s, 3H), 3.86-3.80 (m, 1H), 3.80-3.71 (m, 1H), 3.32-3.21 (m, 1H), 3.08-2.98 (m, 1H), 2.72-2.54 (m, 2H), 2.46-2.27 (m, 1H), 2.21-2.09 (m, 1H), 2.03-1.93 (m, 2H), 1.81-1.70 (m, 2H) MS m/z= 626.9 (M+H)+

[1720] Example 234: (S)-(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)(3,3-difluoropyrrolidin-1-yl)methanone

[1721] The titled compound (14.0 mg) was prepared in accordance with the same procedures as in Step 3 of Example 231, changing the amine reagent to 3,3-difluoropyrrolidine hydrochloride. (Yield: 40.0%) ¹H NMR (CDCl₃, 400MHz) δ 8.67-8.58 (m, 1H), 8.18 (s, 1H), 8.11-8.03 (m, 1H), 7.99 (s, 1H), 7.48-7.33 (m, 2H), 7.27-7.24 (m, 0.6H), 7.13-7.08 (m, 0.2H), 7.03-6.97 (m, 1H), 6.97-6.91 (m, 1H), 5.00-4.77 (m, 1H), 4.09-3.98 (m, 1H), 3.98-3.92 (m, 1H), 3.92 (s, 3H), 3.88-3.80 (m, 1H), 3.80-3.72 (m, 1H), 3.34-3.24 (m, 1H), 3.10-2.99 (m, 1H), 2.76-2.56 (m, 2H), 2.53-2.37 (m, 2H), 2.05-1.93 (m, 1H), 1.91-1.83 (m, 1H), 1.82-1.71 (m, 2H) MS m/z= 644.9 (M+H)+

[1722] Example 235: (S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropan-2-ol hydrochloride

[1723] The titled compound (20.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-23 and C1-1. (Yield: 71.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.91 (d, 1H), 8.27 (s, 2H), 8.04 (s, 1H), 7.83 (q, 1H), 7.66 (d, 1H), 7.47 (s, 1H), 7.25 (d, 1H), 7.13 (t, 1H), 4.35 (s, 2H), 4.07 (s, 3H), 4.00-3.96 (m, 1H), 3.75-3.69 (m, 1H), 3.53-3.42 (m, 1H), 3.20-3.02 (m, 2H), 2.28-2.17 (m, 1H), 1.95-1.63 (m, 3H), 1.32 (d, 6H) MS m/z= 533.0 (M+H)+

[1724] Example 236: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-(dimethylamino)propyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1725] The titled compound (27.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-24 and C1-1. (Yield: 49.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.93 (d, 1H), 8.32 (d, 2H), 7.98 (s, 1H), 7.84 (q, 1H), 7.64 (d, 1H), 7.48 (s, 1H), 7.26 (d, 1H), 7.14 (t, 1H), 4.49 (t, 2H), 4.10 (s, 3H), 3.93-3.91 (m, 1H), 3.55-3.40 (m, 1H), 3.31-3.24 (m, 2H), 3.23-3.07 (m, 2H), 3.00-2.89 (m, 6H), 2.47-2.36 (m, 2H), 2.28-2.19 (m, 1H), 1.94-1.85 (m, 1H), 1.85-1.67 (m, 2H) MS m/z= 547.0 (M+H)+

- [1726] Example 237: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(azetidin-3-ylmethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1727] The titled compound (16.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-25 and C1-1. (Yield: 49.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.91 (d, 1H), 8.31-8.18 (m, 2H), 7.95-7.86 (m, 1H), 7.81 (q, 1H), 7.64 (d, 1H), 7.46 (s, 1H), 7.25 (d, 1H), 7.13 (t, 1H), 4.65-4.56 (m, 2H), 4.27-4.09 (m, 3H), 4.07 (s, 3H), 3.77-3.71 (m, 1H), 3.60-3.42 (m, 2H), 3.26-3.04 (m, 2H), 2.29-2.18 (m, 1H), 1.93-1.84 (m, 1H), 1.84-1.66 (m, 2H) MS m/z= 531.0 (M+H)+
- [1728] Example 238: N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-pyrrolidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1729] The titled compound (18.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-26 and C1-1. (Yield: 75.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.91 (d, 1H), 8.33 (s, 1H), 8.24 (s, 1H), 7.97 (s, 1H), 7.83 (q, 1H), 7.63 (d, 1H), 7.45 (s, 1H), 7.26 (d, 1H), 7.13 (t, 1H), 5.48-5.38 (m, 1H), 4.08 (s, 3H), 3.95-3.93 (m, 1H), 3.93-3.75 (m, 2H), 3.75-3.69 (m, 1H), 3.63-3.52 (m, 1H), 3.52-3.39 (m, 1H), 3.20-3.05 (m, 2H), 2.69-2.58 (m, 1H), 2.58-2.45 (m, 1H), 2.30-2.16 (m, 1H), 1.94-1.85 (m, 1H), 1.85-1.65 (m, 2H) MS m/z= 531.0 (M+H)+
- [1730] Example 239: N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-pyrrolidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1731] The titled compound (15.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-27 and C1-1. (Yield: 69.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.91 (d, 1H), 8.35 (s, 1H), 8.25 (s, 1H), 7.96 (s, 1H), 7.82 (q, 1H), 7.65 (d, 1H), 7.46 (s, 1H), 7.26 (d, 1H), 7.13 (t, 1H), 5.49-5.37 (m, 1H), 4.09 (s, 3H), 3.96-3.94 (m, 1H), 3.93-3.77 (m, 2H), 3.77-3.69 (m, 1H), 3.64-3.53 (m, 2H), 3.53-3.42 (m, 1H), 3.21-3.04 (m, 2H), 2.68-2.56 (m, 1H), 2.56-2.42 (m, 1H), 2.29-2.16 (m, 1H), 1.97-1.83 (m, 1H), 1.83-1.65 (m, 2H) MS m/z= 531.0 (M+H)+
- [1732] Example 240: (S)-4-(3-aminopiperidin-1-yl)-N⁶-(2-(dimethylamino)ethyl)-N⁶-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-[3,3'-bipyridin]-6,6'-diamine hydrochloride
- [1733] The titled compound (4.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-28 and C1-1. (Yield: 70.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.87 (d, 1H), 8.35-8.15 (m, 3H), 7.81 (q, 2H), 7.45-7.29 (m, 2H), 7.24 (d, 1H), 7.09 (t, 1H), 4.08-3.98 (m, 1H), 3.97 (s, 3H), 3.96-3.86 (m, 1H), 3.74-3.67 (m, 2H), 3.67-3.59 (m, 2H), 3.12-2.99 (m, 6H), 2.99-2.90 (m, 1H), 2.27-2.14 (m, 1H), 1.99-1.89 (m, 1H), 1.89-1.72 (m, 1H), 1.68-1.54 (m, 1H) MS m/z= 559.0 (M+H)+
- [1734] Example 241: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperazin-1-yl)-[3,3'-bipyridin]-6-amine hydrochloride

- [1735] The titled compound (20.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-29 and C1-1. (Yield: 80.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.87 (d, 1H), 8.41-8.33 (m, 2H), 8.33 (s, 1H), 7.79-7.60 (m, 3H), 7.48 (s, 1H), 7.24 (d, 1H), 7.11 (t, 1H), 4.26-4.10 (m, 4H), 4.05 (s, 3H), 3.97-3.88 (m, 1H), 3.73-3.64 (m, 1H), 3.64-3.56 (m, 4H), 3.46-3.36 (m, 1H), 3.17-3.08 (m, 1H), 3.08-2.97 (m, 1H), 2.27-2.15 (m, 1H), 2.00-1.88 (m, 1H), 1.88-1.74 (m, 1H), 1.70-1.60 (m, 1H) MS m/z= 556.0 (M+H)+
- [1736] Example 242: (S)-(2-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluorophenyl)methanol hydrochloride
- [1737] The titled compound (11.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-11. (Yield: 62.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.90 (d, 1H), 8.57 (s, 1H), 8.09 (s, 1H), 8.05 (s, 1H), 7.80-7.76 (m, 0.2H), 7.76-7.68 (m, 1H), 7.64-7.62 (m, 0.6H), 7.59 (d, 1H), 7.53-7.50 (m, 1H), 7.49-7.47 (m, 0.2H), 7.43 (t, 1H), 7.29 (s, 1H), 4.73 (s, 2H), 3.98-3.85 (m, 1H), 3.66-3.55 (m, 1H), 3.50-3.42 (m, 1H), 3.16-3.04 (m, 1H), 3.04-2.95 (m, 1H), 2.29-2.15 (m, 1H), 1.93-1.81 (m, 1H), 1.81-1.59 (m, 2H) MS m/z= 510.9 (M+H)+
- [1738] Example 243: (S)-(2-(4-((4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluorophenyl)methanol hydrochloride
- [1739] The titled compound (13.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-3 and C1-11. (Yield: 60.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.86 (d, 1H), 8.52 (s, 1H), 8.28 (s, 1H), 7.99 (s, 1H), 7.77-7.68 (m, 1H), 7.65-7.59 (m, 1H), 7.58-7.56 (m, 0.6H), 7.54 (d, 1H), 7.44-7.35 (m, 1H), 7.15 (s, 1H), 4.76 (s, 2H), 4.49-4.39 (m, 1H), 4.38-4.29 (m, 1H), 3.82-3.62 (m, 1H), 3.51-3.42 (m, 2H), 2.33-2.23 (m, 1H), 2.13-2.02 (m, 1H), 1.98-1.75 (m, 2H) MS m/z= 534.9 (M+H)+
- [1740] Example 244: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methoxy-2-methylpropan-2-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1741] The titled compound (9.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-30 and C1-1. (Yield: 52.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.87 (d, 1H), 8.22 (s, 2H), 7.89 (s, 1H), 7.79 (q, 1H), 7.61 (d, 1H), 7.37 (s, 1H), 7.24 (d, 1H), 7.11 (t, 1H), 4.03 (s, 3H), 3.97-3.92 (m, 1H), 3.73 (s, 3H), 3.55 (s, 2H), 3.47-3.41 (m, 1H), 3.15-3.03 (m, 1H), 3.03-2.92 (m, 1H), 2.28-2.18 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.74 (m, 1H), 1.74-1.69 (m, 1H), 1.68 (s, 6H) MS m/z= 547.0 (M+H)+

- [1742] Example 245: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-((3,3-difluorocyclobutyl)methyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1743] The titled compound (15.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-31 and C1-1. (Yield: 80.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.87 (d, 1H), 8.21 (s, 2H), 7.89 (s, 1H), 7.78 (q, 1H), 7.61-7.51 (m, 1H), 7.35 (s, 1H), 7.22 (d, 1H), 7.11 (t, 1H), 4.46 (d, 2H), 4.03 (s, 3H), 4.01-3.97 (m, 1H), 3.97-3.90 (m, 1H), 3.72-3.66 (m, 1H), 3.66-3.58 (m, 1H), 3.51-3.44 (m, 1H), 3.16-3.07 (m, 1H), 3.07-2.95 (m, 1H), 2.80-2.63 (m, 3H), 2.57-2.42 (m, 2H), 2.26-2.17 (m, 1H), 1.89-1.80 (m, 1H), 1.78-1.63 (m, 2H) MS m/z= 565.0 (M+H)+
- [1744] Example 246: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-(dimethylamino)ethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1745] The titled compound (4.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-32 and C1-1. (Yield: 85.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.83 (d, 1H), 8.32 (s, 1H), 8.24 (s, 1H), 7.99 (s, 1H), 7.74 (q, 1H), 7.62 (s, 1H), 7.34 (s, 1H), 7.21 (d, 1H), 7.07 (t, 1H), 4.79-4.67 (m, 2H), 3.98 (s, 3H), 3.85-3.74 (m, 2H), 3.66-3.57 (m, 1H), 3.54-3.40 (m, 1H), 3.09-3.01 (m, 6H), 3.01-2.92 (m, 2H), 2.29-2.16 (m, 1H), 1.97-1.72 (m, 2H), 1.72-1.55 (m, 1H) MS m/z= 532.0 (M+H)+
- [1746] Example 247: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(fluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1747] The titled compound (4.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-33 and C1-1. (Yield: 42.1%) ¹H NMR (CDCl₃, 400MHz) δ 8.86 (d, 1H), 8.46 (s, 1H), 8.26 (s, 1H), 8.06 (s, 1H), 7.78 (q, 1H), 7.65 (s, 1H), 7.40 (s, 1H), 7.24 (d, 1H), 7.11 (t, 1H), 6.31 (s, 1H), 6.18 (s, 1H), 4.04 (s, 3H), 3.94-3.84 (m, 1H), 3.72 (s, 2H), 3.66-3.57 (m, 1H), 3.49-3.39 (m, 1H), 3.11-2.96 (m, 2H), 2.28-2.16 (m, 1H), 1.92-1.72 (m, 2H), 1.72-1.59 (m, 1H) MS m/z= 492.9 (M+H)+
- [1748] Example 248: (S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperidin-4-yl)-[3,3'-bipyridin]-6-amine hydrochloride
- [1749] The titled compound (4.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-34 and C1-1. (Yield: 29.1%) ¹H NMR (CD₃OD, 400MHz) δ 9.19 (s, 1H), 8.94 (s, 1H), 8.85 (d, 1H), 8.46 (s, 1H), 8.28 (s, 1H), 7.92-7.78 (m, 1H), 7.78 (q, 1H), 7.55 (s, 1H), 7.23 (d, 1H), 7.10 (t, 1H), 4.08 (s, 3H), 3.85-3.74 (m, 2H), 3.72-3.65 (m, 3H), 3.65-3.58 (m, 2H), 3.31-3.26 (m, 1H), 3.14-2.97

- (m, 2H), 2.51-2.38 (m, 2H), 2.34-2.13 (m, 3H), 1.94-1.82 (m, 1H), 1.82-1.70 (m, 1H), 1.70-1.59 (m, 1H) MS m/z= 556.0 (M+H)+
- [1750] Example 249: (S)-4-(3-aminopiperidin-1-yl)-6'-(2-(dimethylamino)ethoxy)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-[3,3'-bipyridin]-6-amine hydrochloride
- [1751] The titled compound (5.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-35 and C1-1. (Yield: 31.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.88 (d, 1H), 8.47 (s, 1H), 8.19 (s, 1H), 8.08 (d, 1H), 7.78 (q, 1H), 7.65 (d, 1H), 7.41 (s, 1H), 7.22 (d, 1H), 7.16 (d, 1H), 7.10 (t, 1H), 4.84 (s, 2H), 4.05 (s, 3H), 3.96-3.89 (m, 1H), 3.79-3.74 (m, 1H), 3.64-3.59 (m, 1H), 3.59-3.55 (m, 1H), 3.45-3.37 (m, 1H), 3.15-3.07 (m, 1H), 3.07-2.97 (m, 6H), 2.23-2.13 (m, 1H), 1.88-1.76 (m, 1H), 1.73-1.57 (m, 2H) MS m/z= 560.0 (M+H)+
- [1752] Example 250: (S)-1-(4'-(3-aminopiperidin-1-yl)-6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-6-yl)-3-ethylurea hydrochloride
- [1753] The titled compound (13.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-36 and C1-1. (Yield: 33.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.91 (d, 1H), 8.63-8.51 (m, 2H), 8.36 (s, 1H), 7.81 (q, 2H), 7.61 (d, 1H), 7.49 (s, 1H), 7.24 (d, 1H), 7.11 (t, 1H), 4.08 (s, 3H), 3.92-3.83 (m, 1H), 3.74-3.65 (m, 1H), 3.65-3.56 (m, 1H), 3.44 (q, 2H), 3.14-3.01 (m, 2H), 2.26-2.14 (m, 1H), 1.94-1.82 (m, 1H), 1.82-1.60 (m, 2H), 1.28 (t, 3H) MS m/z= 558.0 (M+H)+
- [1754] Example 251: (4-(4-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone
- [1755] The titled compound (17.3 mg) was prepared in accordance with the same procedures as in Step 3 of Example 186, changing the amine reagent to (R)-3-fluoropyrrolidine hydrochloride. (Yield: 31.7%) ¹H NMR (CDCl₃, 400MHz) δ 8.63 (d, 1H), 8.28 (s, 1H), 8.17 (s, 2H), 8.02 (s, 1H), 7.57 (s, 1H), 7.44-7.40 (m, 0.2H), 7.37 (s, 1H), 7.28-7.25 (m, 0.6H), 7.13-7.09 (m, 0.2H), 7.05-6.90 (m, 2H), 5.49-5.15 (m, 1H), 4.07-3.89 (m, 1H), 3.88 (s, 3H), 3.82-3.69 (m, 2H), 3.69-3.57 (m, 2H), 3.30-3.19 (m, 1H), 3.19-3.08 (m, 1H), 2.98-2.83 (m, 1H), 2.59-2.45 (m, 1H), 2.41-2.27 (m, 2H), 2.01-1.90 (m, 1H), 1.74-1.63 (m, 1H), 1.63-1.43 (m, 2H), 1.22-1.09 (m, 1H) MS m/z= 625.9 (M+H)+
- [1756] Example 252: N-(4-((2R,5S)-5-amino-2-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1757] The titled compound (3.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-36 and C1-1. (Yield: 40.1%) ¹H NMR (CDCl₃, 400MHz) δ 8.65 (d, 1H), 8.15-8.07 (m, 2H), 8.00 (s, 1H), 7.74 (s, 1H), 7.51-7.42 (m, 1H), 7.41-7.40 (m, 0.2H), 7.39-7.33 (m, 1H), 7.33-7.30 (m, 1H),

- 7.27-7.24 (m, 0.6H), 7.12-7.09 (m, 0.2H), 6.89-6.76 (m, 2H), 3.89 (s, 3H), 3.58-3.46 (m, 1H), 3.12-2.99 (m, 1H), 2.99-2.85 (m, 1H), 2.80-2.68 (m, 1H), 2.06-2.00 (m, 2H), 1.85-1.67 (m, 1H), 1.50 (s, 3H) MS m/z= 524.9 (M+H)+
- [1758] Example 253: N-(4-((3R,4S)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1759] The titled compound (5.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-37 and C1-1. (Yield: 34.1%) ¹H NMR (CDCl₃, 400MHz) δ 8.66 (d, 1H), 8.19-8.08 (m, 2H), 8.03 (s, 1H), 7.62-7.51 (m, 1H), 7.51 (d, 1H), 7.42-7.32 (m, 2.2H), 7.27-7.23 (m, 0.6H), 7.13-7.09 (m, 0.2H), 6.89-6.76 (m, 2H), 3.90 (s, 3H), 3.46-3.40 (m, 1H), 3.40 (s, 3H), 3.06-2.98 (m, 1H), 2.98-2.87 (m, 3H), 2.87-2.78 (m, 1H), 1.97-1.87 (m, 1H), 1.65-1.56 (m, 2H) MS m/z= 540.9 (M+H)+
- [1760] Example 254: N-(4-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1761] The titled compound (5.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-38 and C1-1. (Yield: 38.1%) ¹H NMR (CDCl₃, 400MHz) δ 8.65 (d, 1H), 8.19-8.08 (m, 2H), 8.01 (s, 1H), 7.71 (s, 1H), 7.50 (d, 1H), 7.43-7.32 (m, 2.2H), 7.27-7.24 (m, 0.6H), 7.12-7.08 (m, 0.2H), 6.88-6.78 (m, 2H), 3.89 (s, 3H), 3.46 (s, 3H), 3.36-3.25 (m, 2H), 2.99-2.86 (m, 2H), 2.70-2.56 (m, 1H), 2.54-2.41 (m, 1H), 2.09-1.99 (m, 1H), 1.59-1.47 (m, 2H) MS m/z= 540.9 (M+H)+
- [1762] Example 255: (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(morpholino)methanone hydrochloride
- [1763] The titled compound (38.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-37 and C1-1. (Yield: 87.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.77 (d, 1H), 8.12 (s, 1H), 7.71-7.65 (m 2H), 7.65-7.59 (m, 3H), 7.59-7.46 (m, 1H), 7.22 (s, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 3.94 (s, 3H), 3.86-3.74 (m, 4H), 3.74-3.60 (m, 3H), 3.57-3.45 (m, 3H), 3.31-3.24 (m, 1H), 2.93 (q, 2H), 2.17-2.13 (m, 1H), 1.82-1.78 (m, 1H), 1.72-1.54 (m, 2H) MS m/z= 584.9 (M+H)+
- [1764] Example 256: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1765] The titled compound (31.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-38 and C1-1. (Yield: 94.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.71 (d, 1H), 8.20 (s, 1H), 7.80 (s, 1H), 7.80-7.62 (m 3H), 7.28 (brs, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 4.45 (t, 2H), 3.94 (s, 3H), 3.86 (t, 2H), 3.80

- (d, 1H), 3.51 (d, 1H), 3.40 (s, 3H), 3.35-3.25 (m, 1H), 2.93 (t, 1H), 2.84 (t, 1H), 2.19 (d, 1H), 1.91 (d, 1H), 1.74 (q, 1H), 1.58 (q, 1H) MS m/z= 543.9 (M+H)+
- [1766] Example 257: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1767] The titled compound (16.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-39 and C1-1. (Yield: 64.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 7.96 (s, 1H), 7.66 (q, 1H), 7.48-7.38 (m 1H), 7.14-7.11 (m, 2H), 7.02-6.97 (m, 2H), 6.90-6.84 (m, 2H), 4.32 (t, 2H), 3.94 (s, 3H), 3.91 (d, 1H), 3.64 (d, 1H), 3.37 (t, 2H), 3.37-3.20 (m, 1H), 2.97 (s, 3H), 3.01-2.90 (m, 2H), 2.25-2.15 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.50 (m, 2H) MS m/z= 543.0 (M+H)+
- [1768] Example 258: (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one hydrochloride
- [1769] The titled compound (16.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-40 and C1-1. (Yield: 63.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.04 (s, 1H), 7.63 (q, 1H), 7.55-7.45 (m 2H), 7.42 (s, 1H), 7.16 (s, 1H), 7.11 (d, 1H), 7.07 (d, 1H), 6.98 (t, 1H), 5.42 (s, 2H), 3.93 (s, 3H), 3.82 (d, 1H), 3.55 (d, 1H), 3.34-3.32 (m, 1H), 3.04-2.85 (m, 2H), 2.25-2.10 (m, 1H), 1.85-1.70 (m, 1H), 1.70-1.50 (m, 2H) MS m/z= 542.9 (M+H)+
- [1770] Example 259: (S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)pyrrolidin-2-one hydrochloride
- [1771] The titled compound (25.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-41 and C1-1. (Yield: 42.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 7.96 (s, 1H), 7.77-7.66 (m, 2H), 7.64-7.50 (m, 4H), 7.44 (q, 1H), 6.98 (d, 1H), 6.87 (t, 1H), 3.99 (t, 2H), 3.84 (s, 3H), 3.24 (d, 1H), 3.14 (d, 1H), 2.80-2.70 (m, 1H), 2.64 (t, 2H), 2.57 (t, 1H), 2.34 (t, 1H), 2.30-2.15 (m, 2H), 1.95-1.85 (m, 1H), 1.60-1.45 (m, 1H), 1.40-1.25 (m, 1H), 1.25-1.10 (m, 1H) MS m/z= 554.9 (M+H)+
- [1772] Example 260: (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one hydrochloride
- [1773] The titled compound (14.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-42 and C1-1. (Yield: 65.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 8.04 (s, 1H), 7.60 (q, 1H), 7.55-7.30 (m 1H), 7.19-7.15 (m, 2H), 7.15-7.02 (m, 3H), 6.96 (t, 1H), 4.66 (s, 2H), 3.91 (s, 3H), 3.77 (d, 1H), 3.54 (d, 1H), 2.90 (t, 2H), 2.25-2.15 (m, 1H), 2.10-2.00 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.65 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 542.9 (M+H)+

- [1774] Example 261: (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one hydrochloride
- [1775] The titled compound (11.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-43 and C1-1. (Yield: 45.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.06 (s, 1H), 7.61 (q, 1H), 7.58-7.40 (m, 1H), 7.40-7.25 (m, 2H), 7.25-7.20 (m, 1H), 7.15-7.05 (m, 2H), 6.97 (t, 1H), 4.71 (s, 2H), 3.92 (s, 3H), 3.80 (d, 1H), 3.53 (d, 1H), 3.43 (s, 3H), 3.00-2.85 (m, 2H), 2.25-2.15 (m, 1H), 2.10-2.00 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.50 (m, 2H) MS m/z= 557.0 (M+H)+
- [1776] Example 262: (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-8-methyl-3,4-dihydroquinolin-2(1H)-one hydrochloride
- [1777] The titled compound (10.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-44 and C1-1. (Yield: 70.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.81 (d, 1H), 8.03 (s, 1H), 7.70 (q, 1H), 7.52 (d, 1H), 7.30-7.20 (m 3H), 7.16 (d, 1H), 7.03 (t, 1H), 3.98 (s, 3H), 3.98-3.90 (m, 1H), 3.80-3.70 (m, 1H), 3.65-3.55 (m, 1H), 3.10-3.00 (m, 3H), 3.00-2.90 (m, 1H), 2.63 (t, 2H), 2.35 (s, 3H), 2.25-2.15 (m, 1H), 1.85-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 555.9 (M+H)+
- [1778] Example 263: (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1-methyl-3,4-dihydroquinolin-2(1H)-one hydrochloride
- [1779] The titled compound (7.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-45 and C1-1. (Yield: 91.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.05 (s, 1H), 7.61 (q, 1H), 7.54-7.40 (m, 3H), 7.29 (d, 1H), 7.15-7.05 (m, 2H), 6.97 (t, 1H), 3.92 (s, 3H), 3.82 (d, 1H), 3.60-3.50 (m, 1H), 3.41 (s, 3H), 3.03 (t, 2H), 3.03-2.85 (m, 2H), 2.69 (t, 2H), 2.24-2.14 (m, 1H), 2.10-2.00 (m, 1H), 1.85-1.75 (m, 1H), 1.70-1.50 (m, 2H) MS m/z= 556.0 (M+H)+
- [1780] Example 264: (S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol
- [1781] The titled compound (35.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates A2-20 and C1-1. (Yield: 50.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.15-8.05 (m, 2H), 7.86 (s, 1H), 7.63 (s, 1H), 7.53 (d, 1H), 7.44 (q, 1H), 6.97 (d, 1H), 6.86 (t, 1H), 4.90-4.75 (m, 1H), 3.84 (s, 3H), 3.75-3.65 (m, 1H), 3.35-3.25 (m, 1H), 3.06 (d, 1H), 2.64 (t, 1H), 2.45 (t, 1H),

- 2.15-2.05 (m, 2H), 2.00-1.95 (m, 1H), 1.95-1.85 (m, 2H), 1.80-1.70 (m, 1H), 1.65-1.50 (m, 1H), 1.43 (s, 6H), 1.43-1.32 (m, 1H), 1.31 (s, 6H) MS m/z= 602.0 (M+H)+
- [1782] Example 265: (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(piperazin-1-yl)methanone hydrochloride
- [1783] The titled compound (22.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-46 and C1-1. (Yield: 79.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.68 (d, 1H), 8.10 (s, 1H), 7.80-7.70 (m, 2H), 7.70-7.60 (m, 2H), 7.60-7.40 (m, 2H), 7.19 (brs, 1H), 7.07 (d, 1H), 6.95 (t, 1H), 4.10-3.75 (m, 4H), 3.90 (s, 3H), 3.70-3.55 (m, 1H), 3.50-3.30 (m, 4H), 3.30-3.20 (m, 2H), 2.95-2.75 (m, 2H), 2.20-2.10 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.60 (m, 1H), 1.60-1.45 (m, 1H) MS m/z= 584.0 (M+H)+
- [1784] Example 266: (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1785] The titled compound (30.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-39 and C1-1. (Yield: 67.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.48 (s, 1H), 8.16 (s, 1H), 8.06 (s, 1H), 7.77-7.45 (m, 1H), 7.68 (q, 1H), 7.47 (brs, 1H), 7.29 (s, 1H), 7.15 (d, 1H), 7.01 (t, 1H), 3.96 (s, 3H), 3.77 (d, 1H), 3.58 (d, 1H), 2.95 (d, 2H), 2.95-2.80 (m, 2H), 2.74 (s, 3H), 2.25-2.15 (m, 1H), 2.05-1.95 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 1H), 1.45-1.30 (m, 1H) MS m/z= 539.9 (M+H)+
- [1786] Example 267: (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1787] The titled compound (32.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-40 and C1-1. (Yield: 62.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.80 (d, 1H), 8.49 (s, 1H), 8.16 (s, 1H), 8.06 (s, 1H), 7.78-7.47 (m, 1H), 7.69 (q, 1H), 7.55-7.52 (m, 1H), 7.32 (s, 1H), 7.16 (d, 1H), 7.02 (t, 1H), 3.97 (s, 3H), 3.80 (d, 1H), 3.60 (d, 1H), 2.96 (d, 2H), 2.95-2.82 (m, 2H), 2.74 (s, 3H), 2.30-2.15 (m, 1H), 2.05-1.95 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 1H), 1.45-1.30 (m, 1H) MS m/z= 539.9 (M+H)+
- [1788] Example 268: N-(4-((3R,4R)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1789] The titled compound (9.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-41 and C1-1. (Yield: 28.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.48 (s, 1H), 8.18 (s, 1H), 8.06 (s, 1H), 7.78-7.47 (m,

- 1H), 7.66 (q, 1H), 7.60-7.50 (m, 1H), 7.23 (s, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 3.95 (s, 3H), 3.72 (d, 1H), 3.59 (d, 1H), 3.12-2.98 (m, 2H), 2.71 (t, 1H), 2.15-2.05 (m, 1H), 1.98-1.82 (m, 1H), 1.82-1.70 (m, 1H), 1.00 (d, 3H) MS m/z = 525.0 (M+H)+
- [1790] Example 269: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1791] The titled compound (23.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-47 and C1-1. (Yield: 54.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.19 (s, 1H), 8.15 (s, 1H), 7.86 (s, 1H), 7.68 (q, 1H), 7.60-7.50 (m, 1H), 7.24 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 3.96 (s, 3H), 3.90 (d, 1H), 3.61 (d, 1H), 3.55-3.40 (m, 1H), 3.03 (t, 1H), 2.96 (t, 1H), 2.25-2.15 (m, 1H), 2.15-2.05 (m, 2H), 1.95-1.80 (m, 3H), 1.80-1.55 (m, 3H), 1.43 (s, 6H), 1.31 (s, 6H) MS m/z = 602.0 (M+H)+
- [1792] Example 270: 6-(4-((S)-3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one hydrochloride
- [1793] The titled compound (7.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-48 and C1-1. (Yield: 22.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.48 (d, 1H), 8.02 (s, 1H), 7.66-7.60 (m, 1H), 7.60-7.50 (m, 1H), 7.46 (q, 1H), 7.25-7.20 (m, 1H), 7.19 (s, 1H), 7.19-7.05 (m, 1H), 6.99 (d, 1H), 6.88 (t, 1H), 4.71 (q, 1H), 3.84 (s, 3H), 3.55-3.40 (m, 1H), 3.30-3.20 (m, 1H), 3.20-3.10 (m, 1H), 2.75-2.65 (m, 1H), 2.65-2.55 (m, 1H), 2.15-2.00 (m, 1H), 1.75-1.60 (m, 2H), 1.57 (d, 3H), 1.55-1.40 (m, 1H) MS m/z = 556.9 (M+H)+
- [1794] Example 271: (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-methylpiperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1795] The titled compound (16.3 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-42 and C1-1. (Yield: 20.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 8.38 (s, 1H), 8.14 (s, 1H), 8.09 (s, 1H), 7.78 (s, 1H), 7.78-7.39 (m, 2H), 7.47 (q, 1H), 6.98 (d, 1H), 6.86 (t, 1H), 3.84 (s, 3H), 3.25-3.10 (m, 2H), 2.50-2.40 (m, 1H), 2.16 (t, 1H), 1.85-1.75 (m, 1H), 1.75-1.65 (m, 1H), 1.65-1.55 (m, 2H), 1.05-0.85 (m, 2H), 0.79 (d, 3H) MS m/z = 510.9 (M+H)+
- [1796] Example 272: (S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(fluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1797] The titled compound (29.6 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-43 and C1-1. (Yield: 36.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.43 (d, 1H), 8.38 (s, 1H), 8.15 (s, 1H), 8.09 (s, 1H), 7.79 (s, 1H), 7.79-7.39 (m, 2H), 7.48 (q, 1H), 6.98 (d, 1H), 6.86 (t, 1H), 4.35-4.10 (m, 2H),

- 3.83 (s, 3H), 3.83-3.80 (m, 1H), 3.21 (d, 1H), 2.51 (t, 1H), 2.41 (t, 1H), 2.10-1.95 (m, 1H), 1.85-1.75 (m, 1H), 1.70-1.60 (m, 2H), 1.25-1.10 (m, 1H) MS m/z= 529.9 (M+H)+
- [1798] Example 273: (R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(difluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1799] The titled compound (20.2 mg) was prepared in accordance with the same procedures as in Example 7, using Intermediates B3-44 and C1-1. (Yield: 23.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.44 (d, 1H), 8.39 (s, 1H), 8.16 (s, 1H), 8.09 (s, 1H), 7.77 (s, 1H), 7.77-7.39 (m, 2H), 7.46 (q, 1H), 6.98 (d, 1H), 6.86 (t, 1H), 5.80-5.45 (m, 1H), 3.83 (s, 3H), 3.35-3.25 (m, 1H), 3.22 (d, 1H), 2.60-2.45 (m, 2H), 2.20-2.05 (m, 1H), 1.95-1.85 (m, 1H), 1.75-1.55 (m, 2H), 1.40-1.30 (m, 1H) MS m/z= 546.9 (M+H)+
- [1800] Example 274: (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one hydrochloride
- [1801] The titled compound (10.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-49 and C1-1. (Yield: 50.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 8.23 (s, 1H), 8.14 (s, 1H), 7.66-7.58 (m 3H), 7.20 (s, 1H), 7.11 (d, 1H), 6.98 (t, 1H), 4.82 (s, 2H), 3.93 (s, 3H), 3.85-3.70 (m, 1H), 3.58-3.40 (m, 4H), 3.40-3.25 (m, 1H), 3.05-2.85 (m, 2H), 2.18 (d, 1H), 1.90-1.75 (m, 1H), 1.75-1.50 (m, 2H) MS m/z= 557.9 (M+H)+
- [1802] Example 275: (S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one hydrochloride
- [1803] The titled compound (2.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-50 and C1-1. (Yield: 95.8%) ¹H NMR (CD₃OD, 400MHz) δ 8.47 (d, 1H), 8.13 (s, 1H), 8.04 (s, 1H), 7.66 (s, 1H), 7.66-7.61 (m 1H), 7.61-7.58 (m, 1H), 7.46 (q, 1H), 6.99 (d, 1H), 6.87 (t, 1H), 4.73 (s, 2H), 3.84 (s, 3H), 3.25-3.15 (m, 1H), 3.05-2.90 (m, 1H), 2.67 (t, 1H), 2.50 (t, 1H), 2.10-2.00 (m, 2H), 1.75-1.65 (m, 1H), 1.65-1.50 (m, 2H) MS m/z= 543.9 (M+H)+
- [1804] Example 276: (S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-3,4-dihydro-1,8-naphthyridin-2(1H)-one hydrochloride
- [1805] The titled compound (9.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-51 and C1-1. (Yield: 65.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 8.35 (s, 1H), 8.13 (s, 1H), 7.88 (s, 1H), 7.80-7.40 (m 2H), 7.20 (s, 1H), 7.12 (d, 1H), 6.99 (t, 1H), 3.93 (s, 3H), 3.76 (d, 1H), 3.55-3.45 (m, 1H), 3.40-3.20 (m, 1H), 3.10 (t, 2H), 3.00-2.85 (m, 2H), 2.72 (t, 2H), 2.18 (d, 1H), 1.85-1.75 (m, 1H), 1.70-1.50 (m, 2H) MS m/z= 542.0 (M+H)+

- [1806] Example 277: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1807] The titled compound (6.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-52 and C1-1. (Yield: 21.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.20 (d, 1H), 8.16 (s, 1H), 7.90 (s, 1H), 7.68 (q, 1H), 7.55 (brs, 1H), 7.25 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 4.74-4.60 (m, 1H), 4.05 (d, 2H), 4.01 (d, 2H), 3.96 (s, 3H), 3.89 (d, 1H), 3.63 (d, 1H), 3.50-3.40 (m, 1H), 3.05-2.90 (m, 2H), 2.20 (d, 1H), 1.95-1.75 (m, 2H), 1.70-1.55 (m, 1H) MS m/z= 553.9 (M + Cl)-
- [1808] Example 278: methyl (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropanoate hydrochloride
- [1809] The titled compound (18.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-53 and C1-1. (Yield: 88.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.26 (s, 1H), 8.15 (s, 1H), 7.84 (s, 1H), 7.68 (q, 1H), 7.54 (brs, 1H), 7.23 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 3.96 (s, 3H), 3.90 (d, 1H), 3.78 (s, 3H), 3.64 (d, 1H), 3.45-3.35 (m, 1H), 3.05-2.90 (m, 2H), 2.21 (d, 1H), 1.94 (s, 3H), 1.93 (s, 3H), 1.90-1.85 (m, 1H), 1.85-1.70 (m, 1H), 1.70-1.55 (m, 1H) MS m/z= 562.0 (M+H)+
- [1810] Example 279: (S)-N-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)acetamide hydrochloride
- [1811] The titled compound (15.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-54 and C1-1. (Yield: 92.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.73 (d, 1H), 8.04 (s, 1H), 7.80-7.70 (m, 2H), 7.60-7.50 (m, 3H), 7.50-7.20 (m, 1H), 7.10-7.00 (m, 2H), 6.95 (t, 1H), 3.90 (s, 3H), 3.80-3.65 (m, 1H), 3.60-3.45 (m, 1H), 3.30-3.20 (m, 1H), 2.95-2.80 (m, 2H), 2.18 (s, 3H), 2.18-2.10 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.60 (m, 1H), 1.60-1.45 (m, 1H) MS m/z= 529.0 (M+H)+
- [1812] Example 280: (S)-3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-N,N-dimethylbenzamide hydrochloride
- [1813] The titled compound (12.0 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-55 and C1-1. (Yield: 74.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.77 (d, 1H), 8.12 (s, 1H), 7.70-7.60 (m, 4H), 7.60-7.50 (m, 2H), 7.20 (s, 1H), 7.12 (d, 1H), 6.99 (t, 1H), 3.94 (s, 3H), 3.67 (d, 1H), 3.51 (d, 1H), 3.40-3.35 (m, 1H), 3.16 (s, 3H), 3.07 (s, 3H), 3.00-2.85 (m, 2H), 2.14 (d, 1H), 1.85-1.75 (m, 1H), 1.75-1.65 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 542.9 (M+H)+
- [1814] Example 281: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-(trifluoromethoxy)phenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

- [1815] The titled compound (15.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-56 and C1-1. (Yield: 42.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.08 (s, 1H), 7.67 (q, 1H), 7.65-7.55 (m, 2H), 7.54-7.43 (m, 2H), 7.24 (s, 1H), 7.14 (d, 1H), 7.01 (t, 1H), 3.96 (s, 3H), 3.86 (d, 1H), 3.51 (d, 1H), 3.40-3.30 (m, 1H), 3.04 (t, 1H), 2.93 (t, 1H), 2.42 (s, 3H), 2.25-2.10 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 569.9 (M+H)+
- [1816] Example 282: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-fluoro-3-methylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1817] The titled compound (45.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-57 and C1-1. (Yield: 78.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.81 (d, 1H), 8.05 (s, 1H), 7.69 (q, 1H), 7.65-7.40 (m, 3H), 7.30-7.20 (m, 2H), 7.15 (d, 1H), 7.02 (t, 1H), 3.97 (s, 3H), 3.88 (d, 1H), 3.56 (d, 1H), 3.40-3.30 (m, 1H), 3.03 (t, 1H), 2.94 (t, 1H), 2.37 (s, 3H), 2.25-2.10 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 503.0 (M+H)+
- [1818] Example 283: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1819] The titled compound (31.8 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-58 and C1-1. (Yield: 74.2%) ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.24 (s, 1H), 8.17 (s, 1H), 7.87 (s, 1H), 7.63 (q, 1H), 7.60-7.45 (m, 1H), 7.18 (s, 1H), 7.12 (d, 1H), 6.99 (t, 1H), 4.80-4.65 (m, 1H), 3.94 (s, 3H), 3.85 (d, 1H), 3.70-3.55 (m, 2H), 3.55-3.45 (m, 2H), 3.30-3.20 (m, 2H), 3.01 (t, 1H), 2.93 (t, 1H), 2.45-2.30 (m, 4H), 2.25-2.15 (m, 1H), 1.90-1.70 (m, 2H), 1.70-1.55 (m, 1H) MS m/z= 545.0 (M+H)+
- [1820] Example 284: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-isopropoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1821] The titled compound (25.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-59 and C1-1. (Yield: 61.7%) ¹H NMR (CD₃OD, 400MHz) δ 8.77 (d, 1H), 7.99 (s, 1H), 7.62 (q, 1H), 7.43 (brs, 1H), 7.21 (s, 2H), 7.15-7.05 (m, 2H), 6.98 (t, 1H), 4.40-4.25 (m, 1H), 3.93 (s, 3H), 3.90 (d, 1H), 3.56 (d, 1H), 3.40-3.25 (m, 1H), 2.99 (t, 1H), 2.87 (t, 1H), 2.34 (s, 6H), 2.20-2.10 (m, 1H), 1.80-1.65 (m, 1H), 1.65-1.50 (m, 2H), 1.33 (s, 3H), 1.32 (s, 3H) MS m/z= 557.3 (M+H)+
- [1822] Example 285: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1823] The titled compound (37.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-60 and C1-1. (Yield: 65.3%) ¹H

NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 7.99 (s, 1H), 7.66 (q, 1H), 7.55-7.45 (m, 1H), 7.21 (s, 2H), 7.19 (s, 1H), 7.13 (d, 1H), 7.01 (t, 1H), 3.95 (s, 3H), 3.91 (d, 1H), 3.78 (s, 3H), 3.59 (d, 1H), 3.40-3.25 (m, 1H), 3.02 (t, 1H), 2.91 (t, 1H), 2.36 (s, 6H), 2.20-2.10 (m, 1H), 1.80-1.65 (m, 1H), 1.65-1.50 (m, 2H) MS m/z= 529.3 (M+H)+

[1824] Example 286: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1825] The titled compound (26.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-61 and C1-1. (Yield: 80.8%)
1H NMR (CD₃OD, 400MHz) δ 8.80 (d, 1H), 8.07 (s, 1H), 7.96 (q, 1H), 7.65-7.60 (m, 2H), 7.60-7.55 (m, 1H), 7.55-7.45 (m, 2H), 7.27 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 4.10-4.00 (m, 4H), 3.97 (s, 3H), 3.87 (d, 1H), 3.60-3.45 (m, 5H), 3.40-3.30 (m, 1H), 3.03 (t, 1H), 2.94 (t, 1H), 2.20-2.10 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.50 (m, 2H) MS m/z= 556.3 (M+H)+

[1826] Example 287: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1827] The titled compound (25.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-62 and C1-1. (Yield: 58.0%)
1H NMR (CD₃OD, 400MHz) δ 8.80 (d, 1H), 8.04 (s, 1H), 7.68 (q, 1H), 7.53 (brs, 1H), 7.50-7.40 (m, 2H), 7.40-7.35 (m, 1H), 7.23 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 4.05-3.90 (m, 7H), 3.88 (d, 1H), 3.56 (d, 1H), 3.40-3.35 (m, 1H), 3.25-3.10 (m, 4H), 3.02 (t, 1H), 2.93 (t, 1H), 2.49 (s, 3H), 2.20-2.10 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 570.3 (M+H)+

[1828] Example 288: (S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(4-(2-hydroxyethyl)piperazin-1-yl)methanone hydrochloride

[1829] The titled compound (16.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-63 and C1-1. (Yield: 74.1%)
1H NMR (CD₃OD, 400MHz) δ 8.71 (d, 1H), 8.10 (s, 1H), 7.80-7.65 (m, 4H), 7.65-7.35 (m, 2H), 7.16 (brs, 1H), 7.08 (d, 1H), 6.95 (t, 1H), 4.08 (t, 2H), 3.95 (s, 3H), 3.80-3.55 (m, 4H), 3.55-3.40 (m, 2H), 3.39 (t, 2H), 3.39-3.20 (m, 5H), 2.95-2.80 (m, 2H), 2.20-2.10 (m, 1H), 1.85-1.70 (m, 1H), 1.70-1.50 (m, 2H) MS m/z= 627.4 (M+H)+

[1830] Example 289: 4-(4-((S)-3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-N-((1r,4S)-4-hydroxycyclohexyl)benzamide hydrochloride

[1831] The titled compound (24.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-64 and C1-1. (Yield: 62.5%) 1H

NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.11 (s, 1H), 7.99 (d, 2H), 7.70-7.60 (m, 3H), 7.56 (brs, 1H), 7.24 (s, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 3.95 (s, 3H), 3.95-3.85 (m, 1H), 3.85-3.75 (m, 1H), 3.65-3.55 (m, 1H), 3.50 (d, 1H), 3.05-2.90 (m, 2H), 2.20-2.10 (m, 1H), 2.10-1.95 (m, 4H), 1.80-1.70 (m, 1H), 1.80-1.55 (m, 3H), 1.55-1.35 (m, 4H) MS m/z= 612.3 (M+H)+

[1832] Example 290: (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-fluoro-N,N-dimethylbenzamide hydrochloride

[1833] The titled compound (21.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-65 and C1-1. (Yield: 55.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.17 (s, 1H), 7.66 (q, 1H), 7.65-7.55 (m, 2H), 7.55-7.45 (m, 2H), 7.25 (s, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 3.95 (s, 3H), 3.69 (d, 1H), 3.52 (d, 1H), 3.30-3.25 (m, 1H), 3.18 (s, 3H), 3.03 (s, 3H), 3.00-2.85 (m, 2H), 2.17 (d, 1H), 1.85-1.75 (m, 1H), 1.75-1.65 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 560.9 (M+H)+

[1834] Example 291: (S)-1-(3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)ethan-1-one hydrochloride

[1835] The titled compound (21.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-66 and C1-1. (Yield: 36.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.19 (s, 1H), 8.15 (s, 1H), 7.80-7.60 (m, 3H), 7.60-7.50 (m, 2H), 7.25 (s, 1H), 7.13 (d, 1H), 7.01 (t, 1H), 3.95 (s, 3H), 3.80 (d, 1H), 3.49 (d, 1H), 3.10-2.80 (m, 3H), 2.69 (s, 3H), 2.20-2.10 (m, 1H), 1.75-1.65 (m, 1H), 1.65-1.50 (m, 2H) MS m/z= 514.0 (M+H)+

[1836] Example 292: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-chloro-4-fluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1837] The titled compound (9.5 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-67 and C1-1. (Yield: 47.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.11 (s, 1H), 7.78 (d, 1H), 7.67 (q, 1H), 7.64-7.50 (m, 2H), 7.45 (t, 1H), 7.24 (s, 1H), 7.14 (d, 1H), 7.01 (t, 1H), 3.96 (s, 3H), 3.80 (d, 1H), 3.51 (d, 1H), 3.40-3.30 (m, 1H), 3.05-2.90 (m, 2H), 2.25-2.10 (m, 1H), 1.85-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 523.9 (M+H)+

[1838] Example 293: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1839] The titled compound (18.7 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-68 and C1-1. (Yield: 55.6%) ¹H NMR (CD₃OD, 400MHz) δ 8.81 (d, 1H), 8.16 (s, 1H), 8.00-7.90 (m, 2H), 7.70 (q, 1H), 7.63 (brs, 1H), 7.57 (t, 1H), 7.32 (s, 1H), 7.16 (d, 1H), 7.03 (t, 1H), 3.98 (s, 3H), 3.83 (d, 1H), 3.48 (d, 1H), 3.40-3.25 (m, 1H), 3.04 (t, 1H), 2.95 (t, 1H), 2.25-2.10 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 557.2 (M+H)+

- [1840] Example 294: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3,4-difluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1841] The titled compound (18.9 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-69 and C1-1. (Yield: 56.4%) ¹H NMR (CD₃OD, 400MHz) δ 8.83 (d, 1H), 8.11 (s, 1H), 7.71 (q, 1H), 7.65-7.55 (m, 2H), 7.49 (q, 1H), 7.45-7.40 (m, 1H), 7.32 (s, 1H), 7.17 (d, 1H), 7.04 (t, 1H), 3.98 (s, 3H), 3.86 (d, 1H), 3.55 (d, 1H), 3.45-3.35 (m, 1H), 3.06 (t, 1H), 2.99 (t, 1H), 2.25-2.10 (m, 1H), 1.85-1.75 (m, 1H), 1.75-1.55 (m, 2H) MS m/z= 507.9 (M+H)+
- [1842] Example 295: (3R,4R)-4-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol
- [1843] The titled compound (13.4 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-9 and C1-1. (Yield: 13.0%) ¹H NMR (CD₃OD, 400MHz) δ 8.61 (d, 1H), 8.13 (s, 1H), 8.10 (s, 1H), 7.97 (s, 1H), 7.54 (s, 1H), 7.50-7.35 (m, 3H), 7.40-7.10 (m, 1H), 6.84 (t, 1H), 3.85 (s, 3H), 3.46 (d, 1H), 3.40-3.30 (m, 1H), 3.27 (d, 1H), 2.62 (t, 1H), 2.55-2.45 (m, 2H), 1.85-1.75 (m, 1H), 1.50-1.35 (m, 1H) MS m/z= 527.2 (M+H)+
- [1844] Example 296: (S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-(dimethylamino)-4-fluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1845] The titled compound (31.6 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-70 and C1-1. (Yield: 76.3%) ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.17 (s, 1H), 7.95-7.85 (m, 1H), 7.70-7.55 (m, 3H), 7.53 (q, 1H), 7.28 (s, 1H), 7.14 (d, 1H), 7.01 (t, 1H), 3.96 (s, 3H), 3.82 (d, 1H), 3.49 (d, 1H), 3.45-3.35 (m, 1H), 3.33 (s, 6H), 3.10-2.90 (m, 2H), 2.25-2.10 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 2H) MS m/z= 532.3 (M+H)+
- [1846] Example 297: N-(4-((3R,4S)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1847] The titled compound (33.1 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-10 and C1-1. (Yield: 58.5%) ¹H NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.45 (s, 1H), 8.15 (s, 1H), 8.01 (s, 1H), 7.77-7.47 (m, 1H), 7.69 (q, 1H), 7.56 (brs, 1H), 7.31 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 3.97 (s, 3H), 3.65-3.50 (m, 2H), 3.50-3.40 (m, 1H), 3.35-3.30 (m, 1H), 3.20-3.15 (m, 1H), 2.40-2.30 (m, 1H), 1.95-1.85 (m, 2H), 1.04 (d, 3H) MS m/z= 525.2 (M+H)+
- [1848] Example 298: N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

- [1849] The titled compound (33.3 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-71 and C1-1. (Yield: 93.1%)
1H NMR (CD₃OD, 400MHz) δ 8.79 (d, 1H), 8.16 (s, 1H), 8.14 (s, 1H), 7.85 (s, 1H), 7.67 (q, 1H), 7.54 (brs, 1H), 7.26 (s, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 5.18-5.14 (m, 1H), 4.25-4.15 (m, 1H), 4.15-4.00 (m, 2H), 3.98 (s, 3H), 3.98-3.89 (m, 2H), 3.62 (d, 1H), 3.50-3.40 (m, 1H), 3.04 (t, 1H), 2.97 (t, 1H), 2.60-2.50 (m, 1H), 2.50-2.35 (m, 1H), 2.25-2.15 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.60 (m, 1H) MS m/z= 532.0 (M+H)+
- [1850] Example 299: N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1851] The titled compound (18.2 mg) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-72 and C1-1. (Yield: 61.2%)
1H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.16 (s, 1H), 8.14 (s, 1H), 7.85 (s, 1H), 7.67 (q, 1H), 7.53 (brs, 1H), 7.25 (s, 1H), 7.14 (d, 1H), 7.01 (t, 1H), 5.18-5.14 (m, 1H), 4.25-4.15 (m, 1H), 4.15-4.00 (m, 2H), 3.98 (s, 3H), 3.98-3.85 (m, 2H), 3.60 (d, 1H), 3.50-3.40 (m, 1H), 3.05-2.90 (m, 2H), 2.65-2.50 (m, 1H), 2.50-2.35 (m, 1H), 2.25-2.15 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.60 (m, 1H) MS m/z= 531.2 (M+H)+
- [1852] Example 300: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1853] Step 1: tert-butyl N-[(3S)-1-[2-[[5-cyano-6-(2-fluoro-6-methoxy-phenyl)-2-pyridyl]amino]-5-(1-tetrahydropyran-4-ylpyrazol-4-yl)-4-pyridyl]-3-piperidyl]carbamate
- [1854] The titled compound (42.7 mg) was prepared in accordance with the same procedures as in Step 1 of Example 52, using Intermediates A3-1 and C8-1. (Yield: 59.0%)
1H NMR (CDCl₃, 400MHz) δ 8.12 (s, 1H), 7.90-7.85 (m, 1H), 7.85-7.75 (m, 2H), 7.77 (s, 1H), 7.50-7.35 (m, 2H), 6.95-6.80 (m, 2H), 4.55-4.45 (m, 1H), 4.45-4.35 (m, 1H), 4.18-4.11 (m, 2H), 3.88 (s, 3H), 3.80-3.68 (m, 1H), 3.63-3.56 (m, 2H), 3.45-3.28 (m, 1H), 3.10-2.95 (m, 1H), 2.60-2.50 (m, 1H), 2.50-2.40 (m, 1H), 2.19-1.94 (m, 4H), 1.98-1.88 (m, 1H), 1.70-1.60 (m, 1H), 1.60-1.53 (m, 1H), 1.48 (s, 9H)
- [1855] Step 2: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1856] tert-Butyl N-[(3S)-1-[2-[[5-cyano-6-(2-fluoro-6-methoxy-phenyl)-2-pyridyl]amino]-5-(1-tetrahydropyran-4-ylpyrazol-4-yl)-4-pyridyl]-3-piperidyl]carbamate (42.7 mg, 0.06 mmol) was dissolved in dichloromethane (3.0 ml) and then 4.0M hydrogen chloride solution dissolved in 1,4-dioxane (0.48 mL, 1.92 mmol) was added dropwise

thereto. Then, the mixed solution was stirred at room temperature for 17 hours. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (32.0 mg). (Yield: 78.1%) ¹H NMR (CD₃OD, 400MHz) δ 8.47 (s, 1H), 8.28 (d, 1H), 8.11 (s, 1H), 8.03 (s, 1H), 7.81 (s, 1H), 7.59 (q, 1H), 7.35 (d, 1H), 7.10 (s, 1H), 7.06 (d, 1H), 6.97 (t, 1H), 4.55-4.50 (m, 1H), 4.15-4.05 (m, 2H), 3.90 (s, 3H), 3.84 (d, 1H), 3.65-3.55 (m, 2H), 3.55-3.45 (m, 1H), 3.45-3.35 (m, 1H), 2.98 (t, 1H), 2.89 (t, 1H), 2.25-2.15 (m, 1H), 2.15-2.05 (m, 4H), 1.90-1.80 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 1H) MS m/z= 569.0 (M+H)+

[1857] Example 301: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride

[1858] Step 1: tert-butyl N-[(3S)-1-[2-[[5-cyano-6-(2-fluoro-6-methoxy-phenyl)-2-pyridyl]amino]-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate

[1859] The titled compound (55.1 mg) was prepared in accordance with the same procedures as in Step 1 of Example 52, using Intermediates A3-2 and C8-1. (Yield: 74.4%) ¹H NMR (CDCl₃, 400MHz) δ 8.11 (s, 1H), 7.95 (s, 1H), 7.90 (d, 1H), 7.77 (s, 1H), 7.53 (s, 1H), 7.47-7.11 (m, 3H), 6.91-6.81 (m, 2H), 4.50-4.40 (m, 1H), 3.89 (s, 3H), 3.80-3.68 (m, 1H), 3.45-3.24 (m, 1H), 3.08-2.96 (m, 1H), 2.58-2.40 (m, 2H), 1.98-1.88 (m, 1H), 1.70-1.60 (m, 1H), 1.60-1.50 (m, 1H), 1.48 (s, 9H)

[1860] Step 2: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride

[1861] tert-Butyl N-[(3S)-1-[2-[[5-cyano-6-(2-fluoro-6-methoxy-phenyl)-2-pyridyl]amino]-5-[1-(difluoromethyl)pyrazol-4-yl]-4-pyridyl]-3-piperidyl]carbamate (55.1 mg, 0.09 mmol) was dissolved in dichloromethane (3.0 ml) and then 4.0M hydrogen chloride solution dissolved in 1,4-dioxane (0.65 mL, 2.60 mmol) was added dropwise thereto. Then, the mixed solution was stirred at room temperature for 17 hours. Water was added to the reaction mixture and then the aqueous layer was extracted with ethyl acetate. The extracted organic layer was dried over anhydrous magnesium sulfate and then filtered. The filtrate was concentrated and then purified by silica gel column chromatography to prepare the titled compound (32.0 mg). (Yield: 60.9%) ¹H NMR (CD₃OD, 400MHz) δ 8.48 (s, 1H), 8.29 (d, 1H), 8.11 (s, 1H), 8.05 (s, 1H), 7.75-7.45 (m, 1H), 7.59 (q, 1H), 7.38 (d, 1H), 7.10 (s, 1H), 7.09 (d, 1H), 6.97 (t, 1H), 3.91 (s, 3H), 3.81 (d, 1H), 3.52 (d, 1H), 3.50-3.40 (m, 1H), 3.05-2.90 (m, 2H), 2.25-2.15 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.55 (m, 1H) MS m/z= 534.9 (M+H)+

[1862] Example 302: N-(4-((3S,4S)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

- [1863] The titled compound (16.3 mg, Yield: 91.6%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-45 and C1-1. ¹H NMR (CD₃OD, 400MHz) δ 8.78 (d, 1H), 8.42 (s, 1H), 7.99 (s, 1H), 7.94 (s, 1H), 7.66-7.59 (m, 1H), 7.62 (t, 1H), 7.34 (d, 1H), 7.11 (d, 1H), 7.01-6.95 (m, 2H), 5.00-4.95 (m, 1H), 4.40-4.34 (m, 1H), 3.94 (s, 3H), 3.78-3.72 (m, 1H), 3.50-3.46 (m, 1H), 3.46-3.35 (m, 2H), 2.39-2.35 (m, 1H), 2.06-1.96 (m, 1H) MS m/z= 529.9 (M+H)+
- [1864] Example 303: N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1865] The titled compound (12.8 mg, Yield: 78.5%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-48 and C1-1. ¹H NMR (CDCl₃, 400MHz) δ 8.64-8.56 (m, 1H), 8.18 (s, 1H), 8.12 (s, 2H), 7.95 (s, 1H), 7.72 (s, 1H), 7.43-7.40 (m, 0.2H), 7.40-7.33 (m, 1H), 7.28-7.22 (m, 1.6H), 7.13-7.10 (m, 0.2H), 6.89-6.79 (m, 2H), 4.75-4.64 (m, 0.5H), 4.64-4.51 (m, 0.5H), 3.88 (s, 3H), 3.46-3.31 (m, 1H), 3.25-3.12 (m, 1H), 3.02-2.91 (m, 1H), 2.81-2.66 (m, 1H), 2.48-2.27 (m, 2H), 1.56-1.40 (m, 2H) MS m/z= 529.2 (M+H)+
- [1866] Example 304: N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1867] The titled compound (7.9 mg, Yield: 82.3%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-49 and C1-1. ¹H NMR (CDCl₃, 400MHz) δ 8.64-8.55 (m, 1H), 8.26 (s, 1H), 8.20 (s, 1H), 8.08 (s, 1H), 8.00 (s, 1H), 7.58 (s, 1H), 7.44-7.39 (m, 0.2H), 7.39-7.32 (m, 2H), 7.28-7.23 (m, 0.6H), 7.13-7.08 (m, 0.2H), 6.88-6.76 (m, 2H), 4.94-4.73 (m, 1H), 3.88 (s, 3H), 3.53-3.40 (m, 1H), 3.35-3.22 (m, 2H), 2.81-2.63 (m, 1H), 2.39-2.27 (m, 2H), 1.50-1.35 (m, 1H) MS m/z= 529.2 (M+H)+
- [1868] Example 305: N-(4-((3S,5R)-3-amino-5-(trifluoromethyl)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1869] The titled compound (4.7 mg, Yield: 52.3%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-50 and C1-1. ¹H NMR (CDCl₃, 400MHz) δ 8.65-8.58 (m, 1H), 8.19 (s, 1H), 8.10 (s, 1H), 7.96 (s, 1H), 7.77 (s, 1H), 7.69 (s, 1H), 7.45-7.41 (m, 0.2H), 7.41-7.33 (m, 1H), 7.27-7.25 (m, 0.6H), 7.25-7.21 (m, 1H), 7.13-7.07 (m, 0.2H), 6.89-6.79 (m, 2H), 3.88 (s, 3H), 3.49-3.40 (m, 1H), 3.38-3.29 (m, 1H), 2.99-2.87 (m, 1H), 2.54-2.45 (m, 1H), 2.45-2.33 (m, 1H), 2.28-2.17 (m, 2H), 1.40-1.31 (m, 1H), 1.24-1.11 (m, 2H) MS m/z= 579.2 (M+H)+

- [1870] Example 306: (3S,5S)-5-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol hydrochloride
- [1871] The titled compound (12.2 mg, Yield: 63.2%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-51 and C1-1. ¹H NMR (CDCl₃, 400MHz) δ 8.63-8.56 (m, 1H), 8.21 (s, 1H), 8.15 (s, 1H), 8.02 (s, 1H), 7.97 (s, 1H), 7.57 (s, 1H), 7.43-7.32 (m, 2.2H), 7.27-7.23 (m, 0.6H), 7.13-7.09 (m, 0.2H), 6.88-6.79 (m, 2H), 3.93-3.86 (m, 1H), 3.86 (s, 3H), 3.22-3.12 (m, 1H), 3.11-3.01 (m, 1H), 3.01-2.89 (m, 2H), 2.81-2.72 (m, 1H), 1.99-1.90 (m, 1H), 1.60-1.50 (m, 1H) MS m/z= 527.9 (M+H)+
- [1872] Example 307: N-(4-((3R,4S)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1873] The titled compound (12.9 mg, Yield: 37.6%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-46 and C1-1. ¹H NMR (CD₃OD, 400MHz) δ 8.74 (d, 1H), 8.46 (s, 1H), 8.23 (s, 1H), 8.05 (s, 1H), 7.68-7.55 (m, 2H), 7.59 (t, 1H), 7.28 (s, 1H), 7.13 (d, 1H), 7.00 (t, 1H), 5.11-4.98 (m, 1H), 4.03-3.95 (m, 1H), 3.94 (s, 3H), 3.73-3.62 (m, 2H), 3.40-3.26 (m, 1H), 3.12 (t, 1H), 2.13-2.03 (m, 1H), 1.97-1.94 (m, 1H) MS m/z= 529.2 (M+H)+
- [1874] Example 308: N-(4-((3S,4R)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1875] The titled compound (20.2 mg, Yield: 54.8%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-47 and C1-1. ¹H NMR (CD₃OD, 400MHz) δ 8.76 (d, 1H), 8.47 (s, 1H), 8.23 (s, 1H), 8.05 (s, 1H), 7.69-7.50 (m, 2H), 7.60 (t, 1H), 7.31 (s, 1H), 7.14 (d, 1H), 7.01 (t, 1H), 5.12-4.99 (m, 1H), 4.06-4.00 (m, 1H), 3.95 (s, 3H), 3.77-3.63 (m, 2H), 3.44-3.39 (m, 1H), 3.15 (t, 1H), 2.12-2.03 (m, 1H), 1.98-1.95 (m, 1H) MS m/z= 529.2 (M+H)+
- [1876] Example 309: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1877] The titled compound (31.3 mg, Yield: 84.0%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-1 and C8-2. ¹H NMR (CD₃OD, 400MHz) δ 8.29 (d, 1H), 8.12 (s, 1H), 8.05 (s, 1H), 7.81 (s, 1H), 7.35 (d, 1H), 7.02 (s, 1H), 6.96 (d, 1H), 6.83 (t, 1H), 4.56-4.50 (m, 1H), 4.12-4.08 (m, 2H), 3.90 (s, 3H), 3.87-3.83 (m, 1H), 3.65-3.54 (m, 3H), 3.47-3.41 (m, 1H), 2.99 (t, 1H), 2.90

- (t, 1H), 2.26-2.18 (m, 1H), 2.18-2.00 (m, 4H), 1.85-1.81 (m, 1H), 1.81-1.72 (m, 1H), 1.72-1.60 (m, 1H) MS m/z= 587.2 (M+H)+
- [1878] Example 310: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1879] The titled compound (31.6 mg, Yield: 77.3%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C8-2. ¹H NMR (CD₃OD, 400MHz) δ 8.51 (s, 1H), 8.28 (d, 1H), 8.12 (s, 1H), 8.07 (s, 1H), 7.62 (t, 1H), 7.40 (d, 1H), 7.11 (s, 1H), 6.95 (d, 1H), 6.83 (t, 1H), 3.90 (s, 3H), 3.87-3.78 (m, 1H), 3.55-3.45 (m, 1H), 3.45-3.40 (m, 1H), 3.00 (t, 1H), 2.92 (t, 1H), 2.23-2.19 (m, 1H), 1.86-1.80 (m, 1H), 1.80-1.70 (m, 1H), 1.70-1.59 (m, 1H) MS m/z= 553.2 (M+H)+
- [1880] Example 311: (S)-N-(4-(3-aminopiperidin-1-yl)-5-((4-methyltetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1881] The titled compound (3.1 mg, Yield: 29.9%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-6 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.64-8.51 (m, 1H), 8.26 (s, 1H), 7.65 (s, 1H), 7.47 (s, 1H), 7.19-7.10 (m, 1H), 6.63-6.51 (m, 2H), 3.96-3.83 (m, 4H), 3.83-3.72 (m, 4H), 3.05-2.92 (m, 1H), 2.92-2.80 (m, 1H), 2.65-2.53 (m, 1H), 2.06-1.93 (m, 1H), 1.85-1.73 (m, 3H), 1.73-1.61 (m, 3H), 1.43 (s, 3H) MS m/z= 535.3 (M+H)+
- [1882] Example 312: (S)-4-((4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)ethynyl)tetrahydro-2H-pyran-4-ol
- [1883] The titled compound (4.4 mg, Yield: 54.8%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-7 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.64-8.54 (m, 1H), 8.24 (s, 1H), 7.69 (s, 1H), 7.46 (s, 1H), 7.26 (s, 1H), 6.62-6.51 (m, 2H), 5.50 (s, 1H), 4.99 (s, 1H), 4.39-4.29 (m, 1H), 4.03-3.89 (m, 2H), 3.84 (s, 3H), 3.80-3.68 (m, 2H), 3.32-3.23 (m, 2H), 3.00-2.85 (m, 2H), 1.96-1.87 (m, 2H), 1.81-1.75 (m, 1H), 1.75-1.67 (m, 1H), 1.67-1.59 (m, 1H) MS m/z= 537.2 (M+H)+
- [1884] Example 313: (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methylbut-3-yn-2-ol
- [1885] The titled compound (3.5 mg, Yield: 34.8%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-8 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.63-8.54 (m, 1H), 8.18 (s, 1H), 7.53 (s, 1H), 7.47 (s, 1H), 7.20 (s, 1H), 6.63-6.49 (m, 2H), 4.31-4.20 (m, 1H), 3.86 (s, 3H), 3.31-3.17 (m, 2H), 3.06-2.86 (m, 2H), 2.03-1.92 (m, 1H), 1.87-1.76 (m, 2H), 1.75-1.65 (m, 2H), 1.62 (d, 6H) MS m/z= 495.2 (M+H)+

- [1886] Example 314: (S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)but-3-yn-1-ol
- [1887] The titled compound (8.0 mg, Yield: 42.9%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A7-9 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.62-8.53 (m, 1H), 8.26 (s, 1H), 7.81 (s, 1H), 7.48 (s, 1H), 7.23 (s, 1H), 6.61-6.46 (m, 2H), 3.90-3.83 (m, 1H), 3.83-3.76 (m, 5H), 3.53-3.39 (m, 1H), 3.25-3.16 (m, 1H), 3.16-3.08 (m, 1H), 3.08-2.97 (m, 1H), 2.81-2.66 (m, 2H), 1.99-1.79 (m, 2H), 1.76-1.63 (m, 1H), 1.56-1.46 (m, 1H) MS m/z= 481.2 (M+H)+
- [1888] Example 315: 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-(methylsulfonyl)pyridin-2-yl)pyridin-2-amine hydrochloride
- [1889] The titled compound (16.8 mg, Yield: 59.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-2 and C1-5. ¹H NMR (CD₃OD, 400MHz) δ 8.47-8.45 (m, 2H), 8.12 (s, 1H), 8.06 (s, 1H), 7.59 (t, 1H), 7.59-7.49 (m, 2H), 7.31 (s, 1H), 7.00 (d, 1H), 6.89 (t, 1H), 3.81 (s, 3H), 3.70-3.60 (m, 1H), 3.40-3.33 (m, 2H), 2.99 (s, 3H), 2.90-3.75 (m, 2H), 2.22-2.15 (m, 1H), 1.85-1.65 (m, 2H), 1.65-1.50 (m, 1H) MS m/z= 588.2 (M+H)+
- [1890] Example 316: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile
- [1891] The titled compound (10.4 mg, Yield: 15.2%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A2-6 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.15 (s, 1H), 8.10 (s, 1H), 8.05-7.90 (m, 2H), 7.75 (s, 1H), 7.60-7.45 (m, 2H), 7.02 (d, 1H), 6.92 (t, 1H), 5.01 (q, 2H), 3.88 (s, 3H), 3.75-3.65 (m, 1H), 3.30-3.20 (m, 1H), 3.05-2.95 (m, 1H), 2.65-2.55 (m, 1H), 2.44 (t, 1H), 1.97-1.85 (m, 1H), 1.75-1.62 (m, 1H), 1.62-1.50 (m, 1H), 1.40-1.30 (m, 1H) MS m/z= 568.2 (M+H)+
- [1892] Example 317: 2-(2,4-difluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile
- [1893] The titled compound (1.2 mg, Yield: 1.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A2-6 and C8-2. ¹H NMR (CD₃OD, 400MHz) δ 8.15 (s, 1H), 8.10 (s, 1H), 8.00-7.90 (m, 2H), 7.72 (s, 1H), 7.55 (d, 1H), 6.88 (d, 1H), 6.77 (t, 1H), 5.01 (q, 2H), 3.88 (s, 3H), 3.80-3.70 (m, 1H), 3.30-3.20 (m, 1H), 3.05-2.95 (m, 1H), 2.60-2.55 (m, 1H), 2.50-2.40 (m, 1H), 2.00-1.95 (m, 1H), 1.75-1.65 (m, 1H), 1.65-1.50 (m, 1H), 1.40-1.30 (m, 1H) MS m/z= 586.2 (M+H)+
- [1894] Example 318: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride

- [1895] The titled compound (14.2 mg, Yield: 64.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.18 (s, 1H), 8.14 (s, 1H), 8.09 (d, 1H), 7.96 (s, 1H), 7.65-7.45 (m, 3H), 7.05 (d, 1H), 6.94 (t, 1H), 5.05 (q, 2H), 3.89 (s, 3H), 3.60-3.50 (m, 1H), 3.40-3.20 (m, 2H), 2.80-2.55 (m, 2H), 2.20-2.10 (m, 1H), 1.85-1.65 (m, 2H), 1.60-1.45 (m, 1H) MS m/z= 567.3 (M+H)+
- [1896] Example 319: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1897] The titled compound (19.5 mg, Yield: 89.6%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-23 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.25-8.15 (m, 1H), 8.09 (s, 1H), 8.00 (s, 1H), 7.81 (s, 1H), 7.56 (q, 1H), 7.50-7.40 (m, 1H), 7.40-7.20 (m, 1H), 7.06 (d, 1H), 6.95 (t, 1H), 4.18 (s, 2H), 3.89 (s, 3H), 3.75-3.60 (m, 1H), 3.45-3.35 (m, 2H), 2.90-2.80 (m, 1H), 2.80-2.65 (m, 1H), 2.20-2.10 (m, 1H), 1.90-1.70 (m, 2H), 1.60-1.45 (m, 1H), 1.25 (s, 3H), 1.23 (s, 3H) MS m/z= 557.3 (M+H)+
- [1898] Example 320: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1899] The titled compound (16.7 mg, Yield: 59.5%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-4 and C8-2. ¹H NMR (CD₃OD, 400MHz) δ 8.30-8.25 (m, 1H), 8.11 (s, 1H), 8.00 (s, 1H), 7.93 (s, 1H), 7.50-7.35 (m, 1H), 7.30-7.10 (m, 1H), 6.94 (d, 1H), 6.82 (t, 1H), 5.06 (q, 2H), 3.90 (s, 3H), 3.80-3.65 (m, 1H), 3.50-3.35 (m, 2H), 2.95-2.75 (m, 2H), 2.25-2.15 (m, 1H), 1.90-1.65 (m, 2H), 1.65-1.50 (m, 1H) MS m/z= 585.2 (M+H)+
- [1900] Example 321: 6-((4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1901] The titled compound (2.5 mg, Yield: 40.0%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-7 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.41 (s, 1H), 8.16 (s, 1H), 8.10 (s, 1H), 7.99 (d, 1H), 7.82 (s, 1H), 7.60-7.50 (m, 2H), 7.55 (t, 1H), 7.03 (d, 1H), 6.93 (t, 1H), 4.45-4.20 (m, 1H), 3.88 (s, 3H), 3.30-3.20 (m, 1H), 3.10-2.95 (m, 1H), 2.75 (q, 1H), 2.48 (t, 1H), 2.10-1.95 (m, 1H), 1.90-1.70 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 553.2 (M+H)+
- [1902] Example 322: 6-((4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride

- [1903] The titled compound (2.5 mg, Yield: 40.0%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-6 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.51 (s, 1H), 8.31 (d, 1H), 8.16 (s, 1H), 8.09 (s, 1H), 7.65-7.50 (m, 1H), 7.61 (t, 1H), 7.33 (d, 1H), 7.05 (d, 1H), 6.98 (t, 1H), 5.25-5.10 (m, 1H), 3.88 (s, 3H), 3.75-3.60 (m, 1H), 3.55-3.45 (m, 1H), 3.35- 3.15 (m, 2H), 2.30-2.10 (m, 2H), 2.10-2.00 (m, 1H) MS m/z= 553.2 (M+H)+
- [1904] Example 323: 6-((4-((S)-3-aminopiperidin-1-yl)-6'-morpholino-[3,3'-bipyridin]-6-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1905] The titled compound (21.6 mg, Yield: 68.8%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-19 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.31 (d, 1H), 8.23 (s, 1H), 8.10-7.95 (m, 2H), 7.59 (q, 1H), 7.40-7.30 (m, 2H), 7.09 (d, 1H), 7.04 (s, 1H), 6.97 (t, 1H), 3.91 (s, 3H), 3.90-3.80 (m, 4H), 3.80-3.60 (m, 4H), 3.60-3.50 (m, 1H), 3.40- 3.20 (m, 2H), 3.05-2.90 (m, 2H), 2.25-2.15 (m, 1H), 1.90-1.80 (m, 1H), 1.80-1.65 (m, 1H), 1.65-1.50 (m, 1H) MS m/z= 581.3 (M+H)+
- [1906] Example 324: N-(4-(((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(2-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine
- [1907] The titled compound (6.4 mg, Yield: 57.8%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-54 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.63-8.53 (m, 1H), 8.15 (s, 1H), 7.99 (s, 1H), 7.85-7.76 (m, 2H), 7.59 (s, 1H), 7.39 (s, 1H), 6.65-6.51 (m, 2H), 4.87-4.75 (m, 2H), 4.75-4.66 (m, 1H), 4.63-4.54 (m, 1H), 3.89 (s, 3H), 3.44-3.28 (m, 1H), 3.25-3.14 (m, 1H), 3.06-2.93 (m, 1H), 2.88-2.70 (m, 1H), 2.51-2.38 (m, 1H), 2.38-2.23 (m, 1H), 1.63-1.49 (m, 1H) MS m/z= 579.2 (M+H)+
- [1908] Example 325: 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile
- [1909] The titled compound (17.2 mg, Yield: 23.9%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A2-5 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.10-8.05 (m, 2H), 7.97 (d, 1H), 7.83 (s, 1H), 7.75-7.70 (m, 1H), 7.55-7.45 (m, 2H), 7.02 (d, 1H), 6.91 (t, 1H), 4.30-4.20 (m, 1H), 3.88 (s, 3H), 3.75-3.65 (m, 1H), 3.30-3.20 (m, 1H), 3.10-2.95 (m, 3H), 2.65- 2.50 (m, 1H), 2.45-2.35 (m, 1H), 2.31 (s, 3H), 2.30-2.20 (m, 2H), 2.20-2.00 (m, 5H), 2.00-1.90 (m, 1H), 1.75-1.65 (m, 1H), 1.60-1.50 (m, 1H), 1.40-1.30 (m, 1H) MS m/z= 584.2 (M+H)+
- [1910] Example 326: 6-((4-((3R,4R)-4-amino-3-hydroxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile

- [1911] The titled compound (20.1 mg, Yield: 43.1%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-52 and C8-1. ¹H NMR (CDCl₃, 400MHz) δ 8.15-8.10 (m, 2H), 7.97 (s, 1H), 7.91 (d, 1H), 7.73 (s, 1H), 7.55-7.35 (m, 3H), 7.26 (t, 1H), 6.95-6.85 (m, 2H), 3.89 (s, 3H), 3.50-3.40 (m, 1H), 3.40-3.25 (m, 1H), 3.25-3.15 (m, 1H), 2.65- 2.50 (m, 2H), 2.50-2.40 (m, 1H), 1.85-1.75 (m, 1H), 1.45-1.35 (m, 1H) MS m/z= 551.2 (M+H)+
- [1912] Example 327: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-ethyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1913] The titled compound (16.3 mg, Yield: 62.2%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-73 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.23 (d, 1H), 8.10-8.00 (m, 2H), 7.80 (s, 1H), 7.58 (q, 1H), 7.39 (d, 1H), 7.20-7.10 (m, 1H), 7.08 (d, 1H), 6.96 (t, 1H), 4.28 (q, 2H), 3.90 (s, 3H), 3.80-3.70 (m, 1H), 3.55-3.45 (m, 1H), 3.45-3.35 (m, 1H), 2.95- 2.80 (m, 2H), 2.25-2.15 (m, 1H), 1.90-1.65 (m, 2H), 1.65-1.58 (m, 1H), 1.56 (t, 3H) MS m/z= 513.2 (M+H)+
- [1914] Example 328: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1915] The titled compound (33.6 mg, Yield: 99.9%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-74 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.23 (d, 1H), 8.10-8.00 (m, 2H), 7.80 (s, 1H), 7.58 (q, 1H), 7.40 (d, 1H), 7.20-7.10 (m, 1H), 7.08 (d, 1H), 6.96 (t, 1H), 4.66-4.59 (m, 1H), 3.90 (s, 3H), 3.80-3.70 (m, 1H), 3.55-3.35 (m, 2H), 2.95- 2.80 (m, 2H), 2.25-2.15 (m, 1H), 1.85-1.70 (m, 2H), 1.70-1.60 (m, 1H), 1.56 (d, 6H) MS m/z= 527.2 (M+H)+
- [1916] Example 329: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1917] The titled compound (24.1 mg, Yield: 93.0%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-75 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.21 (d, 1H), 8.10-8.00 (m, 2H), 7.79 (s, 1H), 7.58 (q, 1H), 7.41 (d, 1H), 7.30-7.15 (m, 1H), 7.08 (d, 1H), 6.96 (t, 1H), 3.90 (s, 3H), 3.80-3.70 (m, 2H), 3.50-3.40 (m, 1H), 3.40-3.30 (m, 1H), 2.95- 2.75 (m, 2H), 2.25-2.15 (m, 1H), 1.90-1.70 (m, 2H), 1.70-1.50 (m, 1H), 1.20-1.10 (m, 2H), 1.10-1.05 (m, 2H) MS m/z= 525.2 (M+H)+
- [1918] Example 330: 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1919] The titled compound (23.4 mg, Yield: 90.5%) was prepared in accordance with the same procedures as in Example 52, using Intermediates A3-76 and C8-1. ¹H NMR

(CD₃OD, 400MHz) δ 8.14 (d, 1H), 8.15-8.05 (m, 2H), 7.83 (s, 1H), 7.56 (q, 1H), 7.49 (d, 1H), 7.40-7.30 (m, 1H), 7.06 (d, 1H), 6.95 (t, 1H), 4.15-4.05 (m, 2H), 3.89 (s, 3H), 3.75-3.60 (m, 1H), 3.45-3.35 (m, 2H), 2.90-2.70 (m, 2H), 2.25-2.10 (m, 1H), 1.90-1.70 (m, 2H), 1.65-1.50 (m, 1H), 1.45-1.30 (m, 1H), 0.70-0.62 (m, 2H), 0.50-0.42 (m, 2H)
MS m/z= 539.2 (M+H)+

[1920] Example 331: 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile

[1921] The titled compound (28.2 mg, Yield: 47.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-53 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.43 (s, 1H), 8.15 (s, 1H), 8.11 (s, 1H), 7.98 (d, 1H), 7.84 (s, 1H), 7.54 (t, 1H), 7.54-7.49 (m, 2H), 7.02 (d, 1H), 6.93 (t, 1H), 4.45-4.25 (m, 1H), 3.88 (s, 3H), 3.80-3.65 (m, 1H), 3.30-3.20 (m, 1H), 3.20-3.10 (m, 1H), 2.80-2.65 (m, 1H), 2.60-2.50 (m, 1H), 2.10-1.95 (m, 1H), 1.80-1.65 (m, 1H) MS m/z= 554.2 (M+H)+

[1922] Example 332: N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1923] The titled compound (17.4 mg, Yield: 52.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-55 and C1-1. ¹H NMR (CD₃OD, 400MHz) δ 8.95-8.69 (m, 1H), 8.32-8.11 (m, 2H), 7.99 (s, 1H), 7.82 (s, 1H), 7.66 (s, 1H), 7.51-7.34 (m, 1H), 7.28-7.12 (m, 1H), 7.12-6.92 (m, 1H), 5.26-4.98 (m, 2H), 4.20-4.06 (m, 1H), 4.06 (s, 3H), 3.80-3.60 (m, 1H), 3.49-3.39 (m, 1H), 3.30-3.15 (m, 1H), 2.65-2.42 (m, 1H), 2.15-1.87 (m, 1H) MS m/z= 561.2 (M+H)+

[1924] Example 333: N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride

[1925] The titled compound (28.2 mg, Yield: 47.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-55 and C1-7. ¹H NMR (CD₃OD, 400MHz) δ 8.90 (s, 1H), 8.31-8.15 (m, 2H), 8.00 (s, 1H), 7.67 (s, 1H), 7.50 (s, 1H), 7.12-6.99 (m, 1H), 6.99-6.83 (m, 1H), 5.23-4.98 (m, 2H), 4.17-4.04 (m, 1H), 4.04 (s, 3H), 3.77-3.62 (m, 1H), 3.48-3.38 (m, 1H), 3.29-3.19 (m, 1H), 2.65-2.48 (m, 1H), 2.14-1.88 (m, 1H) MS m/z= 579.2 (M+H)+

[1926] Example 334: 4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine hydrochloride

[1927] The titled compound (12.1 mg, Yield: 62.7%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-7 and C3-1. ¹H NMR (CD₃OD, 400MHz) δ 8.55-8.45 (m, 2H), 8.19 (s, 1H), 8.11 (s, 1H), 7.59 (t, 1H),

7.59-7.40 (m, 3H), 7.00-6.85 (m, 2H), 4.75-4.55 (m, 1H), 3.79 (s, 3H), 3.75-3.60 (m, 1H), 3.55-3.40 (m, 1H), 3.00-2.80 (m, 2H), 2.30-2.15 (m, 1H), 2.10-1.95 (m, 2H) MS m/z = 573.2 (M+H)+

[1928] Example 335: N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine

[1929] The titled compound (6.0 mg, Yield: 53.1%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-56 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.62-8.55 (m, 1H), 8.17 (s, 1H), 7.77 (s, 1H), 7.71 (s, 1H), 7.65 (s, 1H), 7.49 (s, 1H), 7.40-7.32 (m, 1H), 6.63-6.53 (m, 2H), 4.77-4.65 (m, 0.5H), 4.65-4.53 (m, 1.5H), 3.88 (s, 3H), 3.46-3.36 (m, 1H), 3.29-3.20 (m, 1H), 3.04-2.94 (m, 1H), 2.81-2.71 (m, 1H), 2.43-2.28 (m, 2H), 1.63 (d, 6H) MS m/z = 539.2 (M+H)+

[1930] Example 336: N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine

[1931] The titled compound (12.6 mg, Yield: 51.2%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-57 and C1-7. ¹H NMR (CDCl₃, 400MHz) δ 8.60-8.53 (m, 1H), 8.24 (s, 1H), 7.93 (s, 1H), 7.84 (s, 1H), 7.78 (s, 1H), 7.51 (s, 1H), 7.35 (s, 1H), 6.62-6.51 (m, 2H), 4.96-4.89 (m, 0.5H), 4.84-4.76 (m, 0.5H), 4.62-4.50 (m, 1H), 3.88 (s, 3H), 3.58-3.46 (m, 1H), 3.40-3.23 (m, 2H), 2.79-2.69 (m, 0.5H), 2.69-2.60 (m, 0.5H), 2.37-2.25 (m, 2H), 1.63 (d, 6H), MS m/z = 539.2 (M+H)+

[1932] Example 337: 6-((4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-nicotinonitrile hydrochloride

[1933] The titled compound (20.4 mg, Yield: 54.0%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-3 and C8-1. ¹H NMR (CD₃OD, 400MHz) δ 8.47 (s, 1H), 8.28 (d, 1H), 8.12 (s, 1H), 8.06 (s, 1H), 7.60 (t, 1H), 7.60-7.55 (m, 1H), 7.38 (d, 1H), 7.20-7.10 (m, 1H), 7.09 (d, 1H), 6.97 (t, 1H), 3.90 (s, 3H), 3.90-3.80 (m, 1H), 3.60-3.50 (m, 1H), 3.10-3.00 (m, 1H), 3.00-2.80 (m, 2H), 1.90-1.70 (m, 2H), 1.65-1.40 (m, 1H), 1.17 (d, 3H) MS m/z = 549.2 (M+H)+

[1934] Example 338: 6-((4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile hydrochloride

[1935] The titled compound (19.6 mg, Yield: 57.4%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-3 and C8-2. ¹H NMR (CD₃OD, 400MHz) δ 8.48 (s, 1H), 8.26 (d, 1H), 8.13 (s, 1H), 8.06 (s, 1H), 7.60 (t, 1H), 7.40 (d, 1H), 7.20-7.10 (m, 1H), 6.95 (d, 1H), 6.82 (t, 1H), 3.90 (s, 3H), 3.85-3.75

- (m, 1H), 3.60-3.50 (m, 1H), 3.10-3.00 (m, 1H), 3.00-2.80 (m, 2H), 1.90-1.70 (m, 2H), 1.65-1.40 (m, 1H), 1.17 (d, 3H) MS m/z= 567.2 (M+H)+
- [1936] Example 339: N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine hydrochloride
- [1937] The titled compound (11.2 mg, Yield: 38.0%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-58 and C1-7. ¹H NMR (CD₃OD, 400MHz) δ 8.75 (d, 1H), 8.20 (s, 1H), 8.15 (s, 1H), 7.86 (s, 1H), 7.65-7.45 (m, 1H), 7.20 (s, 1H), 6.99 (d, 1H), 6.86 (t, 1H), 4.90-4.70 (m, 1H), 4.70-4.60 (m, 1H), 4.00-3.85 (m, 4H), 3.75-3.65 (m, 1H), 3.65-3.50 (m, 1H), 3.15-2.95 (m, 2H), 2.30-2.20 (m, 1H), 2.00-1.85 (m, 1H), 1.58 (d, 6H) MS m/z= 539.2 (M+H)+
- [1938] Example 340: 6-((4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile hydrochloride
- [1939] The titled compound (10.0 mg, Yield: 51.6%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B3-58 and C8-2. ¹H NMR (CD₃OD, 400MHz) δ 8.25 (d, 1H), 8.15-8.05 (m, 2H), 7.82 (s, 1H), 7.45-7.35 (m, 1H), 7.25-7.10 (m, 1H), 6.95 (d, 1H), 6.83 (t, 1H), 4.85-4.65 (m, 1H), 4.65-4.60 (m, 1H), 3.97-3.82 (m, 4H), 3.70-3.60 (m, 1H), 3.60-3.45 (m, 1H), 3.10-2.90 (m, 2H), 2.30-2.20 (m, 1H), 2.00-1.80 (m, 1H), 1.57 (d, 6H) MS m/z= 563.2 (M+H)+
- [1940] Example 341: 4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine hydrochloride
- [1941] The titled compound (23.6 mg, Yield: 67.9%) was prepared in accordance with the same procedures as in Example 52, using Intermediates B1-7 and C1-2. ¹H NMR (CD₃OD, 400MHz) δ 8.51 (s, 1H), 8.15-8.05 (m, 2H), 7.87 (t, 1H), 7.61 (t, 1H), 7.61-7.52 (m, 1H), 7.34 (d, 1H), 7.06 (d, 1H), 7.05-6.95 (m, 1H), 6.93 (t, 1H), 4.85-4.65 (m, 1H), 3.88 (s, 3H), 3.88-3.80 (m, 1H), 3.65-3.50 (m, 2H), 3.10-2.90 (m, 2H), 2.30-2.20 (m, 1H), 2.00-1.80 (m, 1H) MS m/z= 546.2 (M+H)+
- [1942] Test Example: Evaluation of inhibitory activity against human recombinant HPK1
- [1943] The inhibitory activity against human recombinant HPK1 was evaluated using the Time-Resolved Fluorescence Resonance Energy Transfer (TR-FRET) technology of Perkin-Elmer. The test compound was prepared as a 20 mM stock solution with dimethyl sulfoxide (DMSO), serially diluted in a buffer solution, and used at final compound concentrations of 0.32 to 1000 nM. The evaluation of inhibitory activity was carried out at room temperature, using recombinant human HPK1 (BPS Bioscience). Briefly, recombinant human HPK1, serially diluted each test compound, ULight-p70S6K peptide substrate (PerkinElmer), and ATP at each concentration (Km

and final concentration) were added to a kinase buffer solution (50 mM HEPES pH 7.4, 10 mM MgCl₂, 1 mM EGTA, 3 mM MnCl₂, 2 mM DTT, and 0.01% Tween-20). The resulting mixture was added to each well of a 384-well plate (Optiplate™ 384, white, PerkinElmer). The enzyme reaction was carried out at room temperature for 1 hour. After the reaction was suspended by adding 4 µL of a stop solution (10 mM EDTA) thereto, the mixture was stirred for 1 minute and then a detection solution containing Europium-labeled anti-phosphopeptide antibody (final concentration: 2 nM, PerkinElmer) was added thereto. The signals of TR-FRET at excitation wavelength (320 nm) and emission wavelength (665 nm) were detected using a microplate reader (Envision Multilabel Reader, Perkin-Elmer). Inhibition by the test compound was measured as % inhibition in the signals, compared to the control group treated with DMSO only. The IC₅₀ value of each compound was calculated using the GraphPad Prism program (GraphPad Software, Inc., San Diego, CA, USA). The IC₅₀ values of test compounds for inhibitory activity against HPK1 were classified as follows:

- [1944] A: IC₅₀ ≤ 10 nM
- [1945] B: 10 nM < IC₅₀ ≤ 50 nM
- [1946] C: 50 nM < IC₅₀ ≤ 100 nM
- [1947] D: IC₅₀ > 100 nM
- [1948] The results are shown in Tables 1 to 3 below.
- [1949] Table 1

[1950]

Example	IC ₅₀	Example	IC ₅₀	Example	IC ₅₀	Example	IC ₅₀
1	B	33	B	65	A	97	A
2	B	34	B	66	A	98	A
3	C	35	A	67	A	99	B
4	C	36	A	68	B	100	A
5	B	37	B	69	A	101	A
6	B	38	A	70	A	102	A
7	A	39	A	71	A	103	A
8	B	40	A	72	A	104	A
9	B	41	A	73	A	105	A
10	B	42	B	74	A	106	A
11	A	43	A	75	A	107	A
12	A	44	B	76	A	108	A
13	A	45	D	77	A	109	A
14	A	46	A	78	A	110	A
15	A	47	A	79	A	111	A
16	A	48	A	80	A	112	A
17	A	49	D	81	D	113	B
18	A	50	D	82	A	114	A
19	A	51	C	83	A	115	A
20	A	52	A	84	B	116	A
21	B	53	A	85	A	117	A
22	A	54	B	86	C	118	A
23	B	55	B	87	A	119	A
24	A	56	B	88	A	120	A
25	B	57	C	89	A	121	A
26	C	58	D	90	A	122	A
27	B	59	A	91	A	123	B
28	B	60	A	92	A	124	A
29	A	61	B	93	B	125	A
30	B	62	C	94	A	126	B
31	A	63	C	95	A	127	B
32	B	64	A	96	A	128	D

[1951] Table 2

[1952]

Example	IC ₅₀	Example	IC ₅₀	Example	IC ₅₀	Example	IC ₅₀
129	A	161	A	193	A	225	A
130	A	162	A	194	A	226	A
131	C	163	A	195	A	227	A
132	A	164	A	196	A	228	B
133	A	165	A	197	A	229	A
134	A	166	A	198	A	230	A
135	A	167	A	199	A	231	A
136	A	168	A	200	A	232	A
137	A	169	A	201	A	233	A
138	C	170	A	202	A	234	A
139	A	171	A	203	A	235	A
140	A	172	A	204	A	236	A
141	D	173	A	205	A	237	A
142	A	174	A	206	A	238	A
143	A	175	A	207	A	239	A
144	A	176	A	208	A	240	A
145	A	177	A	209	A	241	A
146	A	178	A	210	A	242	A
147	A	179	A	211	A	243	A
148	A	180	A	212	A	244	A
149	A	181	A	213	A	245	A
150	A	182	A	214	A	246	A
151	A	183	A	215	A	247	A
152	A	184	A	216	A	248	A
153	A	185	A	217	A	249	A
154	A	186	A	218	A	250	A
155	A	187	A	219	A	251	A
156	A	188	B	220	A	252	A
157	A	189	A	221	A	253	A
158	A	190	A	222	A	254	A
159	A	191	A	223	A	255	A
160	A	192	B	224	A	256	A

[1953] Table 3

[1954]

Example	IC ₅₀	Example	IC ₅₀	Example	IC ₅₀
257	A	289	A	321	A
258	A	290	A	322	A
259	A	291	A	323	A
260	A	292	A	324	A
261	A	293	A	325	A
262	A	294	A	326	A
263	A	295	A	327	A
264	A	296	A	328	A
265	A	297	A	329	A
266	A	298	A	330	A
267	A	299	A	331	A
268	A	300	A	332	A
269	A	301	A	333	A
270	A	302	A	334	A
271	A	303	A	335	A
272	A	304	A	336	A
273	A	305	A	337	A
274	A	306	A	338	A
275	A	307	A	339	A
276	A	308	A	340	A
277	A	309	A	341	A
278	A	310	A		
279	A	311	A		
280	A	312	A		
281	A	313	A		
282	A	314	A		
283	A	315	A		
284	A	316	A		
285	A	317	A		
286	A	318	A		
287	A	319	A		
288	A	320	A		

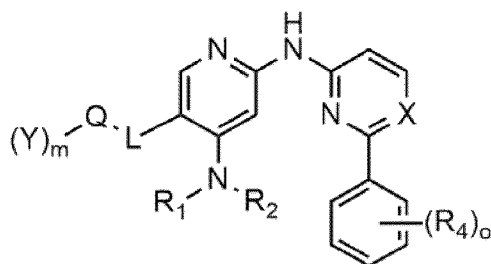
[1955] From the results in Tables 1 to 3, it can be seen that the compounds according to the present invention have excellent inhibitory activity against HPK1.

Claims

[Claim 1]

A compound of Formula 1a or pharmaceutically acceptable salt thereof:

<Formula 1a>



wherein,

R₁ and R₂ form a heterocycloalkyl together with the nitrogen atom to which they are bonded, wherein the heterocycloalkyl is optionally substituted with one or two groups selected from the group consisting of halogen, amino, hydroxy, C₁~C₆ alkyl, C₁~C₆ alkoxy, C₁~C₆ alkyl substituted with halogen, C₁~C₆ alkyl substituted with hydroxy, C₃~C₆ cycloalkyl, C₃~C₆ cycloalkyl substituted with hydroxy, mono- or di-C₁~C₆ alkylamino, aminocarbonyl, C₁~C₆ alkylcarbonylamino, and mono- or di-C₁~C₆ alkylamino-C₁~C₆ alkyl,

X is -C(R₃)= or -N=,

R₃ is hydrogen, halogen, cyano, nitro, amino, C₁~C₃ alkyl, C₁~C₃ alkyl substituted with halogen, hydroxycarbonyl, C₁~C₃ alkoxy, C₁~C₃ alkoxy, aminocarbonyl, mono- or di-C₁~C₃ alkylaminocarbonyl, or C₁~C₃ alkylsulfonyl,

R₄ is, independently each other, halogen, amino, hydroxy, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkoxy, C₃~C₆ cycloalkyl, aldehyde, mono- or di-C₁~C₃ alkylamino, mono- or di-C₁~C₃ alkylamino-C₁~C₆ alkyl, C₁~C₆ alkoxy, C₁~C₆ alkoxy, aminocarbonyl, mono- or di-C₁~C₆ alkylaminocarbonyl, C₁~C₆ alkylaminocarbonyl substituted with halogen, C₃~C₆ cycloalkylaminocarbonyl, C₃~C₆ cycloalkylaminocarbonyl substituted with halogen, C₃~C₆ cycloalkylaminocarbonyl substituted with hydroxy, heterocycloalkyl-C₁~C₃ alkyl optionally substituted with hydroxy, or heterocycloalkylcarbonyl optionally substituted with halogen, o is 0, 1, 2, or 3,

L is a bond, -C(O)-, -(CH₂)_n-, -C(O)NH-, or -C≡C-,

n is 1, 2, or 3,

Q is a bond; C₃~C₆ cycloalkyl; a 3- to 12-membered heterocycloalkyl having one to three heteroatoms selected from N, O and S; a 5- to 12-membered heteroaryl having one to three heteroatoms selected from N, O and S; or a 5- to 12-membered aryl,

m is 1, 2, or 3,

Y is, independently each other, hydrogen, hydroxy, halogen, amino, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkyl substituted with halogen, C₁~C₆ alkyl substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy, C₁~C₆ alkoxy substituted with C₁~C₃ alkoxy, C₁~C₆ alkoxy substituted with halogen, C₁~C₆ alkoxy substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy-C₁~C₆ alkyl, C₃~C₆ cycloalkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl substituted with halogen, C₁~C₃ alkylcarbonyl, C₃~C₆ cycloalkyl-aminocarbonyl substituted with hydroxy, mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkylamino substituted with mono- or di-C₁~C₃ alkylamino, aminocarbonyl-C₁~C₆ alkyl, C₁~C₃ alkoxycarbonyl-C₁~C₆ alkyl, C₁~C₃ alkylcarbonylamino, mono- or di-C₁~C₆ alkylaminocarbonyl, mono- or di-C₁~C₆ alkylaminocarbonylamino, or mono- or di-C₁~C₆ alkylaminocarbonyl-C₁~C₆ alkyl, or a heterocycloalkyl-containing group selected from the group consisting of azetidiny; azetidiny-C₁~C₆ alkyl; tetrahydropyrany; tetrahydrofurany; pyrrolidiny; pyrrolidiny-C₁~C₃ alkyl; piperidiny; piperidiny-C₁~C₃ alkyl; piperidinylcarbonyl; piperidinyloxy; piperazinyl; piperazinyl-C₁~C₃ alkyl; piperazinylcarbonyl; oxetany; morpholinyl; morpholinyl-C₁~C₃ alkyl; and morpholinylcarbonyl, wherein the heterocycloalkyl of the heterocycloalkyl-containing group is optionally substituted with one to four groups selected from the group consisting of halogen, hydroxy, amino, oxo, C₁~C₃ alkyl, C₁~C₃ alkyl substituted with hydroxy, and mono- or di-C₁~C₃ alkylamino.

[Claim 2]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein R₁ and R₂ form piperidine, azetidine,

pyrrolidine, piperazine, or 2,8-diazaspiro[4.5]decane together with the nitrogen atom to which they are bonded.

[Claim 3]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein X is -N=.

[Claim 4]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein X is -C(R₃)= and R₃ is H, -F, -Cl, -CH₃, -CN, -NO₂, -NH₂, -C(O)OH, -C(O)OCH₃, -C(O)NH₂, -C(O)N(CH₃)₂, or -SO₂CH₃.

[Claim 5]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein R₄ is, independently each other, halogen, amino, hydroxy, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkoxy, aldehyde, mono- or di-C₁~C₃ alkylamino-C₁~C₆ alkyl, C₁~C₆ alkoxycarbonyl, mono- or di-C₁~C₆ alkylaminocarbonyl, azetidiny-C₁~C₃ alkyl substituted with hydroxy, azetidiny-carbonyl optionally substituted with one or two halogens, or pyrrolidinyl-carbonyl optionally substituted with one or two halogens.

[Claim 6]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein Q is a bond, C₃~C₆ cycloalkyl, tetrahydropyranyl, pyrrolidinyl, phenyl, pyridinyl, pyrazolyl, thiazolyl, imidazo[1,2-a]pyridinyl, [1,2,4]triazolo[4,3-a]pyridin-6-yl, 2H-benzo[b][1,4]oxazin-3(4H)-onyl, 3,4-dihydroquinolin-2(1H)-onyl, 3,4-dihydro-2H-benzo[b][1,4]oxazinyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 2H-pyrido[3,2-b]-1,4-oxazin-3(4H)-onyl, 1,4-dihydro-2H-benzo[d][1,3]oxazin-2-onyl, or 3,4-dihydro-1,8-naphthyridin-2(1H)-onyl.

[Claim 7]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein Y is, independently each other, hydrogen, hydroxy, halogen, amino, C₁~C₆ alkyl, C₁~C₆ alkyl substituted with hydroxy, C₁~C₆ alkyl substituted with halogen, C₁~C₆ alkyl substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy, C₁~C₆ alkoxy substituted with C₁~C₃ alkoxy, C₁~C₆ alkoxy substituted with halogen, C₁~C₆ alkoxy substituted with mono- or di-C₁~C₃ alkylamino, C₁~C₆ alkoxy-C₁~C₆ alkyl, C₃~C₆ cycloalkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl, C₃~C₆ cycloalkyl-C₁~C₃ alkyl substituted with halogen, C₁~C₃ alkylcarbonyl, C₃~C₆ cycloalkyl-aminocarbonyl substituted

with hydroxy, mono- or di- $C_1\sim C_3$ alkylamino, $C_1\sim C_6$ alkylamino substituted with mono- or di- $C_1\sim C_3$ alkylamino, aminocarbonyl- $C_1\sim C_6$ alkyl, $C_1\sim C_3$ alkoxycarbonyl- $C_1\sim C_6$ alkyl, $C_1\sim C_3$ alkylcarbonylamino, mono- or di- $C_1\sim C_6$ alkylaminocarbonyl, mono- or di- $C_1\sim C_6$ alkylaminocarbonylamino, or mono- or di- $C_1\sim C_6$ alkylaminocarbonyl- $C_1\sim C_6$ alkyl.

[Claim 8]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 1, wherein one of Y is a heterocycloalkyl-containing group selected from the group consisting of azetidinyll; azetidinylmethyl; tetrahydropyranyl; tetrahydrofuranyl; pyrrolidinyl; pyrrolidinylmethyl; pyrrolidinylethyl; piperidinyl; piperidinylmethyl; piperidinylcarbonyl; piperidinylloxy; piperazinyl; piperazinylmethyl; piperazinylcarbonyl; oxetanyl; morpholinyl; morpholinylmethyl; morpholinylethyl; and morpholinylcarbonyl, and the remaining Y is hydrogen.

[Claim 9]

The compound or pharmaceutically acceptable salt thereof as claimed in claim 8, wherein the heterocycloalkyl of the heterocycloalkyl-containing group is substituted with one to four groups selected from the group consisting of halogen, hydroxy, amino, oxo, $C_1\sim C_3$ alkyl, $C_1\sim C_3$ alkyl substituted with hydroxy, and mono- or di- $C_1\sim C_3$ alkylamino.

[Claim 10]

A compound or pharmaceutically acceptable salt thereof, which is selected from the group consisting of:

(S)-cyclopropyl(4-(3-hydroxypiperidin-1-yl)-6-((2-(5-methylpyridin-3-yl)pyrimidin-4-yl)amino)pyridin-3-yl)methanone;
 (S)-(6-((2-(5-aminopyridin-3-yl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)(cyclopropyl)methanone;
 (S)-cyclopropyl(4-(3-hydroxypiperidin-1-yl)-6-((2-(5-methoxy pyridin-3-yl)pyrimidin-4-yl)amino)pyridin-3-yl)methanone;
 (S)-cyclopropyl(6-((2-(3-hydroxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)methanone;
 (S)-cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxypiperidin-1-yl)pyridin-3-yl)methanone;
 cyclopropyl(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-(3-hydroxyazetidin-1-yl)pyridin-3-yl)methanone;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)azetidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(tetrahydro-2H-pyran-4-yl)phenyl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(4-(4-methylpiperazin-1-yl)phenyl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-morpholino-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(4-(hydroxymethyl)thiophen-2-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2,6-difluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(3,6-difluoro-2-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2,3-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2-ethoxy-6-fluorophenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-([1,2,4]triazolo[1,5-a]pyridin-7-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(pyrazolo[1,5-a]pyridin-3-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(quinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(8-fluoroquinolin-7-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((4-methylpiperazin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(morpholinomethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((4-hydroxypiperidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide;

(S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-methylpiperazin-1-yl)methanone;

(S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(morpholino)methanone;

(S)-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-(3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(((S)-3-fluoropyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(3S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-((3-hydroxypyrrolidin-1-yl)methyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

N-(4-(3-(dimethylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-3-methylpyrrolidin-3-yl)methanol;

N-(4-(4-((dimethylamino)methyl)-4-fluoropiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(4-(2,2-difluoroethyl)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)methanol;

(3S)-1-(6'-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

1-((6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)methyl)piperidin-3-ol;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide;

(R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-carboxamide;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(6'-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4'-((S)-3-hydroxypiperidin-1-yl)-[3,3'-bipyridin]-6-yl)(4-hydroxypiperidin-1-yl)methanone;

(S)-1-(6'-((4-aminopiperidin-1-yl)methyl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(S)-1-(6'-ethoxy-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(S)-1-(6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-6'-(trifluoromethyl)-[3,3'-bipyridin]-4-yl)piperidin-3-ol;

(3S)-1-(2-((6-(2-fluoro-6-methoxyphenyl)-5-methylpyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;

methyl 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinate;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(imidazo[1,2-a]pyridin-6-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(5-([1,2,4]triazolo[4,3-a]pyridin-6-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;

2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-yl)amino)nicotinonitrile;

N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)cyclopropan-1-ol;

1-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)ethan-1-ol;

2-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-yl)-2-methylpropan-1-ol;

2-(2-fluoro-6-methoxyphenyl)-N-(4-(4-methylpiperazin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;

(S)-1-(2-((2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-amine;

methyl 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinate;

(S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(3S)-1-(2-((5-chloro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine;

(R)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-3-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)pyridin-2-ol;

(S)-1-(6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-methylpiperidin-4-yl)oxy)-[2,3'-bipyridin]-4'-yl)piperidin-3-ol;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-6-amine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(1-methylpiperidin-4-yl)-[3,3'-bipyridin]-6-amine;

2-(2-fluoro-6-methoxyphenyl)-N-(5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(3-(2,2,2-trifluoroethyl)piperidin-1-yl)pyridin-2-yl)pyrimidin-4-amine;

2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(fluoromethyl)piperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;

N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-yl)acetamide;

2-(2-fluoro-6-methoxyphenyl)-N-(5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-4-(4-(trifluoromethyl)piperidin-1-yl)pyridin-2-yl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-(2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-(2,8-diazaspiro[4.5]decan-2-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(3R,4R)-4-fluoro-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3R,4R)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)-4-(hydroxymethyl)piperidin-3-ol;

(R)-N-(4-(3-aminopyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(2-(1-methylpiperidin-4-yl)thiazol-5-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-yl)-6'-(tetrahydro-2H-pyran-4-yl)-[3,3'-bipyridin]-6-amine;

4-((S)-3-aminopiperidin-1-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine;

(S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol;

(S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol;

(S)-(4-(4-((4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(4-((dimethylamino)methyl)-2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;

2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-N,N-dimethylnicotinamide;

4-((S)-3-aminopiperidin-1-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(7-fluoroquinoxalin-6-yl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-methoxypropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;

(S)-4-(3-aminopiperidin-1-yl)-N⁶-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-N^{6'},N^{6'}-dimethyl-[3,3'-bipyridin]-6,6'-diamine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(pyrrolidin-1-yl)-[3,3'-bipyridin]-6-amine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperidin-1-yl)-[3,3'-bipyridin]-6-amine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine;

(S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(methylamino)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(methylamino)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-2-(2-fluoro-6-methoxyphenyl)-N-(4-(3-(methylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;

(S)-N-(4-(3-(ethylamino)pyrrolidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(R)-N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide;

(S)-3-(6-((4-(3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyridin-2-yl)oxazolidin-2-one;

(S)-N-(1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)pyrrolidin-3-yl)acetamide;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-N,N-dimethylnicotinamide;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-N,N-dimethylacetamide;

(S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)ethan-1-ol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
 2-(2-fluoro-6-methoxyphenyl)-N-(4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)pyrimidin-4-amine;
 N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-4-(2-methyl-2,8-diazaspiro[4.5]decan-8-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine;
 (S)-3-(6-((4-(3-aminopiperidin-1-yl)-6'-morpholino-[3,3'-bipyridin]-6-yl)amino)pyridin-2-yl)oxazolidin-2-one;
 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinic acid;
 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)amino)nicotinamide;
 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-N,N-dimethylnicotinamide;
 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;
 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2-methoxyethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinamide;
 (3S)-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;
 4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
 N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
 4-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-morpholino-[3,3'-bipyridin]-6-amine;
 (3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;
 N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;
 4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-amine;
 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-amine;
 4-((S)-3-aminopiperidin-1-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-amine;
 (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
 (S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
 (S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

6-((5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinamide;

(S)-1-(2-((2-(2-fluoro-4-(hydroxymethyl)-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-3-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)propanamide;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(azetidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;

N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-5-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridazin-3-amine;

(S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(4-methylpiperazin-1-yl)methanone;

(3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

N²-(4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2-fluoro-6-methoxyphenyl)pyridin-2,5-diamine;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

methyl (S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxybenzoate;

(S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N-methylbenzamide;

(S)-4-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxy-N,N-dimethylbenzamide;

(S)-1-(2-((2-(4-((3-hydroxyazetidin-1-yl)methyl)thiophen-2-yl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-3-fluoro-4-(4-((4-(3-hydroxypiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-5-methoxybenzaldehyde;

(S)-1-(2-((2-(2-fluoro-6-methoxy-4-((methylamino)methyl)phenyl)pyrimidin-4-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide;

6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,3S)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-(3-hydroxycyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-N-((1R,2R)-2-hydroxycyclobutyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

N-(3,3-difluorocyclobutyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

N-((1R,3R)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

N-((1R,3S)-3-aminocyclopentyl)-6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-N-((1R,3R)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((5-amino-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)amino)-N-((1R,3S)-3-hydroxycyclopentyl)-4-((S)-3-hydroxypiperidin-1-yl)nicotinamide;

6-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-4-((S)-3-hydroxypiperidin-1-yl)-N-((R)-1-methylpyrrolidin-3-yl)nicotinamide;

N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(3R,4R)-3-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-4-ol;

N-(4-((3S,5S)-3-amino-5-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

(3R,4R)-3-amino-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-4-ol;

(1S,4S)-4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)(methyl)amino)cyclohexan-1-ol;

N²-(4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;

N²-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2,5-diamine;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(trifluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(S)-1-(2-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(5-((1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)ethynyl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(5-((1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)-2-((6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((6-(2,4-difluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)amino)-5-((tetrahydro-2H-pyran-4-yl)ethynyl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(2,2-difluoroethyl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(3S)-1-(2-((5-amino-6-(2,4-difluoro-6-methoxyphenyl)pyridin-2-yl)amino)-5-(2-(tetrahydro-2H-pyran-4-yl)ethyl)pyridin-4-yl)piperidin-3-ol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-methoxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(2-methoxyethoxy)-[3,3'-bipyridin]-6-amine;

(S)-(3,3-difluoroazetidin-1-yl)(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)methanone;

(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((S)-3-fluoropyrrolidin-1-yl)methanone;

(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((S)-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone;

(S)-(4-(4-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)(3,3-difluoropyrrolidin-1-yl)methanone;

(S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropan-2-ol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(3-(dimethylamino)propyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(azetidin-3-ylmethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-pyrrolidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-pyrrolidin-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-4-(3-aminopiperidin-1-yl)-N⁶-(2-(dimethylamino)ethyl)-N⁶-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-[3,3'-bipyridin]-6,6'-diamine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperazin-1-yl)-[3,3'-bipyridin]-6-amine;

(S)-(2-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluorophenyl)methanol;

(S)-(2-(4-((4-(3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)ethynyl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluorophenyl)methanol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(1-methoxy-2-methylpropan-2-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-((3,3-difluorocyclobutyl)methyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2-(dimethylamino)ethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(fluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-4-(3-aminopiperidin-1-yl)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-6'-(piperidin-4-yl)-[3,3'-bipyridin]-6-amine;

(S)-4-(3-aminopiperidin-1-yl)-6'-(2-(dimethylamino)ethoxy)-N-(2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)-[3,3'-bipyridin]-6-amine;

(S)-1-(4'-(3-aminopiperidin-1-yl)-6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-[3,3'-bipyridin]-6-yl)-3-ethylurea;

(4-(4-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)pyrimidin-2-yl)-3-fluoro-5-methoxyphenyl)((R)-3-fluoropyrrolidin-1-yl)methanone;

N-(4-((2R,5S)-5-amino-2-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3R,4S)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-(4-(4-(3-aminopiperidin-1-yl)-6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(morpholino)methanone;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-6-(4-(3-aminopiperidin-1-yl)-6'-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one;

(S)-1-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)pyrrolidin-2-one;

(S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2H-benzo[b][1,4]oxazin-3(4H)-one;

(S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one;

(S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-8-methyl-3,4-dihydroquinolin-2(1H)-one;

(S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1-methyl-3,4-dihydroquinolin-2(1H)-one;

(S)-1-(2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-4-yl)piperidin-3-ol;

(S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(piperazin-1-yl)methanone;

(S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-((methylamino)methyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3R,4R)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

6-(4-((S)-3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one;

(S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-methylpiperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(fluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(R)-N-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-(3-(difluoromethyl)piperidin-1-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-4-methyl-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one;

(S)-7-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one;

(S)-6-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-3,4-dihydro-1,8-naphthyridin-2(1H)-one;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

methyl (S)-2-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-1H-pyrazol-1-yl)-2-methylpropanoate;

(S)-N-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)acetamide;

(S)-3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-N,N-dimethylbenzamide;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-(trifluoromethoxy)phenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-fluoro-3-methylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-isopropoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-methoxy-3,5-dimethylphenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-methyl-4-morpholinophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-(4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)(4-(2-hydroxyethyl)piperazin-1-yl)methanone;

4-(4-((S)-3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-N-((1R,4S)-4-hydroxycyclohexyl)benzamide;

(S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-fluoro-N,N-dimethylbenzamide;

(S)-1-(3-(4-(3-aminopiperidin-1-yl)-6-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)phenyl)ethan-1-one;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-chloro-4-fluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(4-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(3,4-difluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(3R,4R)-4-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-(3-(dimethylamino)-4-fluorophenyl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3R,4S)-4-amino-3-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((S)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((S)-3-aminopiperidin-1-yl)-5-(1-((R)-tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

N-(4-((3S,4S)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,5R)-3-amino-5-(trifluoromethyl)piperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

(3S,5S)-5-amino-1-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-2-((2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-4-yl)piperidin-3-ol;

N-(4-((3R,4S)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,4R)-4-amino-3-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;

(S)-N-(4-(3-aminopiperidin-1-yl)-5-((4-methyltetrahydro-2H-pyran-4-yl)ethynyl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

(S)-4-((4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)ethynyl)tetrahydro-2H-pyran-4-ol;

(S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)-2-methylbut-3-yn-2-ol;

(S)-4-(4-(3-aminopiperidin-1-yl)-6-((2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-yl)amino)pyridin-3-yl)but-3-yn-1-ol;

4-((S)-3-aminopiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-(methylsulfonyl)pyridin-2-yl)pyridin-2-amine;

2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;

2-(2,4-difluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;

6-((4-((S)-3-aminopiperidin-1-yl)-6'-morpholino-[3,3'-bipyridin]-6-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(2-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
 2-(2-fluoro-6-methoxyphenyl)-6-((4-((S)-3-hydroxypiperidin-1-yl)-5-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)nicotinonitrile;
 6-((4-((3R,4R)-4-amino-3-hydroxypiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-ethyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 6-((4-((S)-3-aminopiperidin-1-yl)-5-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 6-((5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-4-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)nicotinonitrile;
 N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2-fluoro-6-methoxyphenyl)pyrimidin-4-amine;
 N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;
 4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(6-(2-fluoro-6-methoxyphenyl)-5-nitropyridin-2-yl)pyridin-2-amine;
 N-(4-((3S,5R)-3-amino-5-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

N-(4-((3S,5S)-3-amino-5-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

6-((4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2-fluoro-6-methoxyphenyl)-nicotinonitrile;

6-((4-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile;

N-(4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-(2,4-difluoro-6-methoxyphenyl)pyrimidin-4-amine;

6-((4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-isopropyl-1H-pyrazol-4-yl)pyridin-2-yl)amino)-2-(2,4-difluoro-6-methoxyphenyl)nicotinonitrile; and

4-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(5-fluoro-6-(2-fluoro-6-methoxyphenyl)pyridin-2-yl)pyridin-2-amine.

[Claim 11]

A pharmaceutical composition for inhibiting hematopoietic progenitor kinase 1 comprising the compound or pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 10 as an active ingredient.

[Claim 12]

The pharmaceutical composition as claimed in claim 11, for preventing or treating a blood cancer or a solid tumor.

[Claim 13]

The pharmaceutical composition as claimed in claim 11, for preventing or treating melanoma, blastoma, sarcoma, lymphoma, leukemia, bladder cancer, brain tumor, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, endometrioma, hepatic cancer, laryngeal cancer, lung cancer, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, thyroid cancer, ependymoma, glioblastoma, bullous cell tumor, neuroblastoma, osteosarcoma, rhabdomyosarcoma, or nephroblastoma.

[Claim 14]

A method for inhibiting hematopoietic progenitor kinase 1 in a mammal, which comprises administering a therapeutically effective amount of the compound or pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 10 to the mammal in need thereof.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2024/007677

A. CLASSIFICATION OF SUBJECT MATTER C07D 401/14(2006.01)i; A61K 31/506(2006.01)i; A61P 35/00(2006.01)i; C07D 403/14(2006.01)i According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C07D 401/14(2006.01); C07D 403/14(2006.01); C07D 473/16(2006.01) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Korean utility models and applications for utility models Japanese utility models and applications for utility models Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) eKOMPASS(KIPO Internal), STN (Registry, Marpat, Caplus), google & keyword: pyrimidine/pyridine derivatives, hematopoietic progenitor kinase 1, cancer		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2023-027518 A1 (YUHAN CORPORATION et al.) 02 March 2023 claims 1, 23	1-13
A	WO 2004-089286 A2 (IRM LLC et al.) 21 October 2004 claims 1-17	1-13
A	WO 2022-246025 A1 (DANA-FARBER CANCER INSTITUTE, INC. et al.) 24 November 2022 claim 1	1-13
A	WO 2010-129053 A2 (DANA FARBER CANCER INSTITUTE et al.) 11 November 2010 (2010-11-11) claim 1	1-13
A	WO 2021-159993 A1 (PHARMABLOCK SCIENCES (NANJING) , INC.) 19 August 2021 claim 1	1-13
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents: “A” document defining the general state of the art which is not considered to be of particular relevance “D” document cited by the applicant in the international application “E” earlier application or patent but published on or after the international filing date “L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) “O” document referring to an oral disclosure, use, exhibition or other means “P” document published prior to the international filing date but later than the priority date claimed “T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention “X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone “Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art “&” document member of the same patent family		
Date of the actual completion of the international search 11 September 2024		Date of mailing of the international search report 11 September 2024
Name and mailing address of the ISA/KR Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon 35208, Republic of Korea Facsimile No. +82-42-481-8578		Authorized officer HEO, Joo Hyung Telephone No. +82-42-481-5373

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2024/007677

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **14**
because they relate to subject matter not required to be searched by this Authority, namely:

Claim 14 pertains to methods for treatment of the human body by surgery or therapy, as well as diagnostic methods (PCT Article 17(2)(a)(i) and Rule 39.1(iv)).
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/KR2024/007677

Patent document cited in search report			Publication date (day/month/year)	Patent family member(s)		Publication date (day/month/year)	
WO	2023-027518	A1	02 March 2023	AR	126892	A1	29 November 2023
				CN	117980297	A	03 May 2024
				EP	4392415	A1	03 July 2024
				KR	10-2024-0052797	A	23 April 2024
				TW	202317106	A	01 May 2023
				US	11981658	B2	14 May 2024
				US	2023-0086884	A1	23 March 2023
WO	2004-089286	A2	21 October 2004	AU	2004-227943	A1	21 October 2004
				AU	2004-227943	B2	04 September 2008
				BR	PI0409173	A	11 April 2006
				CA	2521184	A1	21 October 2004
				CN	1798734	A	05 July 2006
				EP	1613595	A2	11 January 2006
				EP	1613595	A4	01 April 2009
				JP	2006-522143	A	28 September 2006
				MX	PA05010711	A	15 December 2005
				US	2005-0014753	A1	20 January 2005
				WO	2004-089286	A3	21 April 2005
WO	2022-246025	A1	24 November 2022	CA	3173777	A1	20 November 2022
				EP	4341254	A1	27 March 2024
WO	2010-129053	A2	11 November 2010	CA	2760794	A1	11 November 2010
				CA	2760794	C	25 July 2017
				CN	102482277	A	30 May 2012
				CN	102482277	B	19 September 2017
				EP	2440559	A2	18 April 2012
				EP	2440559	A4	21 November 2012
				EP	2440559	B1	10 January 2018
				ES	2659725	T3	19 March 2018
				IL	216140	B	29 March 2018
				JP	2012-526113	A	25 October 2012
				JP	5918693	B2	18 May 2016
				KR	10-1705158	B1	09 February 2017
				KR	10-2012-0047208	A	11 May 2012
				US	2012-0094999	A1	19 April 2012
				US	2019-0040065	A1	07 February 2019
				US	9908884	B2	06 March 2018
				WO	2010-129053	A3	24 March 2011
				WO	2010-129053	A8	15 December 2011
WO	2021-159993	A1	19 August 2021	CN	115151534	A	04 October 2022
				CN	115151534	B	06 February 2024