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(71) Applicants: **RAQUALIA PHARMA INC.** [JP/JP]; 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **NATIONAL UNIVERSITY CORPORATION NAGOYA UNIVERSITY** [JP/JP]; 1, Furo-cho, Chikusa-ku, Nagoya-shi, Aichi, 4648601 (JP).

(72) Inventors: **OHMI, Masashi**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi,

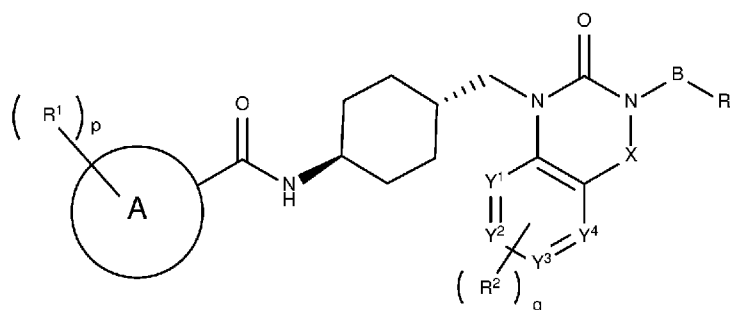
4500003 (JP). **MATSUSHITA, Takeshi**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **ANDO, Kazuo**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **YAMAGUCHI, Ryuichi**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **FUKUMOTO, Yutaka**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **MAGARA, Ryohei**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **YAMAGISHI, Tatsuya**; c/o RaQualia Pharma Inc., 1-21-19 Meieki Minami, Nakamura-ku, Nagoya-shi, Aichi, 4500003 (JP). **TAKEFUJI, Mikito**; c/o National University Corporation Nagoya University, 1, Furo-cho, Chikusa-ku, Nagoya-shi, Aichi, 4648601 (JP).

(74) Agent: **IWATANI, Ryo**; KEIHAN Dojima Bldg. 6F, 1-3-1, Dojima 2-chome, Kita-ku, Osaka-shi, Osaka, 5300003 (JP).

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(54) Title: FUSED CYCLIC UREA DERIVATIVES AS CRHR2 ANTAGONIST



(I)

(57) **Abstract:** The present invention relates to fused cyclic urea derivatives which have antagonistic activities against CRHR1 and/or CRHR2, and which are useful in the treatment or prevention of disorders and diseases in which CRHR1 and/or CRHR2 is involved. The invention also relates to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which CRHR1 and/or CRHR2 is involved.

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, 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).

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Description

Title of Invention: FUSED CYCLIC UREA DERIVATIVES AS CRHR2 ANTAGONIST

Technical Field

[0001] The present invention relates to fused cyclic urea derivatives which have antagonistic activities against both corticotropin releasing hormone receptor 1 (CRHR1) and corticotropin releasing hormone receptor 2 (CRHR2), and which are useful in the treatment or prevention of disorders and diseases in which CRHR1 and/or CRHR2 are involved. The invention also relates to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which CRHR1 and/or CRHR2 is involved.

Background Art

[0002] Corticotropin-releasing hormone receptors (CRHRs), also known as corticotropin-releasing factor receptors (CRFRs) are a G protein-coupled receptor family that binds corticotropin-releasing hormone (CRH) (NPL 1: Hauger RL, et al., Pharmacol. Rev. 55 (1): 21-6, 2003). There are two receptors in the family, designated as type 1 and 2, each encoded by a separate gene (CRHR1 and CRHR2 respectively). CRHRs are important mediators in the stress response. (NPL 2: Grammatopoulos DK, et al., Trends Endocrinol. Metab. 13 (10): 436-44, 2002). Cells in the anterior lobe of the pituitary gland known as corticotropes express the receptors and will secrete adrenocorticotrophic hormone (ACTH) when stimulated. This binding of corticotropin releasing -hormone (CRH) activates the hypothalamic-pituitary-adrenal (HPA) axis, one of the two parts of the fight-or-flight response to stress. (NPL 3: Aguilera G, et al., Neuroendocrinology. 43 (1): 79-88, 1986). CRHRs are also present in other brain areas such as the amygdala, locus coeruleus and hippocampus. Chronic activation of CRHRs by CRH induced by early life stress has been shown to underlie memory deficits and learning impairments and anxiety in adulthood.

[0003] Recently, Takefuji et al., reported that the GPCR corticotropin releasing hormone receptor 2 (CRHR2) is highly expressed in the heart and facilitates heart failure (NPL 4: Takefuji et al., J. Experimental Medicine, 214, 1877-1888, 2017). The results indicate that CRHR2 may be a promising therapeutic target for chronic heart failure.

[0004] The fused cyclic urea derivatives of the present invention are CRHR1 and CRHR2 dual antagonists and have a number of therapeutic applications. More particularly, the fused cyclic urea derivatives of the invention show an excellent CRHR2 antagonistic activities.

[0005]

Citation List

Non Patent Literature

- [0006] {NPL 1} Hauger RL, et al., Pharmacol. Rev. 55 (1): 21-6, 2003.
{NPL 2} Grammatopoulos DK, et al., Trends Endocrinol. Metab. 13 (10): 436-44, 2002 .
{NPL 3} Aguilera G, et al., Neuroendocrinology. 43 (1): 79-88, 1986.
{NPL 4} Takefuji et al., J. Experimental Medicine, 214, 1877-1888, 2017.

Patent Literature

- [0007] {PL 1} WO201 1/092293
{PL 2} WO20 11/095450

Summary of Invention

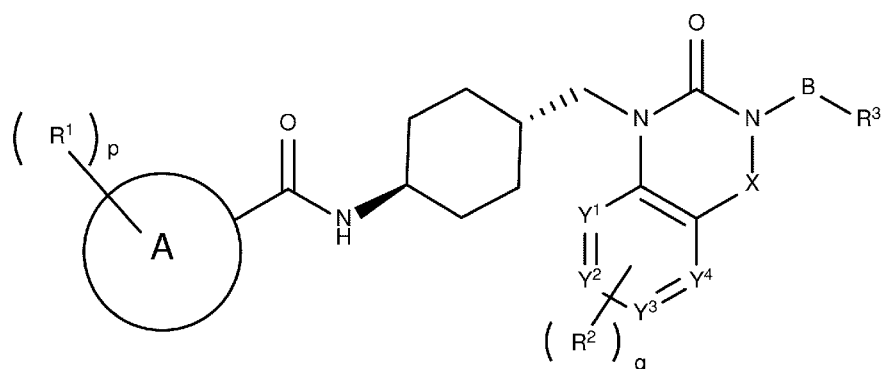
Technical Problem

- [0008] It is an objective of the invention to provide new CRHR1 and CRHR2 dual an-
tagonists that are good drug candidates. Preferred compounds should bind potently to
CRHR1 and CRHR2 whilst showing little affinity for other CRHRs. They possess
favorable pharmacokinetic properties such as absorption, distribution, metabolism, and
excretion. They are non-toxic and demonstrate few side-effects. Lurthermore, the ideal
drug candidate will exist in a physical form that is stable, non-hygroscopic and easily
formulated.

Solution to Problem

- [0009] With respect to other compounds disclosed in the art, the compounds of the present
invention may show less toxicity, favorable absorption and distribution, favorable
solubility, favorable plasma protein binding, less drug-drug interaction, favorable
metabolic stability, reduced inhibitory activity at HERG channel, and/or reduced QT
prolongation.
- [0010] This invention provides:
- [1] A compound of the following formula (I):

[Chem.1]



(I)

wherein:

A is aryl or heteroaryl; preferably A is phenyl or pyridyl;

R¹ is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) C₁₋₆ alkyl, (4) C₃₋₇ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) C₁₋₆ alkoxyC₁₋₆ alkyl, (7) -NHC₁₋₆ alkyl, (8) -N(C₁₋₆ alkyl)₂, and (9) -NHC₃₋₇ cycloalkyl, wherein the C₃₋₆ alkyl, the C₃₋₇ cycloalkyl, the -O-C₁₋₆ alkyl, the C₁₋₆ alkoxyC₁₋₆ alkyl, the -NHC₁₋₆ alkyl, the -N(C₁₋₆ alkyl)₂, or the -NHC₃₋₇ cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl; or two R¹ may form a 5 to 7 membered cycloalkyl ring; preferably R¹ is independently selected from the group consisting of: (1) hydrogen, (2) halogen, and (3) C₁₋₆ alkyl; wherein the C₁₋₆ alkyl is unsubstituted or substituted with one or more halogens;

p is 1, 2, or 3; preferably p is 2 or 3; more preferably p is 2;

R² is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C₁₋₆ alkyl, (5) -O-C₁₋₆ alkyl, and (6) -CN; preferably R² is independently selected from the group consisting of: (1) hydrogen, (2) halogen, (4) C₁₋₆ alkyl, and (6) -CN; more preferably R² is independently selected from the group consisting of: (1) hydrogen, (2) halogen, and (4) C₁₋₆ alkyl;

q is 1, 2, or 3; preferably q is 1;

Y¹, Y², Y³, and Y⁴ are independently selected from the group consisting of CH, CR², and N,

number of nitrogen atom is two at most at the same time; wherein the number of nitrogen atom is preferably one or zero;

X is a chemical bond or CH₂; preferably X is a chemical bond;

B is a chemical bond, -C₁₋₃ alkylene-, -C₁₋₃ alkylene-O-, or -CH₂-(C=O)-; preferably B is a chemical bond;

R³ is selected from the group consisting of:

(1) aryl, preferably phenyl, (2) 5 to 6-membered heteroaryl with 1-3 heteroatoms independently selected from O, N, and S, preferably 5 to 6-membered heteroaryl with 1-2 heteroatoms independently selected from O, N, and S, (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms independently selected from O, N, and S, (4) 5 to 6-membered heterocyclyl with 1-2 heteroatoms independently selected from O, N, and S; and (5) 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl; wherein the aryl, preferably phenyl, the 5 to 6-membered heteroaryl, the 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl, the 5 to 6-membered heterocyclyl, or the 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl is unsubstituted or substituted with one or more substituents independently selected from R⁴; preferably R³ is selected from the group consisting of: (1) phenyl, (2) 5 to 6-membered heteroaryl selected from pyrazole, pyridine, pyrazine, pyridazine, and pyrimidine, and (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms which is selected from the group consisting of indole, pyrrolo[2,3-b]pyridine, pyrrolo[2,3-c]pyridine, indazole, pyrazolo[3,4-b]pyridine, pyrazolo[4,3-b]pyridine, benzoxazole, and 2,3-dihydro-pyrrolo[2,3-b]pyridine, wherein the phenyl the 5 to 6-membered heteroaryl or the 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl is unsubstituted or substituted with one or more substituents independently selected from R⁴; more preferably R³ is phenyl, pyrazole, pyridine, pyrazine, pyridazine, or pyrimidine;

R⁴ is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C₁₋₆ alkyl, (5) -O-C₁₋₆ alkyl, (6) C₂₋₆ alkenyl, (7) C₃₋₇ cycloalkyl, (8) -O-C₃₋₇ cycloalkyl, (9) C₃₋₇ cycloalkylC₁₋₆ alkoxy, (10) - (C=O)-R⁵, (11) -(C=O)-NR⁵R⁶, (12) -NR⁵(C=O)R⁶, (13) -NR⁵R⁶, (14) aryl, preferably phenyl, (15) heterocyclyl which is 4 to 7 membered partially unsaturated or saturated heterocyclic ring with 1-2 heteroatoms independently selected from O, N, and S, (16) -O-heterocyclyl, (17) heterocyclylC₁₋₆ alkyl, (18) heterocyclylC₁₋₆ alkoxy, (19) -NR⁵-S(0)₂R⁶, (20) -S(0)₂-R⁵, (21) -CN, (22) nitro, (23) heteroaryl, (24) -O-heteroaryl, (25) -S-C₁₋₆ alkyl, (26) -O-C₁₋₆ alkyl-(C=O)-NR⁵R⁶, and (26) -(C=O)-NR⁵O-C₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the -O-C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the -O-C₃₋₇ cycloalkyl, or the -S-C₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, -NR⁵R⁶, -O-C₁₋₆ alkyl, and C₃₋₇ cycloalkyl, wherein the aryl, preferably phenyl, the heterocyclyl, the -O-heterocyclyl, the heterocyclylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkoxy, the heteroaryl, or the -O-heteroaryl, is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, C₁₋₆ alkyl, hydroxy C₁₋₆ alkyl, C₁₋₆ alkoxy, and -(C=O)-R⁵; preferably R⁴ is independently selected from the group consisting of:

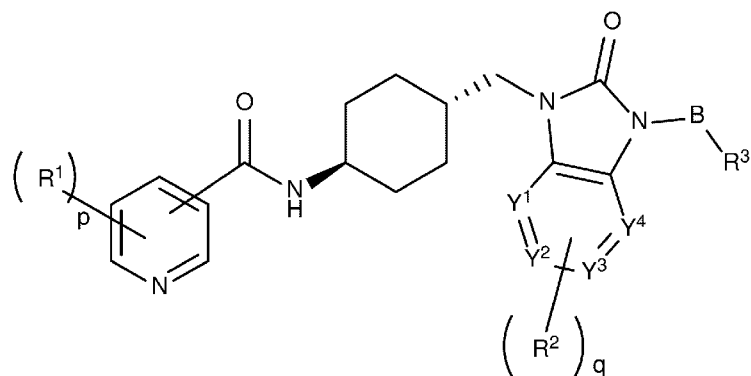
(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C_{1-6} alkyl, (5) $-O-C_{1-6}$ alkyl, (7) C_{3-7} cycloalkyl, (8) $-O-C_{3-7}$ cycloalkyl, (10) $-(C=O)-R^5$, (11) $-(C=O)-NR^5R^6$, (13) $-NR^5R^6$, (14) aryl, and (23) heteroaryl, wherein the C_{1-6} alkyl, the $-O-C_{1-6}$ alkyl, the C_{3-7} cycloalkyl, or the $-O-C_{3-7}$ cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from halogen and hydroxyl; wherein the aryl or the heteroaryl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, C_{1-6} alkyl, hydroxy C_{1-6} alkyl, and $-(C=O)-R^5$; more preferably R^4 is independently selected from the group consisting of: (1) hydrogen, (2) halogen, (3) hydroxyl, (4) C_{1-6} alkyl, (5) $-O-C_{1-6}$ alkyl, and (11) $-(C=O)-NR^5R^6$; wherein the C_{1-6} alkyl or the $-O-C_{1-6}$ alkyl is unsubstituted or substituted with one or more substituents independently selected from halogen and hydroxyl; R^5 is independently selected from the group consisting of: (1) hydrogen and (2) C_{1-6} alkyl;

R^6 is independently selected from the group consisting of:

(1) hydrogen, (2) C_{1-6} alkyl, (3) C_{3-7} cycloalkyl, (4) heterocyclyl, (5) C_{3-7} cycloalkyl C_{1-6} alkyl, (6) heterocyclyl C_{1-6} alkyl, (7) aryl, (8) aryl C_{1-6} alkyl, (9) heteroaryl, and (10) heteroaryl C_{1-6} alkyl, wherein the C_{1-6} alkyl, the C_{3-7} cycloalkyl, the heterocyclyl, the C_{3-7} cycloalkyl C_{1-6} alkyl, the heterocyclyl C_{1-6} alkyl, the aryl, the aryl C_{1-6} alkyl, the heteroaryl, or the heteroaryl C_{1-6} alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy C_{1-6} alkyl, hydroxy C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy, $-NR^7R^8$, and $-(C=O)-NR^7R^8$; or R^5 may form a 4 to 7 membered ring with R^6 which may contain a nitrogen atom, an oxygen atom, or a carbonyl; or R^5 may form a 7 to 11 membered spiro-ring with R^6 which may contain a nitrogen atom, an oxygen atom, or a carbonyl; wherein the 4 to 7 membered ring or the 7 to 11 membered spiro-ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy C_{1-6} alkyl, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy; more preferably R^6 is independently selected from the group consisting of: (1) hydrogen, (2) C_{1-6} alkyl, and (3) C_{3-7} cycloalkyl, wherein the C_{1-6} alkyl or C_{3-7} cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl;

R^7 and R^8 are independently selected from the group consisting of: (1) hydrogen and (2) C_{1-6} alkyl; or R^7 may form a 4 to 7 membered ring with R^8 which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C_{1-6} alkyl, and C_{1-6} haloalkyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[001 1] [2] The compound of the following formula (II) according to [1]:
[Chem.2]



(II)

wherein:

R^1 is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) C_{1-6} alkyl, (4) C_{3-7} cycloalkyl, (5) $-O-C_{1-6}$ alkyl, (6) C_{1-6} alkoxy C_{1-6} alkyl, (7) $-NHC_{1-6}$ alkyl, (8) $-N(C_{1-6} \text{ alkyl})_2$, and (9) $-NHC_{3-7}$ cycloalkyl wherein the C_{1-6} alkyl, the C_{3-7} cycloalkyl, the $-O-C_{1-6}$ alkyl, the C_{1-6} alkoxy C_{1-6} alkyl, the $-NHC_{1-6}$ alkyl, the $-N(C_{1-6} \text{ alkyl})_2$, or the $-NHC_{3-7}$ cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl; or two R^1 may form a 5 to 7 membered cycloalkyl ring;

p is 1, 2, or 3;

R^2 is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (4) C_{1-6} alkyl, and (6) $-CN$;

q is 1, 2, or 3;

Y^1 , Y^2 , Y^3 , and Y^4 are independently selected from the group consisting of: CH , CR^2 , and N ,

number of nitrogen atom is two at most at the same time;

B is a chemical bond, $-CH_2-$, $-CH_2CH_2-$, or $-CH_2-(C=O)-$;

R^3 is selected from the group consisting of:

(1) aryl, preferably phenyl, (2) 5 to 6-membered heteroaryl with 1-3 heteroatoms independently selected from O , N , and S , (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms independently selected from O , N , and S , (4) 5 to 6-membered heterocyclyl with 1-2 heteroatoms independently selected from O , N , and S , and (5) 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl; wherein the aryl, preferably phenyl, the 5 to 6-membered heteroaryl, the 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl, the 5 to 6-membered heterocyclyl, or the 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl is unsubstituted or substituted with one or more substituents inde-

pendently selected from R⁴;

R⁴ is independently selected from the group consisting of: (1) hydrogen, (2) halogen, (3) hydroxyl, (4) C₁₋₆ alkyl, (5) -O-C₁₋₆ alkyl, (6) C₂₋₆ alkenyl, (7) C₃₋₇ cycloalkyl, (8) -O-C₃₋₇ cycloalkyl, (9) C₃₋₇ cycloalkylC₁₋₆ alkoxy, (10) -(C=O)-R⁵, (11) -(C=O)-NR⁵R⁶, (12) -NR⁵(C=O)R⁶, (13) -NR⁵R⁶, (14) aryl, preferably phenyl, (15) heterocyclyl which is 4 to 7 membered partially unsaturated or saturated heterocyclic ring with 1-2 heteroatoms independently selected from O, N, and S, (16) -O-heterocyclyl, (17) heterocyclylC₁₋₆ alkyl, (18) heterocyclylC₁₋₆ alkoxy, (19) -NR⁵-S(O)₂R⁶, (20) -S(O)₂-R⁵, (21) -CN, (22) nitro, (23) heteroaryl, (24) -O-heteroaryl, (25) -S-C₁₋₆ alkyl, (26) -O-C₁₋₆ alkyl-(C=O)-NR⁵R⁶, and (26) -(C=O)-NR⁵O-C₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the -O-C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the -O-C₃₋₇ cycloalkyl, or the -S-C₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, -NR⁵R⁶, -O-C₁₋₆ alkyl, and C₃₋₇ cycloalkyl, wherein the aryl, preferably phenyl, the heterocyclyl, the -O-heterocyclyl, the heterocyclylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkoxy, the heteroaryl, or the -O-heteroaryl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, C₁₋₆ alkyl, hydroxylC₁₋₆ alkyl, and -(C=O)-R⁵;

R⁵ is independently selected from the group consisting of: (1) hydrogen and (2) C₁₋₆ alkyl;

R⁶ is independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) C₃₋₇ cycloalkyl, (4) heterocyclyl, (5) C₃₋₇ cycloalkylC₁₋₆ alkyl, (6) heterocyclylC₁₋₆ alkyl, (7) aryl, (8) arylC₁₋₆ alkyl, (9) heteroaryl, and (10) heteroarylC₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the heterocyclyl, the C₃₋₇ cycloalkylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkyl, the aryl, the arylC₁₋₆ alkyl, the heteroaryl, or the heteroarylC₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxylC₁₋₆ alkyl, hydroxylC₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy, -NR⁷R⁸, and -(C=O)-NR⁷R⁸; or R⁵ may form a 4 to 7 membered ring with R⁶ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxylC₁₋₆ alkyl, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy;

R⁷ and R⁸ are independently selected from the group consisting of: (1) hydrogen and (2) C₁₋₆ alkyl; or R⁷ may form a 4 to 7 membered ring with R⁸ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, and C₁₋₆ haloalkyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof;

[0012] [3] The compound according to [1] or [2]:

wherein:

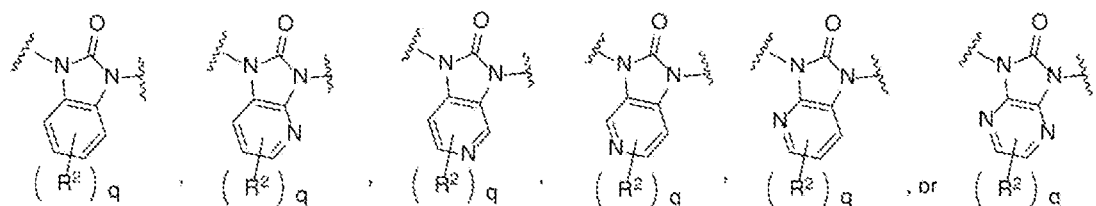
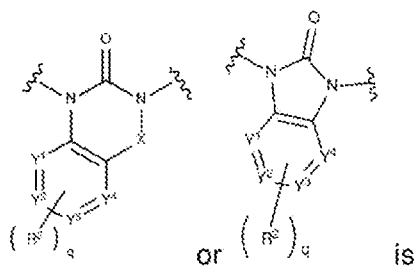
R^1 is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, and (3) C_{1-6} alkyl; wherein the C_{1-6} alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof;

[0013] [4] The compound according to any one of [1] to [3]:

wherein:

[Chem.3]



or a pharmaceutically acceptable salt thereof or a prodrug thereof;

[0014] [5] The compound according to any one of [1] to [4]:

wherein:

B is a chemical bond or $-CH_2-$;

R^3 is selected from the group consisting of: (1) phenyl, (2) 5 to 6-membered heteroaryl selected from pyrazole, pyridine, pyrazine, pyridazine, and pyrimidine, and (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms which is selected from the group consisting of indole, pyrrolo[2,3-b]pyridine, pyrrolo[2,3-c]pyridine, indazole, pyrazolo[3,4-b]pyridine, pyrazolo[4,3-b]pyridine, benzoxazole, and 2,3-dihydro-pyrrolo[2,3-b]pyridine, wherein the phenyl, the 5 to 6-membered heteroaryl or the 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl is unsubstituted or substituted with one or more substituents independently selected from R^4 ;

R^4 is independently selected from the group consisting of: (1) hydrogen, (2) halogen, (3) hydroxyl, (4) C_{1-6} alkyl, (5) $-O-C_{1-6}$ alkyl, (6) C_{3-7} cycloalkyl, (7) $-O-C_{3-7}$ cycloalkyl, (8) $-(C=O)-R^5$, (9) $-(C=O)-NR^5R^6$, (10) $-NR^5R^6$, (11) aryl, and (12) heteroaryl, wherein the C_{1-6} alkyl, the $-O-C_{1-6}$ alkyl, the C_{3-7} cycloalkyl, or the $-O-C_{3-7}$ cycloalkyl is

unsubstituted or substituted with one or more substituents independently selected from halogen and hydroxyl; wherein the aryl or the heteroaryl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, C₁₋₆ alkyl, hydroxylC₁₋₆ alkyl, and -(C=O)-R⁵;

R⁶ is independently selected from the group consisting of: (1) hydrogen, (2) C₁₋₆ alkyl, (3) C₃₋₇ cycloalkyl, (4) heterocyclyl, (5) C₃₋₇ cycloalkylC₁₋₆ alkyl, (6) heterocyclylC₁₋₆ alkyl, (7) aryl, (8) arylC₁₋₆ alkyl, (9) heteroaryl, and (10) heteroarylC₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the heterocyclyl, the C₃₋₇ cycloalkylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkyl, the aryl, the arylC₁₋₆ alkyl, the heteroaryl, or the heteroarylC₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxylC₁₋₆ alkyl, hydroxylC₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy, -NR⁷R⁸, and -(C=O)-NR⁷R⁸; or R⁵ may form a 4 to 7 membered ring with R⁶ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxylC₁₋₆ alkyl, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy;

R⁷ and R⁸ are independently selected from the group consisting of: (1) hydrogen and (2) C₁₋₆ alkyl; or R⁷ may form a 4 to 7 membered ring with R⁸ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, and C₁₋₆ haloalkyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof;

[0015] [6] A compound which is selected from the group consisting of:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-phenyl-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1*r*,4*r*)-4-((3-benzyl-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(3-(methylcarbamoyl)benzyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(pyridin-3-ylmethyl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-yl)methyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(2-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(2,4-difluorophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(4-cyanophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-chlorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2,2-difluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-ethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

2-ethyl-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

2-ethyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

2-ethyl-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

2-(2-hydroxyethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-ethyl-2H-indazole-3-carboxamide;

2-ethyl-N-((1r,4r)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxypyrimidin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3,4-dimethoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxypyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-difluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluoro-2-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluoro-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1S,4r)-4-((3-(6-((S)-3-(dimethylamino)pyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-(2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(2-bromopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
5-chloro-N-((1r,4r)-4-((3-(6-ethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-N-((1r,4r)-4-((3-(4-(2-(dimethylamino)ethoxy)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-2-methyl-N-((1R,4r)-4-((3-(6-((R)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-methyl-N-((1R,4r)-4-((3-(6-(((R)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1R,4r)-4-((3-(6-(((R)-4-acetylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
N-((1r,4r)-4-((3-(6-((1-acetylazetid-3-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
N-((1r,4r)-4-((3-(6-((1-acetylazetid-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
5-chloro-N-((1S,4r)-4-((3-(6-((S)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-vinylpyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(2-ethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(r,2',3',6'-tetrahydro-[2,4-bipyridin]-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-cyclopropylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(tetrahydro-2H-pyran-4-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-phenylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)phenyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3-hydroxypropyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)morpholino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-4-((3-(6-(difluoromethyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((3-(6-(((R)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((cyclopropylmethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((3,3-difluorocyclobutyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-(4-((3-(6-(cyclopropylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-(4-((3-(6-cyclopropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1S,4r)-4-((3-(5-((S)-3-hydroxypyrrolidin-1-yl)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5,6-dimethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-methoxy-5-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((4-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclobutylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-be nzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-methoxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2, 3-dihydro -1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)-4-methylphenyl)-2-oxo-2, 3-dihydro-1H- benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydr o-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-4-methylphenyl)-2-oxo-2, 3-dihydro-1H- benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxetan-3-ylcarbamoyl)phenyl)-2-oxo-2,3-dihyd ro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((5-cyano-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo [d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-4-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-be nzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3 -dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypropoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-b enzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dih ydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenyl-3,4-dihydroquinazolin-1(2H)-yl)met hyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyra zin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-imid azo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((1-(6-(dimethylamino)pyridin-3-yl)-2-oxo-1H-imidazo[4,5-c]py ridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(1H-indol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-aminopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide ;

5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(benzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(1-acetyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide; and

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

or a pharmaceutically acceptable salt thereof or a prodrug thereof;

- [0016] [7] The compound according to [6], which is selected from the group consisting of:
- N-((1r,4r)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-be nzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(2-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-be nzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(2,4-difluorophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-b enzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(4-cyanophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1- yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol- l-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol -l-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imi dazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]i midazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-l- yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol -l-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2,2-difluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-b enzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-ethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imida zol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3,4-dimethoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imid azol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxypyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imi dazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-difluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazo l-l-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-be nzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-ethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-vinylpyridin-4-yl)-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-cyclopropylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-phenylpyridin-3-yl)-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)phenyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3-hydroxypropyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((cyclopropylmethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3,3-difluorocyclobutyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-(4-((3-(6-(cyclopropylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-(4-((3-(6-cyclopropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5,6-dimethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-5-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((4-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclobutylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-methoxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)-4-methylphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxetan-3-ylcarbamoyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypropoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-N-(4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-N-(4-((3-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-N-(4-((3-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-N-(4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(2-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-(3-((4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide;

trans-5-chloro-N-(4-((3-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-N-(4-((3-(benzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(1-methyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-N-(4-((3-(1-acetyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[3,2-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

;

5-chloro-N-((1r,4r)-4-((3-(6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

2-ethyl-N-((1r,4r)-4-((3-(6-(methylcarbamoyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(chroman-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl

l)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((1r,2'-dimethyl-2-oxo-1H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((1r,3'-dimethyl-2,2'-dioxo-2,3-dihydro-1H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[4,3-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(1-methyl-1H-pyrazol-3-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-2-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridazin-3-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(isoxazol-3-ylmethyl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-3-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyrimidin-5-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(oxazol-4-ylmethyl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-((4-methylthiazol-2-yl)methyl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-4-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-ethylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(1H-pyrazol-3-yl)picolinamide;
 5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-inden-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2,3-dimethyl-2H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]

imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinazolin-5-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(2-acetylisoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2, 3-dihydro-1H-inden-5-yl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-indazol-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-N-((1r,4r)-4-((3-(3-(cyclopropylmethyl)-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(3-amino-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(3-aminobenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;
 N-((1r,4r)-4-((3-(benzo[d]thiazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-([2,3'-bipyridin]-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxazol-5-yl)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(6-(1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(4-bromo-2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-

yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((r-methyl-2-oxo-rH-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3'-methyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloro-1-methyl-1H-indazol-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((2',3'-dimethyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloro-1H-indazol-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((1-(5-bromo-2,3-dihydro-1H-inden-2-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1, 3-dimethyl-1H-indazol-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrooxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6'-amino-[2,3'-bipyridin]-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(pyridin-4-yloxy)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl-2H-indazole-3-carboxamide;

N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl-4,5,6,7-tetrahydro-2H-indazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloro-1H-indazol-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imi

dazol-1-yl)methyl)cyclohexyl)-2-methylbenzamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-bromo-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

;

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-nitrophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

2,5-dichloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2,3-dihydro-1H-inden-4-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanobenzyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylbenzo[d]isoxazole-3-carboxamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylbenzo[d]isoxazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-3-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-methylphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-4-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-dimethoxybenzyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(cyclopropylmethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-ethyl-2H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(2-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(2-aminobenzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(benzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-cyclopropyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

2,5-dichloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-3H-[1,2,3]triazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-ethyl-2-oxo-2,3-dihydrooxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-cyclobutylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-ylmethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;
 2,5-dichloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(3-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(1-(2-methoxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-ethyl-3-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyrido[2,3-b]pyrazin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-ethyl-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-oxo-3,4-dihydroquinazolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-formylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(5-bromo-2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-3-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(thiazol-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-cyclopropyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((2-oxo-3-(2-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((3-(4-aminopyrido[3,2-d]pyrimidin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((2-oxo-3-(3-(trifluoromethyl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(2-methoxyethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-cyclobutyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((r-methyl-2-oxo-rH-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(dimethylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(methoxymethyl)-N-(((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((3-(4,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-(((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(methoxymethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2,5-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-phenyl-1H-indazol-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(2,2-difluoroethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-ethyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(quinolin-3-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

ol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2,3-dihydro-1H-inden-4-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((r-methyl-2-oxo-rH-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(benzo[d]thiazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(1,8-naphthyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinazolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-fluoro-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(cyclopentyloxy)-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-ethoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-methyl-1H-indole-2-carboxamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,1-dimethyl-1H-indole-2-carboxamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,N,1-trimethyl-1H-indole-2-carboxamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3'-methyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)picolinamide;

5-chloro-N-(((1r,4r)-4-((3-(6-((2-hydroxyethyl)thio)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((3-(5-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-(((1r,4r)-4-((3-(2,4-dichlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(imidazo[l,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-(((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-(((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(imidazo[l,2-a]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(2-methyl-2H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((2-oxo-3-(quinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(isoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-(((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-(((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-(((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methoxypicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-fluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-morpholinoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(2-amino-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(((1-methyl-1H-pyrazol-4-yl)methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(1,5-naphthyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinazolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-morpholinophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-(isoxazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-phenoxyethyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-dichlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(isopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-

2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-pyrazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-pyrazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(6-(1H-imidazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(2-(1H-imidazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((3,3-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(5-(pyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imi

dazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-5-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-5-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(2-chloro-5-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

N-methyl-5-(3-(((1r,4r)-4-(2-methyl-5-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

N-methyl-5-(3-(((1r,4r)-4-(5-methyl-2-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-(methylamino)-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoazetidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropanecarboxamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

N-((1S,4r)-4-((3-(6-(((S)-l-amino-l-oxopropan-2-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1R,4r)-4-((3-(6-(((R)-l-amino-l-oxopropan-2-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(3-oxomorpholino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4.5-b]pyrazin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4.5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-(pyridin-3-yl)piperidin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(isopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(thiazol-2-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-morpholinopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-imidazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(oxazol-5-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-chloro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methylbenzo[d]thiazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpyrazine-2-carboxamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethoxy)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

N-methyl-5-(3-(((1r,4r)-4-(2-methyl-5-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethoxy)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(2-amino-5-chloronicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-bromo-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

N-((1r,4r)-4-((3-(2-(2H-1,2,3-triazol-2-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(2H-1,2,3-triazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazo

l-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(6-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(3-(1H-pyrazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-(3-(((1r,4r)-4-(2,5-dichloronicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-4-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(oxetan-3-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-ethylpicolinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 3-chloro-5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,6-dimethylpicolinamide;
 N-((1r,4r)-4-((3-(6-(methylcarbamoyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(2-oxoimidazolidin-1-yl)pyri

din-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(6-acetamido-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-propionamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 ;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(cyclopropylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-morpholinophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-(1-methyl-1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 N-((1r,4r)-4-((3-(2-(1H-imidazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-di

hydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(thiazol-5-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(fluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(7-oxo-2-oxa-6-azaspiro[3.4]octan-6-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-(dimethylamino)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1-(2-morpholinoethyl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-3,4-dihydroquinazolin-1(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-aminobenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-hydroxyethyl)benzo[d]isoxazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(methylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-2H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylquinolin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,

5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(2-(1H-pyrazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(6-(1H-pyrazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3

(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(6-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methylureido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylbenzo[d]thiazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(methylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-di

hydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-3-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-ureidopyridin-3-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(1H-imidazol-4-yl)phenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

de;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((7-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(4-fluoro-3-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(2H-1,2,3-triazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-morpholinopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(oxazol-5-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(oxazol-2-yl)pyridin-3-yl)-2-oxo-2,3-d

ihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-(2-oxoimidazolidin-1-yl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
N-((1r,4r)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-3-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-(2-oxopyrrolidin-1-yl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(3-methyl-2-oxoimidazolidin-1-yl)pyri

din-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1, 2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-hydroxypropyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(2-(2-hydroxyethoxy)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-((2-hydroxyethyl)amino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide; 5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-di

hydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 4-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 4-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r, 4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r, 4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(3-(1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(3-(1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2, 3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(4-(1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 and 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-indol-5-yl)-2-

oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
or a pharmaceutically acceptable salt thereof or a prodrug thereof;

[0017] [8] A use of a compound described in any one of [1] to [7] or a pharmaceutically acceptable salt, prodrug, solvate or composition thereof for the manufacture of a medicament for the treatment of a condition or disorder in which CRHR1 and/or CRHR2 are involved;

[0018] [9] The use as described in [8], wherein said condition or disorder is selected from the group consisting of: gastrointestinal disorders, major depressive disorders, schizophrenic disorders, neurodegenerative diseases, pain, dysfunction of appetite and food intake, sleep disorders, cognitive disorders, tolerance to and dependence on a number of substances, inflammation, fertility problems, sexual dysfunctions and pre-term birth and non-inflammatory urogenital disorders, allergic disorders, mast cell activation disorders, Cushing's syndrome, emesis, gastrointestinal disorders, neurotoxic injury, loss of hair, heart disease, and combinations thereof;

[0019] [10] The use as described in [9], wherein the heart disease is selected from the group consisting of: acute and chronic heart failure, cardiovascular disease, hyper tension, myocardial infarction, coronary artery disease, and abdominal aortic aneurysm.

[0020] [11] A method for the treatment of a condition or disorder in which CRHR1 and/or CRHR2 are involved, in an animal, including a human, which comprises administering to the animal in need of such treatment a therapeutically effective amount of a compound or a prodrug thereof or a pharmaceutically acceptable salt thereof, as described in any one of [1] to [7];

[0021] [12] The method as described in [11], wherein said condition or disorder is selected from the group consisting of: gastrointestinal disorders, major depressive disorders, schizophrenic disorders, neurodegenerative diseases, pain, dysfunction of appetite and food intake, sleep disorders, cognitive disorders, tolerance to and dependence on a number of substances, inflammation, fertility problems, sexual dysfunctions and pre-term birth and non-inflammatory urogenital disorders, allergic disorders, mast cell activation disorders, Cushing's syndrome, emesis, gastrointestinal disorders, neurotoxic injury, loss of hair, heart disease, and combinations thereof;

[0022] [13] The method as described in [12], wherein the heart disease is selected from the group consisting of: acute and chronic heart failure, cardiovascular disease, hyper tension, myocardial infarction, coronary artery disease, and abdominal aortic aneurysm;

[0023] [14] A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt thereof or a prodrug thereof, as described in any one of [1] to [7], and a pharmaceutically acceptable carrier;

[0024] [15] The pharmaceutical composition as described in [14], further comprising

another pharmacologically active agent;

[0025] [16] A compound described in any one of [1] to [7] or a prodrug thereof or a pharmaceutically acceptable salt for use in the treatment of a condition or disorder in which CRHR1 and/or CRHR2 are involved;

[0026] [17] A process for preparing a pharmaceutical composition, wherein the process comprises mixing a compound described in any one of [1] to [7] or a pharmaceutically acceptable salt thereof or a prodrug thereof and a pharmaceutically acceptable carrier or excipient;

[0027] [18] An assay process for identifying a compound which has CRHR1 and/or CRHR2 antagonistic activity, comprising administering of a compound described in any one of [1] to [7] to mice loaded exogenous CRHR2 agonist within 1 week and investigating cardiovascular functions; and

[0028] [19] An assay process for identifying a compound which has CRHR1 and/or CRHR2 antagonistic activity, comprising administering of a compound described in any one of [1] to [7] to mice infused urocortin 2 within 2 days and measuring cardiac function by echocardiography.

Advantageous Effects of Invention

[0029] The compounds showed activities against both CRHR1 and CRHR2. In particular, the fused cyclic urea derivatives of the present invention show excellent antagonistic activities against the CRHR2 over the compounds with close chemical structure, leading to better pharmacological profiles. The fused cyclic urea derivatives of the present invention show good selectivity against other receptors than CRHR1 and CRHR2, leading to improvements in the side-effect profile. The fused cyclic urea derivatives of the present invention are therefore useful in the treatment of a wide range of disorders.

[0030] Therefore, according to a further aspect of the invention, we provide a compound of formula (I) and (II), or a salt thereof, for the treatment or alleviation of treatment of any state with increased endogenous level of CRH or in which the HPA (hypothalamic pituitary axis) is dysregulated, or of various diseases induced or facilitated by CRH.

[0031] Compounds of the invention are in particular useful for the treatment or prevention of gastrointestinal disorders including irritable bowel syndrome with or without diarrhea, inflammatory bowel diseases, post-operative ileus, reflux disease and infectious diarrhea.

[0032] Compounds of the invention are also in particular useful for the treatment or prevention of major depressive disorders including bipolar depression, unipolar depression, single or recurrent major depressive episodes with or without psychotic features, catatonic features, melancholic features, atypical features or postpartum onset,

the treatment of anxiety and the treatment of panic disorders. Other mood disorders encompassed within the term major depressive disorders include fatigue syndrome and dysthymic disorder with early or late onset and with or without atypical features, neurotic depression, post traumatic stress disorders, post operative stress and social phobia; dementia of the Alzheimer type, with early or late onset, with depressed mood; vascular dementia with depressed mood; mood disorders induced by alcohol, amphetamines, cocaine, hallucinogens, inhalants, opioids, phencyclidine, sedatives, hypnotics, anxiolytics and other substances; schizoaffective disorder of the depressed type; and adjustment disorder with depressed mood. Major depressive disorders may also result from a general medical condition including, but not limited to, myocardial infarction, diabetes, miscarriage or abortion, etc.

- [0033] Compounds of the invention are also useful in the treatment or prevention of schizophrenic disorders including paranoid schizophrenia, disorganized schizophrenia, catatonic schizophrenia, undifferentiated schizophrenia, residual schizophrenia.
- [0034] Compounds of the invention are also useful in the treatment or prevention of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, senile dementia of the Alzheimer's type, and multiinfarct dementia.
- [0035] Compounds of the invention are useful as analgesics. In particular, they are useful in the treatment of traumatic pain such as postoperative pain; traumatic avulsion pain such as brachial plexus; chronic pain such as arthritic pain such as occurring in osteo-, rheumatoid or psoriatic arthritis; neuropathic pain such as post-herpetic neuralgia, trigeminal neuralgia, segmental or intercostal neuralgia, fibromyalgia, causalgia, peripheral neuropathy, diabetic neuropathy, chemotherapy-induced neuropathy, AIDS related neuropathy, occipital neuralgia, geniculate neuralgia, glossopharyngeal neuralgia, reflex sympathetic dystrophy, phantom limb pain; various forms of headache such as migraine, acute or chronic tension headache, temporomandibular pain, maxillary sinus pain, cluster headache; odontalgia; cancer pain; pain of visceral origin; gastrointestinal pain; nerve entrapment pain; sport's injury pain; dysmenorrhea; menstrual pain; meningitis; arachnoiditis; musculoskeletal pain; low back pain e.g. spinal stenosis; prolapsed disc; sciatica; angina; ankylosing spondylitis; gout; burns; scar pain; itch; and thalamic pain such as post stroke thalamic pain.
- [0036] Compounds of the invention are also useful for the treatment of dysfunction of appetite and food intake and in circumstances such as anorexia, anorexia nervosa, bulimia, obesity and metabolic syndrome.
- [0037] Compounds of the invention are also useful in the treatment of sleep disorders including dyssomnia, insomnia, sleep apnea, narcolepsy, and circadian rhythmic disorders.

- [0038] Compounds of the invention are also useful in the treatment or prevention of cognitive disorders. Cognitive disorders include dementia, amnestic disorders and cognitive disorders not otherwise specified.
- [0039] Furthermore compounds of the invention are also useful as memory and/or cognition enhancers in healthy humans with no cognitive and/or memory deficit.
- [0040] Compounds of the invention are also useful in the treatment of tolerance to and dependence on a number of substances. For example, they are useful in the treatment of dependence on nicotine, alcohol, caffeine, phencyclidine (phencyclidine like compounds), or in the treatment of tolerance to and dependence on opiates (e.g. cannabis, heroin, morphine) or benzodiazepines; in the treatment of cocaine, sedative hypnotic, amphetamine or amphetamine-related drugs (e.g. dextroamphetamine, methylamphetamine) addiction or a combination thereof.
- [0041] Compounds of the invention are also useful as anti-inflammatory agents. In particular, they are useful in the treatment of inflammation in asthma, influenza, chronic bronchitis and rheumatoid arthritis; in the treatment of inflammatory diseases of the gastrointestinal tract such as Crohn's disease, ulcerative colitis, postoperative gastric ileus (POI), inflammatory bowel disease (IBD) and non-steroidal anti-inflammatory drug induced damage; inflammatory diseases of the skin such as herpes and eczema; inflammatory diseases of the bladder such as cystitis and urge incontinence; and eye and dental inflammation.
- [0042] Compounds of the invention are also useful in the treatment of fertility problems, sexual dysfunctions and pre-term birth and non-inflammatory urogenital disorders such as overactive bladder and related urinary incontinence.
- [0043] Compounds of the invention are also useful in the treatment of allergic disorders, in particular allergic disorders of the skin such as urticaria, and allergic disorders of the airways such as rhinitis.
- [0044] Compounds of the invention are also useful in the treatment of mast cell activation disorders such as mastocytosis.
- [0045] Compounds of the invention are also useful the treatment of Cushing's syndrome induced by drugs such as steroids or cancer such as pituitary adenoma.
- [0046] Compounds of the invention are also useful in the treatment of emesis, i.e. nausea, retching and vomiting. Emesis includes acute emesis, delayed emesis and anticipatory emesis. The compounds of the invention are useful in the treatment of emesis however induced. For example, emesis may be induced by drugs such as cancer chemotherapeutic agents such as alkylating agents, e.g. cyclophosphamide, carmustine, lomustine and chlorambucil; cytotoxic antibiotics, e.g. dactinomycin, doxorubicin, mitomycin-C and bleomycin; anti-metabolites, e.g. cytarabine, methotrexate and 5-fluorouracil; vinca alkaloids, e.g. etoposide, vinblastine and vincristine; and others

such as cisplatin, dacarbazine, procarbazine and hydroxyurea; and combinations thereof; radiation sickness; radiation therapy, e.g. irradiation of the thorax or abdomen, such as in the treatment of cancer; poisons; toxins such as toxins caused by metabolic disorders or by infection, e.g. gastritis, or released during bacterial or viral gastrointestinal infection; pregnancy; vestibular disorders, such as motion sickness, vertigo, dizziness and Meniere's disease; post-operative sickness; gastrointestinal obstruction; reduced gastrointestinal motility; visceral pain, e.g. myocardial infarction or peritonitis; migraine; increased intracranial pressure; decreased intracranial pressure (e.g. altitude sickness); opioid analgesics, such as morphine; and gastro-oesophageal reflux disease, acid indigestion, over-indulgence of food or drink, acid stomach, sour stomach, regurgitation, heartburn, such as episodic heartburn, nocturnal heartburn, and meal-induced heartburn and dyspepsia.

- [0047] Compounds of the invention are of particular use in the treatment of gastrointestinal disorders such as irritable bowel syndrome; skin disorders such as psoriasis, pruritus and sunburn; vasospastic diseases such as angina, vascular headache and Reynaud's disease; cerebral ischemia such as cerebral vasospasm following subarachnoid haemorrhage; fibrosing and collagen diseases such as scleroderma and eosinophilic fascioliasis; disorders related to immune enhancement or suppression such as systemic lupus erythematosus and rheumatic diseases such as fibrositis; and cough.
- [0048] Compounds of the invention are useful for the treatment of neurotoxic injury which follows cerebral stroke, thromboembolic stroke, hemorrhagic stroke, cerebral ischemia, cerebral vasospasm, hypoglycemia, hypoxia, anoxia, perinatal asphyxia, and cardiac arrest.
- [0049] Compounds of the invention are useful for hair growth.
- [0050] Compounds of the invention are useful for heart disease including acute and chronic heart failure, cardiovascular disease, hyper tension, myocardial infarction, coronary artery disease, and abdominal aortic aneurysm.
- [0051] The utility of the agents of the invention in the above indicated diseases can be confirmed in a range of standard tests. Examples of such tests may include, but are not limited to, the following:

(1) The anxiolytic activity of the agents of the invention can be confirmed in the mouse elevated plus-maze [see, for example, Rodgers R. J., *Behavioural Pharmacology* 8:477-496 (1997) where the relevance of the elevated plus-maze is discussed on p. 486; for the method, see Rodgers R. J. et al. *Ethology and Psychopharmacology* (Eds SJ Cooper and CA Hendrie), pp 9-44 (1994), J. Wiley, Chichester]. (2) The analgesic activity of the agents of the invention can be confirmed in rat visceral hyperalgesia models following colorectal distension [see for example Schwetz I, *Am J Physiology* 286: G683-G691 (2004); for the method, see Ness T. J., *Brain Research*

450:153-169 (1988)]. (3) The anti-diarrheal activity of the agents of the invention can be confirmed in rat defecation models during stress or CRF challenge [see for example, Maillot C., *Gastroenterology* 119:1569-1579 (2002)]. (4) The hair growth activity of the agents of the invention can be confirmed in the method described in WO 2007/149938. (5) The anti-heart disease activity of the agents of the invention can be confirmed in the method described in this specification and the literature, e.g. *Drug Discovery Today* Volume 20, Number 7, 906-914 (2015). (6) Other activities of the agents of the invention can be confirmed in the method described in literatures known by a person skilled in the art including well-known art and commonly used art.

[0052] Novartis discloses structurally close arts in WO201 1/092293 and WO201 1/095450. The compounds of present invention show much better activities than those of the close arts.

[0053] Namely the present invention is characterized by -B-R³ substituent on the fused cyclic urea ring in the above formula (I) or (II). The structurally closest compounds are synthesized and are described as reference compounds in the present application. The difference between the present invention and the structurally closest art is further well brought out as follows.

[0054] The CRHR2 antagonistic activities of the representative chemical structures in the present invention and the structurally close arts are summarized in the following Tables 1-1 and 1-2.

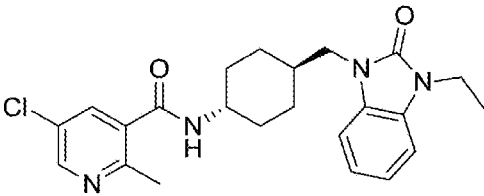
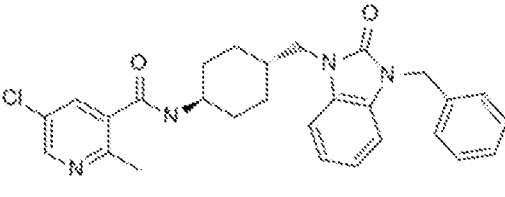
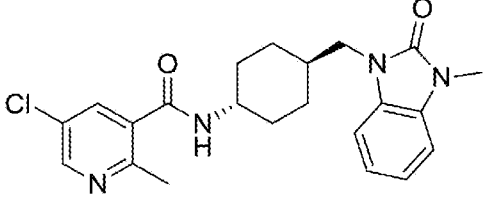
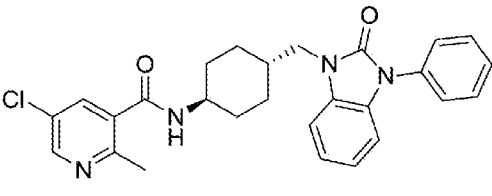
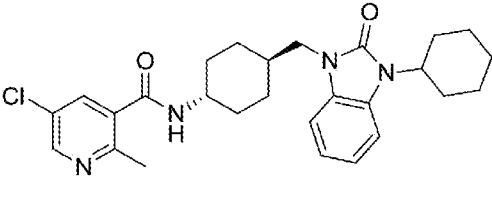
[0055] The reference compound of Example 2.46 in the structurally close art, WO201 1/092293, shows the inhibitory activity against CRHR2 with 3 microM, whereas the compound of Example 2 in the present invention, where phenyl group is introduced to the terminal ethyl group of Example 2.46, has inhibitory activities against CRHR2 with 0.18 microM. The reference compound of Example 2.50 in the structurally close art, WO201 1/092293, shows the inhibitory activity against CRHR2 with 13 microM, whereas the compound of Example 1 in the present invention, where phenyl group is introduced to the terminal methyl group of Example 2.50, has inhibitory activities against CRHR2 with 0.39 microM. The reference compound (A) with cyclohexyl group falls into the claim of the structurally close art, WO201 1/092293, shows the inhibitory activity against CRHR2 with 3.1 microM, whereas the compound of Example 156 in the present invention, where cyclohexyl group of the reference compound (A) is replaced with pyridyl group, has inhibitory activities against CRHR2 with 0.28 microM. In addition the compound of Example 30 with methoxy group on the pyridyl group in the present invention has inhibitory activities against CRHR2 with 0.06 microM. Further the compound of Example 128 with pyrazolopyridyl group in the present invention has inhibitory activities against CRHR2 with 0.28 microM, which shows better activity comparing with the reference

compound (A) of the structurally close art, WO201 1/092293. Then the compound of Example 148 with methyl-introduced pyrropyridyl group in the present invention has inhibitory activities against CRHR2 with 0.06 microM.

[0056] Therefore the compound of the present invention, which has -B-R³ substituent on the bi-cyclic imidazolinone ring in the above formula (I) or (II) shows excellent activity against CRHR2 comparing with the corresponding compound of the structurally close arts.

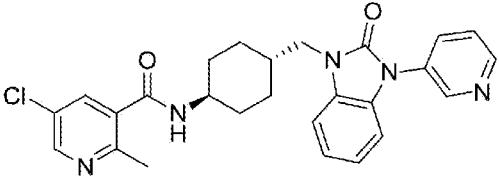
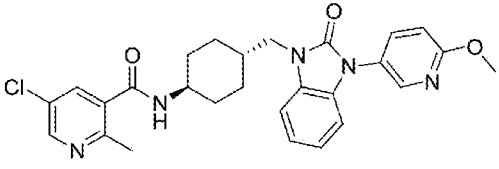
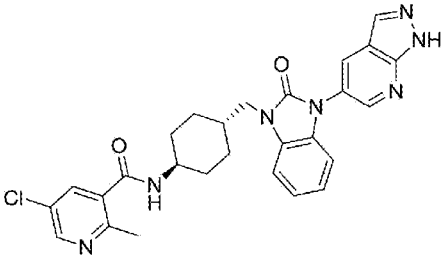
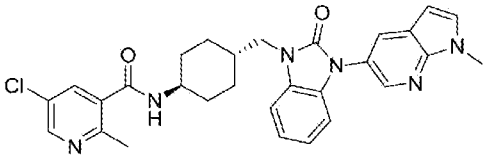
[0057]

[Table 1-1]

Literature / Present invention	Chemical structure	CRHR2 (IC ₅₀)
WO2011/092293	 Example 2.46	3.0 microM
Present invention	 Example 2	0.18 microM
WO2011/092293	 Example 2.50	13 microM
Present invention	 Example 1	0.39 microM
WO2011/092293	 Reference compound (A)	3.1 microM

[0058]

[Table 1-2]

Present invention	 Example 156	0.28 microM
Present invention	 Example 30	0.06 microM
Present invention	 Example 128	0.28 microM
Present invention	 Example 148	0.06 microM

[0059] Examples of conditions or disorders mediated by CRHR1 and/or CRHR2 include, but are not limited to, CRHR1 and/or CRHR2 related diseases. The compounds of the present invention show the CRHR1 and CRHR2 antagonistic activity. The compounds of the present invention may show less toxicity, good absorption and distribution, good solubility, less protein binding affinity other than CRHR1 and/or CRHR2, less drug-drug interaction, good metabolic stability, reduced inhibitory activity at HERG channel, and/or reduced QT prolongation.

Description of Embodiments

[0060] As appreciated by those of skill in the art, "halogen" as used herein is intended to include fluoro, chloro, bromo and iodo. Similarly, 1-6, as in C₁₋₆ is defined to identify the number as having 1, 2, 3, 4, 5, or 6. According to the definition, for example, C₁₋₆, as in C₁₋₆ alkyl is defined to identify the alkyl group as having 1, 2, 3, 4, 5, or 6 carbons. Similarly, C₂₋₆ alkenyl is defined to identify the alkenyl group as having 2, 3, 4, 5, or 6 carbons. A group which is designated as being independently substituted with

substituents may be independently substituted with multiple numbers of such substituents.

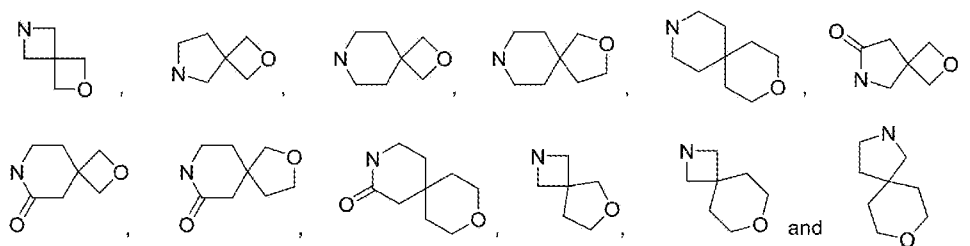
- [0061] The term "alkyl", as used herein, means a linear saturated monovalent hydrocarbon radical of one to six carbon atoms or a branched saturated monovalent hydrocarbon radical of three to six carbon atoms, e.g., methyl, ethyl, propyl, 2-propyl, butyl (including all isomeric forms), pentyl (including all isomeric forms), and the like.
- [0062] The term "alkoxy", as used herein, means an -O-alkyl such as, but not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy (including all isomeric forms), and the like.
- [0063] The term "cycloalkyl", as used herein, means a mono- or bi-cyclic ring such as, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norbornyl, adamantyl groups, and the like. In this specification, preferable cycloalkyl is C₃₋₇ mono cycloalkyl, more preferable cycloalkyl is C₃₋₆ mono cycloalkyl, further preferable cycloalkyl is C₃₋₅ mono cycloalkyl.
- [0064] The term "aryl", as used herein, means unsaturated or partially saturated mono- or bi-cyclic 5-15 membered ring which consists of carbon atoms. Examples of such aryl include, but are not limited to, phenyl, naphthyl, indanyl, indenyl, 1,2,3,4-tetrahydronaphthyl, 1,2-dihydronaphthyl, 2,3-dihydro-1H-indenyl, cyclohexenyl, cyclopentenyl, (1S,4S)-bicyclo[2.2.2]oct-2-enyl, and (1R,4S)-bicyclo[2.2.1]hept-2-enyl and the like. In this specification, preferable aryl is 6-10 membered unsaturated aryl, more preferable aryl is 6-8 membered unsaturated aryl.
- [0065] The term "heteroaryl" as used herein, means unsaturated and partially saturated mono- or bi-cyclic 5-15 membered ring, preferably mono- or bi-cyclic 5-10 membered ring, which may contain 1-4 heteroatoms selected from O, N, and S.
- Examples of such heteroaryl include, but are not limited to, thiophenyl, thiazolyl, isoxazolyl, pyrazolyl, pyrazyl, tetrazolyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, isothiazolyl, triazolyl, thiadiazolyl, pyridyl, pyrimidyl, pyridazinyl, pyrazinyl, pyranyl, triazinyl, 3,6-dihydro-2H-pyran, 1,2,3,6-tetrahydropyridyl, benzofuranyl, benzothiophenyl, benzotriazolyl, benzoxazolyl, indolyl, indazolyl, benzoimidazolyl, pyrrolopyridyl, 2,3-dihydro-pyrrolo[2,3-b]pyridyl, 2,3-dihydro-1H-pyrrolo[2,3-c]pyridyl, pyrrolopyrimidinyl, pyrazolopyridyl, pyrazolopyrimidinyl, imidazopyridinyl, furopyridyl, benzoisoxazolyl, imidazopyrazinyl, imidazopyridazinyl, imidazopyrimidinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolinyl, phthalazinyl, quinoxalyl, naphthyridinyl, pyridopyrimidinyl, 2,3-dihydro-[1,4]dioxino[2,3-b]pyridyl, 2,3-dihydro-[1,4]dioxino[2,3-c]pyridyl and N-oxides thereof and S-oxides thereof and the like. In this specification, preferable heteroaryl is 5-6 membered mono heteroaryl, more preferable heteroaryl is 5-6

membered N-containing mono heteroaryl.

[0066] The term "heterocyclyl" as used herein includes both unsaturated and saturated heterocyclic moieties, wherein the unsaturated heterocyclic moieties (i.e. "heteroaryl") include, but not limited to, benzofuranyl, benzofurazanyl, benzimidazolonyl, benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, benzoxazolyl, benzothiophenyl, benzotriazolyl, carbazolyl, carbolinyl, chromanyl, cinnolyl, 2,3-dioxindolyl, furanyl, furazanyl, furopyridyl, furopyrryl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolazinyl, indolyl, indolyl, isobenzofuranyl, isochromanyl, isoindolyl, isoquinolyl, isoxazolopyridyl, isoxazolyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxazolyl, oxadiazolyl, oxazolyl, oxetanyl, 2-oxindolyl, oxoisindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridyl, pyrimidyl, pyridazinyl, pyridopyrimidinyl, pyrrolopyridyl, pyrrolyl, quinazolyl, quinolyl, quinoxalyl, tetrazolopyridyl, tetrazolyl, thiadiazolyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrryl, triazolopyrimidinyl, triazolyl, 4-oxo-1,4-dihydroquinolyl, 2-oxo-1,2-dihydropyridyl, 4-oxo-1,4-dihydropyrimidinyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidinyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, 3,6-dihydro-2H-pyran, 1,2,3,6-tetrahydropyridinyl, tetrahydro-2H-thiopyran, 1,1-dioxide, and N-oxides thereof, and wherein the saturated heterocyclic moieties include, but not limited to, azetidyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl, morpholinyl, tetrahydrofuranyl, tetrahydropyran, thiomorpholinyl, triazolopyrimidinyl, tetrahydrothienyl, pyrrolidinonyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 5,6,7,8-tetrahydro-1,6-naphthyridyl, 1,4-oxazepanyl, and N-oxides thereof and S-oxides thereof. In this specification, preferable heterocyclyl is 3-6 membered saturated mono heterocyclyl, which may contain 1-4 heteroatoms selected from O, N, and S, more preferable heterocyclyl is 5-6 membered saturated mono heterocyclyl.

[0067] The term "7 to 11 membered spiro-ring", as used herein, means a twisted structure of two rings (a ring system), in which 2 rings are linked together by one common carbon atom, examples of which are shown below, but not limited to.

[Chem.4]



- [0068] The term "protecting group", as used herein, means a hydroxy or amino protecting group which is selected from typical hydroxy or amino protecting groups described in Protective Groups in Organic Synthesis edited by T. W. Greene et al. (John Wiley & Sons, 2007).
- [0069] The term "treating" or "treatment", as used herein, includes prohibiting, restraining, slowing, stopping, or reversing the progression or severity of an existing symptom or disorder. As used herein, the term "preventing" or "to prevent" includes prohibiting, restraining, or inhibiting the incidence or occurrence of a symptom or disorder.
- [0070] As used herein, the article "a" or "an" refers to both the singular and plural form of the object to which it refers unless indicated otherwise.
- [0071] Included within the scope of the "compounds of the invention" are all salts, solvates, hydrates, complexes, polymorphs, prodrugs, radiolabeled derivatives, stereoisomers and optical isomers of the compounds of formula (I) or (II).
- [0072] Compounds of formula (I) or (II) can form acid addition salts thereof. It will be appreciated that for use in medicine the salts of the compounds of formula (I) or (II) should be pharmaceutically acceptable. Suitable pharmaceutically acceptable salts will be apparent to those skilled in the art and include those described in J. Pharm. Sci, 1977, 66, 1-19, such as acid addition salts formed with inorganic acids e.g., but not limited to, hydrochloric, hydrobromic, sulfuric, nitric or phosphoric acid; and organic acids e.g., but not limited to, succinic, maleic, formic, acetic, trifluoroacetic, propionic, fumaric, citric, tartaric, benzoic, p-toluenesulfonic, methanesulfonic or naphthalene-sulfonic acid. Certain of the compounds of formula (I) or (II) may form acid addition salts with one or more equivalents of the acid. The present invention includes within its scope all possible stoichiometric and non-stoichiometric forms. In addition, certain compounds containing an acidic function such as a carboxy can be isolated in the form of their inorganic salt in which the counter ion can be selected from sodium, potassium, lithium, calcium, magnesium and the like, as well as from organic bases such as choline, arginine, benzathine, diethylamine, glycine, lysine, meglumine, olamine, 2-amino-2-methylpropan-1-ol, benethamine, tert-butylamine, epolamine, ethylenediamine, hydrabamine, morpholine, piperazine, procaine, triethanolamine, diethanolamine, monoethanolamine, triisopropanolamine, and tromethamine.

- [0073] Also within the scope of the invention are so-called "prodrugs" of the compounds of formula (I) or (II). Thus certain derivatives of compounds of formula (I) or (II) which may have little or no pharmacological activity themselves can, when administered into or onto the body, be converted into compounds of formula (I) or (II) having the desired activity, for example, by hydrolytic cleavage. Such derivatives are referred to as "prodrugs". Further information on the use of prodrugs may be found in Pro-drugs as Novel Delivery Systems, Vol. 14, ACS Symposium Series (T Higuchi and W Stella) and Bioreversible Carriers in Drug Design, Pergamon Press, 1987 (ed. E B Roche, American Pharmaceutical Association).
- [0074] The term "animal," as used herein, includes a mammalian subject or a non-mammalian subject. Examples of suitable mammalian subject may include, without limit, human, rodents, companion animals, livestock, and primates. Suitable rodents may include, but are not limited to, mice, rats, hamsters, gerbils, and guinea pigs. Suitable companion animals may include, but are not limited to, cats, dogs, rabbits, and ferrets. Suitable livestock may include, but are not limited to, horses, goats, sheep, swine, cattle, llamas, and alpacas. Suitable primates may include, but are not limited to, chimpanzees, lemurs, macaques, marmosets, spider monkeys, squirrel monkeys, and vervet monkeys. Examples of suitable non-mammalian subject may include, without limit, birds, reptiles, amphibians, and fish. Non-limiting examples of birds include chickens, turkeys, ducks, and geese. The preferred mammalian subject is a human.
- [0075] The term "CRHR2 agonist", as used herein, includes but are not limited to, urocortin 2, urocortin 1, urocortin 3, sauvagine, CRF, and CRF peptide family containing CRF analogs.
- [0076] Prodrugs in accordance with the invention can, for example, be produced by replacing appropriate functionalities present in the compounds of formula (I) or (II) with certain moieties known to those skilled in the art as 'pro-moieties' as described, for example, in Design of Prodrugs by H Bundgaard (Elsevier, 1985). Some examples of prodrugs in accordance with the invention include:
- (i) where the compound of formula (I) or (II) contains an alcohol functionality (-OH), compounds wherein the hydroxy group is replaced with a moiety convertible in vivo into the hydroxy group. Said moiety convertible in vivo into the hydroxy group means a moiety transformable in vivo into a hydroxyl group by e.g. hydrolysis and/or by an enzyme, e.g. an esterase. Examples of said moiety include, but are not limited to, ester and ether groups which may be hydrolyzed easily in vivo. Preferred are the moieties replaced the hydrogen of hydroxy group with acyloxyalkyl, l-(alkoxycarbonyloxy)alkyl, phthalidyl and acyloxyalkyloxycarbonyl such as pivaloyloxymethyloxycarbonyl; and

(ii) where the compound of the formula (I) or (II) contains an amino group, a fused cyclic urea derivative prepared by reacting with a suitable acid halide or a suitable acid anhydride is exemplified as a prodrug. A particularly preferred fused cyclic urea derivative as a prodrug is $\text{-NHCO(CH}_2)_2\text{OCH}_3$, $\text{-NHCOCH(NH}_2\text{)CH}_3$ or the like.

[0077] Further examples of replacement groups in accordance with the foregoing examples and examples of other prodrug types may be found in the aforementioned references.

[0078] Salts and solvates having non-pharmaceutically acceptable counter-ions or associated solvents are within the scope of the present invention, for example, for use as intermediates in the preparation of other compounds of formula (I) or (II) and their pharmaceutically acceptable salts.

[0079] Compounds of formula (I) or (II) may have polymorphs in crystalline form, which are within the scope of the present invention.

[0080] Additionally, compounds of formula (I) or (II) may be administered as prodrugs. As used herein, a "prodrug" of a compound of formula (I) or (II) is a functional derivative of the compound which, upon administration to a patient, eventually liberates the compound of formula (I) or (II) in vivo. Administration of a compound of formula (I) or (II) as a prodrug may enable the skilled artisan to do one or more of the following: (a) modify the onset of action of the compound in vivo; (b) modify the duration of action of the compound in vivo; (c) modify the transportation or distribution of the compound in vivo; (d) modify the solubility of the compound in vivo; and (e) overcome a side effect or other difficulty encountered with the compound. Typical functional derivatives used to prepare prodrugs include modifications of the compound that are chemically or enzymatically cleaved in vivo. Such modifications, which include the preparation of phosphates, amides, esters, thioesters, carbonates, and carbamates, are well known to those skilled in the art.

[0081] In certain of the compounds of formula (I) or (II), there may be one or more chiral carbon atoms. In such cases, compounds of formula (I) or (II) exist as stereoisomers. The invention extends to all optical isomers such as stereoisomeric forms of the compounds of formula (I) or (II) including enantiomers, diastereoisomers and mixtures thereof, such as racemates. The different stereoisomeric forms may be separated or resolved one from the other by conventional methods or any given isomer may be obtained by conventional stereoselective or asymmetric syntheses.

[0082] Certain of the compounds herein can exist in various tautomeric forms and it is to be understood that the invention encompasses all such tautomeric forms.

[0083] The invention also includes isotopically-labeled compounds, which are identical to those described herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds

of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, iodine, and chlorine, such as ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{18}F , ^{123}I and ^{125}I . Compounds of the invention that contain the aforementioned isotopes and/or other isotopes of other atoms are within the scope of the present invention. Isotopically-labeled compounds of the present invention, for example those into which radioactive isotopes such as ^3H , ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution assays.

Tritiated, i.e., ^3H , and carbon- 14, i.e., ^{14}C , isotopes are particularly preferred for their ease of preparation and detectability. ^{11}C and ^{18}F isotopes are particularly useful in PET (positron emission tomography), and ^{123}I isotopes are particularly useful in SPECT (single photon emission computerized tomography), all useful in brain imaging.

Further, substitution with heavier isotopes such as deuterium, i.e., ^2H , can afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements and, hence, may be preferred in some circumstances. Isotopically labeled compounds of the invention can generally be prepared by carrying out the procedures disclosed in the Schemes and/or in the Examples below, then substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent.

[0084] With respect to other compounds disclosed in the art, certain compounds exhibit unexpected properties, such as with respect to duration of action and/or metabolism, such as favorable metabolic stability, favorable oral bioavailability or absorption, and/or decreased drug-drug interactions.

[0085] A skilled physician will be able to determine the appropriate situation in which subjects are susceptible to or at risk of, for example, stroke as well as suffering from stroke for administration by methods of the present invention.

[0086] CRHR1 and/or CRHR2 have been implicated in a wide range of biological functions. This has suggested a potential role for these receptors in a variety of disease processes in humans or other species. The compounds of the present invention have utility in treating, preventing, ameliorating, controlling or reducing the risk of a variety of disorders associated with CRHR1 and/or CRHR2, including one or more of the following conditions or diseases: gastrointestinal disorders, major depressive disorders, schizophrenic disorders, neurodegenerative diseases, pain, dysfunction of appetite and food intake, sleep disorders, cognitive disorders, tolerance to and dependence on a number of substances, inflammation, fertility problems, sexual dysfunctions and pre-term birth and non-inflammatory urogenital disorders, allergic disorders, mast cell activation disorders, Cushing's syndrome, emesis, gastrointestinal disorders, neurotoxic injury, loss of hair, heart failure, and the like.

[0087] The dosage of active ingredient in the compositions of this invention may be varied, however, it is necessary that the amount of the active ingredient be such that a suitable

dosage form is obtained. The active ingredient may be administered to patients (animals and human) in need of such treatment in dosages that will provide optimal pharmaceutical efficacy.

[0088] The selected dosage depends upon the desired therapeutic effect, on the route of administration, and on the duration of the treatment. The dose will vary from patient to patient depending upon the nature and severity of disease, the patient's weight, special diets then being followed by a patient, concurrent medication, and other factors which those skilled in the art will recognize.

[0089] For administration to human patients, the total daily dose of the compounds of the invention is typically in the range of 0.1 mg to 1000 mg depending, of course, on the mode of administration. For example, oral administration may require a total daily dose of from 1 mg to 1000 mg, while an intravenous dose may only require from 0.1 mg to 100 mg. The total daily dose may be administered in single or divided doses and may, at the physician's discretion, fall outside of the typical range given herein.

[0090] These dosages are based on an average human subject having a weight of about 60 kg to 70 kg. The physician will readily be able to determine doses for subjects whose weight falls outside this range, such as infants and the elderly.

[0091] In one embodiment, the dosage range will be about 0.5 mg to 500 mg per patient per day; in another embodiment about 0.5 mg to 200 mg per patient per day; in another embodiment about 1 mg to 100 mg per patient per day; and in another embodiment about 5 mg to 50 mg per patient per day; in yet another embodiment about 1 mg to 30 mg per patient per day. Pharmaceutical compositions of the present invention may be provided in a solid dosage formulation such as comprising about 0.5 mg to 500 mg active ingredient, or comprising about 1 mg to 250 mg active ingredient. The pharmaceutical composition may be provided in a solid dosage formulation comprising about 1 mg, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg, 200 mg or 250 mg active ingredient. For oral administration, the compositions may be provided in the form of tablets containing 1.0 to 1000 milligrams of the active ingredient, such as 1, 5, 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 400, 500, 600, 750, 800, 900, and 1000 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. The compounds may be administered on a regimen of 1 to 4 times per day, such as once or twice per day.

[0092] Compounds of the present invention may be used in combination with one or more other drugs in the treatment, prevention, control, amelioration, or reduction of risk of diseases or conditions for which compounds of the present invention or the other drugs may have utility, where the combination of the drugs together are safer or more effective than either drug alone. Such other drug(s) may be administered, by a route and in an amount commonly used therefore, contemporaneously or sequentially with a

compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition in unit dosage form containing such other drugs and the compound of the present invention is envisioned. However, the combination therapy may also include therapies in which the compound of the present invention and one or more other drugs are administered on different overlapping schedules. It is also contemplated that when used in combination with one or more other active ingredients, the compounds of the present invention and the other active ingredients may be used in lower doses than when each is used singly.

[0093] Accordingly, the pharmaceutical compositions of the present invention include those that contain one or more other active ingredients, in addition to a compound of the present invention. The above combinations include combinations of a compound of the present invention not only with one other active compound, but also with two or more other active compounds.

[0094] Likewise, compounds of the present invention may be used in combination with other drugs that are used in the prevention, treatment, control, amelioration, or reduction of risk of the diseases or conditions for which compounds of the present invention are useful. Such other drugs may be administered, by a route and in an amount commonly used therefore, contemporaneously or sequentially with a compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition containing such other drugs in addition to the compound of the present invention is envisioned. Accordingly, the pharmaceutical compositions of the present invention include those that also contain one or more other active ingredients, in addition to a compound of the present invention.

[0095] The weight ratio of the compound of the present invention to the second active ingredient may be varied and will depend upon the effective dose of each ingredient. Generally, an effective dose of each will be used. Thus, for example, when a compound of the present invention is combined with another agent, the weight ratio of the compound of the present invention to the other agent will generally range from about 1000:1 to about 1:1000, including about 200: 1 to about 1:200. Combinations of a compound of the present invention and other active ingredients will generally also be within the aforementioned range, but in each case, an effective dose of each active ingredient should be used. In such combinations the compound of the present invention and other active agents may be administered separately or in conjunction. In addition, the administration of one element may be prior to, concurrent to, or subsequent to the administration of other agent(s).

[0096] A CRHR1 and CRHR2 antagonist may be usefully combined with another pharma-

cologically active compound, or with two or more other pharmacologically active compounds, particularly in the treatment of inflammatory, pain and urological diseases or disorders. For example, a CRHR1 and CRHR2 antagonist, particularly a compound of formula (I) and (II), or a prodrug thereof or a pharmaceutically acceptable salt or solvate thereof, as defined above, may be administered simultaneously, sequentially or separately in combination with one or more agents selected from:

- [0097] - an opioid analgesic, e.g. morphine, heroin, hydromorphone, oxymorphone, lev-orphanol, levallorphan, methadone, meperidine, fentanyl, cocaine, codeine, dihydrocodeine, oxycodone, hydrocodone, propoxyphene, nalmefene, nalorphine, naloxone, naltrexone, buprenorphine, butorphanol, nalbuphine, or pentazocine;
- [0098] - a nonsteroidal antiinflammatory drug (NSAID), e.g. aspirin, diclofenac, diflunisal, etodolac, fenbufen, fenoprofen, flufenisal, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamic acid, mefenamic acid, meloxicam, nabumetone, naproxen, nimesulide, nitroflurbiprofen, olsalazine, oxaprozin, phenylbutazone, piroxicam, sulfasalazine, sulindac, tolmetin, or zomepirac;
- [0099] - a barbiturate sedative, e.g. amobarbital, aprobarbital, butabarbital, butalbital, methobarbital, metharbital, methohexital, pentobarbital, phenobarbital, secobarbital, talbutal, thiamylal, or thiopental;
- [0100] - a benzodiazepine having a sedative action, e.g. chlordiazepoxide, clorazepate, diazepam, flurazepam, lorazepam, oxazepam, temazepam, or triazolam;
- [0101] - an H1 antagonist having a sedative action, e.g. diphenhydramine, pyrilamine, promethazine, chlorpheniramine, or chlorcyclizine;
- [0102] - a sedative such as glutethimide, meprobamate, methaqualone, or dichloralphenazone;
- [0103] - a skeletal muscle relaxant, e.g. baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, methocarbamol, or orphenadrine;
- [0104] - an NMDA receptor antagonist, e.g. dextromethorphan ((+)-3-hydroxy-N-methylmorphinan) or its metabolite dextrorphan ((+)-3-hydroxy-N-methylmorphinan), ketamine, memantine, pyrroloquinoline quinone, cis-4-(phosphonomethyl)-2-piperidinecarboxylic acid, budipine, EN-3231 (MorphiDex (registered trademark), a combination formulation of morphine and dextromethorphan), topiramate, neramexane or perzinfotel including an NR2B antagonist, e.g. ifenprodil, traxoprodil, or (-)-(R)-6-{2-[4-(3-fluorophenyl)-4-hydroxy-1-piperidinyl]-1-hydroxyethyl}-3, 4-dihydro-2(1H)-quinolinone ;
- [0105] - an alpha-adrenergic, e.g. doxazosin, tamsulosin, clonidine, guanfacine, dexmedetomidine, modafinil, or 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5

- (2-pyridyl)quinazoline ;
- [0106] - a tricyclic antidepressant, e.g. desipramine, imipramine, amitriptyline, or nortriptyline;
- [0107] - an anticonvulsant, e.g. carbamazepine, lamotrigine, topiramate, or valproate;
- [0108] - a tachykinin (NK) antagonist, particularly an NK-3, NK-2 or NK-1 antagonist, e.g. (alphaR,9R)-7-[3,5-bis(trifluoromethyl)benzyl]-8,9,10,11-tetrahydro-9-methyl-5-(4-methylphenyl)-7H-[1,4]diazocino[2,1-g][1,7]-naphthyridine-6, 13-dione (TAK-637), 5-[[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy-3-(4-fluorophenyl)-4-morpholinyl]-methyl]-1,2-dihydro-3H-1,2,4-triazol-3-one (MK-869), aprepitant, lanepitant, dapitant, or 3-[[2-methoxy-5-(trifluoromethoxy)phenyl]-methylamino]-2-phenylpiperidine (2S,3S);
- [0109] - a muscarinic antagonist, e.g. oxybutynin, tolterodine, propiverine, trospium chloride, darifenacin, solifenacin, temiverine, or ipratropium;
- [0110] - a COX-2 selective inhibitor, e.g. celecoxib, rofecoxib, parecoxib, valdecoxib, deracoxib, etoricoxib, or lumiracoxib;
- [0111] - a coal-tar analgesic, e.g. paracetamol;
- [0112] - a neuroleptic such as droperidol, chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine, fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonopiprazole, bionanserin, iloperidone, perospirone, raclopride, zotepine, bifeprunox, asenapine, lurasidone, amisulpride, balaperidone, palindore, eplivanserin, osanetant, rimonabant, meclizine, Miraxion (registered trademark), or sarizotan;
- [0113] - a vanilloid receptor agonist (e.g. resiniferatoxin) or antagonist (e.g. capsazepine);
- [0114] - a transient receptor potential cation channel subtype (VI, V2, V3, V4, M8, M2, A1) agonist or antagonist;
- [0115] - a beta-adrenergic such as propranolol;
- [0116] - a local anaesthetic such as mexiletine;
- [0117] - a corticosteroid such as dexamethasone;
- [0118] - a 5-HT receptor agonist or antagonist, particularly a 5-HT1B/1D agonist such as eletriptan, sumatriptan, naratriptan, zolmitriptan, or rizatriptan;
- [0119] - a 5-HT2A receptor antagonist such as R(+)-alpha-(2,3-dimethoxy-phenyl)-1-[2-(4-fluorophenylethyl)]-4-piperidinemethanol (MDL- 100907);
- [0120] - a cholinergic (nicotinic) analgesic, such as ispronicline (TC-1734), (E)-N-methyl-4-(3-pyridinyl)-3-buten- 1-amine (RJR-2403), (R)-5-(2-azetidylmethoxy)-2-chloropyridine (ABT-594), or nicotine;
- [0121] - Tramadol (registered trademark);
- [0122] - a PDEV inhibitor, such as

- 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (sildenafil),
 (6R, 12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',r:6,l]pyrido[3,4-b]indole-1,4-dione (IC-351 or tadalafil),
 2-[2-ethoxy-5-(4-ethyl-piperazin-1-yl-sulphonyl)phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one (vardenafil),
 5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidiny)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one,
 5-(5-acetyl-2-propoxy-3-pyridinyl)-3-ethyl-2-(1-isopropyl-3-azetidiny)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one,
 5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one,
 4-[(3-chloro-4-methoxybenzyl)amino]-2-[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]-N-(pyrimidin-2-ylmethyl)pyrimidine-5-carboxamide, or
 3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-N-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-propoxybenzenesulfonamide;
- [0123] - an alpha-2-delta ligand such as gabapentin, pregabalin, 3-methylgabapentin, (3-(aminomethyl)bicyclo[3.2.0]hept-3-yl)acetic acid, (3S,5R)-3-(aminomethyl)-5-methylheptanoic acid, (3S,5R)-3-amino-5-methylheptanoic acid, (3S,5R)-3-amino-5-methyloctanoic acid, (2S,4S)-4-(3-chlorophenoxy)proline, (2S,4S)-4-(3-fluorobenzyl)proline, [(1R,5R,6S)-6-(aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid, 3-((1-(aminomethyl)cyclohexyl)methyl)-4H-[1,2,4]oxadiazol-5-one, C-[1-((1H-tetrazol-5-yl)methyl)cycloheptyl]methylamine, (3S,4S)-3-(1-(aminomethyl)-3,4-dimethylcyclopentyl)acetic acid, (3S,5R)-3-(aminomethyl)-5-methyloctanoic acid, (3S,5R)-3-amino-5-methylnonanoic acid, (3S,5R)-3-amino-5-methyloctanoic acid, (3R,4R,5R)-3-amino-4,5-dimethylheptanoic acid, or (3R,4R,5R)-3-amino-4,5-dimethyloctanoic acid;
- [0124] - a cannabinoid;
- [0125] - a metabotropic glutamate subtype 1 receptor (mGluR1) antagonist;
- [0126] - a serotonin reuptake inhibitor such as sertraline, sertraline metabolite desmethylsertraline, fluoxetine, norfluoxetine (fluoxetine desmethyl metabolite), fluvoxamine, paroxetine, citalopram, citalopram metabolite desmethylcitalopram, escitalopram, d,l-fenfluramine, femoxetine, ifoxetine, cyanodothiepin, litoxetine, dapoxetine, nefazodone, cericlamine, or trazodone;
- [0127] - a noradrenaline (norepinephrine) reuptake inhibitor, such as maprotiline, lofepramine, mirtazapine, oxaprotiline, fezolamine, tomoxetine, mianserin, bupropion,

- bupropion metabolite hydroxybupropion, nomifensine, or viloxazine (Vivalan (registered trademark)), especially a selective noradrenaline reuptake inhibitor such as reboxetine, in particular (S,S)-reboxetine;
- [0128] - a dual serotonin-noradrenaline reuptake inhibitor, such as venlafaxine, venlafaxine metabolite O-desmethylvenlafaxine, clomipramine, clomipramine metabolite desmethylclomipramine, duloxetine, milnacipran, or imipramine;
- [0129] - an inducible nitric oxide synthase (iNOS) inhibitor such as S-2-[(1-iminoethyl)amino]ethyl-L-homocysteine, S-2-[(1-iminoethyl)amino]ethyl-4,4-dioxo-L-cysteine, S-2-[(1-iminoethyl)amino]ethyl-2-methyl-L-cysteine, (2S,5Z)-2-amino-2-methyl-7-[(1-iminoethyl)amino]-5-heptenoic acid, 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-5-chloro-3-pyridinecarbonitrile; 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-4-chlorobenzonitrile, (2S,4R)-2-amino-4-[[2-chloro-5-(trifluoromethyl)phenyl]thio]-5-thiazolebutanol, 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-6-(trifluoromethyl)-3-pyridinecarbonitrile, 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-5-chlorobenzonitrile, N-[4-[2-(3-chlorobenzylamino)ethyl]phenyl]thiophene-2-carboxamide, or guanidinoethyldisulfide;
- [0130] - an acetylcholinesterase inhibitor such as donepezil;
- [0131] - a prostaglandin E2 subtype 4 (EP4) antagonist such as N-[(2-[4-(2-ethyl-4,6-dimethyl-1H-imidazo[4,5-c]pyridin-1-yl)phenyl]ethyl)amino]carbonyl-4-methylbenzenesulfonamide, or 4-[(1S)-1-([5-chloro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl)amino]ethyl]benzoic acid;
- [0132] - a leukotriene B4 antagonist; such as 1-(3-biphenyl-4-ylmethyl-4-hydroxy-chroman-7-yl)-cyclopentanecarboxylic acid (CP-105696), 5-[2-(2-Carboxyethyl)-3-[6-(4-methoxyphenyl)-5E-hexenyl]oxyphenoxy]-valeric acid (ONO-4057), or DPC-11870,
- [0133] - a 5-lipoxygenase inhibitor, such as zileuton, 6-[(3-fluoro-5-[4-methoxy-3,4,5,6-tetrahydro-2H-pyran-4-yl])phenoxy-methyl]-1-methyl-2-quinolone (ZD-2138), or 2,3,5-trimethyl-6-(3-pyridylmethyl)-1,4-benzoquinone (CV-6504);
- [0134] - a sodium channel blocker, such as lidocaine;
- [0135] - a calcium channel blocker, such as ziconotide, zonisamide, or mibefradil;
- [0136] - a 5-HT3 antagonist, such as ondansetron;
- a chemotherapy drug such as oxaliplatin, 5-fluorouracil, leucovorin, or paclitaxel;

- a calcitonin gene related peptide (CGRP) antagonist;
- a bradykinin (BK1 and BK2) antagonist;
- a voltage gated sodium dependent channel blocker ($\text{Na}_{v1.7}$, $\text{Na}_{v1.8}$);
- a voltage dependent calcium channel blocker (N-type, T-type);
- a P2X (ion channel type ATP receptor) antagonist;
- an acid-sensing ion channel (ASIC1a, ASIC3) antagonist;
- an angiotensin-converting enzyme (ACE) inhibitors, such as AT2 antagonist;
- an Angiotensin receptor blockers (ARBs);
- a direct renin inhibitors (DRIs);
- mineralocorticoid receptor antagonists (MRAs);
- funny channel (If channel) inhibitor, such as ivabradine;
- a Chemokine CCR2B receptor antagonist;
- a Cathepsin (B, S, K) inhibitor;
- a sigma 1 receptor agonist or antagonist;
- cardiac sarcomere modulators, such as omecamtiv mecarbil (OM), or MYK-491, Mavacamten,
- soluble guanylate cyclase (sGC) stimulators, such as vericiguat,
- apelin receptor agonists,
- a drugs for heart failure, such as Entresto (registered trademark) which is a combination of sacubitril and valsartan,

[0137] or the pharmaceutically acceptable salts, or the solvates thereof.

[0138] Such combinations offer significant advantages, including synergistic activity, in therapy.

[0139] A pharmaceutical composition of the invention, which may be prepared by admixture, suitably at ambient temperature and atmospheric pressure, is usually adapted for oral, parenteral or rectal administration and, as such, may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, reconstitutable powders, injectable or infusible solutions or suspensions or suppositories. Orally administered compositions are generally preferred. Tablets and capsules for oral administration may be in unit dose form, and may contain conventional excipients, such as binding agents (e.g. pregelatinised maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (e.g. lactose, microcrystalline cellulose or calcium hydrogen phosphate); tableting lubricants (e.g. magnesium stearate, talc or silica); disintegrants (e.g. potato starch or sodium starch glycollate); and acceptable wetting agents (e.g. sodium lauryl sulphate). The tablets may be coated according to methods well known in normal pharmaceutical practice.

[0140] Oral liquid preparations may be in the form of, for example, aqueous or oily suspension, solutions, emulsions, syrups or elixirs, or may be in the form of a dry

product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents (e.g. sorbitol syrup, cellulose derivatives or hydrogenated edible fats), emulsifying agents (e.g. lecithin or acacia), non-aqueous vehicles (which may include edible oils e.g. almond oil, oily esters, ethyl alcohol or fractionated vegetable oils), preservatives (e.g. methyl or propyl-p-hydroxybenzoates or sorbic acid), and, if desired, conventional flavourings or colorants, buffer salts and sweetening agents as appropriate. Preparations for oral administration may be suitably formulated to give controlled release of the active compound or pharmaceutically acceptable salt thereof.

[0141] For parenteral administration, fluid unit dosage forms are prepared utilising a compound of formula (I) or (II) or pharmaceutically acceptable salt thereof and a sterile vehicle. Formulations for injection may be presented in unit dosage form e.g. in ampoules or in multi-dose, utilising a compound of formula (I) or (II) or pharmaceutically acceptable salt thereof and a sterile vehicle, optionally with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilising and/or dispersing agents. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, e.g. sterile pyrogen-free water, before use. The compound, depending on the vehicle and concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions, the compound can be dissolved for injection and filter sterilised before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilisation cannot be accomplished by filtration. The compound can be sterilised by exposure to ethylene oxide before suspension in a sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

[0142] Lotions may be formulated with an aqueous or oily base and will in general also contain one or more emulsifying agents, stabilising agents, dispersing agents, suspending agents, thickening agents, or colouring agents. Drops may be formulated with an aqueous or non-aqueous base also comprising one or more dispersing agents, stabilising agents, solubilising agents or suspending agents. They may also contain a preservative.

[0143] Compounds of formula (I) or (II) or pharmaceutically acceptable salts thereof may also be formulated in rectal compositions such as suppositories or retention enemas,

e.g. containing conventional suppository bases such as cocoa butter or other glycerides.

[0144] Compounds of formula (I) or (II) or pharmaceutically acceptable salts may also be formulated as depot preparations. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds of formula (I) or (II) or pharmaceutically acceptable salts may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[0145] For intranasal administration, compounds formula (I) or (II) or pharmaceutically acceptable salts thereof may be formulated as solutions for administration via a suitable metered or unitary dose device or alternatively as a powder mix with a suitable carrier for administration using a suitable delivery device. Thus compounds of formula (I) or (II) or pharmaceutically acceptable salts thereof may be formulated for oral, buccal, parenteral, topical (including ophthalmic and nasal), depot or rectal administration or in a form suitable for administration by inhalation or insufflation (either through the mouth or nose). The compounds of formula (I) or (II) and pharmaceutically acceptable salts thereof may be formulated for topical administration in the form of ointments, creams, gels, lotions, pack, tape, pessaries, aerosols or drops (e.g. eye, ear or nose drops). Ointments and creams may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agents. Ointments for administration to the eye may be manufactured in a sterile manner using sterilized components.

[0146] General Synthesis

Throughout the instant application, the following abbreviations are used with the following meanings:

[0147] BINAP tri-o-tolylphosphine, triphenylarsine,
 2,2'-bis(diphenylphosphino)- 1,1'-binaphthyl
 Boc tert-Butoxycarbonyl
 JohnPhos 2-(di-tert-butylphosphino)biphenyl
 CDI 1,1'-Carbonyldiimidazole
 CyJohnPhos 2-(dichlorohexylphosphino)biphenyl
 DABCO 1,4-diazabicyclo [2.2.2]octane
 DavePhos 2-(dicyclohexylphosphino)-2'-(dimethylamino)biphenyl
 dba dibenzylidenacetone
 DBN 1,5-diazabicyclo[4.3.0]non-5-ene
 DBU 1,8-Diazabicyclo[5.4.0]undec-7-ene
 DCM Dichloromethane
 DIEA N,N-Diisopropylethylamine

DME 1,2-Dimethoxyethane
 DMEDA N,N'-Dimethylethylenediamine
 DMF N,N-Dimethylformamide
 DMA N,N-Dimethylacetamide
 DMAP N,N-Dimethyl-4-aminopyridine
 DMSO Dimethyl sulfoxide
 EDC 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide Hydrochloride
 ESI Electrospray ionization
 EtOAc Ethyl acetate
 EtOH Ethanol
 Ex Example
 HOBT 1-Hydroxybenzotriazole
 HATU 0-(7-Aza-1H-benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
 HBTU 0-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
 HPLC High-Performance liquid chromatography
 IPE Diisopropyl ether
 Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ [4,4'-bis(1,1-dimethylethyl)-2,2'-bipyridine-N¹,N¹'-bis[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-N]phenyl-C] iridium(III) hexafluorophosphate
 LC Liquid chromatography
 LG Leaving group
 tR Retention time
 MeCN Acetonitrile
 MeOH Methanol
 MHz Megahertz
 Ms Methanesulfonyl
 MS Mass spectrometry
 MS 4A Molecular sieves 4 angstrom
 NMP N-methylpyrrolidone
 NMR Nuclear magnetic resonance
 Pd(dppf)Cl₂ [1,1-Bis(diphenylphosphino)ferrocene]dichloropalladium(II)
 Pd(PPh₃)₄ Tetrakis(triphenylphosphine)palladium(0)
 rt Room temperature
 SFC Supercritical fluid chromatography
 SPhos 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
 tBuXPhos 2-di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl
 T3P (trademark) Propylphosphonic acid anhydride (Cyclic Trimer)

TEA Triethylamine

TFA Trifluoroacetic Acid

THF Tetrahydrofuran

THP Tetrahydropyranyl

TLC Thin layer chromatography

TMEDA N,N,N',N'-tetramethylethylenediamine

TosMIC p-Toluenesulfonylmethyl isocyanide

UV Ultraviolet

XPhos 2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

Xantphos 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene

[0148] The term of "base" is likewise no particular restriction on the nature of the bases used, and any base commonly used in reactions of this type may equally be used here. Examples of such bases include, but not limited to: alkali metal hydroxides, such as lithium hydroxide, sodium hydroxide, potassium hydroxide, potassium phosphate, and barium hydroxide; alkali metal hydrides, such as lithium hydride, sodium hydride, and potassium hydride; alkali metal alkoxides, such as sodium methoxide, sodium ethoxide, and potassium tert-butoxide; alkali metal carbonates, such as lithium carbonate, sodium carbonate, potassium carbonate, and cesium carbonate; alkali metal hydrogencarbonates, such as lithium hydrogencarbonate, sodium hydrogencarbonate, and potassium hydrogencarbonate; amines, such as N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 2,6-di(tert-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, N,N-dimethyl-4-aminopyridine (DMAP), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), lutidine, and colidine; alkali metal amides, such as lithium amide, sodium amide, potassium amide, lithium diisopropyl amide, potassium diisopropyl amide, sodium diisopropyl amide, lithium bis(trimethylsilyl)amide and potassium bis(trimethylsilyl)amide. Of these, triethylamine, diisopropylethylamine, DMAP, DBU, DBN, DABCO, pyridine, lutidine, colidine, sodium carbonate, sodium hydrogencarbonate, sodium hydroxide, potassium carbonate, potassium hydrogencarbonate, potassium hydroxide, potassium phosphate, barium hydroxide, and cesium carbonate are preferred.

[0149] The reactions are normally and preferably effected in the presence of inert solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve reagents, at least to some extent. Examples of suitable solvents include, but not limited to: halogenated hydrocarbons, such as DCM, chloroform, carbon tetrachloride, and dichloroethane; ethers, such as diethyl ether, diisopropyl ether, THF, and

1,4-dioxane; aromatic hydrocarbons, such as benzene, toluene and nitrobenzene; amides, such as, DMF, DMA, and hexamethylphosphoric triamide; amines, such as N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, N,N-dimethylaniline, and N,N-diethylaniline; alcohols, such as methanol, ethanol, propanol, isopropanol, and butanol; nitriles, such as acetonitrile and benzonitrile; sulfoxides, such as dimethyl sulfoxide (DMSO) and sulfolane; ketones, such as acetone and diethylketone. Of these solvents, including but not limited to DMF, DMA, DMSO, THF, diethylether, diisopropylether, dimethoxyethane, acetonitrile, DCM, dichloroethane and chloroform are preferred.

[0150] The invention is illustrated in the following non-limiting examples in which, unless stated otherwise: all reagents are commercially available, all operations are carried out at room or ambient temperature, that is, in the range of about 18-25 °C; microwave reactions are carried out using Biotage Initiator or Biotage Initiator-i; evaporation of solvent is carried out using a rotary evaporator under reduced pressure with a bath temperature of up to about 60 °C; reactions are monitored by thin layer chromatography (TLC) and reaction times are given for illustration only; the structure and purity of all isolated compounds are assured by at least one of the following techniques: TLC (Merck silica gel 60 F₂₅₄ precoated TLC plates or Merck NFL F₂₅₄ precoated HPTLC plates), mass spectrometry or NMR. Yields are given for illustrative purposes only. Flash column chromatography is carried out using Biotage SNAP KP-Sil, Biotage SNAP Isolute NH2, Merck silica gel 60 (230-400 mesh ASTM), Fuji Silysia Chromatorex (registered trademark) NH-DM 1020 and NH-DM2035, Wako Wakogel C300-HG, Yamazen Hi-FLASH column, or YMC DispoPack-SIL. The pre-purification for the HPLC (preparative LC-MS) is carried out using a strong cation exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage), or strong anion exchange cartridge (ISOLUTE (registered trademark) PE-AX, 1 g/6 mL, Biotage). The purification of compounds using HPLC (preparative LC-MS) or SFC (preparative SFC-MS) is performed by the following apparatus and conditions.

[0151] HPLC:

Apparatus: Waters MS-trigger AutoPurification (registered trademark) system
 Column: Waters XBridge C8, 19 mm x 50 mm, 5 micrometer particle or Waters XBridge C18, 19 mm x 50 mm, 5 micrometer particle

Mobile phase 1: (A) 0.05%(v/v) ammonia aqueous solution, (B) MeOH or MeCN
 Mobile phase 2: (A) 0.05%(v/v) formic acid aqueous solution, (B) MeOH or MeCN
 Mobile phase 3: (A) 10 mM ammonium formate aqueous solution, (B) MeCN/water = 90/10(v/v)

Flow rate: 20 mL/min

Gradient: A/B (95/5) to A/B (5/95) in 5 or 7 or 10 min

[0152] SFC:

Apparatus: Waters Prepl5 SFC system with ACQUITY QDa Detector

Column: Waters Torus 2-PIC, 10 mm x 150 mm, 5 micrometer particle; Waters Torus DEA, 10 mm x 150 mm, 5 micrometer particle; Waters Torus DIOL, 10 mm x 150 mm, 5 micrometer particle; Waters Torus I-AA, 10 mm x 150 mm, 5 micrometer particle

Mobile phase: (A) Carbon dioxide (CO₂), (B) MeOH or 10 mM ammonia in MeOH

Flow rate: 15 mL/min

Gradient: A/B (95/5) to A/B (60/40) in 7 or 10 min

Temperature: 40 °C

Pressure: 120 bar (1740 psi)

Mass spectral data (ESI) are obtained by Waters Alliance HPLC system with ZQ mass spectrometer and UV detector. NMR data are determined by 400 MHz (JEOL JNM-ECZ400S) using deuterated chloroform (99.8% D) or dimethylsulfoxide (99.9% D) as solvent unless indicated otherwise, relative to tetramethylsilane (TMS) as internal standard in parts per million (ppm); conventional abbreviations used are: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, etc. Chemical symbols have their usual meanings; M (mol(s) per liter), L(liter(s)), mL (milliliter(s)), g (gram(s)), mg(milligram(s)), mol (moles), mmol (millimoles).

Each prepared compound is generally named by ChemBioDraw (Ultra, version 12.0, CambridgeSoft).

[0153] Conditions for determining HPLC retention time:

[0154] QC Method:

Apparatus: Waters Acquity Ultra Performance LC with PDA Detector and ZQ mass spectrometer

Column: YMC Triart C18, 2.1 x 100 mm, 1.9 micrometer particle

Column Temperature: 60 °C

PDA detection: 200 - 400 nm scan

MS detection: ESI positive/negative mode

Mobile phase:

A: 10 mM ammonium acetate aqueous solution

B: acetonitrile

[0155]

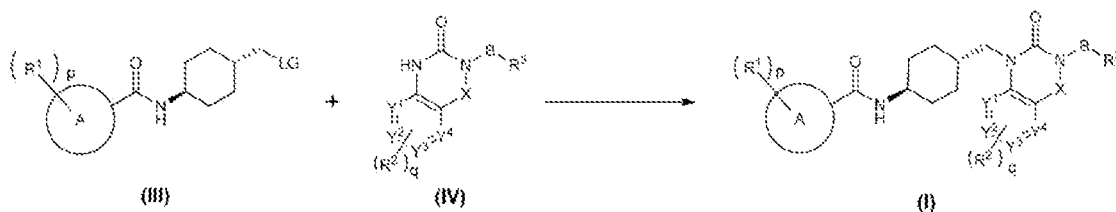
Time(min)	A (%)	B (%)
0	90	10
0.05	90	10
1.9	5	95
2.5	5	95
2.51	90	10
run time		3 min
Flow rate		0.75 mL/min

[0156] All of the compounds of the formula (I) and (II) can be prepared by the procedures described in the general methods presented below or by the specific methods described in the Example synthesis part and Intermediate synthesis part, or by routine modifications thereof. The present invention also encompasses any one or more of these processes for preparing the compound of formula (I) and (II), in addition to any novel intermediates used therein.

[0157] In the following general methods, descriptors (R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , A, B, X, p, q, Y^1 , Y^2 , Y^3 , and Y^4) are as previously defined for the compound of the formula (I) and (II) unless otherwise stated. All starting materials in the following general syntheses may be commercially available or obtained by the conventional methods known to those skilled in the art, otherwise noted in the Intermediate synthesis part.

[0158] <Scheme 1>

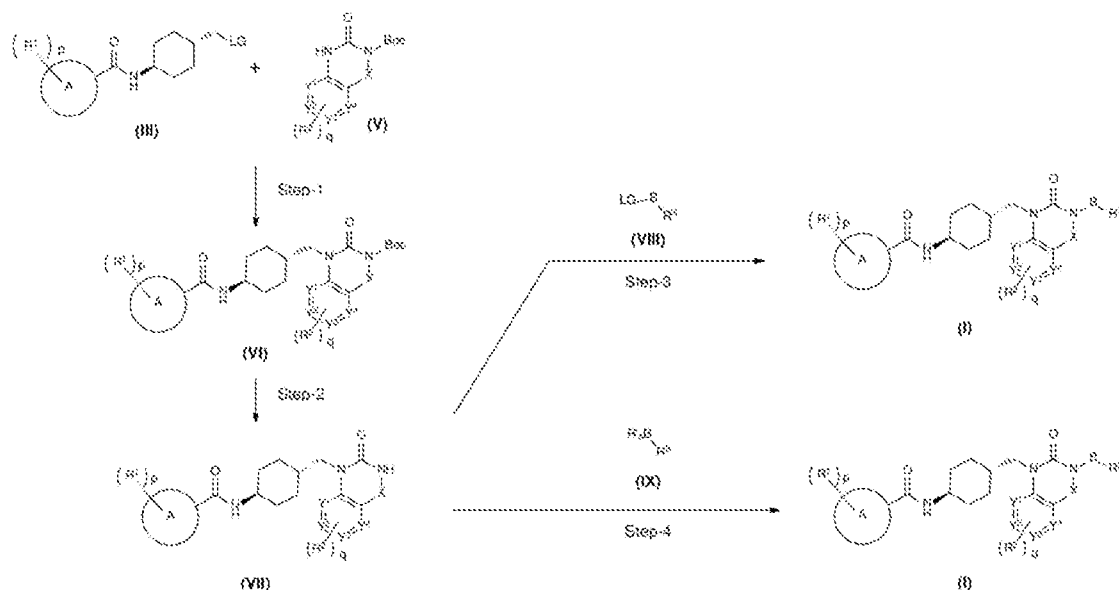
[Chem.5]



[0159] In Scheme 1, a compound of formula (I) can be prepared by the substitution reaction of a compound of formula (III) with a compound of formula (IV) in the presence of a suitable base in an inert solvent. LG is a suitable leaving group such as O-trifluoromethanesulfonate, O-tosylate, O-mesylate, iodide, bromide, chloride, fluoride. Examples of suitable base include, but not limited to, such as sodium hydride, potassium carbonate, cesium carbonate, potassium tert-butoxide, triethyl amine, pyridine, and N,N-diisopropylethylamine. Examples of suitable organic solvent include such as THF, 1,4-dioxane, DMF, DMSO, MeCN, DMA, NMP, toluene. The reaction can be carried out at a temperature from about -20 to 200 °C, more preferably from about 0 to 100 °C. Reaction times are, in general, from about 30 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0160] <Scheme 2>

[Chem.6]



[0161] All compounds in Scheme 2, X is bond.

In Step-1 of Scheme 2, a compound of formula (VI) can be prepared a compound of formula (III) and a compound of formula (V) in the substitution reaction conditions by the similar general protocol in Scheme 1.

In Step-2 of Scheme 2, deprotection of Boc group by usual acidic treatment (for example, hydrogen chloride in 1,4-dioxane, TFA-DCM) to afford a compound of formula (VII).

[0162] In Step-3 of Scheme 2, a compound of formula (I) can be prepared from a compound of formula (VII) and a compound of formula (VIII) by the similar general protocol in Scheme 1.

In Step-3 of Scheme 2, when B is a chemical bond, a compound of formula (I) can be prepared by cross coupling reaction of a compound of formula (VII) with a compound of formula (VIII) under coupling conditions in suitable organic solvents in the presence of a suitable transition metal catalyst and in the presence or absence of a base.

Examples of suitable transition metal catalysts include:

tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) chloride, copper(I), copper(II) acetate, copper(I) bromide, copper(I) chloride, copper(I) iodide, copper(I) oxide, copper(II) trifluoromethanesulfonate, copper(II) acetate, copper(II) bromide, copper(II) chloride, copper(II) iodide, copper(II) oxide, copper(II) trifluoromethanesulfonate, palladium(II) acetate, palladium(II) chloride, bis(acetonitrile)dichloropalladium(II), bis(dibenzylideneacetone)palladium(0), tris(dibenzylideneacetone)dipalladium(0), [1,1'-bis(diphenylphosphino)ferrocene] palladium(II) dichloride and bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II). Preferred

catalysts are tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) chloride, palladium(II) acetate, palladium(II) chloride, bis(acetonitrile)dichloropalladium(0), bis(dibenzylideneacetone)palladium(0), tris(dibenzylideneacetone)dipalladium(0), [1,1-bis(diphenylphosphino)ferrocene]palladium(II) dichloride and bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II). Examples of suitable organic solvent include: THF; 1,4-dioxane; DMF; MeCN; DMSO; DMA; alcohols, such as methanol or ethanol; halogenated hydrocarbons, such as DCM, 1,2-dichloroethane, chloroform or carbon tetrachloride; and diethylether. Example of suitable base include: tripotassium phosphate, sodium bicarbonate, sodium carbonate, cesium carbonate and potassium carbonate. This reaction can be carried out in the presence of a suitable additive agent. Examples of such additive agents include: 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos), triphenylphosphine, tri-tert-butylphosphine, 1,1'-bis(diphenylphosphino)ferrocene, tri-2-furylphosphine, tri-o-tolylphosphine, triphenylarsine, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), 2-(dichlorohexylphosphino)biphenyl (CyJohnPhos), 2-(dicyclohexylphosphino)-2'-(dimethylamino)biphenyl (DavePhos), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (XPhos), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (SPhos), 2-di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl (tBuXPhos), 2-(di-tert-butylphosphino)biphenyl (JohnPhos), N,N'-dimethylethylenediamine (DMEDA), N,N,N',N'-tetramethylethylenediamine (TMEDA), 2,2'-bipyridine, 1,10-phenanthroline. The reaction can be carried out at a temperature from about 50 to 200 °C, more preferably from about 80 to 150 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 30 minutes to 24 hours. In an alternative case, the reaction can be carried out with microwave system. The reaction can be carried out at a temperature in the range from about 100 to 200 °C, preferably in the range from about 120 to 160 °C. Reaction times are, in general, from about 10 minutes to 3 hours, preferably from about 15 minutes to 1 hour.

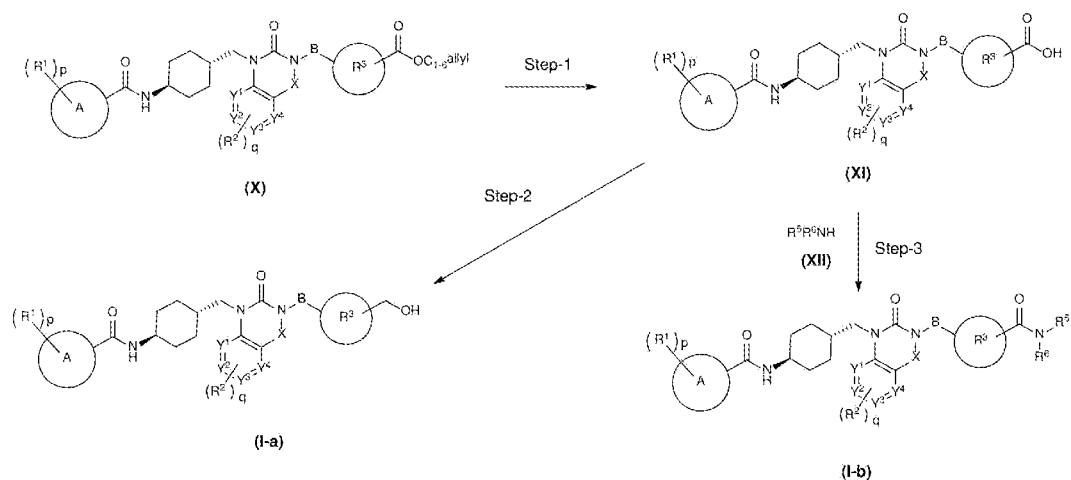
[0163] In Step-4 of Scheme 2, when B is a chemical bond, a compound of formula (I) can be prepared from a compound of formula (VII) and a suitable boronic acid or borate of formula (IX) and a suitable copper salt and in the presence or absence of a base and in the presence or absence of a dehydrating reagent in an inert solvent. In a representation of BR'_s , R' means OH, O-lower alkyl or fluorine, and s is 2 or 3, B is boron atom. As the concrete representation of substituent, $B(OH)_2$, $B(O\text{-lower alkyl})_2$, $B(\text{lower alkyl})_2$, potassium trifluoroborate (BF_3)(BF_3K) are described, but when $B(O\text{-lower alkyl})_2$ may form the cyclic ring between the lower alkyl groups. Example of a suitable copper salt include, copper(0), copper(I) acetate, copper(I) bromide, copper(I) chloride, copper(I)

iodide, copper(I) oxide, copper(II) trifluoromethanesulfonate, copper(II) acetate, copper(II) bromide, copper(II) chloride, copper(II) iodide, copper(II) oxide, copper(II) trifluoromethanesulfonate. Examples of a suitable base include, but not limited to, such as triethyl amine, pyridine, and N,N-diisopropylethylamine. Examples of suitable organic solvent include such as DCM, dichloroethane, MeOH, EtOH, THF, 1,4-dioxane, DMF, MeCN, DMA, toluene. Examples of a suitable dehydrating agent include, but not limited to, such as MS 4A, magnesium sulfate, sodium sulfate. The reaction can be carried out at a temperature from about -20 to 150 °C, more preferably from about 0 to 100 °C. Reaction times are, in general, from about 30 minutes to 7 days, more preferably from about 1 hour to 24 hours.

If a compound of formula (VIII) or (IX) has a protecting group, a deprotecting step is needed to afford a compound of formula (I). The deprotecting step can be carried out by the conventional methods known to those skilled in the art (typical protecting groups described in "Protective Groups in Organic Synthesis Forth Edition" edited by T. W. Greene et al. (John Wiley & Sons, 2007).

[0164] <Scheme 3>

[Chem.7]



[0165] In Scheme 3, a compound of formula (X) can be prepared by the similar general protocol in Scheme 1.

[0166] In Step-1 of Scheme 3, a compound of formula (XI) can be prepared by the hydrolysis of a compound of formula (X). The hydrolysis can be carried out by the conventional procedures. In a typical procedure, the hydrolysis is conducted under basic conditions, e.g. in the presence of sodium hydroxide, potassium hydroxide or lithium hydroxide. Suitable solvents include, for example: alcohols such as water, methanol, ethanol, propanol, butanol, 2-methoxyethanol, and ethylene glycol; ethers such as THF, DME, and 1,4-dioxane; amides such as DMF and hexamethylphosphoric-triamide; and sulfoxides such as DMSO. Preferred solvents are water, methanol,

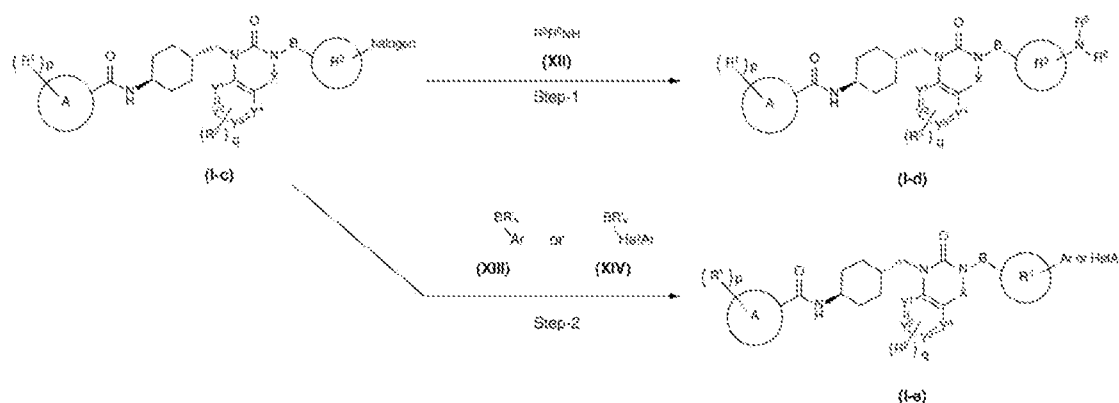
ethanol, propanol, THF, DME, 1,4-dioxane, DMF, and DMSO. This reaction can be carried out at a temperature in the range from about 20 to 100 °C for from about 5 minutes to 24 hours.

[0167] In Step-2 of Scheme 3, a compound of formula (I-a) can be prepared by the reduction of a compound of formula (XI). In a typical procedure, the reduction is conducted by using a reducing agent such as lithium aluminum hydride, borane, lithium borohydride, sodium borohydride in an inert solvent. Suitable solvents include, ethers such as THF, DME, and 1,4-dioxane. This reaction can be carried out at a temperature in the range from about -80 to 100 °C for from about 5 minutes to 24 hours. In an alternative case, before the reduction of a compound of formula (XI) by using sodium borohydride in alcohols (such as water, MeOH, EtOH), a compound of formula (XI) can be reacted with a reagent (such as CDI, isobutyl chloroformate) for activating carboxylic acid moiety in the presence or absence of base (such as TEA, pyridine, DIEA) in an inert solvent (for example, THF, 1,4-dioxane).

[0168] In Step-3 of Scheme 3, a compound of formula (I-b) can be prepared from a compound of formula (XI) by the condensation with a compound of formula (XII) using a suitable condensation reagent such as HBTU, HATU, T3P (registered trademark), EDC, and EDC-HOBT, preferably under the presence of a base such as triethylamine, N,N-diisopropylethylamine, DMAP, DABCO, and DBU in a suitable solvent such as THF, DME, 1,4-dioxane, DMF, DMA, and DCM. This reaction can be carried out at a temperature in the range from about 5 to 60 °C for from about 1 hour to 48 hours.

[0169] <Scheme 4>

[Chem.8]



[0170] In Scheme 4, a compound of formula (I-c) can be prepared by the similar general protocol in Scheme 1.

[0171] In Step-1 of Scheme 4, a compound of formula (I-d) can be prepared from a compound of formula (I-c) and nucleophile (XII) by substitution reaction in the presence of a suitable base in an inert solvent. Examples of a suitable base include, but

not limited to, such as sodium hydride, potassium carbonate, cesium carbonate, potassium tert-butoxide, triethyl amine, pyridine, DBU, and N,N-diisopropylethylamine. Examples of suitable organic solvent include such as THF, 1,4-dioxane, DMF, DMSO, MeCN, DMA, 2-propanol, NMP, toluene. The reaction can be carried out at a temperature from about -20 to 200 °C, more preferably from about 0 to 100 °C. Reaction times are, in general, from about 30 minutes to 48 hours, more preferably from about 1 hour to 24 hours. In an alternative case, the reaction can be carried out with microwave system. The reaction can be carried out at a temperature in the range from about 100 to 300 °C. Reaction times are, in general, from about 10 minutes to 3 hours, preferably from about 15 minutes to 1 hour. As well, when R⁴ is O-substituent (such as -O-C₁₋₆ alkyl, -O-C₃₋₇ cycloalkyl, and -O-heterocyclyl), a compound of formula (II) can be prepared similar manner in Step-1 of Scheme 4 by using suitable alcohol instead of nucleophile (XII).

[0172] In Step-2 of Scheme 4, a compound of formula (I-e) can be prepared by cross coupling reaction of a compound of formula (I-c) with a suitable boronic acid or borate of formula (XIII) and (XIV) in suitable organic solvents and in the presence of a suitable transition metal catalyst and in the presence or absence of a base and in the presence or absence of water. In a representation of BR'_s, R' means OH, O-lower alkyl or fluorine, and s is 2 or 3, B is boron atom. As the concrete representation of substituent, B(OH)₂, B(O-lower alkyl)₂, B(lower alkyl)₂, potassium trifluoroborate (BF₃⁻)(BF₃K) are described, but when B(O-lower alkyl)₂ may form the cyclic ring between the lower alkyl groups. Examples of suitable transition metal catalysts include: tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) chloride, copper(0), copper(I) acetate, copper(I) bromide, copper(I) chloride, copper(I) iodide, copper(I) oxide, copper(II) trifluoromethanesulfonate, copper(II) acetate, copper(II) bromide, copper(II) chloride, copper(II) iodide, copper(II) oxide, copper(II) trifluoromethanesulfonate, palladium(II) acetate, palladium(II) chloride, bis(acetonitrile)dichloropalladium(II), bis(dibenzylideneacetone)palladium(0), tris(dibenzylideneacetone)dipalladium(0), [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride and bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II). Preferred catalysts are tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) chloride, palladium(II) acetate, palladium(II) chloride, bis(acetonitrile)dichloropalladium(0), bis(dibenzylideneacetone)palladium(0), tris(dibenzylideneacetone)dipalladium(0), [1,1-bis(diphenylphosphino)ferrocene]palladium(II) dichloride and bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II). Examples of suitable organic solvent include: THF; 1,4-dioxane; DMF; MeCN; alcohols, such as

methanol or ethanol; halogenated hydrocarbons, such as DCM, 1,2-dichloroethane, chloroform or carbon tetrachloride; and diethyl ether. Example of suitable base include: tripotassium phosphate, sodium bicarbonate, sodium carbonate and potassium carbonate. This reaction can be carried out in the presence of a suitable additive agent. Examples of such additive agents include:

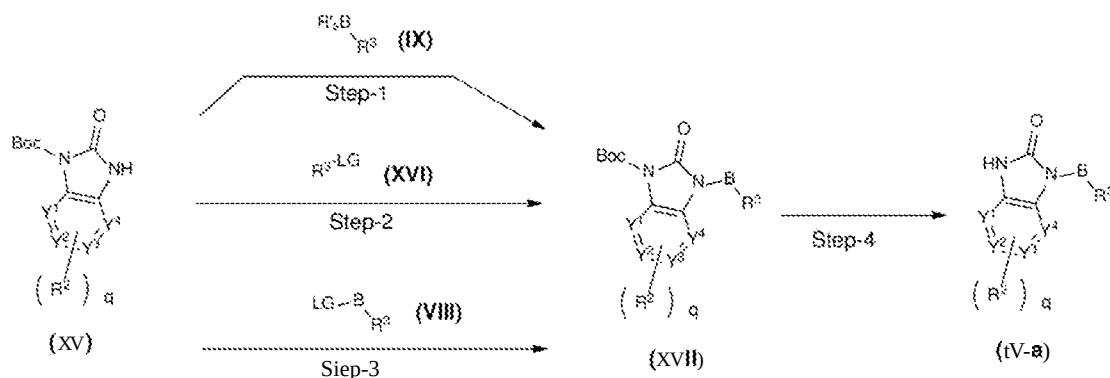
4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene, triphenylphosphine, tri-tert-butylphosphine, 1,1'-bis(diphenylphosphino)ferrocene, tri-2-furylphosphine, tri-o-tolylphosphine, 2-(dichlorohexylphosphino)biphenyl, triphenylarsine. The reaction can be carried out at a temperature from about 50 to 200 °C, more preferably from about 80 to 150 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 30 minutes to 24 hours. In an alternative case, the reaction can be carried out with microwave system. The reaction can be carried out at a temperature in the range from about 100 to 200 °C, preferably in the range from about 120 to 160 °C. Reaction times are, in general, from about 10 minutes to 3 hours, preferably from about 15 minutes to 1 hour.

[0173] As well, when R⁴ is unsaturated substituent (such as alkenyl, cycloalkenyl, partially saturated heterocyclic ring), a compound of formula (I) can be prepared similar manner in Step-2 of Scheme 4. Furthermore, the unsaturated substituent can be transformed to saturated substituent (such as alkyl, cycloalkyl, saturated heterocyclic ring) by a general hydrogenation. A general hydrogenation can be carried out in the presence of a suitable transition metal catalyst under hydrogen atmosphere in suitable organic solvents. Examples of suitable transition metal catalysts include: platinum (IV) oxide, palladium on carbon, palladium-fibroin, palladium hydroxide, ruthenium on carbon. Examples of suitable organic solvent include such as THF, 1,4-dioxane, EtOAc, MeOH, EtOH, DMF, DMSO, MeCN, DMA, toluene. The reaction can be carried out at a temperature from about 0 to 100 °C. Reaction times are, in general, from about 30 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0174] If a compound of formula (XII), (XIII), or (XIV) has a protecting group, deprotecting step is needed to afford a compound of formula (I-d) and (I-e). The deprotecting step can be carried out by the conventional methods known to those skilled in the art (typical protecting groups described in "Protective Groups in Organic Synthesis Forth Edition" edited by T. W. Greene et al. (John Wiley & Sons, 2007).

[0175] <Scheme 5>

[Chem.9]



[0176] In Step-1 of Scheme 5, a compound of formula (XVII) can be prepared from a compound of formula (XV) and a suitable boronic acid or borate of formula (IX) by the similar general protocol in Step 4 of Scheme 2.

[0177] In Step-2 of Scheme 5, when B is a chemical bond, a compound of formula (XVII) can be prepared by cross coupling reaction of a compound of formula (XV) with a compound of formula (XVI) under coupling conditions in suitable organic solvents in the presence of a suitable transition metal catalyst and in the presence or absence of a base. Examples of suitable transition metal catalysts include:

tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) chloride, copper(0), copper(I) acetate, copper(I) bromide, copper(I) chloride, copper(I) iodide, copper(I) oxide, copper(II) trifluoromethanesulfonate, copper(II) acetate, copper(II) bromide, copper(II) chloride, copper(II) iodide, copper(II) oxide, copper(II) trifluoromethanesulfonate, palladium(II) acetate, palladium(II) chloride, bis(acetonitrile)dichloropalladium(II), bis(dibenzylideneacetone)palladium(0), tris(dibenzylideneacetone)dipalladium(0), [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride and

bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II). Preferred catalysts are tetrakis(triphenylphosphine)palladium(0),

bis(triphenylphosphine)palladium(II) chloride, palladium(II) acetate, palladium(II) chloride, bis(acetonitrile)dichloropalladium(0),

bis(dibenzylideneacetone)palladium(0), tris(dibenzylideneacetone)dipalladium(0),

[1,1-bis(diphenylphosphino)ferrocene]palladium(II) dichloride and

bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II). Examples

of suitable organic solvent include: THF; 1,4-dioxane; DMF; DMSO; DMA; MeCN; alcohols, such as methanol or ethanol; halogenated hydrocarbons, such as DCM, 1,2-dichloroethane, chloroform or carbon tetrachloride; and diethylether. Example of suitable base include: tripotassium phosphate, sodium bicarbonate, sodium carbonate, cesium carbonate and potassium carbonate.

[0178] This reaction can be carried out in the presence of a suitable additive agent.

Examples of such additive agents include:

4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos), triphenylphosphine, tri-*tert*-butylphosphine, 1,1'-bis(diphenylphosphino)ferrocene, tri-2-furylphosphine, tri-*o*-tolylphosphine, triphenylarsine, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), 2-(dichlorohexylphosphino)biphenyl (CyJohnPhos), 2-(dicyclohexylphosphino)-2'-(dimethylamino)biphenyl (DavePhos), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (XPhos), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (SPhos), 2-di-*tert*-butylphosphino-2',4',6'-triisopropylbiphenyl (tBuXPhos), 2-(di-*tert*-butylphosphino)biphenyl (JohnPhos), *N,N'*-dimethylethylenediamine (DMEDA), *N,N,N',N'*-tetramethylethylenediamine (TMEDA), 2,2'-bipyridine, 1,10-phenanthroline.

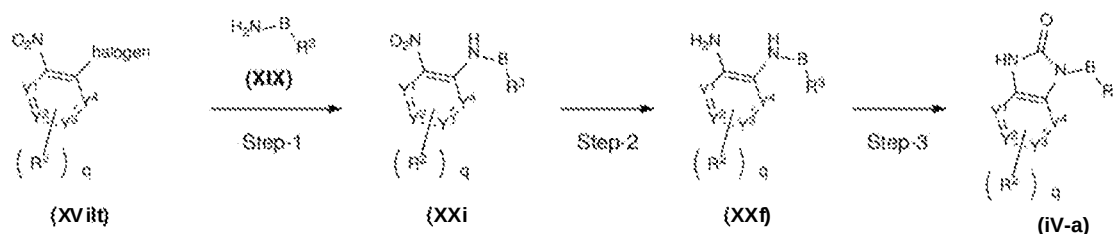
[0179] The reaction can be carried out at a temperature from about 50 to 200 °C, more preferably from about 80 to 150 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 30 minutes to 24 hours. In an alternative case, the reaction can be carried out with microwave system. The reaction can be carried out at a temperature in the range from about 100 to 200 °C, preferably in the range from about 120 to 160 °C. Reaction times are, in general, from about 10 minutes to 3 hours, preferably from about 15 minutes to 1 hour.

[0180] In Step-3 of Scheme 5, a compound of formula (XVII) can be prepared from a compound of formula (XV) and a compound of formula (VIII) by the similar general protocol in Scheme 1.

[0181] In Step-4 of Scheme 5, deprotection of Boc group in a compound of formula (XVII) by usual acidic treatment (for example, hydrogen chloride in 1,4-dioxane, TFA-DCM) to afford a compound of formula (IV).

[0182] <Scheme 6>

[Chem.10]



[0183] In Step-1 of Scheme 6, a compound of formula (XX) can be prepared from a compound of formula (XVIII) and a compound of formula (XIX) by the similar general protocol in Scheme 1. In alternative, a compound of formula (XX) can be prepared from a compound of formula (XVIII) and a compound of formula (XIX) by

the similar general protocol of cross coupling reaction described in Step-2 of Scheme 5.

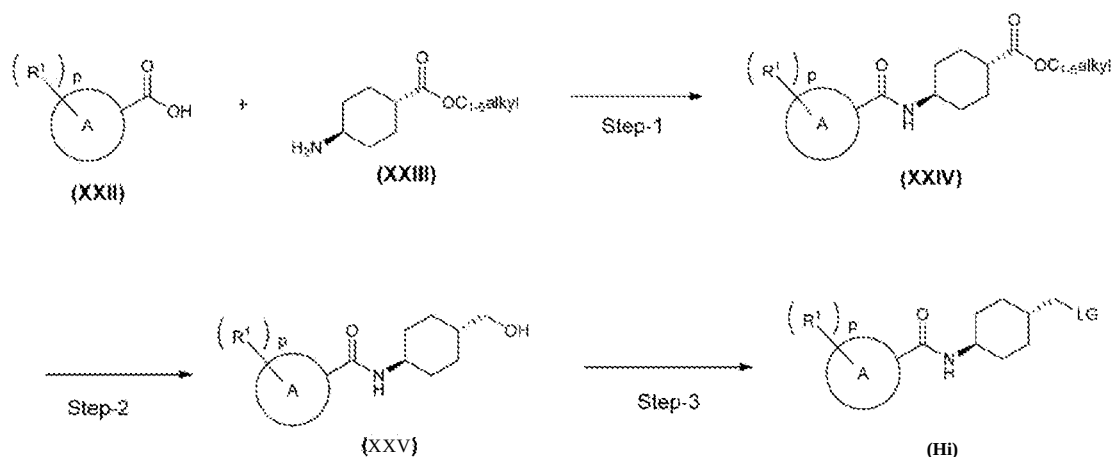
[0184] In Step-2 of Scheme 6, a compound of formula (XXI) can be prepared from a compound of formula (XX) by the similar general hydrogenation described in Step-2 of Scheme 4.

In alternative, a compound of formula (XXI) can be prepared from a compound of formula (XX) and suitable reducing agent (for example, iron, SnCl_2 , zinc, osmium on carbon) and in the presence or absence acid (for example, acetic acid, hydrochloric acid, ammonium chloride) in suitable organic solvents (for example, MeOH, EtOH, water).

[0185] In Step-3 of Scheme 6, a compound of formula (IV-a) can be prepared from a compound of formula (XXI) reacted with CDI, phosgene, diphosgene, triphosgene or N,N'-disuccinimidyl carbonate, in suitable organic solvents in the presence or absence of a base. Examples of a suitable base include, but not limited to, such as triethyl amine, pyridine, DMAP, and N,N-diisopropylethylamine. Examples of suitable organic solvent include such as THF, 1,4-dioxane, DMF, DMSO, MeCN, DMA, toluene, DCM. The reaction can be carried out at a temperature from about -20 to 100 °C, more preferably from about 0 to 50 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0186] <Scheme 7>

[Chem.11]



[0187] In Step-1 of Scheme 7, a compound of formula (XXIV) can be prepared from a compound of formula (XXII) and a compound of formula (XXIII) by the similar general protocol in Step 3 of Scheme 3.

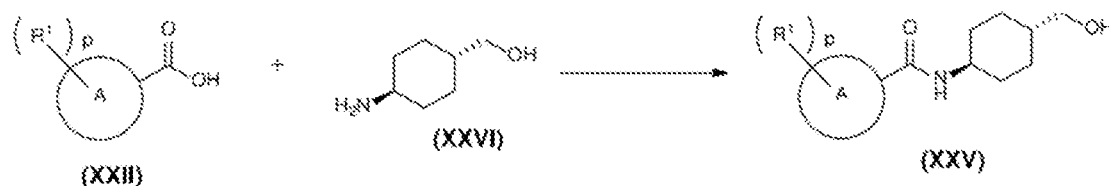
[0188] In Step-2 of Scheme 7, a compound of formula (XXV) can be prepared from a compound of formula (XXIV) by the similar general protocol in Step 2 of Scheme 3.

[0189] In Step-3 of Scheme 7, when LG is O-mesylate, a compound of formula (III) can be prepared by mesylation of a compound of formula (XXV) with Ms_2O or MsCl in

suitable organic solvents in the presence of a base. Examples of a suitable base include, but not limited to, such as sodium hydride, potassium carbonate, cesium carbonate, potassium tert-butoxide, triethyl amine, pyridine, and N,N-diisopropylethylamine. Examples of suitable organic solvent include such as DCM, THF, 1,4-dioxane, DMF, DMSO, MeCN, DMA, toluene. The reaction can be carried out at a temperature from about -20 to 100 °C, more preferably from about 0 to 50 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0190] <Scheme 8>

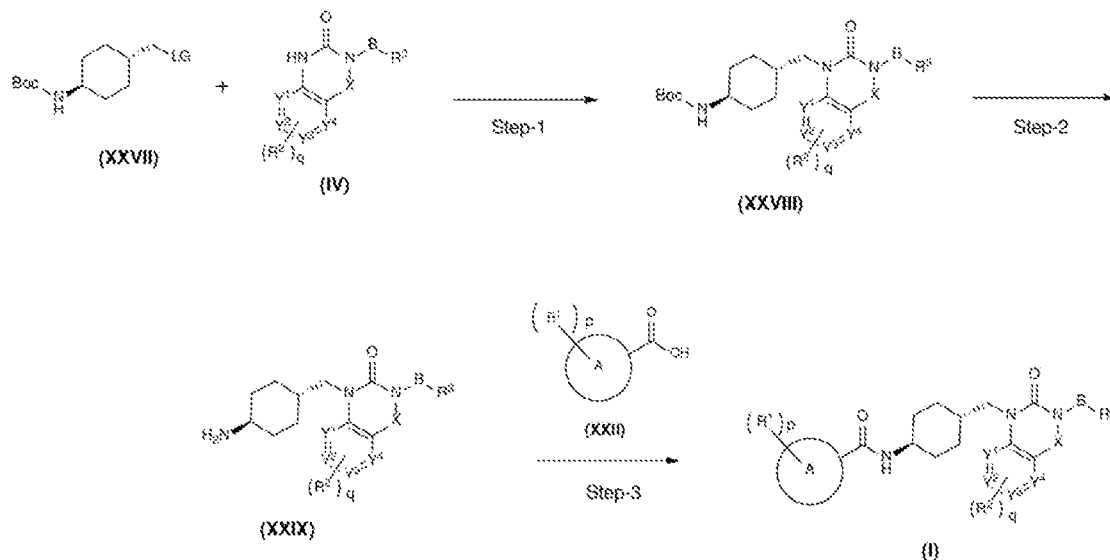
[Chem.12]



[0191] In Scheme 8, a compound of formula (XXV) can be prepared from a compound of formula (XXII) and a compound of formula (XXVI) by the similar general protocol in Step 3 of Scheme 3.

[0192] <Scheme 9>

[Chem.13]



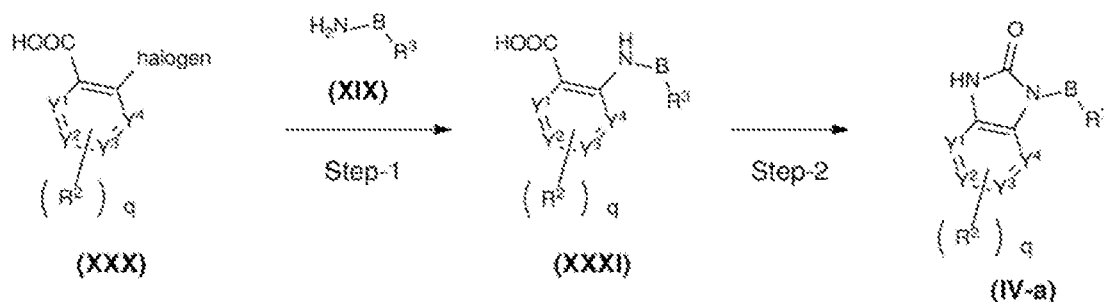
[0193] In Step-1 of Scheme 9, a compound of formula (XXVIII) can be prepared from a compound of formula (XXVII) and a compound of formula (IV) by the similar general protocol in Scheme 1.

[0194] In Step-2 of Scheme 9, deprotection of Boc group by usual acidic treatment (for example, hydrogen chloride in 1,4-dioxane, TFA-DCM) to afford a compound of formula (XXIX).

[0195] In Step-3 of Scheme 9, a compound of formula (I) can be prepared from a compound of formula (XXII) and a compound of formula (XXIX) by the similar general protocol in Step-3 of Scheme 3.

[0196] <Scheme 10>

[Chem.14]

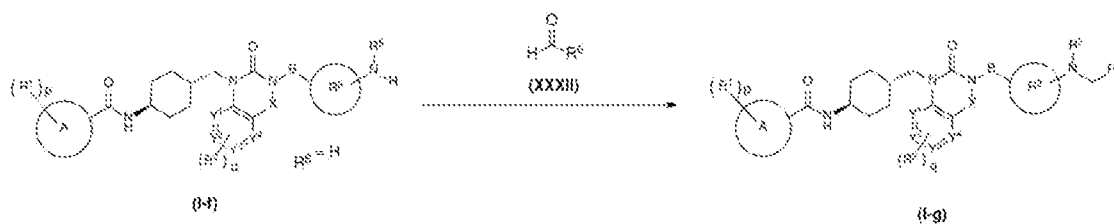


[0197] In Step-1 of Scheme 10, a compound of formula (XXXI) can be prepared from a compound of formula (XXX) and a compound of formula (XIX) by the similar general protocol in Scheme 1. In alternative, a compound of formula (XXXI) can be prepared from a compound of formula (XXX) and a compound of formula (XIX) by the similar general protocol of cross coupling reaction described in Step-2 of Scheme 5. In alternative, a compound of formula (XXXI) can be prepared from a compound of formula (XXX) and a compound of formula (XIX) in the presence or absence of suitable acid in an inert solvent. Example of suitable acid include, but not limited to, p-toluenesulfonic acid, benzenesulfonic acid, acetic acid, TFA. Examples of suitable organic solvent include such as water, THF, 1,4-dioxane, DMF, DMSO, MeCN, DMA, toluene. The reaction can be carried out at a temperature from about -20 to 200 °C, more preferably from about 20 to 100 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0198] In Step-2 of Scheme 10, a compound of formula (IV-a) can be prepared from a compound of formula (XXXI) under Curtius rearrangement conditions. The Curtius rearrangement can be carried out by the conventional procedures. In a typical procedure, the Curtius rearrangement can be conducted by using a suitable reagent such as diphenylphosphoryl azide in the presence or absence suitable base (such as TEA, DIEA, and pyridine) in an inert solvent (such as toluene, THF, and 1,4-dioxane). The reaction can be carried out at a temperature from about -20 to 200 °C, more preferably from about 20 to 100 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0199] <Scheme 11>

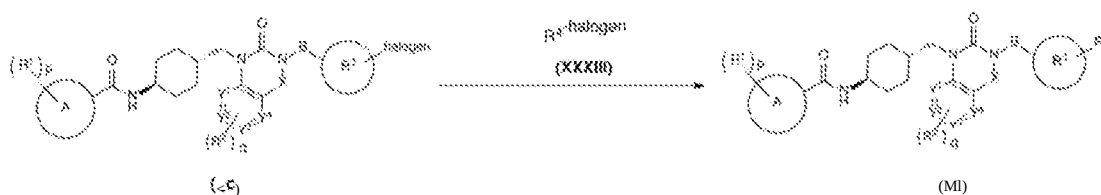
[Chem.15]



[0200] In Scheme 11, a compound of formula (I-g) can be prepared from a compound of formula (I-f) and a compound of formula (XXXII) under reductive amination conditions. The reductive amination can be carried out by the conventional procedures. In a typical procedure, the reductive amination can be conducted by using a suitable reducing reagent such as sodium borohydride, sodium triacetoxyborohydride, and sodium cyanoborohydride in the presence or absence suitable acid (such as acetic acid) in an inert solvent (such as DCM, 1,2-dichloroethane). The reaction can be carried out at a temperature from about -20 to 200 °C, more preferably from about 0 to 30 °C. Reaction times are, in general, from about 5 minutes to 48 hours, more preferably from about 1 hour to 24 hours.

[0201] <Scheme 12>

[Chem.16]

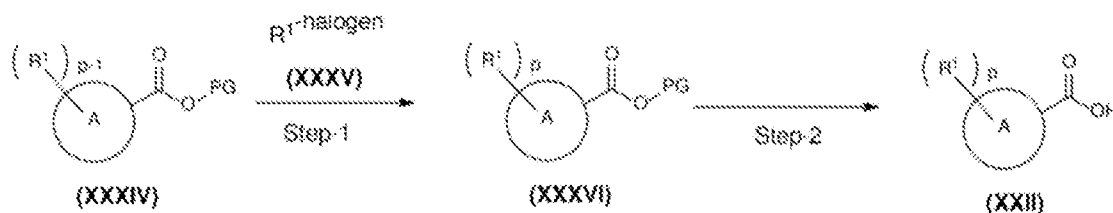


[0202] In Scheme 12, a compound of formula (I-h) can be prepared from a compound of formula (I-c) and a compound of formula (XXXIII) under photochemical reaction conditions. The photochemical reaction can be carried out by the conventional procedures. In a typical procedure, iridium catalyst (such as $\text{Ir}(\text{dF}(\text{CF}_3)\text{ppy})_2(\text{dtbbpy})\text{PF}_6$), nickel catalyst (such as

$\text{NiCl}_2\text{-glyme}$, $\text{Ni}(\text{BF}_4)_2$, nickel(II) acetate, and nickel(II) acetylacetonate), ligand (such as 4,4'-di-*tert*-butyl-2,2'-dipyridine), additive (such as tris(trimethylsilyl) silane), and base (such as 2,6-lutidine, LiOH, and Na_2CO_3) in an inert solvent (such as DME, MeCN, 1,4-dioxane, and DMA) irradiated with Blue LED lamp. The reaction can be carried out at a temperature from about -20 to 100 °C, more preferably from about 10 to 50 °C. Reaction times are, in general, from about 5 minutes to 72 hours, more preferably from about 1 hour to 24 hours.

[0203] <Scheme 13>

[Chem.17]



[0204] In Step-1 of Scheme 13, a compound of formula (XXXVI) can be prepared from a compound of formula (XXIV) and a compound of formula (XXXV) by the similar general protocol in Scheme 12.

[0205] In Step-2 of Scheme 13, a compound of formula (XXII) can be prepared from a compound of formula (XXXVI) by the similar general protocol in Step-1 of Scheme 3.

[0206] Intermediate synthesis part

Each chemical structure of Intermediate synthesis part is described as a free-base.

[0207] Mesylate- 1:

((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methanesulfonate

[0208] <Step-1>: (1r,4r)-methyl 4-(5-chloro-2-methylnicotinamido)cyclohexanecarboxylate

A mixture of 5-chloro-2-methylnicotinic acid (5.23 g, 30.5 mmol), (1r,4r)-methyl 4-aminocyclohexanecarboxylate hydrochloride (5.90 g, 30.5 mmol), HOBT (9.34 g, 61.0 mmol), EDC (11.7 g, 61.0 mmol), and TEA (17 mL, 122 mmol) in DCM (200 mL) is stirred at room temperature overnight. To the mixture is added saturated aqueous sodium bicarbonate. The resultant mixture is extracted with EtOAc. The organic phase is washed with water and brine, dried over MgSO₄, filtered and concentrated in vacuo. The resultant residue is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 8.55 g (90% yield) of the title compound as a white solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.50 (1H, d, J = 2.3 Hz), 7.62 (1H, d, J = 2.7 Hz), 5.57 (1H, d, J = 8.2 Hz), 4.00-3.91 (1H, m), 3.69 (3H, s), 2.62 (3H, s), 2.29 (1H, tt, J = 12.3, 3.6 Hz), 2.21-2.18 (2H, m), 2.11-2.07 (2H, m), 1.68-1.56 (5H, m), 1.28-1.22 (2H, m). MS (ESI) m/z: 311.2 (M+H)⁺.

[0209] <Step-2>: 5-chloro-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2-methylnicotinamide

To a solution of (1r,4r)-methyl

4-(5-chloro-2-methylnicotinamido)cyclohexanecarboxylate (8.55 g, 27.5 mmol, Step-1 of Mesylate- 1) in THF (180 mL) is added lithium aluminum hydride (1.57 g, 41.3 mmol) portion wise at 0 °C. The reaction mixture is stirred at 0 °C. After 1 hr the reaction is quenched with water (150 mL) and Rochelle salt (75 g). The resultant mixture is stirred at room temperature for 1 day. The resultant mixture is extracted with EtOAc, dried over MgSO₄, filtered and concentrated in vacuo to give 7.49 g (96% yield) of the title compound as a white solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.50 (1H, d, J = 2.3 Hz), 7.62 (1H, d, J = 2.3 Hz), 5.58 (1H, d, J = 7.8 Hz), 4.03-3.85 (1H, m), 3.54-3.46 (2H, m), 2.62 (3H, s), 2.22-2.11 (2H, m), 1.96-1.86 (2H, m), 1.60-1.44 (1H, m), 1.35 (1H, br s), 1.31-1.08 (4H, m). MS (ESI) m/z: 283.2 (M+H)⁺.

[0210] <Step-3>: ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methanesulfonate

To a mixture of 5-chloro-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2-methylnicotinamide (10.2 g, 35.9 mmol, Step-2 of Mesylate-1) and TEA (15 mL) in DCM (120 mL) / THF (60 mL) is added portionwise methanesulfonic anhydride (14.1 g, 81 mmol) at room temperature. The mixture is stirred at room temperature for 18 hrs. To the resultant mixture is added methanesulfonic anhydride (3.13 g, 18.0 mmol) and stirred at room temperature. After 1 hr, to the mixture is added methanesulfonic anhydride (3.13 g, 18.0 mmol) and stirred at room temperature. After 1.5 hrs, the reaction is quenched with saturated aqueous sodium bicarbonate (100 mL) and extracted with DCM (3 x 150 mL). The combined organic phase is dried over sodium sulfate, filtered and concentrated in vacuo. The residual solid is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in DCM to give 10.5 g (81% yield) of the title compound as a white solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.50 (1H, d, J = 2.3 Hz), 7.62 (1H, d, J = 2.3 Hz), 5.61 (1H, d, J = 7.8 Hz), 4.07 (2H, d, J = 6.6 Hz), 4.01-3.85 (1H, m), 3.02 (3H, s), 2.62 (3H, s), 2.24-2.15 (2H, m), 1.98-1.89 (2H, m), 1.85-1.71 (1H, m), 1.32-1.18 (4H, m). MS (ESI) m/z: 361.1 (M+H)⁺.

[0211] Mesylate-2:
((1r,4r)-4-(2-ethyl-2H-indazole-3-carboxamido)cyclohexyl)methyl methanesulfonate

[0212] <Step-1>: ethyl 2-ethyl-2H-indazole-3-carboxylate

A mixture of 1H-indazole-3-carboxylic acid (500 mg, 3.08 mmol), iodoethane (1.44 g, 9.25 mmol) in DMSO (5 mL) is stirred at 80 °C for 5 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc:n-hexane (1:1). The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-25% EtOAc in n-hexane to give 265 mg (39% yield) of the title compound as a pale yellow oil.

¹H -NMR (400 MHz, CDCl₃) delta 8.04 (1H, dt, J = 8.7, 1.4 Hz), 7.79 (1H, dt, J = 8.7, 1.4 Hz), 7.32-7.25 (1H, m), 7.38-7.33 (1H, m), 4.96 (2H, q, J = 7.3 Hz), 4.50 (2H, q, J = 7.3 Hz), 1.58 (3H, t, J = 7.3 Hz), 1.51 (3H, t, J = 7.3 Hz). MS (ESI) m/z: 219.4 (M+H)⁺.

[0213] <Step-2>: 2-ethyl-2H-indazole-3-carboxylic acid

A mixture of ethyl 2-ethyl-2H-indazole-3-carboxylate (265 mg, 1.21 mmol, Step-1 of

Mesylate-2) and 2 M aqueous sodium hydroxide solution (2 mL) in THF (1 mL) and MeOH (1 mL) is stirred at 50 °C for 2 hrs. The mixture is acidified with 2 M hydrochloric acid. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 224 mg (97% yield) of the title compound as a yellow solid.

MS (ESI) m/z: 189.3 (M-H)⁻.

[0214] <Step-3>: (1r,4r)-methyl

4-(2-ethyl-2H-indazole-3-carboxamido)cyclohexanecarboxylate

To a mixture of 2-ethyl-2H-indazole-3-carboxylic acid (224 mg, 1.18 mmol, Step-2 of Mesylate-2), (1r,4r)-methyl 4-aminocyclohexanecarboxylate hydrochloride (228 mg, 1.18 mmol), and TEA (0.66 mL, 4.71 mmol) in DCM (2 mL) is added 1.7 M T3P (registered trademark) in EtOAc (1.39 mL, 2.36 mmol) at rt. The mixture is stirred at rt for 1 hr. The mixture is quenched with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 210 mg (54% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.79 (1H, d, J = 8.7 Hz), 7.63 (1H, d, J = 8.7 Hz), 7.38-7.32 (1H, m), 7.28-7.22 (1H, m), 6.00 (1H, br d, J = 7.8 Hz), 4.87 (2H, q, J = 7.3 Hz), 4.12-3.98 (1H, m), 3.70 (3H, s), 2.38-2.24 (3H, m), 2.18-2.09 (2H, m), 1.73-1.53 (2H, m), 1.59 (3H, t, J = 7.3 Hz), 1.42-1.30 (2H, m). MS (ESI) m/z: 330.3 (M+H)⁺.

[0215] <Step-4>:

2-ethyl-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2H-indazole-3-carboxamide

To a mixture of (1r,4r)-methyl 4-(2-ethyl-2H-indazole-3-carboxamido)cyclohexanecarboxylate (210 mg, 0.64 mmol, Step-3 of Mesylate-2) in THF (4 mL) is added lithium aluminum hydride (36 mg, 0.96 mmol) at 0 °C. The mixture is stirred at 0 °C for 1 hr. The mixture is acidified with 2 M hydrochloric acid and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 192 mg (quantitative yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.79 (1H, dd, J = 8.7, 0.9 Hz), 7.65 (1H, dd, J = 8.7, 0.9 Hz), 7.37-7.31 (1H, m), 6.02 (1H, br d, J = 7.8 Hz), 4.87 (2H, q, J = 7.3 Hz), 4.09-3.97 (1H, m), 3.52 (2H, d, J = 5.9 Hz), 2.29-2.22 (2H, m), 1.99-1.91 (2H, m), 1.59 (3H, t, J = 7.3 Hz), 1.60-1.51 (1H, m), 1.41-1.30 (3H, m), 1.27-1.13 (2H, m). MS (ESI) m/z: 302.3 (M+H)⁺.

[0216] <Step-5>: ((1r,4r)-4-(2-ethyl-2H-indazole-3-carboxamido)cyclohexyl)methyl methanesulfonate

To a mixture of

2-ethyl-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2H-indazole-3-carboxamide (192 mg, 0.64 mmol, Step-4 of Mesylate-2) and TEA (0.18 mL, 1.27 mmol) in DCM (3 mL) is added methanesulfonic anhydride (166 mg, 0.96 mmol) at rt. The mixture is stirred at rt for 1 hr. The mixture is quenched with saturated aqueous sodium bicarbonate. The mixture is extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 253 mg (quantitative yield) of the title compound as a pale orange solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.79 (1H, dd, J = 8.7, 0.9 Hz), 7.63 (1H, d, J = 8.7 Hz), 7.38-7.30 (1H, m), 7.29-7.21 (1H, m), 6.02 (1H, d, J = 7.3 Hz), 4.87 (2H, q, J = 7.3 Hz), 4.09 (2H, d, J = 6.4 Hz), 4.05-3.96 (1H, m), 3.03 (3H, s), 2.28 (2H, br d, J = 12.3 Hz), 1.98 (2H, br d, J = 12.3 Hz), 1.91-1.63 (1H, m), 1.59 (3H, t, J = 7.3 Hz), 1.45-1.18 (4H, m). MS (ESI) m/z: 380.2 (M+H)⁺.

[0217] Mesylate-3:

((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate

<Step-1>:

5-chloro-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

A mixture of 5-chloro-2-(trifluoromethyl)nicotinic acid (2.28 g, 6.84 mmol), ((1r,4r)-4-aminocyclohexyl)methanol hydrochloride (1.47 g, 8.89 mmol), HBTU (3.89 g, 10.3 mmol), and TEA (3.81 mL, 27.4 mmol) in DMF (35 mL) is stirred at room temperature overnight. To the mixture is added water. The resultant mixture is extracted with EtOAc (x2). The organic phase is washed with 0.5 M HCl, water, then saturated aqueous sodium bicarbonate. The organic layer is dried over MgSO₄, filtered and concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 30-75% EtOAc in n-hexane to give 1.62 g (70% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, DMSO-d₆) delta 8.87 (1H, d, J = 2.3 Hz), 8.57 (1H, d, J = 7.8 Hz), 8.22 (1H, d, J = 2.3 Hz), 4.40 (1H, t, J = 5.5 Hz), 3.69-3.57 (1H, m), 3.22 (1H, t, J = 5.5 Hz), 1.91 (2H, br d, J = 11.9 Hz), 1.77 (2H, br d, J = 11.9 Hz), 1.38-1.26 (1H, m), 1.29-1.14 (2H, m), 1.03-0.99 (2H, m).

MS (ESI) m/z: 337.4 (M+H)⁺.

[0218] <Step-2>: ((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate

To a mixture of

5-chloro-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

(1.62 g, 4.81 mmol, Step-1 of Mesylate-3) and TEA (2.34 mL, 16.9 mmol) in DCM (10 mL) / THF (20 mL) is added portionwise methanesulfonic anhydride (1.26 g, 7.22 mmol) at 0 °C. The mixture is stirred at room temperature for 1.5 hrs. The mixture is

quenched with saturated aqueous sodium bicarbonate and extracted with DCM (x2). The combined organic phase is dried over MgSO_4 , filtered and concentrated. The residual solid is purified by column chromatography on silica-gel eluting with 10-80% EtOAc in n-hexane to give 1.89 g (95% yield) of the title compound as an off-white solid.

^1H -NMR (400 MHz, CDCl_3) δ 8.69 (1H, d, $J = 2.3$ Hz), 7.89 (1H, d, $J = 2.3$ Hz), 5.64 (1H, d, $J = 7.8$ Hz), 4.07 (2H, d, $J = 6.4$ Hz), 4.00-3.89 (1H, m), 3.02 (3H, s), 2.23-2.14 (2H, m), 1.99-1.88 (2H, m), 1.85-1.68 (1H, m), 1.33-1.15 (4H, m).

MS (ESI) m/z : 415.4 ($\text{M}+\text{H}$) $^+$.

[0219] Mesylate-4:

((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate

<Step-1>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)nicotinamide

A mixture of 5-chloro-2-(difluoromethyl)nicotinic acid (500 mg, 2.41 mmol), ((1r,4r)-4-aminocyclohexyl)methanol hydrochloride (599 mg, 3.61 mmol), HBTU (1.37 g, 3.61 mmol), and TEA (1.68 mL, 12.0 mmol) in DCM (10 mL) is stirred at room temperature overnight. To the mixture is added saturated aqueous sodium bicarbonate. The resultant mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 768 mg (quantitative yield) of the title compound as a pale yellow solid.

^1H -NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.83 (1H, d, $J = 2.3$ Hz), 8.64 (1H, d, $J = 7.8$ Hz), 8.15 (1H, d, $J = 2.3$ Hz), 7.15 (1H, t, $J = 54.0$ Hz), 4.40 (1H, t, $J = 5.5$ Hz), 3.70-3.60 (1H, m), 3.22 (2H, t, $J = 5.5$ Hz), 1.99-1.88 (2H, m), 1.82-1.72 (2H, m), 1.40-1.13 (3H, m), 1.17-0.90 (2H, m).

MS (ESI) m/z : 319.3 ($\text{M}+\text{H}$) $^+$.

[0220] <Step-2>: ((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate

To a mixture of

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)nicotinamide (768 mg, 2.41 mmol, Step-1 of Mesylate-4) and TEA (1.00 mL, 7.23 mmol) in DCM (4 mL) / THF (4 mL) is added portionwise methanesulfonic anhydride (630 mg, 3.61 mmol) at 0 °C. The mixture is stirred at room temperature for 1 hr. The mixture is quenched with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate, filtered and concentrated. The residual solid is purified by column chromatography on silica-gel eluting with 0-60% EtOAc in n-hexane to give 777 mg (81% yield) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.84 (1H, d, J = 2.3 Hz), 8.67 (1H, d, J = 7.8 Hz), 8.16 (1H, d, J = 2.3 Hz), 7.15 (1H, t, J = 54.0 Hz), 4.04 (2H, d, J = 6.4 Hz), 3.75-3.62 (1H, m), 3.17 (3H, s), 1.95 (2H, br d, J = 11.4 Hz), 1.80 (2H, br d, J = 11.4 Hz), 1.72-1.61 (1H, m), 1.36-1.22 (2H, m), 1.18-1.14 (2H, m).

MS (ESI) m/z: 397.2 (M+H)⁺.

[0221] Intermediate- 1:

1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-benzo[d]imidazol-2(3H)-one

[0222] <Step-1>: tert-butyl

2-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

To a mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (100 mg, 0.43 mmol), 4-(iodomethyl)tetrahydro-2H-pyran (193 mg, 0.85 mmol), and cesium carbonate (278 mg, 0.85 mmol) in DMSO (1 mL) is stirred at 80 °C for 5 hrs. The mixture is diluted with water, extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-80% EtOAc in n-hexane to give 113 mg (80% yield) of the title compound as a pale yellow gum.

¹H -NMR (400 MHz, CDCl₃) delta 7.83 (1H, dd, J = 7.8, 0.9 Hz), 7.20 (1H, td, J = 7.8, 0.9 Hz), 7.12 (1H, td, J = 7.8, 0.9 Hz), 6.96 (1H, dd, J = 7.8, 0.9 Hz), 3.97 (2H, dd, J = 11.4, 2.7 Hz), 3.73 (2H, d, J = 7.3 Hz), 3.33 (2H, td, J = 11.9, 2.3 Hz), 2.22-2.08 (1H, m), 1.68 (9H, s), 1.65-1.55 (2H, m), 1.52-1.39 (2H, m). MS (ESI) m/z: 332.9 (M+H)⁺.

[0223] <Step-2>: 1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-benzo[d]imidazol-2(3H)-one

A solution of tert-butyl

2-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (113 mg, 0.34 mmol, Step-1 of Intermediate- 1) in 4 M HCl in 1,4-dioxane (1 mL) is stirred at room temperature for 1 hr. The mixture is concentrated to give 79 mg (quantitative yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 233.0 (M+H)⁺.

[0224] Intermediate-2:

3-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid

[0225] <Step-1>: tert-butyl

3-(3-(methoxycarbonyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 91% yield (372 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate- 1 using methyl 3-(bromomethyl)benzoate in place of 4-(iodomethyl)tetrahydro-2H-pyran.

MS (ESI) m/z: 383.1 (M+H)⁺.

- [0226] <Step-2>: methyl 3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate
The title compound is prepared in quantitative yield (368 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl 3-(3-(methoxycarbonyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (372 mg, 0.97 mmol, Step-1 of Intermediate-2).
¹H -NMR (400 MHz, DMSO-d₆) delta 10.98 (1H, br s), 7.88 (1H, s), 7.83 (1H, d, J = 7.8 Hz), 7.58 (1H, d, J = 7.8 Hz), 7.47 (1H, t, J = 7.8 Hz), 7.03-6.88 (4H, m), 5.06 (2H, s), 3.80 (3H, s). MS (ESI) m/z: 283.2 (M+H)⁺.
- [0227] <Step-3>: methyl 3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate
A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (100 mg, 0.28 mmol, Mesylate-l), methyl 3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate (78 mg, 0.28 mmol, Step-2 of Intermediate-2), and cesium carbonate (181 mg, 0.55 mmol) in DMSO (0.5 mL) is stirred at 80 °C for 2 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 86 mg (57% yield) of the title compound as a yellow gum.
MS (ESI) m/z: 547.2 (M+H)⁺.
- [0228] <Step-4>:
3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid
A mixture of methyl 3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate (86 mg, 0.16 mmol, Step-3 of Intermediate-2) and 2 M aqueous sodium hydroxide solution (0.5 mL) in THF (1 mL) and MeOH (1 mL) is stirred at 50 °C for 2 hrs. The mixture is neutralized with 2 M hydrochloric acid. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 88 mg (quantitative yield) of the title compound as a yellow gum.
MS (ESI) m/z: 533.1 (M+H)⁺.
- [0229] Intermediate- 3:
2-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid
- [0230] <Step-1>: tert-butyl 3-(2-(methoxycarbonyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in quantitative yield (408 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate- 1 using methyl 2-(chloromethyl)benzoate in place of 4-(iodomethyl)tetrahydro-2H-pyran.

¹H -NMR (400 MHz, CDCl₃) delta 8.05 (1H, dd, J = 7.8, 1.8 Hz), 7.88 (1H, dd, J = 7.8, 1.8 Hz), 7.39 (1H, td, J = 7.8, 1.8 Hz), 7.32 (1H, td, J = 7.8, 1.8 Hz), 7.17-7.08 (2H, m), 7.05 (1H, d, J = 7.8 Hz), 6.80 (1H, dd, J = 7.8, 1.8 Hz), 5.54 (2H, s), 3.97 (3H, s), 7.70 (9H, s). MS (ESI) m/z: 383.3 (M+H)⁺.

[0231] <Step-2>: methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate

The title compound is prepared in quantitative yield (301 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl 3-(2-(methoxycarbonyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (408 mg, 1.07 mmol, Step-1 of Intermediate-3).

MS (ESI) m/z: 283.2 (M+H)⁺.

[0232] <Step-3>: methyl

2-(((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate

A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (150 mg, 0.42 mmol, Mesylate-1), methyl

2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate (117 mg, 0.42 mmol, Step-2 of Intermediate-3), and cesium carbonate (271 mg, 0.83 mmol) in DMSO (0.5 mL) is stirred at 80 °C for 2 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 111 mg (49% yield) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.48 (1H, d, J = 2.3 Hz), 8.05 (1H, dd, J = 7.8, 1.8 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.38 (1H, td, J = 7.8, 1.8 Hz), 7.32 (1H, td, J = 7.8, 1.4 Hz), 7.11 (1H, td, J = 7.8, 1.4 Hz), 7.05-6.96 (3H, m), 6.83 (1H, d, J = 7.8 Hz), 5.62 (1H, d, J = 8.2 Hz), 5.55 (2H, s), 3.97 (3H, s), 4.00-3.90 (1H, m), 3.82 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.20-2.10 (2H, m), 2.01-1.83 (3H, m), 1.40-1.14 (4H, m). MS (ESI) m/z: 547.2 (M+H)⁺.

[0233] <Step-4>:

2-(((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid

The title compound is prepared in quantitative yield (108 mg, a pale yellow solid) by the similar manner to Step-4 of Intermediate-2 using methyl

2-(((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate (111 mg, 0.20 mmol, Step-3 of Intermediate-3).

MS (ESI) m/z: 533.2 (M+H)⁺.

[0234] Intermediate-4:

1-(4-fluorophenyl)- 1H-benzo [d]imidazol-2(3H)-one

[0235] <Step-1>: tert-butyl

3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

A mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (150 mg, 0.64 mmol), (4-fluorophenyl)boronic acid (134 mg, 0.96 mmol), MS 4A (150 mg), copper (II) acetate (233 mg, 1.28 mmol), and pyridine (0.16 mL, 1.92 mmol) in DCM (3 mL) is stirred at room temperature for 2 days. The mixture is filtered by using Celite pad. The filtrate is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-25% EtOAc in n-hexane to give 77 mg (37% yield) of the title compound as a pale yellow gum.

MS (ESI) m/z: 329.1 (M+H)⁺.

[0236] <Step-2>: 1-(4-fluorophenyl)- 1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 99% yield (53 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (77 mg, 0.24 mmol, Step-1 of Intermediate-4).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.16 (1H, s), 7.58 (2H, dd, J = 9.2, 5.0 Hz), 7.40 (2H, t, J = 9.2 Hz), 7.09-7.06 (2H, m), 7.05-6.98 (1H, m), 6.98-6.94 (1H, m). MS (ESI) m/z: 229.2 (M+H)⁺.

[0237] Intermediate- 5:

1-(3-fluorophenyl)-1H-benzo[d]imidazol-2(3H)-one

[0238] <Step-1>: tert-butyl

3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 75% yield (105 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using methyl (3-fluorophenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 329.2 (M+H)⁺.

[0239] <Step-2> : 1-(3-fluorophenyl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in 97% yield (71 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (105 mg, 0.43 mmol, Step-1 of Intermediate-5).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.23 (1H, s), 7.65-7.57 (1H, m), 7.48-7.40 (2H, m), 7.29 (1H, td, J = 7.8, 1.8 Hz), 7.11-7.00 (4H, m). MS (ESI) m/z: 229.2 (M+H)⁺.

[0240] Intermediate- 6:

1-(3-acetylphenyl)-1H-benzo[d]imidazol-2(3H)-one

[0241] <Step-1>: tert-butyl

3-(3-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 76% yield (115 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using methyl (3-acetylphenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 353.2 (M+H)⁺.

[0242] <Step-2>: 1-(3-acetylphenyl)- 1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 97% yield (80 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(3-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (115 mg, 0.33 mmol, Step-1 of Intermediate-6).

MS (ESI) m/z: 253.2 (M+H)⁺.

[0243] Intermediate-7:

1-(4-acetylphenyl)-1H-benzo[d]imidazol-2(3H)-one

[0244] <Step-1>: tert-butyl

3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 68% yield (102 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (4-acetylphenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 353.2 (M+H)⁺.

[0245] <Step-2>: 1-(4-acetylphenyl)- 1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 86% yield (63 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (102 mg, 0.29 mmol, Step-1 of Intermediate-7).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.28 (1H, s), 8.13 (2H, d, J = 8.7 Hz), 7.74 (2H, d, J = 8.7 Hz), 7.16-7.00 (4H, m), 2.63 (3H, s). MS (ESI) m/z: 253.2 (M+H)⁺.

[0246] Intermediate- 8:

3-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol- 1-yl)benzoic acid

[0247] <Step-1>: tert-butyl

3-(3-(ethoxycarbonyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 60% yield (98 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (3-(ethoxycarbonyl)phenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 383.1 (M+H)⁺.

[0248] <Step-2>: ethyl 3-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate

The title compound is prepared in 91% yield (66 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(3-(ethoxycarbonyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (98 mg, 0.26 mmol, Step-1 of Intermediate- 8).

MS (ESI) m/z: 283.2 (M+H)⁺.

[0249] <Step-3>: ethyl

3-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate

The title compound is prepared in 69% yield (88 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using ethyl

3-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate (66 mg, 0.23 mmol, Step-2 of Intermediate- 8) in place of methyl

3-(((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 547.2 (M+H)⁺.

[0250] <Step-4>:

3-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoic acid

The title compound is prepared in quantitative yield (88 mg, a pale yellow gum) by the similar manner to Step-4 of Intermediate-2 using ethyl

3-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate (88 mg, 0.16 mmol, Step-3 of Intermediate- 8).

MS (ESI) m/z: 519.1 (M+H)⁺.

[0251] Intermediate-9 :

4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoic acid

[0252] <Step-1>: tert-butyl

3-(4-(methoxycarbonyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 32% yield (51 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (4-(methoxycarbonyl)phenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 369.1 (M+H)⁺.

[0253] <Step-2>: methyl 4-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate

The title compound is prepared in quantitative yield (39 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(4-(methoxycarbonyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (51 mg, 0.14 mmol, Step-1 of Intermediate-9).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.29 (1H, s), 8.14 (2H, d, J = 8.7 Hz), 7.75

(2H, d, J = 8.7 Hz), 7.15 (1H, d, J = 8.2 Hz), 7.14-7.09 (2H, m), 7.08-7.01 (1H, m), 3.90 (3H, s). MS (ESI) m/z: 269.2 (M+H)⁺.

[0254] <Step-3>: methyl

4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate

The title compound is prepared in 49% yield (38 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using methyl

4-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate (39 mg, 0.15 mmol, Step-2 of Intermediate-9) in place of methyl

3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 533.2 (M+H)⁺.

[0255] <Step-4>:

4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoic acid

The title compound is prepared in quantitative yield (37 mg, a pale yellow gum) by the similar manner to Step-4 of Intermediate-2 using methyl

4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate (38 mg, 0.16 mmol, Step-3 of Intermediate-9).

MS (ESI) m/z: 519.1 (M+H)⁺.

[0256] Intermediate- 10:

4-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid

[0257] <Step-1>: tert-butyl

3-(4-(methoxycarbonyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 90% yield (368 mg, a pale yellow solid) by the similar manner to Step-1 of Intermediate- 1 using methyl 4-(bromomethyl)benzoate in place of 4-(iodomethyl)tetrahydro-2H-pyran.

MS (ESI) m/z: 383.3 (M+H)⁺.

[0258] <Step-2>: methyl 3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate

The title compound is prepared in quantitative yield (308 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(4-(methoxycarbonyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (368 mg, 0.96 mmol, Step-1 of Intermediate- 10).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.02 (1H, s), 7.92 (2H, d, J = 8.7 Hz), 7.43 (2H, d, J = 8.7 Hz), 7.03-6.90 (4H, m), 5.09 (2H, s), 3.83 (3H, s). MS (ESI) m/z: 283.2 (M+H)⁺.

[0259] <Step-3>: methyl

4-((3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)benzoate

The title compound is prepared in 77% yield (88 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using methyl

4-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoate (59 mg, 0.21 mmol, Step-2 of Intermediate- 10) in place of methyl

3-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) *m/z*: 547.2 (M+H)⁺.

[0260] <Step-4>:

4-((3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)benzoic acid

The title compound is prepared in quantitative yield (88 mg, a pale yellow gum) by the similar manner to Step-4 of Intermediate-2 using methyl

4-((3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)benzoate (88 mg, 0.16 mmol, Step-3 of Intermediate- 10).

MS (ESI) *m/z*: 533.2 (M+H)⁺.

[0261] Intermediate- 11:

1-(6-(trifluoromethyl)pyridin-3-yl)-1*H*-benzo[d]imidazol-2(3*H*)-one

[0262] <Step-1>: tert-butyl

2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1*H*-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 25% yield (40 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (6-(trifluoromethyl)pyridin-3-yl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) *m/z*: 380.1 (M+H)⁺.

[0263] <Step-2>: 1-(6-(trifluoromethyl)pyridin-3-yl)-1*H*-benzo[d]imidazol-2(3*H*)-one

The title compound is prepared in 92% yield (27 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1*H*-benzo[d]imidazole-1-carboxylate (40 mg, 0.11 mmol, Step-1 of Intermediate- 11).

MS (ESI) *m/z*: 280.1 (M+H)⁺.

[0264] Intermediate- 12:

1-(6-methoxypyridin-3-yl)-1*H*-benzo[d]imidazol-2(3*H*)-one

[0265] <Step-1>: tert-butyl

3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 31% yield (45 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using

2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 342.1 (M+H)⁺.

[0266] <Step-2>: 1-(6-methoxypyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield (36 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl 2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (45 mg, 0.13 mmol, Step-1 of Intermediate- 12).

MS (ESI) m/z: 242.3 (M+H)⁺.

[0267] Intermediate- 13:

1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0268] <Step-1>: 6-methyl-N-(2-nitrophenyl)pyridin-3-amine

To a mixture of 1-fluoro-2-nitrobenzene (250 mg, 1.77 mmol) and 6-methylpyridin-3-amine (192 mg, 1.77 mmol) in THF (3 mL) is added sodium hydride (60% dispersion in mineral oil, 142 mg, 3.54 mmol) at room temperature. The mixture is stirred at room temperature for 1 day. The mixture is diluted with saturated aqueous ammonium chloride. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 170 mg (42% yield) of the title compound as a brown gum.

MS (ESI) m/z: 230.3 (M+H)⁺.

[0269] <Step-2>: N¹-(6-methylpyridin-3-yl)benzene-1, 2-diamine

A mixture of 6-methyl-N-(2-nitrophenyl)pyridin-3-amine (170 mg, 0.74 mmol, Step-1 of Intermediate- 13) and palladium-fibroin (20 mg, purchased from WAKO) in THF (2 mL) and MeOH (2 mL) is stirred at room temperature for 1 day under hydrogen atmosphere. Palladium-fibroin and solvent are removed to give 148 mg (quantitative yield) of the title compound as a brown gum.

MS (ESI) m/z: 200.3 (M+H)⁺.

[0270] <Step-3> : 1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of N¹-ib-methylpyridin-3-ylbenzene-1, 2-diamine (148 mg, 0.74 mmol, Step-2 of Intermediate- 13) and CDI (164 mg, 1.17 mmol) in 1,4-dioxane (3 mL) is stirred at room temperature for 3 hrs. The mixture is diluted with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 135 mg (81% yield) of the title compound as a brown solid.

MS (ESI) m/z: 226.3 (M+H)⁺.

[0271] Intermediate- 14:

1-(2,6-dimethylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0272] <Step-1>: 2,6-dimethyl-N-(2-nitrophenyl)pyridin-3-amine

The title compound is prepared in 12% yield (52 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate- 13 using 2,6-dimethylpyridin-3-amine in place of 6-methylpyridin-3-amine.

MS (ESI) m/z: 244.3 (M+H)⁺.

[0273] <Step-2>: N¹-(2,6-dimethylpyridin-3-yl)benzene-1, 2-diamine

The title compound is prepared in quantitative yield (45 mg, a brown gum) by the similar manner to Step-2 of Intermediate- 13 using 2,6-dimethyl-N-(2-nitrophenyl)pyridin-3-amine (52 mg, 0.21 mmol, Step-1 of Intermediate- 14) in place of 6-methyl-N-(2-nitrophenyl)pyridin-3-amine.

MS (ESI) m/z: 214.3 (M+H)⁺.

[0274] <Step-3>: 1-(2,6-dimethylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 81% yield (41 mg, a brown solid) by the similar manner to Step-3 of Intermediate- 13 using N¹-(2,6-dimethylpyridin-3-yl)benzene-1, 2-diamine (45 mg, 0.21 mmol, Step-2 of Intermediate- 14) in place of N¹-methylpyridin-3-ylbenzene-1, 2-diamine.

MS (ESI) m/z: 240.3 (M+H)⁺.

[0275] Intermediate- 15:

1-(6-(2,2-difluoroethoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0276] <Step-1>: tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 82% yield (345 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (6-fluoropyridin-3-yl)boronic acid in place of (4-fluorophenyl)boronic acid.

¹H -NMR (400 MHz, CDCl₃) delta 8.42 (1H, dd, J = 2.7, 1.4 Hz), 8.03-7.91 (2H, m), 7.26-7.17 (2H, m), 7.14 (1H, dd, J = 8.7, 3.2 Hz), 6.95 (1H, dd, J = 7.9, 3.2 Hz), 1.69 (9H, s). MS (ESI) m/z: 330.2 (M+H)⁺.

[0277] <Step-2>: 1-(6-(2,2-difluoroethoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (35

mg, 0.11 mmol, Step-1 of Intermediate- 15) and 2,2-difluoroethanol (44 mg, 0.53

mmol) in DMF (1 mL) is added potassium tert-butoxide (36 mg, 0.32 mmol) at rt. The mixture is stirred at rt for 3 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 29 mg (94% yield) of the title compound as a yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.82 (1H, br s), 8.35 (1H, d, J = 2.7 Hz), 7.83 (1H,

dd, J = 8.7, 2.7 Hz), 7.18-7.05 (3H, m), 7.02-6.95 (2H, m), 6.19 (1H, tt, J = 55.3, 4.1 Hz), 4.61 (2H, td, J = 13.7, 4.1 Hz). MS (ESI) m/z: 292.2 (M+H)⁺.

[0278] Intermediate- 16:

1-(6-ethoxypyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0279] To a mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (35 mg, 0.11 mmol, Step-1 of Intermediate- 15) in DMF (1 mL) is added 20% sodium ethanolate in EtOH (108 mg, 0.32 mmol) at rt. The mixture is stirred at rt for 3 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 17 mg (63% yield) of the title compound as a yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.83 (1H, br s), 8.33 (1H, d, J = 2.7 Hz), 7.74 (1H, dd, J = 8.7, 2.7 Hz), 7.15-7.05 (3H, m), 6.97 (1H, d, J = 7.7 Hz), 6.89 (1H, d, J = 8.7 Hz), 4.43 (2H, q, J = 6.9 Hz), 1.44 (3H, t, J = 6.9 Hz). MS (ESI) m/z: 256.2 (M+H)⁺.

[0280] Intermediate- 17:

1-(2-methoxypyrimidin-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

[0281] <Step-1>: tert-butyl

3-(2-methoxypyrimidin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 34% yield (50 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (2-methoxypyrimidin-5-yl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 343.3 (M+H)⁺.

[0282] <Step-2>: 1-(2-methoxypyrimidin-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield (45 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl 2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (50 mg, 0.15 mmol, Step-1 of Intermediate- 17).

MS (ESI) m/z: 243.3 (M+H)⁺.

[0283] Intermediate- 18:

1-(3,4-dimethoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one

[0284] <Step-1>: tert-butyl

3-(3,4-dimethoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 18% yield (28 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (3,4-dimethoxyphenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 371.3 (M+H)⁺.

[0285] <Step-2>: 1-(3,4-dimethoxyphenyl)- 1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 98% yield (20 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl 3-(3,4-dimethoxyphenyl)-2-oxo-2, 3-dihydro- 1H-benzo[d] imidazole- 1-carboxylate (28 mg, 0.076 mmol, Step-1 of Intermediate- 18).

MS (ESI) m/z: 271.4 (M+H)⁺.

[0286] Intermediate- 19:

1-(2-methoxypyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

[0287] <Step-1>: tert-butyl

3-(2-methoxypyridin-4-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazole- 1-carboxylate

The title compound is prepared in 30% yield (43 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (2-methoxypyridin-4-yl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 342.3 (M+H)⁺.

[0288] <Step-2>: 1-(2-methoxypyridin-4-yl)- 1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield (31 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl

3-(2-methoxypyridin-4-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazole- 1-carboxylate (43 mg, 0.13 mmol, Step-1 of Intermediate- 19).

MS (ESI) m/z: 242.3 (M+H)⁺.

[0289] Intermediate-20:

1-(2,4-difluorophenyl)-1H-benzo[d]imidazol-2(3H)-one

[0290] <Step-1>: 2,4-difluoro-N-(2-nitrophenyl)aniline

To a mixture of 1-fluoro-2-nitrobenzene (200 mg, 1.42 mmol) and 2,4-difluoroaniline (183 mg, 1.42 mmol) in THF (3 mL) is added potassium tert-butoxide (318 mg, 2.83 mmol) at room temperature. The mixture is stirred at room temperature for 1 hr. The mixture is diluted with saturated aqueous ammonium chloride. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-25% EtOAc in n-hexane to give 240 mg (68% yield) of the title compound as a brown solid.

[0291] <Step-2>: N¹-(2,4-difluorophenyl)benzene-1, 2-diamine

A mixture of 2,4-difluoro-N-(2-nitrophenyl)aniline (225 mg, 0.92 mmol, Step-1 of Intermediate-20) and palladium-fibroin (20 mg, purchased from WAKO) in THF (2 mL) and MeOH (2 mL) is stirred at room temperature for 1 day under hydrogen atmosphere. Palladium-fibroin and solvent are removed to give 211 mg (quantitative yield) of the title compound as a brown solid.

MS (ESI) m/z: 221.3 (M+H)⁺.

[0292] <Step-3>: 1-(2,4-difluorophenyl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine (211 mg, 0.92 mmol,

Step-2 of Intermediate-20) and CDI (233 mg, 1.44 mmol) in THF (3 mL) is stirred at room temperature for 1 day. The mixture is diluted with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 154 mg (65% yield) of the title compound as a brown solid. ¹H-NMR (400 MHz, CDCl₃) delta 9.20 (1H, br s), 7.58-7.48 (1H, m), 7.16-7.11 (2H, m), 7.12-7.03 (3H, m), 6.80 (1H, d, J = 6.9 Hz). MS (ESI) m/z: 247.3 (M+H)⁺.

[0293] Intermediate-2 1:

1-(4-fluoro-2-methylphenyl)- 1H-benzo [d]imidazol-2(3H)-one

[0294] <Step-1>: 4-fluoro-2-methyl-N-(2-nitrophenyl)aniline

The title compound is prepared in 65% yield (225 mg, a brown oil) by the similar manner to Step-1 of Intermediate-20 using 4-fluoro-2-methylaniline (177 mg, 1.42 mmol) in place of 2,4-difluoroaniline.

MS (ESI) m/z: 247.3 (M+H)⁺.

[0295] <Step-2>: N¹-(4-fluoro-2-methylphenyl)benzene-l, 2-diamine

The title compound is prepared in quantitative yield (198 mg, a brown oil) by the similar manner to Step-2 of Intermediate-20 using 4-fluoro-2-methyl-N-(2-nitrophenyl)aniline (225 mg, 1.07 mmol, Step-1 of Intermediate-20) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 217.4 (M+H)⁺.

[0296] <Step-3>: 1-(4-fluoro-2-methylphenyl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in 19% yield (42 mg, a brown gum) by the similar manner to Step-3 of Intermediate-20 using N¹-(4-fluoro-2-methylphenyl)benzene-l, 2-diamine (198 mg, 0.92 mmol, Step-2 of Intermediate-20) in place of N¹-(2,4-difluorophenyl)benzene-l, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.19 (1H, br s), 7.32 (1H, dd, J = 8.2, 5.0 Hz), 7.18-7.00 (5H, m), 6.67 (1H, d, J = 7.3 Hz), 2.20 (3H, s). MS (ESI) m/z: 243.3 (M+H)⁺.

[0297] Intermediate-22:

1-(4-fluoro-3-methoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one

[0298] <Step-1>: 4-fluoro-3-methoxy-N-(2-nitrophenyl)aniline

The title compound is prepared in 58% yield (215 mg, a brown solid) by the similar manner to Step-1 of Intermediate-20 using 4-fluoro-3-methoxyaniline (200 mg, 1.42 mmol) in place of 2,4-difluoroaniline.

MS (ESI) m/z: 263.1 (M+H)⁺.

[0299] <Step-2>: N¹-(4-fluoro-3-methoxyphenyl)benzene-l, 2-diamine

The title compound is prepared in quantitative yield (190 mg, a brown solid) by the similar manner to Step-2 of Intermediate-20 using

4-fluoro-3-methoxy-N-(2-nitrophenyl)aniline (215 mg, 0.82 mmol, Step-1 of Intermediate-22) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 233.3 (M+H)⁺.

[0300] <Step-3>: 1-(4-fluoro-3-methoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 77% yield (162 mg, a brown solid) by the similar manner to Step-3 of Intermediate-20 using N¹-

(4-fluoro-3-methoxyphenyl)benzene-1, 2-diamine (190 mg, 0.82 mmol, Step-2 of Intermediate-22) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 10.00 (1H, br s), 7.30-7.20 (2H, m), 7.20-7.04 (4H, m), 7.01 (1H, d, J = 7.8 Hz), 3.93 (3H, s). MS (ESI) m/z: 259.2 (M+H)⁺.

[0301] Intermediate-23:

1-(2-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0302] <Step-1>: 2-methyl-N-(2-nitrophenyl)pyridin-3-amine

The title compound is prepared in 52% yield (170 mg, a brown oil) by the similar manner to Step-1 of Intermediate-20 using 2-methylpyridin-3-amine in place of 2,4-difluoroaniline.

MS (ESI) m/z: 230.3 (M+H)⁺.

[0303] <Step-2>: N¹-(2-methylpyridin-3-yl)benzene-1, 2-diamine

The title compound is prepared in quantitative yield (148 mg, a brown oil) by the similar manner to Step-2 of Intermediate-20 using 2-methyl-N-(2-nitrophenyl)pyridin-3-amine (170 mg, 0.74 mmol, Step-1 of Intermediate-23) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 200.3 (M+H)⁺.

[0304] <Step-3>: 1-(2-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 88% yield (148 mg, a brown gum) by the similar manner to Step-3 of Intermediate-20 using N¹-

(2-methylpyridin-3-yl)benzene-1, 2-diamine (148 mg, 0.47 mmol, Step-2 of Intermediate-23) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.01 (1H, br s), 8.67 (1H, dd, J = 5.0, 1.8 Hz), 7.70 (1H, dd, J = 8.2, 1.8 Hz), 7.35 (1H, dd, J = 8.2, 5.0 Hz), 7.18-7.10 (2H, m), 7.08-7.01 (1H, m), 6.67 (1H, d, J = 7.8 Hz), 2.47 (3H, s). MS (ESI) m/z: 226.3 (M+H)⁺.

[0305] Intermediate-24:

1-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0306] To a mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (30 mg, 0.091 mmol, Step-1 of Intermediate-15) and

2-((tetrahydro-2H-pyran-2-yl)oxy)ethanol (67 mg, 0.46 mmol) in DMF (1 mL) is added potassium tert-butoxide (31 mg, 0.27 mmol) at rt. The mixture is stirred at rt for 3 hrs. The mixture is diluted with water and extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 24 mg (74% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 356.3 (M+H)⁺.

[0307] Intermediate-25:

1-(3-methylpyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

[0308] <Step-1>: 3-methyl-N-(2-nitrophenyl)pyridin-4-amine

The title compound is prepared in 56% yield (182 mg, a brown solid) by the similar manner to Step-1 of Intermediate-20 using 3-methylpyridin-4-amine (153 mg, 1.42 mmol) in place of 2,4-difluoroaniline.

¹H-NMR (400 MHz, CDCl₃) delta 9.27 (1H, br s), 8.45 (1H, s), 8.39 (1H, d, J = 5.5 Hz), 8.25 (1H, dd, J = 8.7, 1.4 Hz), 7.58-7.44 (2H, m), 7.28 (1H, d, J = 5.5 Hz), 7.00 (1H, td, J = 7.3, 1.4 Hz), 2.34 (3H, s). MS (ESI) m/z: 230.3 (M+H)⁺.

[0309] <Step-2>: N¹-(3-methylpyridin-4-yl)benzene-1, 2-diamine

The title compound is prepared in quantitative yield (158 mg, a brown solid) by the similar manner to Step-2 of Intermediate-20 using 3-methyl-N-(2-nitrophenyl)pyridin-4-amine (182 mg, 0.79 mmol, Step-1 of Intermediate-25) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 200.3 (M+H)⁺.

[0310] <Step-3>: 1-(3-methylpyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 79% yield (141 mg, a pale yellow solid) by the similar manner to Step-3 of Intermediate-20 using N¹-(3-methylpyridin-4-yl)benzene-1, 2-diamine (158 mg, 0.79 mmol, Step-2 of Intermediate-25) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.21 (1H, br s), 8.73 (1H, br s), 8.65 (1H, d, J = 5.0 Hz), 7.34 (1H, d, J = 5.0 Hz), 7.20-7.10 (2H, m), 7.07 (1H, t, J = 7.7 Hz), 6.75 (1H, d, J = 7.7 Hz), 2.29 (3H, s). MS (ESI) m/z: 226.3 (M+H)⁺.

[0311] Intermediate-26 :

1-(6-(dimethylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0312] A mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (50 mg, 0.15 mmol, Step-1 of Intermediate-15), dimethylamine hydrochloride (62 mg, 0.76 mmol) and DIEA (0.13 mL, 0.76 mmol) in NMP (0.6 mL) is irradiated with microwave at 200 °C for 20 min. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a

strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 16 mg (41% yield) of the title compound as a yellow gum.

MS (ESI) m/z: 255.4 (M+H)⁺.

[0313] Intermediate-27 :

1-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0314] The title compound is prepared in 44% yield (20 mg, a pale yellow gum) by the similar manner to Intermediate-26 using 2-methoxy-N-methylethanamine in place of dimethylamine hydrochloride.

MS (ESI) m/z: 299.4 (M+H)⁺.

[0315] Intermediate-28 :

1-(6-morpholinopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0316] The title compound is prepared in 58% yield (26 mg, a pale yellow gum) by the similar manner to Intermediate-26 using morpholine in place of dimethylamine hydrochloride.

MS (ESI) m/z: 297.4 (M+H)⁺.

[0317] Intermediate-29:

1-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0318] The title compound is prepared in 23% yield (11 mg, a pale yellow gum) by the similar manner to Intermediate-26 using 1-methylpiperazine in place of dimethylamine hydrochloride.

MS (ESI) m/z: 310.3 (M+H)⁺.

[0319] Intermediate-30:

1-(2-methylpyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

[0320] <Step-1>: 2-methyl-N-(2-nitrophenyl)pyridin-4-amine

The title compound is prepared in 30% yield (72 mg, an orange solid) by the similar manner to Step-1 of Intermediate-20 using 2-methylpyridin-4-amine in place of 2,4-difluoroaniline.

¹H-NMR (400 MHz, CDCl₃) delta 9.26 (1H, br s), 8.40 (1H, d, J = 5.5 Hz), 8.22 (1H, dd, J = 8.2, 1.4 Hz), 7.62-7.49 (2H, m), 7.05-6.95 (3H, m), 2.54 (3H, s). MS (ESI) m/z: 230.3 (M+H)⁺.

[0321] <Step-2>: N¹-(2-methylpyridin-4-yl)benzene-1, 2-diamine

The title compound is prepared in quantitative yield (63 mg, a brown gum) by the similar manner to Step-2 of Intermediate-20 using 2-methyl-N-(2-nitrophenyl)pyridin-4-amine (72 mg, 0.31 mmol, Step-1 of Intermediate-30) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 200.4 (M+H)⁺.

[0322] <Step-3>: 1-(2-methylpyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 21% yield (45 mg, a pale yellow solid) by the

similar manner to Step-3 of Intermediate-20 using N¹-

(2-methylpyridin-4-yl)benzene-1, 2-diamine (63 mg, 0.31 mmol, Step-2 of Intermediate-30) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.32 (1H, br s), 8.59 (1H, d, J = 5.5 Hz), 7.53 (1H, d, J = 2.3 Hz), 7.47 (1H, dd, J = 5.5, 2.3 Hz), 7.27 (1H, dd, J = 7.8, 0.9 Hz), 7.15-7.02 (3H, m), 2.56 (3H, s). MS (ESI) m/z: 226.5 (M+H)⁺.

[0323] Intermediate-31:

7-methyl-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0324] <Step-1>: 6-methyl-N-(2-methyl-6-nitrophenyl)pyridin-3-amine

The title compound is prepared in 58% yield (136 mg, an orange gum) by the similar manner to Step-1 of Intermediate-20 using 6-methylpyridin-3-amine (105 mg, 0.97 mmol) and 2-fluoro-1-methyl-3-nitrobenzene (150 mg, 0.97 mmol) in place of 2,4-difluoroaniline and 1-fluoro-2-nitrobenzene.

¹H-NMR (400 MHz, CDCl₃) delta 8.23 (1H, br s), 8.07 (1H, d, J = 2.7 Hz), 7.99 (1H, d, J = 7.8 Hz), 7.44 (1H, d, J = 7.3 Hz), 7.10 (1H, t, J = 7.8 Hz), 7.03 (1H, d, J = 8.2 Hz), 6.94 (1H, dd, J = 7.3, 5.5 Hz), 2.50 (3H, s), 2.07 (3H, s). MS (ESI) m/z: 244.5 (M+H)⁺.

[0325] <Step-2>: 6-methyl-N'-(6-methylpyridin-3-yl)benzencene-1,2-diamine

The title compound is prepared in quantitative yield (119 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate-20 using 6-methyl-N-(2-methyl-6-nitrophenyl)pyridin-3-amine (136 mg, 0.56 mmol, Step-1 of Intermediate-31) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 214.6 (M+H)⁺.

[0326] <Step-3>: 7-methyl-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 6-methyl-N'-(6-methylpyridin-3-yl)benzene-1, 2-diamine (119 mg, 0.56 mmol, Step-2 of Intermediate-31) and CDI (271 mg, 1.67 mmol) in THF (3 mL) is stirred at room temperature for 3 hrs. The mixture is diluted with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 195 mg of the title compound as a pale yellow crude oil.

MS (ESI) m/z: 240.5 (M+H)⁺.

[0327] Intermediate-32:

1-(6-methoxypyridin-3-yl)-7-methyl-1H-benzo[d]imidazol-2(3H)-one

[0328] <Step-1>: 6-methoxy-N-(2-methyl-6-nitrophenyl)pyridin-3-amine

The title compound is prepared in 21% yield (53 mg, an orange gum) by the similar manner to Step-1 of Intermediate-20 using 6-methoxypyridin-3-amine (120 mg, 0.97 mmol) and 2-fluoro-1-methyl-3-nitrobenzene (150 mg, 0.97 mmol) in place of

2,4-difluoroaniline and 1-fluoro-2-nitrobenzene.

¹H-NMR (400 MHz, CDCl₃) delta 8.38 (1H, br s), 8.01 (1H, dd, J = 8.7, 1.4 Hz), 7.74 (1H, d, J = 3.2 Hz), 7.38 (1H, d, J = 7.3 Hz), 7.13 (1H, dd, J = 8.7, 3.2 Hz), 7.01 (1H, dd, J = 8.2, 7.3 Hz), 6.68 (1H, d, J = 8.7 Hz), 3.90 (3H, s), 2.02 (3H, s). MS (ESI) m/z: 260.4 (M+H)⁺.

[0329] <Step-2>: N'-(6-methoxypyridin-3-yl)-6-methylbenzidine-1,2-diamine

The title compound is prepared in quantitative yield (47 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate-20 using 6-methoxy-N-(2-methyl-6-nitrophenyl)pyridin-3-amine (53 mg, 0.20 mmol, Step-1 of Intermediate-32) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 230.5 (M+H)⁺.

[0330] <Step-3>: 1-(6-methoxypyridin-3-yl)-7-methyl-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 105 mg (a pale yellow crude oil) by the similar manner to Step-3 of Intermediate-31 using N¹-(6-methoxypyridin-3-yl)-6-methylbenzene-1,2-diamine (47 mg, 0.20 mmol, Step-2 of Intermediate-32) in place of 6-methyl-N¹-(2-methyl-6-nitrophenyl)pyridin-3-amine, 2-diamine.

MS (ESI) m/z: 256.4 (M+H)⁺.

[0331] Intermediate-33:

1-(6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-7-methyl-1H-benzo[d]imidazol-2(3H)-one

[0332] <Step-1>: 6-(2-(dimethylamino)ethoxy)-N-(2-methyl-6-nitrophenyl)pyridin-3-amine

The title compound is prepared in 12% yield (37 mg, an orange gum) by the similar manner to Step-1 of Intermediate-20 using 6-(2-(dimethylamino)ethoxy)pyridin-3-amine (175 mg, 0.97 mmol) and 2-fluoro-1-methyl-3-nitrobenzene (150 mg, 0.97 mmol) in place of 2,4-difluoroaniline and 1-fluoro-2-nitrobenzene.

¹H-NMR (400 MHz, CDCl₃) delta 8.39 (1H, br s), 8.01 (1H, dd, J = 8.2, 0.9 Hz), 7.71 (1H, dd, J = 3.2, 0.9 Hz), 7.38 (1H, dd, J = 6.8, 0.9 Hz), 7.11 (1H, dd, J = 8.7, 2.7 Hz), 7.01 (1H, dd, J = 8.2, 0.9 Hz), 6.73 (1H, d, J = 8.7 Hz), 4.36 (2H, t, J = 5.9 Hz), 2.70 (2H, t, J = 5.9 Hz), 2.32 (6H, s), 2.02 (3H, s). MS (ESI) m/z: 317.5 (M+H)⁺.

[0333] <Step-2>: N¹-

6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-6-methylbenzene-1,2-diamine

The title compound is prepared in quantitative yield (34 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate-20 using 6-(2-(dimethylamino)ethoxy)-N-(2-methyl-6-nitrophenyl)pyridin-3-amine (37 mg, 0.12 mmol, Step-1 of Intermediate-33) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 287.5 (M+H)⁺.

[0334] <Step-3>:

1-(6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-7-methyl-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 50 mg (a pale yellow crude oil) by the similar manner to Step-3 of Intermediate-31 using N¹-

(6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-7-methyl-1H-benzo[d]imidazol-2(3H)-one (34 mg, 0.12 mmol, Step-2 of Intermediate-33) in place of 6-methyl- N¹-(6-methylpyridin-3-yl)benzene-1,2-diamine.

MS (ESI) m/z: 313.5 (M+H)⁺.

[0335] Intermediate-34:

1-(6-methoxypyridin-3-yl)-4-methyl-1H-benzo[d]imidazol-2(3H)-one

[0336] <Step-1>: 6-methoxy-N-(3-methyl-2-nitrophenyl)pyridin-3-amine

The title compound is prepared in 4% yield (11 mg, an orange gum) by the similar manner to Step-1 of Intermediate-20. 6-Methoxypyridin-3-amine and 1-fluoro-3-methyl-2-nitrobenzene are used instead of 2,4-difluoroaniline and 1-fluoro-2-nitrobenzene.

MS (ESI) m/z: 260.5 (M+H)⁺.

[0337] <Step-2>: N¹-(6-methoxypyridin-3-yl)-3-methylbenzene-1,2-diamine

The title compound is prepared in quantitative yield (10 mg, a yellow gum) by the similar manner to Step-2 of Intermediate-20 using 6-methoxy-N-(3-methyl-2-nitrophenyl)pyridin-3-amine (11 mg, 0.042 mmol, Step-1 of Intermediate-34) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 230.5 (M+H)⁺.

[0338] <Step-3>: 1-(6-methoxypyridin-3-yl)-4-methyl-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 36% yield (4 mg, a pale yellow oil) by the similar manner to Step-3 of Intermediate-31 using N¹-

(6-methoxypyridin-3-yl)-3-methylbenzene-1,2-diamine (10 mg, 0.044 mmol, Step-2 of Intermediate-34) in place of N¹-(2,4-difluorophenyl)benzene-1,2-diamine.

MS (ESI) m/z: 256.4 (M+H)⁺.

[0339] Intermediate-35:

(S)-1-(6-(3-(dimethylamino)pyrrolidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0340] The title compound is prepared in 54% yield (21 mg, a pale yellow gum) by the similar manner to Intermediate-26 using (S)-N,N-dimethylpyrrolidin-3-amine in place of dimethylamine hydrochloride.

MS (ESI) m/z: 324.5 (M+H)⁺.

[0341] Intermediate-36:

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihy

dro-1H-benzo[d]imidazol-1-yl)picolinic acid

[0342] <Step-1>: methyl 5-((2-nitrophenyl)amino)picolinate

A mixture of methyl 5-aminopicolinate (300 mg, 1.97 mmol), 1-bromo-2-nitrobenzene (398 mg, 1.97 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride dichloromethane adduct (161 mg, 0.20 mmol), 1,1'-bis(diphenylphosphino)ferrocene (22 mg, 0.039 mmol), and tripotassium phosphate (837 mg, 3.4 mmol) in toluene (5 mL) is stirred at 100 °C for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 242 mg (45% yield) of the title compound as a brown gum.

¹H-NMR (400 MHz, CDCl₃) delta 9.45 (1H, br s), 8.68 (1H, d, J = 2.3 Hz), 8.25 (1H, dd, J = 8.2, 1.4 Hz), 8.17 (1H, d, J = 8.2 Hz), 7.71 (1H, dd, J = 8.2, 2.7 Hz), 7.55-7.48 (1H, m), 7.42 (1H, dd, J = 8.2, 0.9 Hz), 7.03-6.98 (1H, m), 4.02 (3H, s). MS (ESI) m/z: 274.6 (M+H)⁺.

[0343] <Step-2>: methyl 5-((2-aminophenyl)amino)picolinate

The title compound is prepared in quantitative yield (214 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate-13 using methyl 5-((2-nitrophenyl)amino)picolinate (242 mg, 0.89 mmol, Step-1 of Intermediate-36) in place of 6-methyl-N-(2-nitrophenyl)pyridin-3-amine.

MS (ESI) m/z: 244.5 (M+H)⁺.

[0344] <Step-3>: methyl 5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

A mixture of methyl 5-((2-aminophenyl)amino)picolinate (215 mg, 0.88 mmol, Step-2 of Intermediate-36) and CDI (358 mg, 2.21 mmol) in THF (3 mL) is stirred at room temperature for 2 hrs. The mixture is diluted with 10% aqueous citric acid. The precipitate is collected and dried to give 220 mg (92% yield) of the title compound as a purple solid.

¹H-NMR (400 MHz, CDCl₃) delta 11.37 (1H, br s), 8.96 (1H, t, J = 1.8 Hz), 8.22 (2H, d, J = 1.8 Hz), 7.20-7.00 (4H, m), 3.90 (3H, s). MS (ESI) m/z: 270.4 (M+H)⁺.

[0345] <Step-4>:

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinic acid

A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (161 mg, 0.45 mmol, Mesylate-1), methyl 5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (120 mg, 0.45 mmol, Step-3 of Intermediate-36), cesium carbonate (436 mg, 1.33 mmol) in DMSO (2 mL) is stirred at 80 °C for 5 hrs. Then, the mixture is diluted with water and stirred at rt for 30 min. The mixture is acidified with 2 M hydrochloric acid and extracted with DCM.

The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 320 mg (quantitative yield) of the title compound as a yellow solid.

MS (ESI) m/z : 520.5 (M+H)⁺.

[0346] Intermediate-37:

1-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0347] The title compound is prepared in 49% yield (21 mg, a pale yellow gum) by the similar manner to Intermediate-26 using 2-(methylamino)ethanol in place of dimethylamine hydrochloride.

MS (ESI) m/z : 285.5 (M+H)⁺.

[0348] Intermediate-38:

1-(6-(4-(2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0349] The title compound is prepared in 83% yield (43 mg, a pale yellow gum) by the similar manner to Intermediate-26 using 2-(piperazin-1-yl)ethanol in place of dimethylamine hydrochloride.

MS (ESI) m/z : 340.5 (M+H)⁺.

[0350] Intermediate-39:

1-(6-bromopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0351] <Step-1>: 6-bromo-N-(2-nitrophenyl)pyridin-3-amine

To a mixture of 1-fluoro-2-nitrobenzene (1 g, 7.09 mmol) and 6-bromopyridin-3-amine (1.23 g, 7.09 mmol) in THF (12 mL) is added potassium tert-butoxide (1.59 g, 14.2 mmol) at rt. The mixture is stirred at rt for 1 hr. The reaction mixture is diluted with water. The mixture is extracted with EtOAc and dried over sodium sulfate. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in hexane to give 1.14 g (55% yield) of the desired product as an orange solid.

¹H-NMR (400 MHz, CDCl₃) δ 9.32 (1H, s), 8.38 (1H, d, J = 3.1 Hz), 8.24 (1H, dd, J = 8.6, 1.8 Hz), 7.54-7.43 (3H, m), 7.17 (1H, d, J = 8.6 Hz), 6.91 (1H, dd, J = 8.6, 7.3 Hz).

[0352] <Step-2>: N'-(6-bromopyridin-3-yl)benzidine-1,2-diamine

A mixture of 6-bromo-N-(2-nitrophenyl)pyridin-3-amine (1.00 g, 3.40 mmol), iron powder (1.14 g, 20.4 mmol) and ammonium chloride (0.546 g, 10.2 mmol) in ethanol (12.75 mL) and water (4.25 mL) is refluxed with stirring for 2 hrs. After cooling to room temperature, the reaction mixture is filtered through a pad of celite, and filtrate is concentrated in vacuo, the residue is poured into 2 M aqueous sodium hydroxide solution and extracted with EtOAc, dried over sodium sulfate then filtrated and concentrated, to give N'-ih-bromopyridin-S-yObenzene-l, 2-diamine (0.845 g, 3.20 mmol, 94 % yield).

¹H -NMR (400 MHz, CDCl₃) delta 7.92 (1H, d, J = 3.1 Hz), 7.24 (1H, d, J = 8.6 Hz), 7.10-7.06 (2H, m), 6.85 (1H, dd, J = 5.5, 3.1 Hz), 6.82 (1H, dd, J = 5.5, 1.8 Hz), 6.77 (1H, ddd, J = 8.0, 7.3, 1.2 Hz), 5.26 (1H, br), 3.77 (2H, br).

[0353] <Step-3>: 1-(6-bromopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of N'-iO-bromopyridin-S-yObenzene-l, 2-diamine (0.840 g, 3.18 mmol) and CDI (0.774 g, 4.77 mmol) in THF (30 mL) is stirred at rt for 3 hrs. The reaction mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The resulting solution is dried over sodium sulfate and concentrated. The residue is purified by solidification with isopropyl acetate (25 mL)-ethanol (18 mL) to give desired product (0.686g, 80 % yield) as pale brown solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.66 (1H, d, J = 2.7 Hz), 7.85 (1H, dd, J = 8.7, 2.7 Hz), 7.69 (1H, d, J = 7.8 Hz), 7.18-7.07 (4H, m). A signal due to NH is not observed.

[0354] Intermediate-40:

1-(6-(dimethylamino)pyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0355] <Step-1>: 6-chloro-N-(2-nitrophenyl)pyridazin-3-amine

A mixture of 6-chloropyridazin-3-amine (750 mg, 5.79 mmol) and 1-fluoro-2-nitrobenzene (1.23 g, 8.68 mmol) in THF is added potassium tert-butoxide (1.30 g, 11.6 mmol) at 0 °C. The mixture is stirred at rt for 2 hrs. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 547 mg (38% yield) of the title compound as a brown solid.

MS (ESI) m/z: 251.6 (M+H)⁺.

[0356] <Step-2>: N¹-(6-chloropyridazin-3-yl)benzene-l, 2-diamine

A mixture of 6-chloro-N-(2-nitrophenyl)pyridazin-3-amine (547 mg, 2.18 mmol, Step-1 of Intermediate-40), iron (501 mg, 8.97 mmol) and ammonium chloride (79 mg, 14.9 mmol) in EtOH (3 mL) and water (1 mL) is stirred at 80 °C for 2 hrs. The mixture is filtered by using Celite pad. The mixture is extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 471 mg (98% yield) of the title compound as a brown oil.

[0357] <Step-3>: 1-(6-chloropyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 90% yield (472 mg, a pale orange solid) by the similar manner to Step-3 of Intermediate- 36 using N¹-(6-chloropyridazin-3-yl)benzene-l, 2-diamine (471 mg, 2.14 mmol, Step-2 of Intermediate-40) in place of methyl 5-((2-aminophenyl)amino)picolinate.

MS (ESI) m/z: 247.5 (M+H)⁺.

[0358] <Step-4>: 1-(6-(dimethylamino)pyridazin-3-yl)- 1H-benzo[d]imidazol-2(3H)-one

A mixture of 1-(6-chloropyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (50 mg, 0.20 mmol, Step-3 of Intermediate-40), dimethylamine hydrochloride (165 mg, 2.03

mmol), and DIEA (0.11 mL, 0.61 mmol) in NMP (0.7 mL) is irradiated with microwave at 200 °C for 30 min. The mixture is diluted with water. The mixture is extracted with DCM. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 42 mg (81% yield) of the title compound as a brown solid.

MS (ESI) m/z: 256.7 (M+H)⁺.

[0359] Intermediate-4 1:

1-(6-(4-methylpiperazin-1-yl)pyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0360] The title compound is prepared in 67% yield (42 mg, a brown solid) by the similar manner to Step-4 of Intermediate-40 using 1-methylpiperazine in place of dimethylamine hydrochloride.

MS (ESI) m/z: 311.7 (M+H)⁺.

[0361] Intermediate-42:

1-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0362] A mixture of 1-(6-chloropyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (50 mg, 0.20 mmol, Step-3 of Intermediate-40) and 2-((tetrahydro-2H-pyran-2-yl)oxy)ethanol (89 mg, 0.61 mmol) in DMF (5 mL) is added potassium tert-butoxide (227 mg, 2.03 mmol) at rt. The mixture is stirred at 50 °C for 6 hrs. The mixture is diluted with saturated aqueous ammonium chloride and extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 41 mg (57% yield) of the title compound as a brown solid.

MS (ESI) m/z: 355.7 (M-H)⁻.

[0363] Intermediate-43:

1-(2-bromopyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

[0364] <Step-1>: 2-bromo-N-(2-nitrophenyl)pyridin-4-amine

The title compound is prepared in 45 % yield (1.40 g, an orange solid) by the similar manner to Step-1 of Intermediate-39 using 2-bromopyridin-4-amine in place of 6-bromopyridin-3-amine.

¹H-NMR (400 MHz, CDCl₃) delta 9.20 (1H, s), 8.24-8.22 (2H, m), 7.60 (1H, d, J = 3.7 Hz), 7.32 (1H, d, J = 2.4 Hz), 7.14-7.08 (1H, m), 7.05 (1H, dd, J = 5.5, 2.4 Hz).

[0365] <Step-2>: N¹-(2-bromopyridin-4-yl)benzene-1, 2-diamine

A mixture of 2-bromo-N-(2-nitrophenyl)pyridin-4-amine (1.45 g, 4.93 mmol), iron (1.595 g, 28.6 mmol), and ammonium chloride (0.764 g, 14.28 mmol) in ethanol (18 mL) and water (6 mL) is refluxed with stirring for 2 hrs. After cooling to room temperature, the reaction mixture is filtered through a pad of celite, and filtrate is concentrated in vacuo, the residue is poured into 2 M aqueous sodium hydroxide solution

and extracted with EtOAc, dried over sodium sulfate then filtrated and concentrated.

To give the title compound (1.30 g, 4.92 mmol, 100 % yield).

¹H -NMR (400 MHz, CDCl₃) delta 7.98 (1H, d, J = 5.5 Hz), 7.15 (1H, ddd, J = 8.0, 7.3, 1.2 Hz), 7.10 (1H, d, J = 7.3 Hz), 6.84 (1H, dd, J = 8.0, 1.2 Hz), 6.80 (1H, ddd, J = 8.0, 7.3, 1.2 Hz), 6.69 (1H, d, J = 1.8 Hz), 6.50 (1H, dd, J = 5.5, 1.8 Hz), 5.63 (1H, br), 3.77 (2H, br).

[0366] <Step-3>: 1-(2-bromopyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of N¹-(2-bromopyridin-4-yl)benzene-1, 2-diamine (1.3 g, 4.92 mmol) and CDI (1.04 g, 6.4 mmol) in THF (30 mL) is stirred at rt for 3 hrs. The reaction mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The resulting solution is dried over sodium sulfate and concentrated. The residual solid is purified by repulped with ethyl acetate (10 mL) and ethanol (15 mL) to give the title compound (1.18 g, 89 % yield) as a pale brown solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.53 (1H, d, J = 5.5 Hz), 8.34 (1H, br), 7.86 (1H, d, J = 1.8 Hz), 7.64 (1H, dd, J = 5.5, 1.8 Hz), 7.30-7.26 (1H), 7.23-7.13 (3H, m).

[0367] Intermediate-44:

1-(4-(2-(dimethylamino)ethoxy)phenyl)-1H-benzo[d]imidazol-2(3H)-one

[0368] <Step-1>: N-(4-(2-(dimethylamino)ethoxy)phenyl)-2-nitroaniline

The title compound is prepared in 47% yield (64 mg, a brown gum) by the similar manner to Step-1 of Intermediate-20 using 4-(2-(dimethylamino)ethoxy)aniline (81 mg, 0.45 mmol) in place of 2,4-difluoroaniline.

¹H -NMR (400 MHz, CDCl₃) delta 9.40 (1H, br s), 8.19 (1H, dd, J = 8.7, 1.8 Hz), 7.35-7.30 (1H, m), 7.19 (2H, d, J = 8.7 Hz), 7.05-6.95 (3H, m), 6.71 (1H, ddd, J = 8.7, 7.3, 1.8 Hz), 4.09 (2H, t, J = 5.5 Hz), 2.75 (2H, t, J = 5.5 Hz), 2.36 (6H, s). MS (ESI) m/z: 302.6 (M+H)⁺.

[0369] <Step-2>: N¹-(4-(2-(dimethylamino)ethoxy)phenyl)benzene-1, 2-diamine

The title compound is prepared in 99% yield (57 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate-20 using N-(4-(2-(dimethylamino)ethoxy)phenyl)-2-nitroaniline (64 mg, 0.21 mmol, Step-1 of Intermediate-44) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

[0370] <Step-3>: 1-(4-(2-(dimethylamino)ethoxy)phenyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 83% yield (52 mg, a pale yellow solid) by the similar manner to Step-3 of Intermediate-20 using N¹-(4-(2-(dimethylamino)ethoxy)phenyl)benzene-1, 2-diamine (57 mg, 0.21 mmol, Step-2 of Intermediate-44) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

MS (ESI) m/z: 298.5 (M+H)⁺.

[0371] Intermediate-45:

(R)-tert-butyl

2-(((5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate

[0372] A mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (75 mg, 0.23 mmol, Step-1 of Intermediate- 15) and (R)-tert-butyl

2-(hydroxymethyl)morpholine-4-carboxylate (99 mg, 0.46 mmol) in 1,4-dioxane (1 mL) is added sodium hydride (60% dispersion in mineral oil, 36 mg, 0.91 mmol) at rt. The mixture is stirred at rt for 5 hrs. The mixture is diluted with saturated aqueous ammonium chloride and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 46 mg (47% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 427.7 (M+H)⁺.

[0373] Intermediate-46:

5-chloro-2-methyl-N-((1S,4r)-4-(((3-(6-((S)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[0374] <Step-1>: (S)-tert-butyl

2-(((5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate

[0375] A mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (75 mg, 0.23 mmol, Step-1 of Intermediate- 15) and (S)-tert-butyl

2-(hydroxymethyl)morpholine-4-carboxylate (99 mg, 0.46 mmol) in 1,4-dioxane (1 mL) is added sodium hydride (60% dispersion in mineral oil, 36 mg, 0.91 mmol) at rt. The mixture is stirred at rt for 5 hrs. The mixture is diluted with saturated aqueous ammonium chloride and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 23 mg (24% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 427.7 (M+H)⁺.

[0376] <Step-2>: (S)-tert-butyl

2-(((5-(3-(((1r,4S)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate

The title compound is prepared in 75% yield (28 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using (S)-tert-butyl

2-(((5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate (23 mg, 0.054 mmol, Step-1 of Intermediate-46) in place of methyl 3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 691.8 (M+H)⁺.

[0377] <Step-3>:

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-((S)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A solution of (S)-tert-butyl

2-(((5-(3-(((1r,4S)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate (28 mg, 0.041 mmol, Step-2 of Intermediate-46) in DCM (1 mL) and TFA (1 mL) is stirred at rt for 1 hr. The mixture is concentrated. The residue is basified with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 25 mg (quantitative yield) of the title compound as a pale yellow gum.

MS (ESI) m/z: 591.6 (M+H)⁺.

[0378] Intermediate-47 :

N-((1r,4r)-4-((3-(6-(azetidin-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[0379] <Step-1>: tert-butyl

3-(((5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)azetidine-1-carboxylate

The title compound is prepared in 77% yield (67 mg, a pale yellow solid) by the similar manner to Step-1 of Intermediate-46 using tert-butyl

3-hydroxyazetidine-1-carboxylate in place of (S)-tert-butyl

2-(hydroxymethyl)morpholine-4-carboxylate.

MS (ESI) m/z: 383.8 (M+H)⁺.

[0380] <Step-2>: tert-butyl

3-(((5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)azetidine-1-carboxylate

The title compound is prepared in 67% yield (76 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using tert-butyl

3-(((5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)azetidine-1-carboxylate (67 mg, 0.18 mmol, Step-1 of Intermediate-47) in place of methyl

3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 647.6 (M+H)⁺.

[0381] <Step-3>: N-

((1r,4r)-4-((3-(6-(azetidin-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound is prepared in 92% yield (59 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-46 using tert-butyl

3-(((5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)azetidine-1-carboxylate (76 mg, 0.12 mmol, Step-2 of Intermediate-47).

MS (ESI) *m/z*: 547.5 (M+H)⁺.

[0382] Intermediate-48:

N-(((1*r*,4*r*)-4-((3-(6-(azetidin-3-ylmethoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[0383] <Step-1>: tert-butyl

3-(((5-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)azetidine-1-carboxylate

The title compound is prepared in quantitative yield (94 mg, a pale yellow solid) by the similar manner to Step- 1 of Intermediate-46 using tert-butyl

3-(hydroxymethyl)azetidine-1-carboxylate in place of (S)-tert-butyl

2-(hydroxymethyl)morpholine-4-carboxylate.

MS (ESI) *m/z*: 397.8 (M+H)⁺.

[0384] <Step-2>: tert-butyl

3-(((5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo [d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)azetidine-1-carboxylate

The title compound is prepared in 52% yield (82 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using tert-butyl

3-(((5-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)azetidine-1-carboxylate (94 mg, 0.24 mmol, Step-1 of Intermediate-48) in place of methyl

3-((2-oxo-2, 3-dihydro-1*H*-benzo [d]imidazol-1-yl)methyl)benzoate.

MS (ESI) *m/z*: 661.7 (M+H)⁺.

[0385] <Step-3>: N-

((1*r*,4*r*)-4-((3-(6-(azetidin-3-ylmethoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound is prepared in quantitative yield (74 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-46 using tert-butyl

3-(((5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo [d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)azetidine-1-carboxylate (76 mg, 0.12 mmol, Step-2 of Intermediate-48).

[0386] Intermediate-49:

(S)-1-(6-(3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-1*H*-benzo[d]imidazol-2(3*H*)-one

[0387] The title compound is prepared in 39% yield (25 mg, a brown gum) by the similar manner to Step-4 of Intermediate-40 using (S)-pyrrolidin-3-ol in place of dimethylamine hydrochloride.

MS (ESI) *m/z*: 297.5 (M+H)⁺.

[0388] Intermediate- 50:

(R)-1-(6-(3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0389] The title compound is prepared in 39% yield (25 mg, a brown gum) by the similar manner to Step-4 of Intermediate-40 using (R)-pyrrolidin-3-ol in place of dimethylamine hydrochloride.

MS (ESI) m/z: 297.6 (M+H)⁺.

[0390] Intermediate-51:

1-(6-cyclopropylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0391] <Step-1>: 6-bromo-N-(2-nitrophenyl)pyridin-3-amine

To a mixture of 1-fluoro-2-nitrobenzene (2.00 g, 14.2 mmol) and 6-bromopyridin-3-amine (2.45 g, 14.2 mmol) in THF (14 mL) is added potassium tert-butoxide (3.18 g, 28.3 mmol) at 0 °C and stirred at rt. After 1 hr, the reaction mixture is diluted with water and extracted with EtOAc. The organic phase is washed with brine, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 2.77 g (66% yield) of the title compound as an orange solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.32 (1H, s), 8.38 (1H, d, J = 2.7 Hz), 8.24 (1H, dd, J = 8.2, 1.6 Hz), 7.53 (1H, d, J = 8.2 Hz), 7.50 (1H, dd, J = 8.2, 2.7 Hz), 7.45 (1H, t, J = 7.8 Hz), 7.17 (1H, d, J = 7.8 Hz), 6.91 (1H, t, J = 8.2 Hz).

[0392] <Step-2>: N'-(6-bromopyridin-3-yl)benzidine-1,2-diamine

A mixture of 6-bromo-N-(2-nitrophenyl)pyridin-3-amine (2.77 g, 9.42 mmol), iron (1.58 g, 28.3 mmol) and ammonium chloride (3.1 g, 56.5 mmol) in ethanol (125 mL) and water (50 mL) is refluxed with stirring for 2.5 hr. After cooling to room temperature, the reaction mixture is filtered through a pad of celite, and the filtrate is concentrated in vacuo, the residue is poured into 2 M aqueous sodium hydroxide solution and extracted with EtOAc. The organic phase is dried over sodium sulfate then filtrated and concentrated to give 2.50 g (100 % yield) of the title compound as a beige solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.92 (1H, d, J = 2.7 Hz), 7.24 (1H, d, J = 8.7 Hz), 7.11-7.04 (2H, m), 6.88-6.80 (2H, m), 6.77 (1H, td, J = 7.5, 1.4 Hz), 5.25 (1H, s), 3.76 (2H, s). MS (ESI) m/z: 264.4 (M+H)⁺.

[0393] <Step-3>: 1-(6-bromopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of N'-iO-bromopyridin-3-ylbenzene-1,2-diamine (2.50 g, 9.47 mmol) and CDI (1.84 g, 11.4 mmol) in THF is stirred at rt. After 3 hrs, CDI (2.0 g, 12.3 mmol) is added to the reaction mixture and stirred at rt overnight. The reaction mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic phase is concentrated. The residual solid is washed with EtOAc then collected by filtration to give 1.9 g (69% yield) of the title compound as a beige solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.19 (1H, br s), 8.66 (1H, dd, J = 2.7, 0.9 Hz),

7.85 (1H, dd, J = 8.2, 2.7 Hz), 7.69 (1H, d, J = 8.2 Hz), 7.21-7.09 (3H, m), 7.08 (1H, d, J = 7.3 Hz).

[0394] <Step-4>: 1-(6-cyclopropylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of 1-(6-bromopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (30 mg, 0.103 mmol), cyclopropylboronic acid (13.3 mg, 0.155 mmol), bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II) (3.7 mg, 0.0052 mmol) in 1,4-dioxane (0.5 mL) is added 2 M aqueous tripotassium phosphate solution (0.129 mL) and stirred at 150 °C for 10 min under microwave irradiation. After cooled to rt, the organic phase of the reaction mixture is directly purified by column chromatography on silica-gel eluting with 12-80% EtOAc in n-hexane to give 3 mg (12% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 252.4 (M+H)⁺.

[0395] Intermediate-52:

1-(6-(tetrahydro-2H-pyran-4-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0396] <Step-1>:

1-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of 1-(6-bromopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (30 mg, 0.103 mmol, Step-3 of Intermediate-51),

2-(3,6-dihydro-2H-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (26.1 mg, 0.124 mmol),

bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II) (3.7 mg, 0.0052 mmol) in 1,4-dioxane (0.6 mL) is added 2 M aqueous tripotassium phosphate solution (0.129 mL) and stirred at 120 °C for 10 min under microwave irradiation.

After cooled to rt, the organic phase of the reaction mixture is directly purified by column chromatography on silica-gel eluting with 10-100% EtOAc in n-hexane to give 21 mg (69% yield) of the title compound as a beige solid.

MS (ESI) m/z: 294.4 (M+H)⁺.

[0397] <Step-2>:

1-(6-(tetrahydro-2H-pyran-4-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A solution of

1-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (21 mg, 0.072 mmol) in EtOAc (2 mL) and DMF (1 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (wet) (8 mg). The mixture is evacuated and backfilled with H₂ gas and stirred at rt under H₂ atmosphere. After 1 h, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 17 mg (80% yield) of the title compound. It is used for a next reaction without further purification.

¹H-NMR (400 MHz, CDCl₃) delta 9.27 (1H, br s), 8.79 (1H, d, J = 2.7 Hz), 7.89 (1H,

dd, J = 8.2, 2.7 Hz), 7.39 (1H, d, J = 8.2 Hz), 7.17-7.13 (2H, m), 7.13-7.05 (2H, m), 4.18-4.11 (2H, m), 3.64-3.55 (2H, m), 3.12-2.99 (1H, m), 2.03-1.89 (4H, m). MS (ESI) m/z: 296.4 (M+H)⁺.

[0398] Intermediate-53:

1-(1-methyl-1H-pyrazol-4-yl)-1H-benzo[d]imidazol-2(3H)-one

[0399] <Step-1>: 1-methyl-N-(2-nitrophenyl)-1H-pyrazol-4-amine

The title compound is prepared in 29% yield (66 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-36 using 1-methyl-1H-pyrazol-4-amine (100 mg, 1.03 mmol) in place of methyl 5-aminopicolinate.

MS (ESI) m/z: 219.5 (M+H)⁺.

[0400] <Step-2>: N¹-(1-methyl-1H-pyrazol-4-yl)benzene-1,2-diamine

The title compound is prepared in quantitative yield (57 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate-13 using 1-methyl-N-(2-nitrophenyl)-1H-pyrazol-4-amine (66 mg, 0.30 mmol, Step-1 of Intermediate-53).

MS (ESI) m/z: 189.5 (M+H)⁺.

[0401] <Step-3>: 1-(1-methyl-1H-pyrazol-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 69% yield (45 mg, a pale yellow solid) by the similar manner to Step-3 of Intermediate-20 using N¹-(1-methyl-1H-pyrazol-4-yl)benzene-1,2-diamine (57 mg, 0.30 mmol, Step-2 in Intermediate-53).

¹H-NMR (400 MHz, DMSO-d₆) delta 11.10 (1H, br s), 8.15 (1H, s), 7.76 (1H, d, J = 0.9 Hz), 7.11-7.00 (4H, m), 3.91 (3H, s). MS (ESI) m/z: 215.4(M+H)⁺.

[0402] Intermediate-54:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[0403] A mixture of ((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (200 mg, 0.55 mmol, Mesylate-1), tert-butyl 3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (183 mg, 0.55 mmol, Step-1 of Intermediate-15), and cesium carbonate (542 mg, 1.66 mmol) in DMSO (1 mL) is stirred at 90 °C for 5 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 182 mg (67% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 494.4 (M+H)⁺.

[0404] Intermediate-55:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-chloropyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[0405] The title compound is prepared in 65% yield (49 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using 1-(6-chloropyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (34 mg, 0.14 mmol, Step-3 of Intermediate-40) in place of methyl 3-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 511.4 (M+H)⁺.

[0406] Intermediate-56:

tert-butyl

3-(2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

[0407] A mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (105 mg, 0.449 mmol), copper (II) acetate (61 mg, 0.336 mmol), pyridine (0.033 mL, 0.404 mmol),

7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-[1,4]dioxino[2,3-b]pyridine (59 mg, 0.224 mmol), and MS 4A (100 mg) in DCM (1 mL) is stirred at rt for 2 days. The reaction mixture is filtered through celite pad. The filtrate is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 10-100% EtOAc in n-hexane to give 12 mg (14% yield) of the title compound as an off-white solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.98 (1H, d, J = 2.3 Hz), 7.94-7.89 (1H, m), 7.38 (1H, d, J = 2.3 Hz), 7.22-7.14 (2H, m), 6.97-6.91 (1H, m), 4.55-4.48 (2H, m), 4.35-4.28 (2H, m), 1.69 (9H, s). MS (ESI) m/z: 370.4 (M+H)⁺.

[0408] Intermediate- 57:

5-chloro-N-((1r,4r)-4-((3-(5-chloropyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[0409] <Step-1>: 1-(5-chloropyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 1H-benzo[d]imidazol-2(3H)-one (225 mg, 1.68 mmol), 2,5-dichloropyrazine (250 mg, 1.68 mmol), and cesium carbonate (820 mg, 2.52 mmol) in DMSO (2 mL) is stirred at 80 °C for 2 hrs. The mixture is diluted with water. The precipitate is collected and washed with diisopropyl ether to give 356 mg (86% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, DMSO-d₆) delta 9.31 (1H, d, J = 1.4 Hz), 8.77 (1H, d, J = 1.4 Hz), 7.90 (1H, d, J = 8.2 Hz), 7.18-7.01 (3H, m). A signal due to NH is not observed.

MS (ESI) m/z: 247.2 (M+H)⁺.

[0410] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(5-chloropyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-

sulfonate (250 mg, 0.69 mmol, Mesylate- 1),

1-(5-chloropyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one (171 mg, 0.69 mmol, Step-1 of Intermediate-57), and cesium carbonate (677 mg, 2.08 mmol) in DMSO (1 mL) is stirred at 80 °C for 5 hrs. The mixture is diluted with water. The precipitate is collected and dried in vacuo to give 471 mg (quantitative yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 511.3 (M+H)⁺.

[0411] Intermediate- 58:

tert-butyl

3-(5,6-dimethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

[0412] A mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (100 mg, 0.427 mmol), copper (II) acetate (155 mg, 0.854 mmol), TEA (0.298 mL, 2.13 mmol), 2,3-dimethoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (226 mg, 0.854 mmol), and molecular sieves 4 angstrom (100 mg) in DCM (3 mL) is stirred at rt for 4 days. The reaction mixture is filtered through celite pad. The filtrate is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 10-100% EtOAc in n-hexane to give 113 mg (71% yield) of the title compound as a yellow viscous oil.

¹H -NMR (400 MHz, CDCl₃) delta 7.94-7.90 (1H, m), 7.87 (1H, d, J = 2.3 Hz), 7.20-7.16 (3H, m), 6.96-6.93 (1H, m), 4.08 (3H, s), 3.89 (3H, s), 1.70 (9H, s). MS (ESI) m/z: 372.3 (M+H)⁺.

[0413] Intermediate- 59:

tert-butyl

3-(5,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

[0414] The title compound is prepared by the similar manner to Intermediate- 58 using 2,3-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (199 mg, 0.854 mmol) in place of 2,3-dimethoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 8.48 (1H, d, J = 2.3 Hz), 7.94-7.92 (1H, m), 7.60 (1H, d, J = 2.3 Hz), 7.21-7.14 (2H, m), 6.95-6.94 (1H, m), 2.58 (3H, s), 2.36 (3H, s), 1.69 (9H, s). MS (ESI) m/z: 340.3 (M+H)⁺.

[0415] Intermediate- 60:

1-(6-methoxy-5-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0416] <Step-1>: 6-methoxy-5-methylpyridin-3-amine

A solution of 2-methoxy-3-methyl-5-nitropyridine (490 mg, 2.91 mmol) in EtOAc (10 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (wet) (50 mg). The resulting mixture is evacuated and backfilled with H₂ and vigorously stirred

at rt under H₂ atmosphere for 1 h. After evacuated and backfilled with N₂, the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 394 mg (98% yield) of the title compound as a pale green oil. It is used for a next step without further purification.

¹H-NMR (400 MHz, CDCl₃) delta 7.50 (1H, d, J = 2.3 Hz), 6.87 (1H, d, J = 2.3 Hz), 3.88 (3H, s), 3.28 (2H, br s), 2.13 (3H, s).

[0417] <Step-2>: 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine

A solution 2-fluoro-nitrobenzene (30 mg, 0.213 mmol) and 6-methoxy-5-methylpyridin-3-amine (29.4 mg, 0.213 mmol) in THF (1 mL) is added potassium tert-butoxide (47.7 mg, 0.425 mmol) and stirred at rt. After 1 h, the reaction mixture is diluted with EtOAc and 0.5 M hydrochloric acid. The resulting mixture is extracted with EtOAc. The organic phase is dried over MgSO₄, filtered and concentrated. The crude mixture is purified by column chromatography on silica-gel eluting with 10-90% EtOAc in n-hexane to give 24 mg (44% yield) of the title compound as a beige solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.27 (1H, s), 8.21 (1H, dd, J = 8.7, 1.4 Hz), 7.96 (1H, d, J = 2.7 Hz), 7.38-7.32 (2H, m), 6.92 (1H, dd, J = 8.7, 0.9 Hz), 6.78-6.73 (1H, m), 3.99 (3H, s), 2.22 (3H, s).

[0418] <Step-3>: N'-(6-methoxy-5-methylpyridin-3-yl)benzidine-1,2-diamine

A solution of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine (24 mg, 0.093 mmol) in EtOAc (3 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (wet) (10 mg). The resulting mixture is evacuated and backfilled with H₂ and vigorously stirred at rt under H₂ atmosphere for 1 hr. After evacuated and backfilled with N₂, the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 20 mg (94% yield) of the title compound as a brown oil. It is used for a next step without further purification.

¹H-NMR (400 MHz, CDCl₃) delta 7.62 (1H, d, J = 2.3 Hz), 7.01 (1H, d, J = 2.3 Hz), 6.98-6.90 (2H, m), 6.80 (1H, dd, J = 7.8, 0.9 Hz), 6.74 (1H, t, J = 7.8 Hz), 3.93 (3H, s), 2.15 (3H, s).

[0419] <Step-4> : 1-(6-methoxy-5-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 90% yield (20 mg, a beige solid) by the similar manner to Step-3 of Intermediate- 51 using N¹-(6-methoxy-5-methylpyridin-3-yl)benzene-1,2-diamine (20 mg, 0.087 mmol) in place of N'-(6-bromopyridin-3-yl)benzidine-1,2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 8.88 (1H, br s), 8.18 (1H, d, J = 2.7 Hz), 7.57 (1H, d, J = 2.7 Hz), 7.14-7.04 (3H, m), 6.96 (1H, d, J = 7.8 Hz), 4.03 (3H, s), 2.27 (3H, s).

[0420] Intermediate- 61:

7-fluoro-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0421] <Step-1>: N-(2-fluoro-6-nitrophenyl)-6-methylpyridin-3-amine

The title compound is prepared in 72% yield (112 mg, a yellow solid) by the similar manner to Step-2 of Intermediate- 60 using 1,2-difluoro-3-nitrobenzene (100 mg, 0.629 mmol) and 6-methylpyridin-3-amine (68 mg, 0.629 mmol) in place of 2-fluoro-nitrobenzene and 6-methoxy-5-methylpyridin-3-amine, respectively.

¹H -NMR (400 MHz, CDCl₃) delta 8.72 (1H, br s), 8.28 (1H, t, J = 2.7 Hz), 8.03 (1H, dt, J = 8.7, 1.4 Hz), 7.32 (1H, ddd, J = 12.0, 7.9, 1.4 Hz), 7.22 (1H, dt, J = 8.2, 2.7 Hz), 7.10 (1H, d, J = 8.2 Hz), 6.96 (1H, td, J = 8.2, 4.7 Hz), 2.54 (3H, s).

[0422] <Step-2>: 7-fluoro-l-(6-methylpyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 78% yield (86 mg) by the similar manner to both Step-3 of Intermediate-60 and Step-3 of Intermediate- 51 using N-(2-fluoro-6-nitrophenyl)-6-methylpyridin-3-amine (112 mg, 0.453 mmol) as a starting material for the former step in place of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.66 (1H, s), 8.67 (1H, t, J = 2.3 Hz), 7.74 (1H, dt, J = 8.7, 2.3 Hz), 7.32 (1H, d, J = 8.7 Hz), 7.07 (1H, td, J = 8.2, 4.6 Hz), 6.95 (1H, dd, J = 8.2, 0.9 Hz), 6.85 (1H, ddd, J = 11.2, 8.2, 0.9 Hz), 2.66 (3H, s). MS (ESI) m/z: 244.3 (M+H)⁺.

[0423] Intermediate- 62:

6-fluoro-l-(6-methylpyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

[0424] <Step-1>: N-(5-fluoro-2-nitrophenyl)-6-methylpyridin-3-amine

The title compound is prepared in 72% yield (112 mg, a yellow solid) by the similar manner to Step-2 of Intermediate- 60 using 2,4-difluoro- 1-nitrobenzene (100 mg, 0.629 mmol) and 6-methylpyridin-3-amine (68 mg, 0.629 mmol) in place of 2-fluoro-nitrobenzene and 6-methoxy-5-methylpyridin-3-amine, respectively.

¹H -NMR (400 MHz, CDCl₃) delta 9.52 (1H, br s), 8.48 (1H, d, J = 2.7 Hz), 8.28 (1H, dd, J = 9.6, 5.9 Hz), 7.52 (1H, dd, J = 8.2, 2.7 Hz), 7.26 (1H, d, J = 8.2 Hz), 6.65 (1H, dd, J = 11.0, 2.7 Hz), 6.52 (1H, ddd, J = 9.6, 7.8, 2.3 Hz), 2.62 (3H, s).

[0425] <Step-2>: 6-fluoro-l-(6-methylpyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 62% yield (86 mg) by the similar manner to both Step-3 of Intermediate-60 and Step-3 of Intermediate- 51 using N-(5-fluoro-2-nitrophenyl)-6-methylpyridin-3-amine (112 mg, 0.453 mmol) as a starting material for the former step in place of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.31 (1H, br s), 8.70 (1H, d, J = 2.7 Hz), 7.78 (1H, dd, J = 8.2, 2.7 Hz), 7.37 (1H, d, J = 8.2 Hz), 7.05 (1H, dd, J = 8.9, 4.3 Hz), 6.85 (1H, td, J = 8.9, 2.3 Hz), 6.77 (1H, dd, J = 8.9, 2.3 Hz), 2.67 (3H, s). MS (ESI) m/z: 244.3 (M+H)⁺.

[0426] Intermediate-63:

5-fluoro-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0427] <Step-1>: N-(4-fluoro-2-nitrophenyl)-6-methylpyridin-3-amine

The title compound is prepared in 23% yield (35 mg, a yellow solid) by the similar manner to Step-2 of Intermediate- 60 using 1,4-difluoro-2-nitrobenzene (100 mg, 0.629 mmol) and 6-methylpyridin-3-amine (68 mg, 0.629 mmol) in place of 2-fluoro-nitrobenzene and 6-methoxy-5-methylpyridin-3-amine, respectively.

¹H -NMR (400 MHz, CDCl₃) delta 9.21 (1H, br s), 8.47 (1H, d, J = 2.7 Hz), 7.94 (1H, dd, J = 8.9, 2.7 Hz), 7.49 (1H, dd, J = 8.5, 2.7 Hz), 7.25-7.16 (2H, m), 7.07 (1H, dd, J = 9.6, 4.6 Hz), 2.60 (3H, s).

[0428] <Step-2>: 5-fluoro-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 72% yield (21 mg) by the similar manner to both Step-3 of Intermediate-60 and Step-3 of Intermediate- 51 using N-(4-fluoro-2-nitrophenyl)-6-methylpyridin-3-amine (35 mg, 0.142 mmol) as a starting material for the former step in place of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.06 (1H, br s), 8.70 (1H, d, J = 2.7 Hz), 7.79 (1H, dd, J = 8.2, 2.7 Hz), 7.36 (1H, d, J = 8.2 Hz), 6.94 (1H, dd, J = 8.7, 4.6 Hz), 6.90 (1H, dd, J = 8.2, 2.3 Hz), 6.81 (1H, ddd, J = 10.0, 8.7, 2.3 Hz), 2.66 (3H, s). MS (ESI) m/z: 244.3 (M+H)⁺.

[0429] Intermediate- 64:

4-fluoro-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0430] <Step-1>: N-(3-fluoro-2-nitrophenyl)-6-methylpyridin-3-amine

The title compound is prepared in 72% yield (112 mg, a yellow solid) by the similar manner to Step-2 of Intermediate- 60 using 1,3-difluoro-2-nitrobenzene (100 mg, 0.629 mmol) and 6-methylpyridin-3-amine (68 mg, 0.629 mmol) in place of 2-fluoro-nitrobenzene and 6-methoxy-5-methylpyridin-3-amine, respectively.

¹H -NMR (400 MHz, CDCl₃) delta 8.44 (1H, d, J = 2.7 Hz), 8.37 (1H, br s), 7.46 (1H, dd, J = 8.2, 2.7 Hz), 7.31-7.23 (1H, m), 7.21 (1H, d, J = 8.2 Hz), 6.83 (1H, dt, J = 8.7, 1.2 Hz), 6.62 (1H, ddd, J = 11.0, 8.2, 1.2 Hz), 2.58 (3H, s).

[0431] <Step-2>: 4-fluoro-1-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 88% yield (97 mg) by the similar manner to both Step-3 of Intermediate-60 and Step-3 of Intermediate- 51 using N-(3-fluoro-2-nitrophenyl)-6-methylpyridin-3-amine (112 mg, 0.453 mmol) as a starting material for the former step in place of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.11 (1H, br s), 8.70 (1H, d, J = 2.3 Hz), 7.80 (1H, dd, J = 8.2, 2.3 Hz), 7.35 (1H, d, J = 8.2 Hz), 7.02 (1H, td, J = 8.2, 5.0 Hz), 6.94-6.89

(1H, m), 6.83 (1H, dd, J = 8.2, 0.9 Hz), 2.66 (3H, s). MS (ESI) m/z: 244.3 (M+H)⁺.

[0432] Intermediate-65:

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-2-methylbenzoic acid

[0433] <Step-1>: methyl 2-methyl-5-((2-nitrophenyl)amino)benzoate

A mixture of 1-bromo-2-nitrobenzene (293 mg, 1.45 mmol), methyl 5-amino-2-methylbenzoate (200 mg, 1.21 mmol), [1,1'-bis(diphenylphosphino)ferrocene] dichloropalladium(II) complex with dichloromethane (99 mg, 0.12 mmol), 1,1'-bis(diphenylphosphino)ferrocene (13 mg, 0.024 mmol), and tripotassium phosphate (514 mg, 2.42 mmol) in toluene (3 mL) is stirred at 100 °C for 1 day. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-25% EtOAc in n-hexane to give 246 mg (71% yield) of the title compound as a brown gum. ¹H-NMR (400 MHz, CDCl₃) delta 9.45 (1H, br s), 8.21 (1H, dd, J = 8.2, 1.8 Hz), 7.83 (1H, d, J = 2.3 Hz), 7.41-7.28 (3H, m), 7.14 (1H, dd, J = 8.7, 1.4 Hz), 6.79 (1H, ddd, J = 8.2, 7.3, 1.4 Hz), 3.90 (3H, s), 2.62 (3H, s).

[0434] <Step-2>: methyl 5-((2-aminophenyl)amino)-2-methylbenzoate

The title compound is prepared in quantitative yield (246 mg, a brown gum) by the similar manner to Step-2 of Intermediate-20 using methyl 2-methyl-5-((2-nitrophenyl)amino)benzoate (275 mg, 0.96 mmol, Step-1 in Intermediate-65) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

[0435] <Step-3>: methyl

2-methyl-5-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoate

A mixture of methyl 5-((2-aminophenyl)amino)-2-methylbenzoate (246 mg, 0.96 mmol, Step-2 of Intermediate-65) and CDI (233 mg, 1.44 mmol) in THF (3 mL) is stirred at room temperature for 3 hrs. The mixture is concentrated. The residual solid is washed with diisopropyl ether to give 175 mg (65% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.21 (1H, br s), 7.95 (1H, d, J = 2.3 Hz), 7.70-7.62 (1H, m), 7.52 (1H, d, J = 8.2 Hz), 7.10-6.95 (4H, m), 3.85 (3H, m), 2.59 (3H, s). MS (ESI) m/z: 283.3 (M+H)⁺.

[0436] <Step-4>:

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-2-methylbenzoic acid

A mixture of ((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (224 mg, 0.62 mmol, Mesylate-1), methyl 2-methyl-5-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoate (175 mg, 0.62

mmol, Step-3 of Intermediate-65), and cesium carbonate (606 mg, 1.86 mmol) in DMSO (2 mL) is stirred at 80 °C for 5 hrs. Then, the mixture is diluted with water and stirred at rt for 3 days. The mixture is acidified with 2 M hydrochloric acid. The precipitate is collected and dried in vacuo to give 120 mg (36% yield) of the title compound as a purple solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.53 (1H, d, J = 2.7 Hz), 8.41 (1H, d, J = 7.8 Hz), 7.96 (1H, d, J = 2.3 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.65 (1H, dd, J = 8.2, 2.3 Hz), 7.51 (1H, d, J = 8.2 Hz), 7.34 (1H, d, J = 7.8 Hz), 7.19-7.13 (1H, m), 7.10-7.01 (2H, m), 3.77 (2H, d, J = 6.9 Hz), 3.78-3.63 (1H, m), 2.60 (3H, s), 2.51 (3H, s), 1.94-1.69 (5H, m), 1.30-1.13 (4H, m). A signal due to COOH is not observed. MS (ESI) m/z: 533.2 (M+H)⁺.

[0437] Intermediate-66:

2-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-methylbenzoic acid

[0438] <Step-1>: ethyl 5-methyl-2-((2-nitrophenyl)amino)benzoate

A mixture of 1-bromo-2-nitrobenzene (336 mg, 1.67 mmol), ethyl 2-amino-5-methylbenzoate (249 mg, 1.39 mmol), [1,1'-bis(diphenylphosphino)ferrocene] dichloropalladium(II) complex with dichloromethane (113 mg, 0.14 mmol), 1,1'-bis(diphenylphosphino)ferrocene (15 mg, 0.028 mmol), and tripotassium phosphate (589 mg, 2.77 mmol) in toluene (3 mL) is stirred at 100 °C for 1 day. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 368 mg (88% yield) of the title compound as a yellow oil. MS (ESI) m/z: 301.2 (M+H)⁺.

[0439] <Step-2>: ethyl 2-((2-aminophenyl)amino)-5-methylbenzoate

The title compound is prepared in quantitative yield (331 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate-20 using ethyl 5-methyl-2-((2-nitrophenyl)amino)benzoate (368 mg, 1.22 mmol, Step-1 in Intermediate-66) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

[0440] <Step-3>: ethyl 5-methyl-2-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate

The title compound is prepared in 35% yield (166 mg, a pale yellow solid) by the similar manner to Step-3 of Intermediate-20 using ethyl 2-((2-aminophenyl)amino)-5-methylbenzoate (331 mg, 1.22 mmol, Step-2 in Intermediate-66).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.06 (1H, m), 7.78 (1H, d, J = 1.8 Hz), 7.61 (1H, t, J = 1.4 Hz), 7.47 (1H, d, J = 8.2 Hz), 7.10-6.91 (3H, m), 6.70 (1H, d, J = 7.8 Hz), 4.02 (2H, q, J = 7.3 Hz), 2.45 (3H, s), 0.95 (3H, t, J = 7.3 Hz). MS (ESI) m/z:

297.3 (M+H)⁺.

[0441] <Step-4>:

2-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-5-methylbenzoic acid

A mixture of ((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (224 mg, 0.62 mmol, Mesylate-1), ethyl

5-methyl-2-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoate (166 mg, 0.56 mmol, Step-3 of Intermediate-66), and cesium carbonate (365 mg, 1.12 mmol) in DMSO (2 mL) is stirred at 80 °C for 5 hrs. Then, the mixture is diluted with water and stirred at rt for 3 hrs. The mixture is acidified with 2 M hydrochloric acid. The precipitate is collected and dried in vacuo to give 245 mg (82% yield) of the title compound as a purple solid.

MS (ESI) *m/z*: 533.2 (M+H)⁺.

[0442] Intermediate- 67:

3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro- 1*H*-benzo [d]imidazole- 5-carbonitrile

[0443] <Step- 1>: 3-((6-methylpyridin-3-yl)amino)-4-nitrobenzonitrile

The title compound is prepared in 19% yield (27 mg) by the similar manner to Step-2 of Intermediate-60 using 4-fluoro-3-nitrobenzonitrile (94 mg, 0.565 mmol), 6-methylpyridin-3-amine (67 mg, 0.621 mmol) and sodium tert-amylate (124 mg, 1.13 mmol) in place of 2-fluoro-nitrobenzene, 6-methoxy-5-methylpyridin-3-amine and potassium tert-butoxide, respectively.

¹H-NMR (400 MHz, CDCl₃) δ 9.36 (1H, s), 8.48 (1H, d, *J* = 2.7 Hz), 8.32 (1H, d, *J* = 8.7 Hz), 7.52 (1H, dd, *J* = 8.2, 2.7 Hz), 7.31 (1H, d, *J* = 8.2 Hz), 7.27 (1H, d, *J* = 1.4 Hz), 7.03 (1H, dd, *J* = 8.7, 1.4 Hz), 2.64 (3H, s).

[0444] <Step-2>: 4-amino-3-((6-methylpyridin-3-yl)amino)benzonitrile

A crude mixture of the title compound, which is prepared by the similar manner to Step-3 of Intermediate-60 using 3-((6-methylpyridin-3-yl)amino)-4-nitrobenzonitrile (27 mg, 0.106 mmol) in place of

6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine, is purified by column chromatography on silica-gel eluting with 7-100% EtOAc in n-hexane followed by 0-10% MeOH in EtOAc to give 17 mg (72% yield) of the title compound as a beige solid.

MS (ESI) *m/z*: 225.3 (M+H)⁺.

[0445] <Step-3>:

3-(6-methylpyridin-3-yl)-2-oxo-2, 3-dihydro- 1*H*-benzo [d]imidazole-5-carbonitrile

The title compound is prepared in 79% yield (15 mg, a beige solid) by the similar manner to Step-3 of Intermediate- 51 using

4-amino-3-((6-methylpyridin-3-yl)amino)benzonitrile (17 mg, 0.076 mmol) in place of N¹-(6-bromopyridin-3-yl)benzene-1, 2-diamine.

MS (ESI) m/z: 251.2 (M+H)⁺.

[0446] Intermediate-68:

1-(6-methoxy-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0447] <Step- 1>: 6-methoxy-4-methyl-N-(2-nitrophenyl)pyridin-3-amine

A mixture of 1-bromo-2-nitrobenzene (227 mg, 1.12 mmol), 6-methoxy-4-methylpyridin-3-amine (155 mg, 1.12 mmol), tris(dibenzylideneacetone)dipalladium(0) (205 mg, 0.224 mmol), XPhos (214 mg, 0.449 mmol), and sodium tert-pentoxide (247 mg, 2.24 mmol) in 1,4-dioxane (5 mL) is stirred at 110 °C overnight. After cooled to rt, the mixture is diluted with EtOAc and water then filtered. The filtrate is extracted with EtOAc. The filtrate is extracted with EtOAc. The organic phase is washed with brine, dried over MgSO₄ filtered and concentrated in vacuo. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 300 mg (quantitative yield) of the title compound as a brown solid.

MS (ESI) m/z: 260.3 (M+H)⁺.

[0448] <Step-2>: N¹-(6-methoxy-4-methylpyridin-3-yl)benzene-1, 2-diamine

A crude mixture of the title compound, which is prepared by the similar manner to Step-3 of Intermediate-60 using 6-methoxy-4-methyl-N-(2-nitrophenyl)pyridin-3-amine (300 mg, 1.157 mmol) in place of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine, is purified by column chromatography on silica-gel eluting with 7-100% EtOAc in n-hexane to give 170 mg (64% yield) of the title compound as a beige solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.68 (1H, s), 6.88 (1H, td, J = 7.5, 1.4 Hz), 6.79 (1H, dd, J = 7.5, 1.4 Hz), 6.71 (1H, td, J = 7.5, 1.4 Hz), 6.65-6.61 (2H, m), 4.80 (1H, br s), 3.89 (3H, s), 3.65 (2H, br s), 2.18 (3H, s).

[0449] <Step-3>: 1-(6-methoxy-4-methylpyridin-3-yl)- 1H-benzo[d]imidazol-2(3H)-one

To a solution of N¹-(6-methoxy-4-methylpyridin-3-yl)benzene-1, 2-diamine (170 mg, 0.741 mmol) in THF (1 mL) is added CDI (120 mg, 0.741 mmol) and stirred at rt for 1 h. The reaction is monitored by TLC and CDI is further added to the reaction mixture until the starting material is completely consumed. After confirmation of disappearance of the starting material by TLC, saturated aqueous sodium bicarbonate is added to the reaction mixture and stirred for 2 min. The resultant mixture is extracted with EtOAc. The organic phase is dried over MgSO₄, filtered and concentrated in vacuo. The crude mixture is purified by column chromatography on silica-gel eluting with 30-85% EtOAc in n-hexane to give 164 mg (87% yield) of the title compound as an ivory solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.88 (1H, br s), 8.15 (1H, s), 7.16 (1H, dd, J = 7.5, 1.4 Hz), 7.11 (1H, td, J = 7.5, 1.4 Hz), 7.05 (1H, td, J = 7.5, 1.4 Hz), 6.80 (1H, s), 6.71

(1H, d, J = 7.5 Hz), 3.99 (3H, s), 2.18 (3H, s).

[0450] Intermediate- 69:

1-(5-methyl-6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0451] <Step-1>: N,3-dimethyl-5-nitropyridin-2-amine

A mixture of 2-chloro-3-methyl-5-nitropyridine (200 mg, 1.16 mmol), methanamine (1.16 mL, 2.32 mmol) and TEA (0.808 mL, 5.79 mmol) in 2-propanol (3 mL) is stirred at reflux temperature overnight. After cooled to rt, the mixture is concentrated. The residue is dissolved into DCM and EtOAc (ratio 1/1), washed with water and brine, dried over MgSO_4 , filtered and concentrated in vacuo to give 172 mg (89% yield) of the title compound as a yellow solid.

^1H -NMR (400 MHz, CDCl_3) δ 8.99 (1H, d, J = 2.3 Hz), 8.01 (1H, d, J = 2.3 Hz), 4.96 (1H, br s), 3.16 (3H, d, J = 5.0 Hz), 2.16 (3H, s).

[0452] <Step-2>: N^2 ,3-dimethylpyridine-2, 5-diamine

The title compound is prepared in quantitative yield (133 mg, a pale red oil) by the similar manner to Step-1 of Intermediate- 60 using N,3-dimethyl-5-nitropyridin-2-amine (155 mg, 0.927 mmol) in place of N^1 -(6-bromopyridin-3-yl)benzene- 1,2-diamine.

^1H -NMR (400 MHz, CDCl_3) δ 7.64 (1H, d, J = 2.7 Hz), 6.80 (1H, d, J = 2.7 Hz), 3.79 (1H, s), 3.16 (2H, s), 2.98 (3H, s), 2.05 (3H, s).

[0453] <Step-3>: N^2 ,3-dimethyl- N^5 -(2-nitrophenyl)pyridine-2, 5-diamine

A mixture of 1-bromo-2-nitrobenzene (81 mg, 0.400 mmol), N^2 ,3-dimethylpyridine-2, 5-diamine (64 mg, 0.467 mmol), XPhos (63.5 mg, 0.133 mmol), tris(dibenzylideneacetone)dipalladium(0) (61 mg, 0.067 mmol), and Cs_2CO_3 (271 mg, 0.832 mmol) in 1,4-dioxane (1 mL) is stirred at 110 °C overnight. After cooled to rt, the reaction mixture is directly purified by column chromatography on silica-gel eluting with 10-100% EtOAc in n-hexane to give 104 mg (quantitative yield) of the title compound.

^1H -NMR (400 MHz, CDCl_3) δ 9.25 (1H, s), 8.19 (1H, dd, J = 8.7, 1.8 Hz), 8.01 (1H, d, J = 2.3 Hz), 7.35-7.28 (1H, m), 7.16 (1H, d, J = 2.3 Hz), 6.88 (1H, d, J = 7.8 Hz), 6.74-6.67 (1H, m), 4.30 (1H, s), 3.09 (3H, d, J = 5.0 Hz), 2.12 (3H, s). MS (ESI) m/z: 259.3 (M+H)⁺.

[0454] <Step-4>: N^5 -(2-aminophenyl)- N^2 ,3-dimethylpyridine-2, 5-diamine

A crude mixture of the title compound, which is prepared by the similar manner to Step-3 of Intermediate-60 using N^2 ,3-dimethyl- N^5 -(2-nitrophenyl)pyridine-2, 5-diamine (100 mg, 0.387 mmol) in place of 6-methoxy-5-methyl-N-(2-nitrophenyl)pyridin-3-amine, is purified by column chromatography on silica-gel eluting with 7-100% EtOAc in n-hexane to give 51 mg (45% yield) of the title compound as a brown solid.

¹H -NMR (400 MHz, CDCl₃) delta 7.79 (1H, d, J = 2.7 Hz), 6.96 (1H, d, J = 2.7 Hz), 6.89-6.82 (2H, m), 6.80-6.75 (1H, m), 6.75-6.69 (1H, m), 4.84 (1H, br s), 3.99 (1H, br s), 3.63 (2H, br s), 3.03 (3H, s), 2.07 (3H, s). MS (ESI) m/z: 229.3 (M+H)⁺.

[0455] <Step-5>:

1-(5-methyl-6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a solution of N¹-(6-methoxy-4-methylpyridin-3-yl)benzene-1, 2-diamine (51 mg, 0.223 mmol) in THF (1 mL) is added CDI (36 mg, 0.222 mmol) and stirred at rt for 1h. The reaction is monitored by TLC and CDI is further added to the reaction mixture until the starting material is completely consumed. After confirmation of disappearance of the starting material by TLC, saturated aqueous sodium bicarbonate is added to the reaction mixture and stirred for 2 min. The resultant mixture is diluted with water and DCM, then insoluble substance is collected by filtration to give 44 mg (78% yield) of the title compound as an ivory solid.

¹H -NMR (400 MHz, CDCl₃) delta 10.40 (1H, s), 8.14 (1H, d, J = 2.3 Hz), 7.35 (1H, d, J = 2.3 Hz), 7.12-6.96 (3H, m), 6.91 (1H, d, J = 7.3 Hz), 4.70 (1H, s), 3.08 (3H, d, J = 5.0 Hz), 2.14 (3H, s).

[0456] Intermediate-70:

1-(p-tolyl)-1H-imidazo[4,5-b]pyrazin-2(3H)-one

[0457] A mixture of 2,3-dichloropyrazine (198 mg, 1.33 mmol), 1-(p-tolyl)urea (200 mg, 1.33 mmol), and tripotassium phosphate (1.13 g, 5.33 mmol) in 1,4-dioxane (1 mL) is stirred at 110 °C for 7 hrs. The mixture is diluted with water, extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residual solid is washed with EtOAc to give 62 mg (21% yield) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 7.71 (1H, d, J = 3.2 Hz), 7.60 (2H, d, J = 7.8 Hz), 7.53 (1H, d, J = 3.2 Hz), 7.26 (2H, d, J = 7.8 Hz), 2.34 (3H, s). A signal due to NH is not observed. MS (ESI) m/z: 227.3 (M+H)⁺.

[0458] Intermediate-7 1:

3-(6-(dimethylamino)pyridin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

[0459] <Step-1>: N²,N²-dimethyl-N⁵-(3-nitropyridin-2-yl)pyridine-2, 5-diamine

A mixture of 2-fluoro-3-nitropyridine (104 mg, 0.73 mmol), N²,N²-dimethylpyridine-2, 5-diamine (100 mg, 0.73 mmol), and potassium carbonate (302 mg, 2.19 mmol) in DMF (3 mL) is stirred at rt for 1 day. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 155 mg (82% yield) of the title compound as a pale yellow gum.

¹H -NMR (400 MHz, CDCl₃) delta 9.78 (1H, br s), 8.50 (1H, dd, J = 8.2, 1.8 Hz),

8.41 (1H, dd, J = 4.6, 1.8 Hz), 8.31 (1H, d, J = 2.7 Hz), 7.66 (1H, dd, J = 9.1, 2.7 Hz), 6.76 (1H, dd, J = 8.2, 4.6 Hz), 6.57 (1H, d, J = 9.1 Hz), 3.11 (6H, s). MS (ESI) m/z: 260.3 (M+H)⁺.

[0460] <Step-2>: N²-(6-(dimethylamino)pyridin-3-yl)pyridine-2, 3-diamine

The title compound is prepared in quantitative yield (137 mg, a brown gum) by the similar manner to Step-2 of Intermediate- 13 using N²,N²-dimethyl-N⁵-(3-nitropyridin-2-yl)pyridine-2, 5-diamine (155 mg, 0.60 mmol, Step-1 of Intermediate-71).

MS (ESI) m/z: 230.3 (M+H)⁺.

[0461] <Step-3>: 3-(6-(dimethylamino)pyridin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

A mixture of methyl N²-(6-(dimethylamino)pyridin-3-yl)pyridine-2, 3-diamine (137 mg, 0.60 mmol, Step-2 of Intermediate-71) and CDI (194 mg, 1.20 mmol) in THF (3 mL) is stirred at room temperature for 1 day. The mixture is diluted with water. The precipitate is collected and dried to give 64 mg (45% yield) of the title compound as a gray solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.32 (1H, s), 8.23 (1H, d, J = 2.7 Hz), 7.90 (1H, dd, J = 9.1, 2.7 Hz), 7.67 (1H, dd, J = 5.0, 1.8 Hz), 7.37 (1H, dd, J = 7.8, 1.8 Hz), 7.06 (1H, dd, J = 7.8, 5.0 Hz), 6.75 (1H, d, J = 9.1 Hz), 3.08 (6H, s). MS (ESI) m/z: 256.3 (M+H)⁺.

[0462] Intermediate-72:

1-(6-(dimethylamino)pyridin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

[0463] <Step-1>: N²,N²-dimethyl-N⁵-(3-nitropyridin-4-yl)pyridine-2, 5-diamine

The title compound is prepared in 76% yield (143 mg, a pale yellow gum) by the similar manner to Step-1 of Intermediate-71 using 4-chloro-3-nitropyridine (116 mg, 0.73 mmol) in place of 2-fluoro-3-nitropyridine.

¹H -NMR (400 MHz, CDCl₃) delta 9.38 (1H, br s), 9.27 (1H, s), 8.21 (1H, d, J = 6.4 Hz), 8.10 (1H, d, J = 2.7 Hz), 7.35 (1H, dd, J = 9.1, 2.7 Hz), 6.70 (1H, d, J = 5.9 Hz), 6.59 (1H, d, J = 9.1 Hz), 3.15 (6H, s). MS (ESI) m/z: 260.3 (M+H)⁺.

[0464] <Step-2>: N⁵-(3-aminopyridin-4-yl)-N²,N²-dimethylpyridine-2, 5-diamine

The title compound is prepared in quantitative yield (127 mg, a brown gum) by the similar manner to Step-2 of Intermediate- 13 using N²,N²-dimethyl-N⁵-(3-nitropyridin-4-yl)pyridine-2, 5-diamine (143 mg, 0.55 mmol, Step-1 of Intermediate-72).

MS (ESI) m/z: 230.3 (M+H)⁺.

[0465] <Step-3>: 1-(6-(dimethylamino)pyridin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound is prepared in 50% yield (70 mg, a brown solid) by the similar manner to Step-3 of Intermediate-72 using N⁵-(3-aminopyridin-4-yl)-N²,N²-dimethylpyridine-2, 5-diamine (127 mg, 0.55 mmol, Step-2 of Intermediate-72).

¹H -NMR (400 MHz, DMSO-d₆) delta 11.37 (1H, br s), 8.27 (1H, s), 8.18 (1H, dd, J = 2.7, 0.9 Hz), 8.16 (1H, d, J = 5.5 Hz), 7.63 (1H, dd, J = 9.1, 2.7 Hz), 6.91 (1H, dd, J = 5.5, 0.9 Hz), 6.78 (1H, d, J = 9.1 Hz), 3.09 (6H, s). MS (ESI) m/z: 256.3 (M+H)⁺.

[0466] Intermediate-73:

1-(1-methyl- 1H-indazol-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

[0467] <Step-1>: 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine

A mixture of 1-bromo-2-nitrobenzene (100 mg, 0.495 mmol), 1-methyl-1H-indazol-5-amine (109 mg, 0.743 mmol), Xphos (71 mg, 0.149 mmol) and tris(dibenzylideneacetone)dipalladium(0) (68 mg, 0.074 mmol) in 1,4-dioxane (2 mL) is stirred at 110 °C overnight. After cooled to rt, the mixture is directly purified by column chromatography on silica-gel eluting with 5-90% EtOAc in n-hexane to give 140 mg (quantitative yield) of the title compound as a brown solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.56 (1H, s), 8.23 (1H, dd, J = 8.5, 1.6 Hz), 7.98 (1H, d, J = 0.9 Hz), 7.64 (1H, d, J = 1.8 Hz), 7.46 (2H, d, J = 9.1 Hz), 7.36-7.28 (2H, m), 7.00 (1H, dd, J = 8.7, 0.9 Hz), 6.78-6.71 (1H, m), 4.12 (3H, s).

[0468] <Step-2>: N¹-(1-methyl- 1H-indazol-5-yl)benzene- 1,2-diamine

A solution of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine (133 mg, 0.495 mmol) in EtOAc is evacuated and backfilled by N₂ gas. To the mixture is added 10% Pd/C (wet) (53 mg). The mixture is evacuated and backfilled with H₂ gas and vigorously stirred at rt under H₂ atmosphere. After 1 hr, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. After the filtrate is concentrated in vacuo, the residue is purified by column chromatography on silica-gel eluting with 10-60% EtOAc in n-hexane to give 105 mg (89% yield) of the title compound as a beige solid.

MS (ESI) m/z: 239.3 (M+H)⁺.

[0469] <Step-3> : 1-(1-methyl- 1H-indazol-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in 73% yield (85 mg, an off-white solid) by the similar manner to Step-3 of Intermediate-20 using N¹-(1-methyl-1H-indazol-5-yl)benzene-1, 2-diamine (105 mg, 0.441 mmol, Step-2 of Intermediate-73) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H -NMR (400 MHz, CDCl₃) delta 8.96 (1H, s), 8.06 (1H, s), 7.89 (1H, s), 7.60-7.51 (2H, m), 7.18-7.03 (3H, m), 6.98 (1H, d, J = 7.8 Hz), 4.15 (3H, s).

[0470] Intermediate-74:

1-(1H-indol-6-yl)- 1H-benzo [d]imidazol-2(3H)-one

[0471] <Step-1>: N-(2-nitrophenyl)-1H-indol-6-amine

The title compound is prepared in 57% yield (71 mg) by the similar manner to Step-1 of Intermediate-73 using 1H-indol-6-amine (98 mg, 0.743 mmol) in place of 1-methyl- 1H-indazol-5-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.62 (1H, s), 8.32 (1H, s), 8.21 (1H, dd, J = 8.7, 1.4 Hz), 7.67 (1H, d, J = 8.2 Hz), 7.34-7.28 (1H, m), 7.28-7.24 (5H, m), 7.13 (1H, dd, J = 8.7, 1.4 Hz), 7.05 (1H, dd, J = 8.2, 1.8 Hz), 6.74-6.69 (1H, m), 6.61-6.57 (1H, m).

[0472] <Step-2>: N¹-(1H-indol-6-yl)bcnzcnc- 1,2-diamine

The title compound is prepared in 54% yield (34 mg) by the similar manner to Step-2 of Intermediate-73 using N-(2-nitrophenyl)-1H-indol-6-amine (71 mg, 0.280 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H -NMR (400 MHz, CDCl₃) delta 7.89 (1H, s), 7.49 (1H, d, J = 8.2 Hz), 7.13 (1H, dd, J = 7.8, 1.4 Hz), 7.06-7.03 (1H, m), 7.02-6.97 (1H, m), 6.82 (1H, dd, J = 7.8, 1.4 Hz), 6.79-6.71 (2H, m), 6.70-6.68 (1H, m), 6.47-6.44 (1H, m), 5.20 (1H, s), 3.77 (2H, s).

[0473] <Step-3>: 1-(1H-indol-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 74% yield (28 mg, a beige solid) by the similar manner to Step-3 of Intermediate-20 using N¹-1H-indol-6-ylbenzene-1, 2-diamine (34 mg, 0.152 mmol, Step-2 of Intermediate-74) in place of N¹-(2,4-difluorophenyl)benzene- 1,2-diamine.

[0474] Intermediate-75:

1-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0475] <Step-1>: 2-(3-methoxyazetidin-1-yl)-5-nitropyridine

A mixture of 2-chloro-5-nitropyridine (75 mg, 0.473 mmol), 3-methoxyazetidine hydrochloride (62 mg, 0.568 mmol) and potassium carbonate (372 mg, 2.37 mmol) in DMF is stirred at 50 °C overnight. After cooled to rt, the mixture is diluted with EtOAc and water then extracted with EtOAc. Organic phase is washed with water and brine, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-60% EtOAc in n-hexane to give 84 mg (85% yield) of the title compound as a brown solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.04 (1H, d, J = 2.3 Hz), 8.19 (1H, dd, J = 9.4, 2.3 Hz), 6.20 (1H, d, J = 9.4 Hz), 4.50-4.29 (3H, m), 4.17-4.00 (2H, m), 3.37 (3H, s).

[0476] <Step-2>: 6-(3-methoxyazetidin-1-yl)pyridin-3-amine

The title compound is prepared in 81% yield (58 mg, a purple solid) by the similar manner to Step-2 of Intermediate-73 using 2-(3-methoxyazetidin-1-yl)-5-nitropyridine (84 mg, 0.400 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H -NMR (400 MHz, CDCl₃) delta 7.75 (1H, d, J = 2.7 Hz), 6.98 (1H, dd, J = 8.7, 2.7 Hz), 6.26 (1H, d, J = 8.7 Hz), 4.37-4.29 (1H, m), 4.18-4.12 (2H, m), 3.79 (2H, dd, J = 8.7, 4.6 Hz), 3.33 (3H, s), 3.26 (2H, s).

[0477] <Step-3>: N¹-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)benzene- 1,2-diamine

A mixture of 1-bromo-2-nitrobenzene (103 mg, 0.508 mmol), 6-(3-methoxyazetidin-1-yl)pyridin-3-amine (58 mg, 0.324 mmol), cesium carbonate

(276 mg, 0.847 mmol), Xphos (81 mg, 0.169 mmol) and tris(dibenzylideneacetone)dipalladium(0) (78 mg, 0.085 mmol) in 1,4-dioxane (2 mL) is stirred at 110 °C overnight. After cooled to rt, the mixture is directly purified by column chromatography on silica-gel eluting with 5-90% EtOAc in n-hexane. The fractions containing 6-(3-methoxyazetidin-1-yl)-N-(2-nitrophenyl)pyridin-3-amine are collected and concentrated. The residue (115 mg) is dissolved into EtOAc (2 mL) and treated with 10% Pd/C (wet) (36 mg) and H₂ gas in a similar manner to Step-2 of Intermediate-73 to give the title compound (75 mg, 82% yield) as a brown gum.

¹H-NMR (400 MHz, CDCl₃) delta 7.89 (1H, d, J = 2.7 Hz), 7.12 (1H, dd, J = 8.7, 2.7 Hz), 6.92-6.85 (2H, m), 6.78 (1H, dd, J = 8.2, 1.4 Hz), 6.76-6.70 (1H, m), 6.31 (1H, d, J = 8.7 Hz), 4.90 (1H, s), 4.38-4.32 (1H, m), 4.23-4.16 (2H, m), 3.88-3.82 (2H, m), 3.65 (2H, s), 3.34 (3H, s).

[0478] <Step-4>:

1-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 74% yield (61 mg, a beige powder) by the similar manner to Step-3 of Intermediate-20 using N¹-

(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)benzene-1, 2-diamine (75 mg, 0.277 mmol, Step-3 of Intermediate-75) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.39 (1H, s), 8.30 (1H, d, J = 2.5 Hz), 7.60 (1H, dd, J = 8.9, 2.5 Hz), 7.17-7.02 (3H, m), 6.94 (1H, d, J = 7.3 Hz), 6.45 (1H, d, J = 8.9 Hz), 4.43-4.36 (1H, m), 4.34-4.26 (2H, m), 3.98 (2H, dd, J = 9.6, 4.1 Hz), 3.37 (3H, s).

[0479] Intermediate-76:

1-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0480] <Step-1>: 2-(3-fluoroazetidin-1-yl)-5-nitropyridine

The title compound is prepared in 85% yield (79 mg, a brown solid) by the similar manner to Step-1 of Intermediate-75 using 3-fluoroazetidine hydrochloride (63 mg, 0.568 mmol) in place of 3-methoxyazetidine hydrochloride.

¹H-NMR (400 MHz, CDCl₃) delta 9.05 (1H, d, J = 2.7 Hz), 8.23 (1H, dd, J = 9.1, 2.7 Hz), 6.25 (1H, d, J = 9.1 Hz), 5.66-5.37 (1H, m), 4.59-4.41 (2H, m), 4.41-4.23 (2H, m).

[0481] <Step-2>: 6-(3-fluoroazetidin-1-yl)pyridin-3-amine

The title compound is prepared in 93% yield (62 mg, a purple gum) by the similar manner to Step-2 of Intermediate-73 using 2-(3-methoxyazetidin-1-yl)-5-nitropyridine (79 mg, 0.400 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H-NMR (400 MHz, CDCl₃) delta 7.76 (1H, t, J = 1.4 Hz), 7.00 (1H, dd, J = 9.1, 2.7 Hz), 6.28 (1H, d, J = 9.1 Hz), 5.53-5.29 (1H, m), 4.31-4.17 (2H, m), 4.10-3.96 (2H, m), 3.29 (2H, s).

[0482] <Step-3>: N¹-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)benzene-1,2-diamine

The title compound is prepared in 89% yield (78 mg, a brown gum) by the similar manner to Step-3 of Intermediate-75 using 6-(3-fluoroazetidin-1-yl)pyridin-3-amine (62 mg, 0.371 mmol) and 6-(3-fluoroazetidin-1-yl)-N-(2-nitrophenyl)pyridin-3-amine in place of 6-(3-methoxyazetidin-1-yl)pyridin-3-amine and 6-(3-methoxyazetidin-1-yl)-N-(2-nitrophenyl)pyridin-3-amine, respectively.

¹H-NMR (400 MHz, CDCl₃) delta 7.89 (1H, d, J = 2.7 Hz), 7.12 (1H, dd, J = 8.9, 2.7 Hz), 6.93-6.88 (2H, m), 6.79 (1H, dd, J = 8.0, 1.6 Hz), 6.76-6.71 (1H, m), 6.32 (1H, d, J = 8.9 Hz), 5.58-5.29 (1H, m), 4.92 (1H, s), 4.40-4.21 (2H, m), 4.19-3.97 (2H, m), 3.67 (2H, s).

[0483] <Step-4>: 1-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 83% yield (71 mg, a pink powder) by the similar manner to Step-3 of Intermediate-20 using N¹-

(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)benzene-1, 2-diamine (78 mg, 0.302 mmol, Step-3 of Intermediate-76) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 10.21 (1H, s), 8.30 (1H, d, J = 1.8 Hz), 7.64 (1H, dd, J = 8.7, 1.8 Hz), 7.19-6.97 (3H, m), 6.92 (1H, d, J = 7.8 Hz), 6.48 (1H, d, J = 8.7 Hz), 5.61-5.36 (1H, m), 4.49-4.31 (2H, m), 4.28-4.12 (2H, m).

[0484] Intermediate-77:

1-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0485] <Step-1>: 2-(3,3-difluoroazetidin-1-yl)-5-nitropyridine

The title compound is prepared in 84% yield (86 mg, a brown solid) by the similar manner to Step-1 of Intermediate-75 using 3,3-difluoroazetidine hydrochloride (74 mg, 0.57 mmol) in place of 3-methoxyazetidine hydrochloride.

¹H-NMR (400 MHz, CDCl₃) delta 9.07 (1H, d, J = 2.7 Hz), 8.29 (1H, dd, J = 9.1, 2.7 Hz), 6.34 (1H, d, J = 9.1 Hz), 4.52 (4H, t, J = 11.7 Hz).

[0486] <Step-2>: 6-(3,3-difluoroazetidin-1-yl)pyridin-3-amine

The title compound is prepared in 88% yield (65 mg, a purple solid) by the similar manner to Step-2 of Intermediate-73 using

2-(3,3-difluoroazetidin-1-yl)-5-nitropyridine (86 mg, 0.40 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H-NMR (400 MHz, CDCl₃) delta 7.76 (1H, d, J = 2.3 Hz), 7.01 (1H, dd, J = 8.7, 2.3 Hz), 6.32 (1H, dd, J = 8.7, 0.9 Hz), 4.27 (4H, t, J = 12.1 Hz), 3.34 (2H, s).

[0487] <Step-3>: N¹-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)benzene-1, 2-diamine

The title compound is prepared in 59% yield (55 mg, a brown solid) by the similar manner to Step-3 of Intermediate-75 using

6-(3,3-difluoroazetidin-1-yl)pyridin-3-amine (65 mg, 0.351 mmol) and

6-(3,3-difluoroazetidin-1-yl)-N-(2-nitrophenyl)pyridin-3-amine in place of 6-(3-methoxyazetidin-1-yl)pyridin-3-amine and

6-(3-methoxyazetidin-1-yl)-N-(2-nitrophenyl)pyridin-3-amine, respectively.

¹H-NMR (400 MHz, CDCl₃) delta 7.89 (1H, d, J = 2.3 Hz), 7.12 (1H, dd, J = 8.7, 2.3 Hz), 6.96-6.91 (2H, m), 6.79 (1H, dd, J = 8.2, 1.4 Hz), 6.77-6.71 (1H, m), 6.37 (1H, d, J = 8.7 Hz), 4.96 (1H, s), 4.31 (4H, t, J = 12.1 Hz), 3.69 (2H, s).

[0488] <Step-4>:

1-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 70% yield (42 mg, a purple powder) by the similar manner to Step-3 of Intermediate-20 using N¹-

(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)benzene-1, 2-diamine (55 mg, 0.199 mmol, Step-3 of Intermediate-77) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 10.11 (1H, s), 8.35 (1H, d, J = 2.7 Hz), 7.70 (1H, dd, J = 8.7, 2.7 Hz), 7.13-7.00 (3H, m), 6.93 (1H, d, J = 7.8 Hz), 6.55 (1H, d, J = 8.7 Hz), 4.43 (4H, t, J = 12.1 Hz).

[0489] Intermediate-78:

1-(6-(oxetan-3-ylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

[0490] <Step-1>: 5-nitro-N-(oxetan-3-yl)pyridin-2-amine

A mixture of 2-chloro-5-nitropyridine (75 mg, 0.473 mmol), oxetan-3-amine (45 mg, 0.615 mmol) and triethylamine (0.330 mL, 2.37 mmol) in 2-propanol (1 mL) is stirred at 70 °C overnight then at 120 °C for 1 hr under microwave irradiation. After the reaction mixture is concentrated, the residue is dissolved into EtOAc, washed with water and brine, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-90% EtOAc in n-hexane to give 84 mg (85% yield) of the title compound as a brown solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.01 (1H, d, J = 2.7 Hz), 8.22 (1H, dd, J = 9.1, 2.7 Hz), 6.39 (1H, d, J = 9.1 Hz), 5.63 (1H, s), 5.19-5.07 (1H, m), 5.04 (2H, t, J = 6.6 Hz), 4.58 (2H, t, J = 6.6 Hz).

[0491] <Step-2>: N²-(oxetan-3-yl)pyridine-2, 5-diamine

The title compound is prepared in quantitative yield (50 mg, a red gum) by the similar manner to Step-2 of Intermediate-73 using

5-nitro-N-(oxetan-3-yl)pyridin-2-amine (55 mg, 0.282 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H-NMR (400 MHz, CDCl₃) delta 7.68 (1H, d, J = 2.7 Hz), 6.95 (1H, dd, J = 8.7, 2.7 Hz), 6.27 (1H, d, J = 8.7 Hz), 4.99 (2H, t, J = 6.9 Hz), 4.62-4.44 (3H, m), 3.25 (2H, s).

[0492] <Step-3>: N⁵-(2-nitrophenyl)-N²-(oxetan-3-yl)pyridine-2, 5-diamine

The title compound is prepared in 21% yield (20 mg) by the similar manner to Step-3 of Intermediate-69 using N²-(oxetan-3-yl)pyridine-2, 5-diamine (50 mg, 0.30 mmol) in place of N²,3-dimethyl-N⁵-(2-nitrophenyl)pyridine-2, 5-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.24 (1H, s), 8.20 (1H, dd, J = 8.7, 2.3 Hz), 8.05

(1H, d, J = 2.3 Hz), 7.41-7.31 (2H, m), 6.87 (1H, d, J = 8.7 Hz), 6.74 (1H, t, J = 7.8 Hz), 6.45 (1H, d, J = 8.7 Hz), 5.15-4.92 (4H, m), 4.59 (2H, t, J = 5.5 Hz).

[0493] <Step-4>: N⁵-(2-aminophenyl)-N²-(oxetan-3-yl)pyridine-2, 5-diamine

The title compound is prepared in 39% yield (7 mg) by the similar manner to Step-2 of Intermediate-73 using N⁵-(2-nitrophenyl)-N²-(oxetan-3-yl)pyridine-2, 5-diamine (20 mg, 0.070 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H -NMR (400 MHz, CDCl₃) delta 7.79 (1H, d, J = 2.3 Hz), 7.08 (1H, dd, J = 8.7, 2.3 Hz), 6.94-6.84 (2H, m), 6.78 (1H, dd, J = 8.2, 1.4 Hz), 6.73 (1H, td, J = 7.7, 1.4 Hz), 6.33 (1H, d, J = 8.7 Hz), 5.00 (2H, t, J = 6.6 Hz), 4.96-4.84 (2H, m), 4.70 (1H, d, J = 6.9 Hz), 4.54 (2H, t, J = 6.6 Hz).

[0494] <Step-5>: 1-(6-(oxetan-3-ylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a solution of N⁵-(2-aminophenyl)-N²-(oxetan-3-yl)pyridine-2, 5-diamine (7 mg, 0.027 mmol) in THF is added CDI (5 mg, 0.031 mmol) is stirred at rt for 1 hr. Further CDI is added until the starting material is completely consumed. After confirmation of disappearance of starting material, the reaction mixture is diluted with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is dried over MgSO₄, filtered and concentrated to give the title compound which is used without further purification.

MS (ESI) m/z: 283.2 (M+H)⁺.

[0495] Intermediate-79:

tert-butyl

3-(1-methyl-1H-pyrrolo[2, 3-b]pyridin-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazole-1-carboxylate

[0496] The title compound is prepared in 57% yield (80 mg, an off-white solid) by the similar manner to Intermediate-58 using

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine (100 mg, 0.908 mmol) in place of

2,3-dimethoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 8.40 (1H, d, J = 2.3 Hz), 8.00 (1H, d, J = 2.3 Hz), 7.94 (1H, dd, J = 7.3, 1.8 Hz), 7.30 (1H, d, J = 3.7 Hz), 7.21-7.11 (2H, m), 6.87 (1H, dd, J = 7.5, 1.1 Hz), 6.52 (1H, d, J = 3.7 Hz), 3.95 (3H, s), 1.70 (9H, s).

[0497] Intermediate-80:

1-(benzo[d]oxazol-6-yl)-1H-benzo[d]imidazol-2(3H)-one

[0498] <Step-1>: N-(2-nitrophenyl)benzo[d]oxazol-6-amine

The title compound is prepared in 49% yield (62 mg) by the similar manner to Step-1 of Intermediate-73 using benzo[d]oxazol-6-amine (100 mg, 0.743 mmol) in place of 1-methyl-1H-indazol-5-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.58 (1H, s), 8.24 (1H, dd, J = 8.7, 1.8 Hz), 8.12

(1H, s), 7.82 (1H, d, J = 8.2 Hz), 7.54 (1H, d, J = 1.8 Hz), 7.43-7.36 (1H, m), 7.31 (1H, dd, J = 8.2, 1.8 Hz), 7.22 (1H, dd, J = 8.7, 0.9 Hz), 6.86-6.79 (1H, m).

[0499] <Step-2>: N¹-(benzo[d]oxazol-6-yl)benzene-1, 2-diamine

The title compound is prepared in 51% yield (28 mg) by the similar manner to Step-2 of Intermediate-73 using N-(2-nitrophenyl)benzo[d]oxazol-6-amine (62 mg, 0.243 mmol) in place of 1-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine.

¹H-NMR (400 MHz, CDCl₃) delta 7.91 (1H, s), 7.59 (1H, d, J = 9.1 Hz), 7.14 (2H, dd, J = 7.8, 1.4 Hz), 7.07 (2H, td, J = 7.8, 1.4 Hz), 6.86-6.81 (3H, m), 6.79 (1H, td, J = 7.8, 1.4 Hz), 5.36 (1H, s), 3.80 (2H, s).

[0500] <Step-3>: 1-(benzo[d]oxazol-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 51% yield (16 mg, an off-white solid) by the similar manner to Step-3 of Intermediate-20 using N¹-(benzo[d]oxazol-6-yl)benzene-1, 2-diamine (28 mg, 0.124 mmol, Step-2 of Intermediate-80) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.04 (1H, s), 8.21 (1H, s), 7.96 (1H, d, J = 8.2 Hz), 7.86 (1H, d, J = 1.8 Hz), 7.59 (1H, dd, J = 8.7, 1.8 Hz), 7.19-7.14 (2H, m), 7.11-7.06 (2H, m).

[0501] Intermediate-81:

tert-butyl

3-(1-methyl-1H-pyrrolo[3, 2-b]pyridin-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazole-1-carboxylate

[0502] <Step-1>:

1-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[3,2-b]pyridine

A mixture of 6-bromo-1-methyl-1H-pyrrolo[3,2-b]pyridine (90 mg, 0.426 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (162 mg, 0.640 mmol), potassium acetate (126 mg, 1.28 mmol) and Pd(dppf)Cl₂ (31 mg, 0.043 mmol) in 1,4-dioxane (2 mL) is stirred at 130 °C for 30 min. After cooled to rt, the mixture is directly purified by column chromatography on silica-gel eluting with 10-90% EtOAc in n-hexane to give 30 mg of the title compound with impurities. This is used for the next step without further purification.

¹H-NMR (400 MHz, CDCl₃) delta 8.83 (1H, d, J = 1.4 Hz), 8.06 (1H, s), 7.33 (1H, d, J = 3.2 Hz), 6.71 (1H, dd, J = 3.2, 0.9 Hz), 3.84 (3H, s), 1.39 (12H, s).

[0503] <Step-2>: tert-butyl

3-(1-methyl-1H-pyrrolo[3, 2-b]pyridin-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 17% yield (7 mg) by the similar manner to Intermediate-58 using

1-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[3,2-b]pyridine

(30 mg, 0.116 mmol, Step-1 of Intermediate-81) in place of
2,3-dimethoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine.

¹H-NMR (400 MHz, CDCl₃) delta 8.55 (1H, d, J = 1.8 Hz), 7.94 (1H, dd, J = 7.1, 2.1 Hz), 7.81 (1H, d, J = 1.8 Hz), 7.41 (1H, d, J = 3.2 Hz), 7.22-7.12 (2H, m), 6.95 (1H, dd, J = 6.9, 2.1 Hz), 6.78 (1H, d, J = 3.2 Hz), 3.83 (3H, s), 1.70 (9H, s).

MS (ESI) m/z: 365.1 (M+H)⁺.

[0504] Intermediate-82:

tert-butyl

2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 65% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-81 using

6-bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-b]pyridine in place of
6-bromo-1-methyl-1H-pyrrolo[3,2-b]pyridine.

MS (ESI) m/z: 481.1 (M+H)⁺.

[0505] Intermediate-83:

tert-butyl

7-(3-(tert-butoxycarbonyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-2H-pyrido[3,2-b][1,4]oxazine-4(3H)-carboxylate

The title compound is prepared in 17% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-81 using tert-butyl

7-bromo-2H-pyrido[3,2-b][1,4]oxazine-4(3H)-carboxylate in place of
6-bromo-1-methyl-1H-pyrrolo[3,2-b]pyridine.

¹H-NMR (400 MHz, CDCl₃) delta 8.22 (1H, d, J = 2.3 Hz), 7.91-7.90 (1H, m), 7.39 (1H, d, J = 2.3 Hz), 7.18-7.16 (2H, m), 7.00-6.99 (1H, m), 4.31 (2H, t, J = 4.6 Hz), 3.99 (2H, t, J = 4.6 Hz), 1.69 (9H, s), 1.57 (9H, s).

[0506] Intermediate-84:

1-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (149 mg, 0.637 mmol), copper (II) acetate (347 mg, 1.91 mmol), TEA (0.266 mL, 1.91 mmol),

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine (165 mg, 0.637 mmol), and molecular sieves 4 A (100 mg) in DMF (0.5 mL) is stirred at 90 °C for 7 hrs. The reaction mixture is filtered through celite pad. The filtrate is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 2-20% MeOH in DCM to give 27 mg (16% yield) of the title compound as a yellow solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.72 (1H, s), 8.24 (1H, d, J = 1.6 Hz), 8.10 (1H, s),

7.16-7.05 (4H, m), 6.97 (1H, d, J = 7.5 Hz), 4.23 (3 H, s).

MS (ESI) m/z: 266.2 (M+H)⁺.

[0507] Intermediate- 85:

tert-butyl

3-(3-methyl-2-oxo-2, 3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazole- 1-carboxylate

The title compound is prepared in 58% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate- 81 using 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one in place of 6-bromo-1-methyl-1H-pyrrolo[3,2-b]pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 7.93-7.91 (1H, m), 7.37 (1H, d, J = 1.8 Hz), 7.34 (1H, dd, J = 8.2, 1.8 Hz), 7.20-7.15 (2H, m), 7.10 (1H, d, J = 8.2 Hz), 6.91-6.90 (1H, m), 3.47 (3H, s), 1.69 (9H, s).

MS (ESI) m/z: 382.2 (M+H)⁺.

[0508] Intermediate- 86:

tert-butyl

2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound (orange oil) is prepared in 72% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-8 1 using 6-bromoquinoxaline in place of 6-bromo- 1-methyl- 1H-pyrrolo[3,2-b]pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 8.92 (2H, d, J = 1.4 Hz), 8.31-8.27 (2H, m), 8.02-7.97 (2H, m), 7.24-7.18 (2H, m), 7.16-7.13 (1H, m), 1.71 (9H, s).

MS (ESI) m/z: 363.1 (M+H)⁺.

[0509] Intermediate- 87:

N-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

A mixture of methyl 5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (9.00 g, 33.4 mmol, Step-3 of Intermediate-36) and 40% methylamine in MeOH (300 mL) is stirred at room temperature for 2 hrs. The mixture is concentrated. The residual solid is washed with EtOAc to give 8.27 g (92% yield) of the title compound as a pale pink solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.19 (1H, br s), 8.87 (1H, t, J = 1.4 Hz), 8.85 (1H, q, J = 5.0 Hz), 8.24-8.18 (2H, m), 7.19-7.10 (3H, m), 7.10-7.00 (1H, m), 2.86 (3H, d, J = 5.0 Hz).

MS (ESI) m/z: 269.2 (M+H)⁺.

[0510] Intermediate- 88:

1-(chroman-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step- 1>: N-(2-nitrophenyl)chroman- 3-amine

To a mixture of chroman-3-amine hydrochloride (105 mg, 0.567 mmol), 1-fluoro-2-nitrobenzene (80 mg, 0.567 mmol) and potassium carbonate (157 mg, 1.134

mmol) in DMF (2 mL) is stirred at 90 °C for 25 hrs. The mixture is poured into water, extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-10% EtOAc in n-hexane to give 102 mg (67% yield) of the title compound as a yellow solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.21 (1H, br s), 8.20 (1H, dd, J = 8.7, 1.6 Hz), 7.55-7.45 (1H, m), 7.19-7.13 (1H, m), 7.12-7.06 (1H, m), 6.99 (1H, d, J = 8.7 Hz), 6.96-6.88 (2H, m), 6.74-6.68 (1H, m), 4.38-4.33 (1H, m), 4.22-4.13 (1H, m), 4.12-4.05 (1H, m), 3.25 (1H, dd, J = 16.0, 4.7 Hz), 2.96 (1H, dd, J = 16.0, 6.7 Hz). MS (ESI) m/z: 271.2 (M+H)⁺.

[0511] <Step-2>: N'-(chroman-3-yl)bcnzcnc-1,2-diamine

A solution of N-(2-nitrophenyl)chroman-3-amine (102 mg, 0.377 mmol, Step-1 of Intermediate-88) in MeOH (2 mL) and THF (4 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (10 mg). The mixture is evacuated and backfilled with H₂ gas and stirred at rt under H₂ atmosphere. After 1hr, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 91 mg (99% yield) of the title compound.

¹H-NMR (400 MHz, DMSO-d₆) delta 7.11-7.05 (2H, m), 6.84 (1H, td, J = 7.3, 1.4 Hz), 6.80-6.76 (1H, m), 6.61 (1H, dd, J = 7.4, 1.4 Hz), 6.56 (1H, dd, J = 7.3, 1.6 Hz), 6.51 (1H, td, J = 7.4, 1.6 Hz), 6.45 (1H, td, J = 7.3, 1.4 Hz), 4.50 (2H, s), 4.34 (1H, d, J = 7.1 Hz), 4.28-4.23 (1H, m), 3.86-3.78 (2H, m), 3.11-3.04 (1H, m), 2.78 (1H, dd, J = 15.8, 8.1 Hz). MS (ESI) m/z: 241.2 (M+H)⁺.

[0512] <Step-3>: 1-(chroman-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of N'-chroman-3-ylbenzene-1,2-diamine (91 mg, 0.377 mmol) and CDI (123 mg, 0.757 mmol) in THF (2 mL) is stirred at rt for 19 hrs. The reaction mixture is poured into water and extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane. The residue is purified by solidification with IPE (5 mL). The obtained solid is washed with IPE to give 86 mg (85% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.01 (1H, br s), 7.21-7.15 (1H, m), 7.13-7.04 (5H, m), 6.97-6.91 (2H, m), 4.92-4.83 (1H, m), 4.70 (1H, t, J = 10.5 Hz), 4.37 (1H, ddd, J = 10.5, 4.1, 2.0 Hz), 3.78 (1H, dd, J = 16.1, 11.1 Hz), 3.12-3.05 (1H, m). MS (ESI) m/z: 267.2 (M+H)⁺.

[0513] Intermediate- 89:

tert-butyl 1,2'-dimethyl-2-oxo-1H-[1,5'-bibenzo[d]imidazole]-3(2H)-carboxylate

The title compound (beige solid) is prepared in quantitative yield (182 mg, beige solid) by the similar manner to Step-1 and Step-2 of Intermediate- 81 using

5-bromo-1, 2-dimethyl- 1H-benzo[d] imidazole in place of
6-bromo- 1-methyl- 1H-pyrrolo[3,2-b]pyridine.

MS (ESI) m/z: 379.2 (M+H)⁺.

[0514] Intermediate-90:

tert-butyl
r,3'-dimethyl-2,2 '-dioxo-2',3'-dihydro-rH-[1,5 '-bibenzo[d]imidazole]-3(2H)-carboxyl
ate

The title compound (brown solid) is prepared in 30% yield in 2 steps by the similar
manner to Step-1 and Step-2 of Intermediate-8 1 using

5-bromo-1, 3-dimethyl- 1H-benzo[d]imidazol-2(3H)-one in place of
6-bromo- 1-methyl- 1H-pyrrolo[3,2-b]pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 7.95-7.91 (1H, m), 7.20-7.13 (3H, m), 7.10 (1H, d,
J = 1.8 Hz), 7.08 (1H, d, J = 8.2 Hz), 6.92-6.88 (1H, m), 3.48 (3H, s), 3.43 (3H, s),
1.69 (9H, s).

MS (ESI) m/z: 395.2 (M+H)⁺.

[0515] Intermediate-9 1:

tert-butyl
3-(3-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazol-5-yl)-2-oxo-2, 3-dihydro-
1H-benzo[d]imidazole- 1-carboxylate

The title compound is prepared in 23% yield in 2 steps by the similar manner to Step-
1 and Step-2 of Intermediate- 8 1 using

5-bromo-3-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole in place of
6-bromo- 1-methyl- 1H-pyrrolo[3,2-b]pyridine.

MS (ESI) m/z: 495.2 (M+H)⁺.

[0516] Intermediate-92:

1-(3-methylbenzo [d]isoxazol-6-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in 20% yield in 2 steps by the similar manner to Step-
1 and Step-2 of Intermediate- 8 1 using 6-bromo-3-methylbenzo[d]isoxazole in place of
6-bromo- 1-methyl- 1H-pyrrolo[3,2-b]pyridine.

MS (ESI) m/z: 466.2 (M+H)⁺.

[0517] Intermediate-93:

1-(3-methyl- 1-(tetrahydro-2H-pyran-2-yl)- 1H-pyrazolo[4,3-b]pyridin-6-yl)- 1H-benz
o[d]imidazol-2(3H)-one

The title compound (brown gum) is prepared in 51% yield in 2 steps by the similar
manner to Step-1 and Step-2 of Intermediate-8 1 using
6-bromo-3-methyl- 1-(tetrahydro-2H-pyran-2-yl)- 1H-pyrazolo[4,3-b]pyridine in place
of 6-bromo- 1-methyl- 1H-pyrrolo[3,2-b]pyridine.

MS (ESI) m/z: 450.3 (M+H)⁺.

[05 18] Intermediate-94:

1-(2,3-dihydro-1H-inden-2-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: 5-bromo-N-(2-nitrophenyl)-2, 3-dihydro- 1H-inden-2-amine

A mixture of 1-fluoro-2-nitrobenzene (50 mg, 0.354 mmol), 5-bromo-2, 3-dihydro- 1H-inden-2-amine hydrobromide (104 mg, 0.354 mmol) and potassium carbonate (171 mg, 1.24 mmol) in DMA (1 mL) is stirred at 80 °C for 6 hrs. After cooled to rt, the reaction mixture is diluted with EtOAc, washed with water, dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-40% EtOAc in n-hexane to give 118 mg (quantitative yield) of the title compound as a yellow oil.

^1H -NMR (400 MHz, CDCl_3) δ 8.24 (1H, d, J = 5.9 Hz), 8.19 (1H, dd, J = 8.7, 1.4 Hz), 7.48 (1H, ddd, J = 8.7, 7.8, 1.4 Hz), 7.39 (1H, s), 7.33 (1H, dd, J = 7.8, 1.8 Hz), 7.12 (1H, d, J = 8.2 Hz), 6.94 (1H, d, J = 7.8 Hz), 6.72-6.66 (1H, m), 4.55-4.45 (1H, m), 3.44 (2H, td, J = 16.1, 7.2 Hz), 2.97 (2H, td, J = 17.2, 5.0 Hz).

[0519] <Step-2>: N'-(2, 3-dihydro- 1H-inden-2-yl)benzene-1, 2-diamine

A solution of 5-bromo-N-(2-nitrophenyl)-2,3-dihydro-1H-inden-2-amine (118 mg, 0.354 mmol, Step-1 of Intermediate-94) in EtOAc (1 mL) in a round bottle flask is evacuated and backfilled with N_2 gas (three times). To this is added 10% Pd on carbon (38 mg). The resultant mixture is evacuated and backfilled with hydrogen gas and vigorously stirred at rt for 1 hr. To the reaction mixture is added 1 M hydrochloric acid (0.1 mL) and stirring is continued for 1.5 hrs. After replacing H_2 with N_2 , the mixture is filtered through celite pad and the filtrate is concentrated. The residual oil is purified by column chromatography on silica-gel eluting with 2-40% EtOAc in n-hexane to give 31 mg (50%) of the title compound as a purple oil.

^1H -NMR (400 MHz, CDCl_3) δ 7.25-7.20 (2H, m), 7.20-7.15 (2H, m), 6.88-6.82 (1H, m), 6.77 (1H, d, J = 7.3 Hz), 6.74-6.67 (2H, m), 4.37-4.31 (1H, m), 3.70-3.30 (4H, m), 2.92 (2H, dd, J = 16.0, 4.6 Hz).

MS (ESI) m/z: 225.3 ($\text{M}+\text{H}$) $^+$.

[0520] <Step-3>: 1-(2,3-dihydro-1H-inden-2-yl)-1H-benzo[d]imidazol-2(3H)-one

To a solution of N'-(2, 3-dihydro- 1H-inden-2-yl)benzene-1, 2-diamine (40 mg, 0.178 mmol, Step-2 of Intermediate-94) in THF (1.5 mL) is added CDI (31 mg, 0.191 mmol) and stirred at rt for 2 days. The reaction mixture is diluted with EtOAc, washed with water, dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-90% EtOAc in n-hexane to give 26 mg (54%) of the title compound as a beige solid.

^1H -NMR (400 MHz, CDCl_3) δ 8.43-8.24 (1H, m), 7.31-7.21 (4H, m), 7.09-7.04 (1H, m), 7.02 (1H, dd, J = 7.8, 0.9 Hz), 6.93 (1H, td, J = 7.5, 1.4 Hz), 6.68 (1H, d, J = 8.7 Hz), 5.58-5.47 (1H, m), 3.50 (2H, dd, J = 16.7, 7.5 Hz), 3.43 (2H, dd, J = 16.5, 9.6

Hz).

MS (ESI) m/z: 251.2 (M+H)⁺.

[0521] Intermediate-95

1-(2,3-dimethyl-2H-indazol-5-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: 5-bromo-2,3-dimethyl-2H-indazole

To a solution of 5-bromo-3-methyl-1H-indazole (116 mg, 0.551 mmol) in THF (1 mL) and DMF (1 mL) is added NaH (60% in oil, 26 mg, 0.661 mmol) at 0 °C and stirred for 20 min. To the reaction mixture is added iodomethane (0.041 mL, 0.661 mmol) at 0 °C and stirred for 15 min. The reaction is quenched by adding ice-water and the resultant mixture is extracted with EtOAc. The organic phase is washed with water, dried over MgSO₄, filtered and concentrated under reduced pressure. The residue is purified by column chromatography on silica-gel eluting with 10-70% EtOAc in n-hexane to give 20 mg (16%) of the title compound as a white solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.70 (1H, d, J = 1.8 Hz), 7.49 (1H, d, J = 9.1 Hz), 7.29 (1H, dd, J = 9.1, 1.8 Hz), 4.08 (3H, s), 2.56 (3H, s).

[0522] <Step-2>: 1-(2,3-dimethyl-2H-indazol-5-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 1H-benzo[d]imidazol-2(3H)-one (60 mg, 0.444 mmol), 5-bromo-2,3-dimethyl-2H-indazole (20 mg, 0.089 mmol, Step-1 of Intermediate-95), copper(I) iodide (42 mg, 0.222 mmol), N,N'-dimethylethane-1,2-diamine (0.048 mL, 0.444 mmol) and Cs₂CO₃ (217 mg, 0.666 mmol) in DMA (1 mL) is stirred at 100 °C overnight then at 150 °C for 16 hrs. After cooled to rt, the reaction mixture is diluted with EtOAc, washed with 28% ammonia aqueous solution, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-10% methanol in EtOAc to give 9 mg (36%) of the title compound.

¹H-NMR (400 MHz, CDCl₃) delta 10.02 (1H, s), 7.78 (1H, d, J = 8.9 Hz), 7.74 (1H, d, J = 2.1 Hz), 7.35 (1H, dd, J = 8.9, 2.1 Hz), 7.15 (1H, dd, J = 7.3, 1.1 Hz), 7.10 (1H, td, J = 7.3, 1.1 Hz), 7.05 (1H, td, J = 7.3, 1.1 Hz), 6.98 (1H, d, J = 7.3 Hz), 4.16 (3H, s), 2.64 (3H, s).

MS (ESI) m/z: 279.3 (M+H)⁺.

[0523] Intermediate-96:

1-(imidazo[1,2-a]pyridin-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 18% yield (10 mg) by the similar manner to Step-2 of Intermediate-95 using 6-bromoimidazo[1,2-a]pyridine (44 mg, 0.222 mmol) in place of 5-bromo-2,3-dimethyl-2H-indazole.

¹H-NMR (400 MHz, CDCl₃) delta 9.76 (1H, br s), 8.49 (1H, d, J = 1.4 Hz), 7.80 (1H, d, J = 9.6 Hz), 7.76 (1H, s), 7.70 (1H, s), 7.34 (1H, dd, J = 9.6, 1.8 Hz), 7.20-7.07 (3H, m), 7.03 (1H, d, J = 7.3 Hz).

MS (ESI) m/z: 251.3 (M+H)⁺.

[0524] Intermediate-97:

1-(quinazolin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 10% yield (6 mg) by the similar manner to Step-2 of Intermediate-95 using 5-bromoquinazoline (46 mg, 0.222 mmol) in place of 5-bromo-2,3-dimethyl-2H-indazole.

¹H -NMR (400 MHz, CDCl₃) delta 9.43 (1H, s), 9.33 (1H, s), 8.88 (1H, s), 8.22 (1H, d, J = 7.8 Hz), 8.09 (1H, t, J = 7.8 Hz), 7.78 (1H, d, J = 7.8 Hz), 7.22-7.00 (3H, m), 6.74 (1H, d, J = 7.8 Hz).

MS (ESI) m/z: 263.3 (M+H)⁺.

[0525] Intermediate-98:

3-(2,3-dihydro-1H-inden-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step-1>: 2-((2,3-dihydro-1H-inden-5-yl)amino)nicotinic acid

A mixture of 2-chloronicotinic acid (150 mg, 0.95 mmol), 2,3-dihydro-1H-inden-5-amine (127 mg, 0.95 mmol), and p-toluenesulfonic acid monohydrate (91 mg, 0.47 mmol) in water (3 mL) is stirred at 100 °C for 1 day. The mixture is concentrated to give the title compound as a crude. The crude is used next step without purification.

MS (ESI) m/z: 255.3 (M+H)⁺.

[0526] <Step-2>: 3-(2,3-dihydro-1H-inden-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

A mixture of 2-((2,3-dihydro-1H-inden-5-yl)amino)nicotinic acid (crude, 0.95 mmol, Step-1 of Intermediate-98), diphenylphosphoryl azide (0.31 mL, 1.43 mmol), and TEA (0.27 mL, 1.90 mmol) in 1,4-dioxane (3 mL) is stirred at 100 °C for 3 hrs. The mixture is quenched with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-75% EtOAc in n-hexane to give 140 mg (59% yield in 2 steps) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 10.31-10.02 (1H, m), 8.07 (1H, dd, J = 5.0, 1.4 Hz), 7.46 (1H, s), 7.43-7.32 (3H, m), 7.03 (1H, dd, J = 7.3, 5.0 Hz), 3.08-2.90 (4H, m), 2.19-2.18 (2H, m).

MS (ESI) m/z: 252.2 (M+H)⁺.

[0527] Intermediate-99:

3-(4-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step-1>: 2-((4-methoxyphenyl)amino)nicotinic acid

A mixture of 2-chloronicotinic acid (150 mg, 0.95 mmol), 4-methoxyaniline (117 mg, 0.95 mmol), and p-toluenesulfonic acid monohydrate (91 mg, 0.47 mmol) in water (3 mL) is stirred at 100 °C for 1 day. The mixture is concentrated to give the title compound as a crude. The crude is used next step without purification.

MS (ESI) m/z: 245.3 (M+H)⁺.

[0528] <Step-2>: 3-(4-methoxyphenyl)- 1H-imidazo[4,5-b]pyridin-2(3H)-one

A mixture of 2-((4-methoxyphenyl)amino)nicotinic acid (crude, 0.95 mmol, Step-1 of Intermediate-99), diphenylphosphoryl azide (0.31 mL, 1.43 mmol), and TEA (0.27 mL, 1.90 mmol) in 1,4-dioxane (3 mL) is stirred at 100 °C for 3 hrs. The mixture is quenched with saturated aqueous sodium bicarbonate. The precipitate is collected and washed with diisopropyl ether to give 101 mg (44% yield in 2 steps) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.69 (1H, br s), 8.07 (1H, dd, J = 5.0, 1.4 Hz), 7.57 (2H, d, J = 9.1 Hz), 7.35 (1H, dd, J = 7.8, 1.4 Hz), 7.08 (2H, d, J = 9.1 Hz), 7.11-7.02 (1H, m), 3.87 (3H, s).

MS (ESI) m/z: 242.3 (M+H)⁺.

[0529] Intermediate- 100:

1-(1,3-dimethyl- 1H-indazol-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 45% yield (41 mg, brown solid) by the similar manner to Intermediate- 84 using

1,3-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (111 mg, 0.33 mmol) in place of

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 7.79 (1H, d, J = 8.5 Hz), 7.54 (1H, s), 7.26 (1H, m), 7.16-7.04 (4H, m), 6.97 (1H, d, J = 7.5 Hz), 4.02 (3H, s), 2.61 (3H, s).

MS (ESI) m/z: 279.2 (M+H)⁺.

[0530] Intermediate- 101:

N-methyl-5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

<Step-1>: methyl 5-((2-methyl-6-nitrophenyl)amino)picolinate

A mixture of 2-bromo-1-methyl-3-nitrobenzene (142 mg, 0.66 mmol), methyl 5-aminopicolinate (100 mg, 0.66 mmol), Pd₂(dba)₃ (48 mg, 0.053 mmol), Xantphos (61 mg, 0.11 mmol), and K₃P0₄ (279 mg, 1.31 mmol) in 1,4-dioxane (3 mL) is stirred at 80 °C for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 170 mg (90% yield) of the title compound as an orange gum.

¹H -NMR (400 MHz, CDCl₃) delta 8.22 (1H, d, J = 2.3 Hz), 8.05-7.93 (3H, m), 7.54 (1H, d, J = 7.8 Hz), 7.31-7.23 (1H, m), 6.90 (1H, dd, J = 8.2, 2.3 Hz), 3.97 (3H, s), 2.17 (3H, s).

MS (ESI) m/z: 288.3 (M+H)⁺.

[0531] <Step-2>: methyl 5-((2-amino-6-methylphenyl)amino)picolinate

The title compound is prepared in quantitative yield (152 mg, brown gum) by the

similar manner to Step-2 of Intermediate-20 using methyl 5-((2-methyl-6-nitrophenyl)amino)picolinate (170 mg, 0.59 mmol, Step-1 of Intermediate- 101) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.
MS (ESI) m/z: 258.3 (M+H)⁺.

[0532] <Step-3>: methyl

5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

The title compound is prepared in quantitative yield (167 mg, brown solid) by the similar manner to Step-3 of Intermediate-20 using methyl 5-((2-amino-6-methylphenyl)amino)picolinate (152 mg, 0.59 mmol, Step-2 of Intermediate- 101) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

MS (ESI) m/z: 284.2(M+H)⁺.

[0533] <Step-4>: N-

methyl-5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in quantitative yield (166 mg, brown solid) by the similar manner to Intermediate- 87 using methyl

5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (Step-3 of Intermediate- 101) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

MS (ESI) m/z: 283.1 (M+H)⁺.

[0534] Intermediate- 102:

5-(6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

<Step-1>: methyl 5-((5-fluoro-2-nitrophenyl)amino)picolinate

The title compound is prepared in 16% yield (32 mg, orange gum) by the similar manner to Step-1 of Intermediate- 101 using 2-bromo-4-fluoro- 1-nitrobenzene in place of 2-bromo-1-methyl-3-nitrobenzene.

¹H -NMR (400 MHz, CDCl₃) delta 9.69 (1H, br s), 8.70 (1H, d, J = 2.3 Hz), 8.32 (1H, dd, J = 9.2, 5.9 Hz), 8.21 (1H, d, J = 8.7 Hz), 7.76 (1H, dd, J = 8.2, 2.7 Hz), 6.99 (1H, dd, J = 10.5, 2.7 Hz), 6.72-6.64 (1H, ddd, J = 9.2, 8.7, 2.7 Hz), 4.04 (3H, s).

MS (ESI) m/z: 292.2 (M+H)⁺.

[0535] <Step-2>: methyl 5-((2-amino-5-fluorophenyl)amino)picolinate

The title compound is prepared in 97% yield (27 mg, pale yellow gum) by the similar manner to Step-2 of Intermediate- 88 using methyl

5-((5-fluoro-2-nitrophenyl)amino)picolinate (31 mg, 0.11 mmol, Step-1 of Intermediate- 102) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 262.2 (M+H)⁺.

[0536] <Step-3>: methyl

5-(6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

A mixture of methyl 5-((2-amino-5-fluorophenyl)amino)picolinate (27 mg, 0.10

mmol, Step-2 of Intermediate- 102) and CDI (34 mg, 0.21 mmol) in THF (3 mL) is stirred at room temperature for 1 day. The mixture is quenched with 1 M hydrochloric acid. The precipitate is collected and washed with diisopropyl ether to give 17 mg (57% yield) of the title compound as a gray solid.

MS (ESI) m/z: 288.2 (M+H)⁺.

[0537] <Step-4>:

5-(6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound is prepared in 95% yield (16 mg, gray solid) by the similar manner to Intermediate- 87 using methyl

5-(6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (17 mg, 0.059 mmol, Step-3 of Intermediate- 102) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.90-8.80 (2H, m), 8.23-8.16 (2H, m), 7.13-7.05 (2H, m), 6.97-6.90 (1H, m), 2.86 (3H, d, J = 5.0 Hz). A signal due to NH is not observed.

MS (ESI) m/z: 287.1 (M+H)⁺.

[0538] Intermediate- 103:

5-(5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

<Step-1>: methyl 5-((4-methoxy-2-nitrophenyl)amino)picolinate

The title compound is prepared in 41% yield (82 mg, orange gum) by the similar manner to Step-1 of Intermediate- 101 using 1-bromo-4-methoxy-2-nitrobenzene (153 mg, 0.66 mmol) in place of 2-bromo-1-methyl-3-nitrobenzene.

¹H -NMR (400 MHz, CDCl₃) delta 9.09 (1H, s), 8.60 (1H, d, J = 2.3 Hz), 8.12 (1H, d, J = 8.7 Hz), 7.68 (1H, d, J = 2.7 Hz), 7.60 (1H, dd, J = 8.2, 2.7 Hz), 7.42 (1H, d, J = 9.1 Hz), 7.18 (1H, dd, J = 9.1, 2.7 Hz), 4.01 (3H, s), 3.87 (3H, s).

MS (ESI) m/z: 304.2 (M+H)⁺.

[0539] <Step-2>: methyl 5-((2-amino-4-methoxyphenyl)amino)picolinate

The title compound is prepared in quantitative yield (74 mg, brown gum) by the similar manner to Step-2 of Intermediate-20 using methyl methyl 5-((4-methoxy-2-nitrophenyl)amino)picolinate (82 mg, 0.27 mmol, Step-1 of Intermediate- 103) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 274.2 (M+H)⁺.

[0540] <Step-3>: methyl

5-(5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

The title compound is prepared in 42% yield (34 mg, gray solid) by the similar manner to Step-3 of Intermediate- 102 using methyl

5-((2-amino-4-methoxyphenyl)amino)picolinate (74 mg, 0.27 mmol, Step-2 of Intermediate- 103) in place of methyl 5-((2-amino-5-fluorophenyl)amino)picolinate.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.35 (1H, br s), 8.98 (1H, t, J = 1.8 Hz), 8.22 (2H, d, J = 1.8 Hz), 7.15 (1H, d, J = 8.7 Hz), 6.69 (1H, d, J = 2.7 Hz), 6.64 (1H, dd, J = 8.7, 2.7 Hz), 3.92 (3H, s), 3.76 (3H, s).

MS (ESI) m/z: 300.2 (M+H)⁺.

[0541] <Step-4>:

5-(5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound is prepared in 97% yield (34 mg, gray solid) by the similar manner to Intermediate- 87 using methyl

5-(5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (34 mg, 0.11 mmol, Step-3 of Intermediate- 103) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

MS (ESI) m/z: 299.1 (M+H)⁺.

[0542] Intermediate- 104:

6-bromo-3-(cyclopropylmethyl)benzo[d]oxazol-2(3H)-one

To a stirred solution of 6-bromobenzo[d]oxazol-2(3H)-one (100 mg, 0.467 mmol) and (bromomethyl)cyclopropane (0.054 mL, 0.561 mmol) in DMF (1.8 mL) and THF (0.2 mL) is added NaH (60% in oil, 22 mg, 0.561 mmol) at 0 °C and stirred at rt for 15 min. To the reaction mixture is added sodium iodide (30 mg, 0.200 mmol) and stirred at rt overnight. After the reaction mixture is diluted with EtOAc then the reaction is quenched by adding ice-water. The resultant mixture is extracted with EtOAc. The organic phase is dried over MgSO₄, filtered and concentrated under reduced pressure. The residue is purified by column chromatography on silica-gel eluting with 5-25% EtOAc in n-hexane to give 99 mg (79%) of the title compound as a colorless oil.

¹H -NMR (400 MHz, CDCl₃) delta 7.38 (1H, d, J = 1.8 Hz), 7.33 (1H, dd, J = 8.2, 1.8 Hz), 6.91 (1H, d, J = 8.2 Hz), 3.70 (2H, d, J = 7.3 Hz), 1.28-1.16 (1H, m), 0.65-0.58 (2H, m), 0.46-0.40 (2H, m).

[0543] Intermediate- 105:

N,4-dimethyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

<Step-1>: methyl 4-methyl-5-((2-nitrophenyl)amino)picolinate

The title compound is prepared in 66% yield (solid) by the similar manner to Step-1 of Intermediate- 101 using 1-bromo-2-nitrobenzene in place of 2-bromo-1-methyl-3-nitrobenzene, and methyl 5-amino-4-methylpicolinate in place of methyl 5-aminopicolinate, respectively.

¹H -NMR (400 MHz, CDCl₃) delta 9.34 (1H, s), 8.72 (1H, s), 8.26 (1H, dd, J = 8.5, 1.6 Hz), 8.11 (1H, s), 7.45 (1H, ddd, J = 8.6, 7.2, 1.6 Hz), 7.09 (1H, dd, J = 8.5, 1.1 Hz), 6.93 (1H, ddd, J = 8.4, 6.8, 1.2 Hz), 4.02 (3H, s), 2.40 (3H, s).

MS (ESI) m/z: 288.1 (M+H)⁺.

[0544] <Step-2>: methyl 5-((2-aminophenyl)amino)-4-methylpicolinate

The title compound is prepared in nearly quantitative yield (solid) by the similar manner to Step-2 of Intermediate- 88 using methyl 4-methyl-5-((2-nitrophenyl)amino)picolinate (Step-1 of Intermediate- 105) in place of N-(2-nitrophenyl)chroman- 3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 7.94 (1H, s), 7.91 (1H, s), 7.12-7.06 (2H, m), 6.89 (1H, d, J = 7.3 Hz), 6.81 (1H, td, J = 7.6, 1.2 Hz), 5.55 (1H, br), 3.94 (3H, s), 3.00 (2H, br), 2.33 (3H, s).

MS (ESI) m/z: 258.2 (M+H)⁺.

[0545] <Step-3>: methyl

4-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

To a mixture of methyl 5-((2-aminophenyl)amino)-4-methylpicolinate (611 mg, 2.38 mmol, Step-2 of Intermediate- 105) in MeCN (20 mL) is added CDI (2.44 g, 15.04 mmol) and stirred at rt overnight. The mixture is diluted with 1 M hydrochloric acid and saturated aqueous sodium bicarbonate, extracted with DCM and passed through sodium sulfate. The solvent is removed under vacuum, the title compound is prepared in nearly quantitative yields (672 mg, solid).

¹H -NMR (400 MHz, CDCl₃) delta 10.23 (1H, br), 8.74 (1H, s), 8.24 (1H, s), 7.21-7.12 (2H, m), 7.07 (1H, td, J = 7.5, 1.8 Hz), 6.72 (1H, d, J = 7.8 Hz), 4.07 (3H, s), 2.39 (3H, s).

MS (ESI) m/z: 284.1 (M+H)⁺.

[0546] <Step-4>:

N,4-dimethyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in 95% yield (solid) by the similar manner to Intermediate- 87 using methyl

4-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (Step-3 of Intermediate- 105) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

¹H -NMR (400 MHz, CDCl₃) delta 10.32 (1H, s), 8.53 (1H, s), 8.29 (1H, s), 8.04 (1H, brd, J = 5.0 Hz), 7.21-7.10 (2H, m), 7.06 (1H, td, J = 7.5, 1.8 Hz), 6.69 (1H, d, J = 7.8 Hz), 3.08 (3H, d, J = 5.0 Hz), 2.35 (3H, s).

MS (ESI) m/z: 283.1 (M+H)⁺.

[0547] Intermediate- 106:

3-(benzo[d]thiazol-6-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (solid) is prepared in quantitative yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-99 using benzo[d]thiazol-6-amine in place of 4-methoxyaniline.

MS (ESI) m/z: 269.1 (M+H)⁺.

[0548] Intermediate- 107:

1-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-6-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>:

3-methyl-1-(tetrahydro-2H-pyran-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole

A mixture of 6-bromo-3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (136 mg, 0.461 mmol), bis(pinacolato)diboron (234 mg, 0.921 mmol), potassium acetate (90 mg, 0.921 mmol), palladium (II) acetate (10 mg, 0.046 mmol), and 2-(dicyclohexylphosphino)biphenyl (32 mg, 0.092 mmol) in 1,4-dioxane (0.5 mL) is stirred overnight at 80 °C. The reaction mixture is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 6-50% EtOAc in n-hexane to give 127 mg (81% yield) of the title compound as a brown gum.
¹H-NMR (400 MHz, CDCl₃) delta 7.95 (1H, s), 7.63 (1H, dd, J = 8.0, 1.0 Hz), 7.55 (1H, d, J = 8.0 Hz), 5.71 (1H, dd, J = 10.0, 2.5 Hz), 4.11-4.05 (1H, m), 3.77 (1H, td, J = 11.5, 2.5 Hz), 2.68-2.60 (1H, m), 2.57 (3H, s), 2.18-2.09 (1H, m), 2.02-1.92 (1H, m), 1.86-1.68 (2H, m), 1.66-1.58 (1H, m), 1.38 (12H, s).
 MS (ESI) m/z: 343.2 (M+H)⁺.

[0549] <Step-2>:

1-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield by the similar manner to Intermediate- 84 using

3-methyl-1-(tetrahydro-2H-pyran-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole in place of

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine.

MS (ESI) m/z: 349.2 (M+H)⁺.

[0550] Intermediate- 108:

1'-methyl- 1H-[1,5'-bibenzo[d]imidazol]-2(3H)-one

The title compound is prepared in 21% yield (40 mg, brown solid) by the similar manner to Intermediate- 84 using

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo[d]imidazole (184 mg, 0.714 mmol) in place of

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine

¹H-NMR (400 MHz, CDCl₃) delta 7.98 (1H, s), 7.95 (1H, s), 7.56 (1H, d, J = 8.2 Hz), 7.50 (1H, d, J = 8.2 Hz), 7.17-6.96 (5H, m), 3.92 (3H, s).

MS (ESI) m/z: 265.2 (M+H)⁺.

[0551] Intermediate- 109:

3--methyl-3'H-[1,5'-bibenzo[d]imidazol]-2(3H)-one

The title compound is prepared in 55% yield (64 mg, brown solid) by the similar manner to Intermediate- 84 using

1-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo[d]imidazole (114 mg, 0.441 mmol) in place of

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine

¹H-NMR (400 MHz, CDCl₃) delta 7.97 (1H, s), 7.95 (1H, d, J = 8.0 Hz), 7.62 (1H, d, J = 2.0 Hz), 7.42 (1H, dd, J = 8.0, 2.0 Hz), 7.17-6.98 (5H, m), 3.89 (3H, s).

MS (ESI) m/z: 265.2 (M+H)⁺.

[0552] Intermediate- 110:

1-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

<Step-1>: N⁴-(5-bromo-2,3-dihydro-1H-inden-2-yl)pyridine-3,4-diamine

A mixture of 4-chloro-3-nitropyridine (25 mg, 0.16 mmol),

5-bromo-2,3-dihydro-1H-inden-2-amine hydrobromide (46 mg, 0.16 mmol), TEA

(0.078 mL, 0.57 mmol) in MeOH (1 mL) is stirred overnight at 60 °C. After the

reaction mixture is cooled down to rt, tin(II) chloride (269 mg, 1.42 mmol) is added

and stirred for 1 hr at rt. The mixture is purified by column chromatography on amino-functional silica gel eluting with 100% EtOAc to give 31 mg (64% yield) of the title compound as a brown gum.

MS (ESI) m/z: 304.1 (M+H)⁺.

[0553] <Step-2>:

1-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

A mixture of N⁴-(5-bromo-2,3-dihydro-1H-inden-2-yl)pyridine-3,4-diamine (31 mg,

0.10 mmol, Step-1 of Intermediate- 110) and CDI (164 mg, 1.01 mmol) in MeCN (1

mL) is stirred for 2 days at rt. After the reaction mixture is concentrated, the residue is

added with water. The resultant mixture is extracted with EtOAc and concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 24-100% EtOAc in n-hexane followed by 100% MeOH to give 34 mg (quantitative yield) of the title compound as a brown solid.

MS (ESI) m/z: 330.1 (M+H)⁺.

[0554] Intermediate- 111:

3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (brown gum) is prepared in 81% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate- 110 using

3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-amine and

2-fluoro-3-nitropyridine in place of 5-bromo-2,3-dihydro-1H-inden-2-amine and 4-chloro-3-nitropyridine.

MS (ESI) m/z: 350.3 (M+H)⁺.

[0555] Intermediate- 112:

1-(4-(pyridin-4-yloxy)phenyl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: 2-nitro-N-(4-(pyridin-4-yloxy)phenyl)aniline

A mixture of 1-bromo-2-nitrobenzene (163 mg, 0.81 mmol), 4-(pyridin-4-yloxy)aniline (150 mg, 0.81 mmol), Pd₂(dba)₃ (37 mg, 0.040 mmol), Xantphos (47 mg, 0.081 mmol) and Cs₂CO₃ (525 mg, 1.61 mmol) in 1,4-dioxane (5 mL) is stirred at 80 °C overnight. The mixture is filtered through a pad of Celite, washed with EtOAc. The filtrate is diluted with H₂O, extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated in vacuo. The resultant residue is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 211 mg (85% yield) of the title compound as a solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.47 (1H, br s), 8.50 (2H, dd, J = 4.6, 1.4 Hz), 8.22 (1H, dd, J = 8.6, 1.4 Hz), 7.41 (1H, ddd, J = 8.7, 6.8, 2.3 Hz), 7.34 (2H, dd, J = 6.8, 2.3 Hz), 7.20 (1H, dd, 8.7, 1.4 Hz), 7.15 (2H, dd, J = 6.8, 2.3 Hz), 6.88 (2H, dd, 4.6, 1.4 Hz), 6.81 (1H, ddd, J = 8.7, 6.8, 1.4 Hz).

MS (ESI) m/z: 308.1 (M+H)⁺.

[0556] <Step-2>: N¹-(4-(pyridin-4-yloxy)phenyl)benzene- 1,2-diamine

The title compound is prepared in 94% yield (179 mg) by the similar manner to Step-2 of Intermediate- 88 using 2-nitro-N-(4-(pyridin-4-yloxy)phenyl)aniline (212 mg, 0.69 mmol, Step-1 of Intermediate- 112) in place of N-(2-nitrophenyl)chroman-3-amine.

¹H-NMR (400 MHz, CDCl₃) delta 8.42 (2H, dd, J = 5.04, 1.8 Hz), 7.13 (1H, dd, J = 7.8, 1.4 Hz), 7.04 (1H, td, J = 7.8, 1.4 Hz), 6.95 (2H, dd, J = 6.9, 2.3 Hz), 6.83 (1H, dd, J = 7.8, 1.4 Hz), 6.81 (2H, dd, J = 7.8, 1.4 Hz), 6.81-6.80 (1H, m), 6.77 (2H, dd, J = 6.9, 2.3 Hz), 5.23 (1H, s), 3.80 (2H, br s). A signal due to NH is not observed.

MS (ESI) m/z: 278.0 (M+H)⁺.

[0557] <Step-3>: 1-(4-(pyridin-4-yloxy)phenyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 95% yield (186 mg) by the similar manner to Step-3 of Intermediate-20 using N¹-(4-(pyridin-4-yloxy)phenyl)benzene-1, 2-diamine (179 mg, 0.64 mmol, Step-2 of Intermediate- 112) in place of N¹-(2,4-difluorophenyl)benzene- 1,2-diamine.

¹H-NMR (400 MHz, DMSO-d₆) delta 8.49 (2H, dd, J = 4.6, 1.4 Hz), 7.62 (2H, dd, J = 6.4, 1.8 Hz), 7.35 (2H, dd, J = 6.4, 1.8 Hz), 7.07-7.05 (2H, m), 7.03-7.01 (2H, m), 7.00 (2H, dd, J = 4.6, 1.4 Hz). A signal due to NH is not observed.

MS (ESI) m/z: 303.9 (M+H)⁺.

[0558] Intermediate- 113:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(6-methoxypyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step- 1>: (((1r,4r)-4-((tert-butoxycarbonyl)amino)cyclohexyl)methyl methane-

sulfonate

To a mixture of tert-butyl ((1r,4r)-4-(hydroxymethyl)cyclohexyl)carbamate (1.0 g, 4.4 mmol) and pyridine (690 mg, 8.7 mmol) is added methanesulfonic anhydride (990 mg, 5.7 mmol) at 0 °C and stirred at rt overnight. The mixture is added water and extracted with DCM, and passed through sodium sulfate. The solvent is removed under vacuum, the title compound is prepared in nearly quantitative yields (1.37 g, solid).

¹H -NMR (400 MHz, CDCl₃) delta 4.39 (1H, br), 4.03 (2H, d, J = 6.9 Hz), 3.50-3.26 (1H, m), 3.00 (3H, s), 2.18-1.97 (2H, m), 1.95-1.79 (2H, m), 1.79-1.64 (1H, m), 1.44 (9H, s), 1.22-1.03 (4H, m).

MS (ESI) m/z: 308.0 (M+H)⁺.

[0559] <Step-2>: tert-butyl

((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)carbamate

The title compound is prepared in 95% yield (solid) by the similar manner to Intermediate-54 using ((1r,4r)-4-((tert-butoxycarbonyl)amino)cyclohexyl)methyl methanesulfonate (Step-1 of Intermediate- 113) and Intermediate- 12 in place of Mesylate- 1 and tert-butyl-3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate.

¹H -NMR (400 MHz, CDCl₃) delta 8.34 (1H, d, J = 2.3 Hz), 7.75 (1H, dd, J = 8.7, 2.7 Hz), 7.19-6.99 (4H, m), 6.90 (1H, d, J = 8.7 Hz), 4.44-4.24 (1H, m), 4.00 (3H, s), 3.77 (2H, d, J = 6.9 Hz), 3.41 (1H, br), 2.03 (2H, brd, J = 11.9 Hz), 1.96-1.73 (3H, m), 1.43 (9H, s), 1.35-1.16 (2H, m), 1.16-0.98 (2H, m).

MS (ESI) m/z: 453.1 (M+H)⁺.

[0560] <Step-3>:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(6-methoxypyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)carbamate (1.92 g, 4.24 mmol, Step-2 of Intermediate- 113) in 4 M HCl in 1,4-dioxane (30 mL) is stirred at rt for 1 hr. The solvent is removed under vacuum, the title compound is prepared in nearly quantitative yields (1.66 g, HCl salt).

¹H -NMR (400 MHz, CDCl₃) delta 8.26 (1H, d, J = 2.3 Hz), 7.71-7.62 (1H, m), 7.12-7.03 (1H, m), 7.02-6.90 (3H, m), 6.85-6.78 (1H, m), 3.90 (3H, d, J = 3.2 Hz), 3.70 (2H, brd, J = 6.9 Hz), 2.57 (1H, br), 1.87-1.66 (5H, m), 1.28-0.82 (4H, m). A signal due to NH₂ is not observed.

MS (ESI) m/z: 353.0 (M+H)⁺.

[0561] Intermediate- 114:

N-methyl-5-(5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound (brown solid) is prepared in 76% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate- 102 using 1-bromo-4-methyl-2-nitrobenzene in place of 2-bromo-4-fluoro- 1-nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.86 (1H, t, J = 1.8 Hz), 8.84 (1H, br q, J = 5.0 Hz), 8.19 (2H, d, J = 1.8 Hz), 7.06 (1H, d, J = 8.2 Hz), 6.93 (1H, s), 6.87 (1H, d, J = 8.2 Hz), 2.85 (3H, d, J = 5.0 Hz), 2.34 (3H, s). A signal due to NH is not observed.

MS (ESI) m/z: 283.3 (M+H)⁺.

[0562] Intermediate- 115:

5-(5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound (gray solid) is prepared in 63% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate- 102 using 1-bromo-4-fluoro-2-nitrobenzene in place of 2-bromo-4-fluoro-1 -nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.86 (1H, t, J =1.8 Hz), 8.85 (1H, q, J = 5.0 Hz), 8.19 (2H, d, J = 1.8 Hz), 7.14 (1H, dd, J = 8.7, 4.6 Hz), 6.99 (1H, dd, J = 8.7, 2.3 Hz), 6.87 (1H, ddd, J = 10.1, 8.7, 2.3 Hz), 2.85 (3H, d, J = 5.0 Hz). A signal due to NH is not observed.

MS (ESI) m/z: 287.3 (M+H)⁺.

[0563] Intermediate- 116:

1-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-1H-benzo[d]imidazol-2 (3H)-one

<Step-1>: 1-(2-(methoxymethoxy)ethyl)-3-methyl-5-nitro-1H-indazole

A mixture of 3-methyl-5-nitro-1H-indazole (2.00 g, 11.29 mmol), 2-iodoethanol (2.91 g, 16.93 mmol) and Cs₂CO₃ (6.62 g, 20.32 mmol) in DMF (10 mL) is stirred at 100 °C overnight. The mixture is added water and extracted with EtOAc/Hexane = 4/1 and passed through sodium sulfate. The solvent is removed under vacuum, the mixture of 2-(3-methyl-5-nitro-1H-indazol-1-yl)ethanol and

2-(3-methyl-5-nitro-2H-indazol-2-yl)ethanol is obtained. Next, the mixture in DCM (20 mL) is added DIEA (7.30 g, 56.4 mmol) and chloromethyl methyl ether (2.73 g, 33.9 mmol) at 0°C, and stirred at rt overnight. The mixture is added water, extracted with DCM and passed through sodium sulfate. The solvent is removed under vacuum, the crude product is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane, the title compound is prepared in 66% yield (1.97 g, solid).

¹H -NMR (400 MHz, CDCl₃) delta 8.64 (1H, d, J = 1.8 Hz), 8.24 (1H, dd, J = 9.1, 2.3 Hz), 7.49 (1H, d, J = 9.1 Hz), 4.55 (2H, t, J = 5.3 Hz), 4.51 (2H, s), 3.97 (2H, t, J = 5.3 Hz), 3.15 (3H, s), 2.63 (3H, s).

MS (ESI) m/z: 266.0 (M+H)⁺.

[0564] <Step-2>: 1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-amine

To a mixture of 1-(2-(methoxymethoxy)ethyl)-3-methyl-5-nitro-1H-indazole (1.97 g,

7.43 mmol, Step-1 of Intermediate- 116) in MeOH (30 mL) is added Os/C (100 mg) and hydrazine monohydrate (5.58 g, 111 mmol), and stirred at 60 °C for 4 hrs. The mixture is passed through celite and the solvent is removed under vacuum, the title compound is prepared in 89% yield (1.56 g, solid).

¹H -NMR (400 MHz, CDCl₃) delta 7.23 (1H, dd, J = 8.2, 1.4 Hz), 6.84 (1H, dd, J = 8.7, 1.8 Hz), 6.83 (1H, d, J = 1.2 Hz), 4.51 (2H, s), 4.43 (2H, t, J = 5.5 Hz), 3.92 (2H, t, J = 5.5 Hz), 3.65 (2H, br), 3.18 (3H, s), 2.47 (3H, s).

MS (ESI) m/z: 236.0 (M+H)⁺.

[0565] <Step-3>:

1-(2-(methoxymethoxy)ethyl)-3-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine

The title compound is prepared in 96% yield (solid) by the similar manner to Step-1 of Intermediate- 101 using

1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-amine (Step-2 of Intermediate - 116) and 1-bromo-2-nitrobenzene in place of methyl 5-aminopicolinate and 2-bromo-1-methyl-3-nitrobenzene.

¹H -NMR (400 MHz, CDCl₃) delta 9.55 (1H, s), 8.22 (1H, dd, J = 8.8, 1.2Hz), 7.57-7.51 (1H, m), 7.49 (1H, d, J = 9.2 Hz), 7.33 (1H, ddd, J = 9.2, 6.8, 0.8 Hz), 7.27 (1H, dd, J = 9.2, 1.6 Hz), 6.99 (1H, dd, J = 8.7, 1.0 Hz), 6.73 (1H, ddd, J = 8.0, 6.8, 1.6 Hz), 4.55 (2H, s), 4.53 (2H, t, J = 5.6 Hz), 3.99 (2H, t, J = 5.5 Hz), 3.22 (3H, s), 2.56 (3H, s).

MS (ESI) m/z: 356.9 (M+H)⁺.

[0566] <Step-4>: N¹-

(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)benzene-1, 2-diamine

A mixture of

1-(2-(methoxymethoxy)ethyl)-3-methyl-N-(2-nitrophenyl)-1H-indazol-5-amine (2.26 g, 6.34 mmol, Step-3 of Intermediate- 116) and Os/C (100 mg) in MeOH (30 mL) is added hydrazine monohydrate (6.64 g, 133 mmol), and stirred at 60 °C overnight. The mixture is passed through celite and the solvent is removed under vacuum. The mixture is diluted with water and extracted with EtOAc, and passed through sodium sulfate. The solvent is removed under vacuum, the title compound is prepared in nearly quantitative yield (2.09 g, solid).

¹H -NMR (400 MHz, CDCl₃) delta 7.30 (1H, d, J = 8.2 Hz), 7.09-6.93 (3H, m), 6.89 (1H, d, J = 1.4 Hz), 6.81 (1H, dd, J = 7.8, 1.4 Hz), 6.75 (1H, td, J = 7.5, 1.4 Hz), 5.24 (1H, s), 4.53 (2H, s), 4.46 (2H, t, J = 5.7 Hz), 3.93 (2H, t, J = 5.7 Hz), 3.76 (2H, br), 3.21 (3H, s), 2.46 (3H, s).

MS (ESI) m/z: 326.9 (M+H)⁺.

[0567] <Step-5>:

1-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-1H-benzo[d]imidazol-2(3

H)-one

The title compound is prepared in 87% yield (solid) by the similar manner to Step-3 of Intermediate- 105 using N¹-

(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)benzene-1, 2-diamine (2.09 g, 6.40 mmol, Step-4 of Intermediate- 116) in place of methyl 5-((2-aminophenyl)amino)-4-methylpicolinate.

¹H -NMR (400 MHz, CDCl₃) delta 10.38 (1H, br), 7.80 (1H, d, J = 1.8 Hz), 7.59 (1H, d, J = 9.6 Hz), 7.49 (1H, dd, J = 9.1, 1.8 Hz), 7.19-7.02 (3H, m), 6.95 (1H, d, J = 7.3 Hz), 4.57 (4H, t, J = 4.8 Hz), 4.00 (2H, t, J = 5.5 Hz), 3.26 (3H, s), 2.59 (3H, s).

MS (ESI) m/z: 352.9 (M+H)⁺.

[0568] Intermediate- 117:

3-(2-chlorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 96% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-chloroaniline in place of 2,3-dihydro- 1H-inden-5-amine.

MS (ESI) m/z: 246.3 (M+H)⁺.

[0569] Intermediate- 118:

5-(7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

<Step-1>: methyl 5-((2-fluoro-6-nitrophenyl)amino)picolinate

A mixture of methyl 5-aminopicolinate (105 mg, 0.69 mmol), 1,2-difluoro-3-nitrobenzene (105 mg, 0.66 mmol) and Cs₂CO₃ (428 mg, 1.31 mmol) in DMSO (3 mL) is stirred at room temperature for 5 hrs. The mixture is diluted with H₂O, extracted with EtOAc three times. The organic layer is dried over sodium sulfate, filtered and concentrated in vacuo. The resultant residue is purified by column chromatography on silica-gel eluting with 0-60% EtOAc in n-hexane to give 52 mg (27% yield) of the title compound as a yellow solid.

MS (ESI) m/z: 292.0 (M+H)⁺.

[0570] <Step-2>: methyl 5-((2-amino-6-fluorophenyl)amino)picolinate

The title compound is prepared in quantitative yield (49 mg) by the similar manner to Step-2 of Intermediate-88 using methyl 5-((2-fluoro-6-nitrophenyl)amino)picolinate (52 mg, 0.18 mmol, Step-1 of Intermediate- 118) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 262.1 (M+H)⁺.

[0571] <Step-3>: methyl

5-(7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

The title compound is prepared in 44% yield (24 mg) by the similar manner to Step-3 of Intermediate-20 using methyl methyl 5-((2-amino-6-fluorophenyl)amino)picolinate (49 mg, 0.18 mmol, Step-2 of Intermediate- 118) in place of N¹-

(2,4-difluorophenyl)benzene- 1,2-diamine.

MS (ESI) m/z: 288.0 (M+H)⁺.

[0572] <Step-4>:

5-(7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound is prepared in quantitative yield (24 mg) by the similar manner to Intermediate-87 using methyl

5-(7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (24 mg, 0.083 mmol, Step-3 of Intermediate- 118) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

MS (ESI) m/z: 287.1 (M+H)⁺.

[0573] Intermediate- 119:

1-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 54 % yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-118 using 1-fluoro-2-nitrobenzene and 2-(1-methyl-1H-pyrazol-4-yl)ethanamine in place of 1,2-difluoro-3-nitrobenzene and methyl 5-aminopicolinate.

MS (ESI) m/z: 243.1 (M+H)⁺.

[0574] Intermediate- 120:

1-(2,3-dihydro-1H-inden-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 39% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 4-chloronicotinic acid and 2,3-dihydro- 1H-inden-4-amine in place of 2-chloronicotinic acid and 2,3-dihydro- 1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.38 (1H, br s), 8.29 (1H, s), 8.15 (1H, d, J = 5.0 Hz), 7.38 (1H, d, J = 7.3 Hz), 7.33 (1H, t, J = 7.3 Hz), 7.21 (1H, d, J = 7.3 Hz), 6.77 (1H, d, J = 5.0 Hz), 3.03-2.95 (2H, m), 2.82-2.71 (1H, m), 2.65-2.53 (1H, m), 2.09-1.93 (2H, m).

MS (ESI) m/z: 252.3 (M+H)⁺.

[0575] Intermediate- 121:

5-(3-(((1r,4r)-4-aminocyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound (solid) is prepared in 92% yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 113 using Intermediate- 87 in place of Intermediate- 12.

¹H -NMR (400 MHz, CDCl₃) delta 8.84 (1H, d, J = 1.8 Hz), 8.37 (1H, d, J = 8.7 Hz), 8.10 (1H, dd, J = 8.5, 2.5 Hz), 8.01 (1H, br d, J = 4.6 Hz), 7.25-7.01 (4H, m), 3.80 (2H, d, J = 6.8 Hz), 3.07 (3H, d, J = 5.6 Hz), 2.78-2.53 (1H, m), 1.98-1.66 (5H, m), 1.33-0.88 (4H, m). A signal due to NH₂ is not observed.

MS (ESI) m/z: 380.1 (M+H)⁺.

[0576] Intermediate- 122:

3-(2,4-dimethoxybenzyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step- 1>: N-(2,4-dimethoxybenzyl)-3-nitropyridin-2-amine

To a mixture of (2,4-dimethoxyphenyl)methanamine (2.53 g, 15.14 mmol), 2-chloro-3-nitropyridine (2.0 g, 12.61 mmol), and TEA (5.27 mL, 37.8 mmol) in DMF (65 mL) is stirred at rt for 4 hrs. The mixture is stirred at 50 °C for 2.5 hrs. The mixture is poured into water, extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-15% EtOAc in n-hexane to give 3.11 g (85% yield) of the title compound as a yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.68 (1H, br s), 8.43 (1H, dd, J = 4.3, 1.8 Hz), 8.40 (1H, dd, J = 8.2, 1.8 Hz), 7.27-7.23 (1H, m), 6.61 (1H, dd, J = 8.2, 4.3 Hz), 6.49 (1H, d, J = 2.5 Hz), 6.43 (1H, dd, J = 8.2, 2.5 Hz), 4.78 (2H, d, J = 5.7 Hz), 3.88 (3H, s), 3.80 (3H, s).

MS (ESI) m/z: 290.4 (M+H)⁺.

[0577] <Step-2>: N²-(2,4-dimethoxybenzyl)pyridine-2, 3-diamine

A solution of N-(2,4-dimethoxybenzyl)-3-nitropyridin-2-amine (3.11 g, 10.75 mmol, Step-1 of Intermediate- 122) in EtOAc (90 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (311 mg) and 5% Pt-alumina (311 mg). The mixture is evacuated and backfilled with H₂ gas and stirred at rt under H₂ atmosphere. After 1.5 hrs, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 2.75 g (99% yield) of the title compound.

¹H -NMR (400 MHz, CDCl₃) delta 7.78 (1H, dd, J = 5.0, 1.6 Hz), 7.30-7.21 (1H, m), 6.84 (1H, dd, J = 7.3, 1.6 Hz), 6.53 (1H, dd, J = 7.3, 5.0 Hz), 6.49 (1H, d, J = 2.3 Hz), 6.45 (1H, dd, J = 8.1, 2.3 Hz), 4.61-4.47 (3H, m), 3.84 (3H, s), 3.80 (3H, s), 3.18 (2H, br s).

MS (ESI) m/z: 260.4 (M+H)⁺.

[0578] <Step-3>: 3-(2,4-dimethoxybenzyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

To a mixture of N²-(2,4-dimethoxybenzyl)pyridine-2, 3-diamine (2.66 g, 10.27 mmol, Step-2 of Intermediate- 122) and CDI (3.33 g, 20.55 mmol) in THF (75 mL) is stirred at rt for 16 hrs. The mixture is poured into saturated aqueous sodium bicarbonate, extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The obtained solid is washed with IPE. The residue is poured into EtOAc and saturated aqueous citric acid. The precipitated is collected by filter, washed with EtOAc (10 mL) and dried to give 2.23 g (76% yield) of the title compound as a beige solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.28 (1H, br s), 8.05 (1H, dd, J = 5.2, 1.4 Hz), 7.31-7.22 (1H, m), 7.02-6.94 (2H, m), 6.45 (1H, d, J = 2.5 Hz), 6.37 (1H, dd, J = 8.4, 2.3 Hz), 5.17 (2H, s), 3.83 (3H, s), 3.76 (3H, m).

MS (ESI) m/z: 286.4 (M+H)⁺.

[0579] Intermediate- 123:

5-bromo-2-ethyl-2H-pyrazolo [3,4-b]pyridine

A mixture of 5-bromo-1H-pyrazolo[3,4-b]pyridine (100 mg, 0.505 mmol), iodethane (0.045 mL, 0.555 mmol) and cesium carbonate (411 mg, 1.26 mmol) in DMF (2 mL) is stirred at rt overnight. The reaction mixture is diluted with EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-25% EtOAc in n-hexane to give 15 mg (13%) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.67 (1H, d, J = 2.3 Hz), 8.17 (1H, d, J = 2.3 Hz), 7.90 (1H, s), 4.51 (2H, q, J = 7.3 Hz), 1.66 (3H, t, J = 7.3 Hz).

[0580] Intermediate- 124:

1-(2-chlorophenyl)- 1H-imidazo [4,5-b]pyridin-2(3H)-one

<Step-1>: 1-(3-bromopyridin-2-yl)-3-(2-chlorophenyl)urea

A mixture of 1-chloro-2-isocyanatobenzene (107 mg, 0.69 mmol) and 3-bromopyridin-2-amine (100 mg, 0.58 mmol) in THF (3 mL) is stirred at room temperature for 1 day. The mixture is concentrated to give the title compound as a crude. The crude is used next step without purification.

MS (ESI) m/z: 326.3 (M+H)⁺.

[0581] <Step-2> : 1-(2-chlorophenyl)- 1H-imidazo [4,5-b]pyridin-2(3H)-one

A mixture of 1-(3-bromopyridin-2-yl)-3-(2-chlorophenyl)urea (crude, 0.58 mmol, Step-1 of Intermediate- 124), CuI (132 mg, 0.69 mmol), and 1,10-phenanthroline (125 mg, 0.69 mmol) in DMSO (1 mL) is stirred at 100 °C for 1 day. The mixture is diluted with 28% aqueous ammonia solution. The precipitate is collected and washed with diisopropyl ether to give 142 mg (quantitative yield in 2 steps) of the title compound as a brown solid.

MS (ESI) m/z: 246.4 (M+H)⁺.

[0582] Intermediate- 125:

1-(2-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 56% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate- 124 using 1-isocyanato-2-(trifluoromethyl)benzene in place of 1-chloro-2-isocyanatobenzene.

MS (ESI) m/z: 280.4 (M+H)⁺.

[0583] Intermediate- 126:

5-(6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound (gray solid) is prepared in 27% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate- 102 using 2-iodo-4-methoxy- 1-nitrobenzene in place of 2-bromo-4-fluoro- 1-nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 10.28 (1H, br s), 8.86 (1H, t, J = 1.8 Hz), 8.84 (1H, q, J = 5.0 Hz), 8.20 (2H, d, J = 2.3 Hz), 7.01 (1H, d, J = 8.7 Hz), 6.75-6.65 (2H, m), 3.71 (3H, s), 2.85 (3H, d, J = 5.0 Hz).

MS (ESI) m/z: 299.5 (M+H)⁺.

[0584] Intermediate- 127:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(6-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 88% yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 113 using Intermediate- 13 in place of Intermediate- 12.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.91 (1H, d J = 2.3 Hz), 8.39 (1H, dd, J = 8.7, 2.3 Hz), 8.03 (2H, br s), 7.82 (1H, d, J = 8.2 Hz), 7.34 (1H, d, J = 7.8 Hz), 7.20-7.15 (2H, m), 7.11-7.06 (1H, m), 3.74 (2H, d, J = 6.9 Hz), 2.91 (1H, br s), 2.70 (3H, s), 1.94-1.92 (2H, m), 1.76-1.73 (3H, m), 1.29-1.12 (4H, m).

MS (ESI) m/z: 337.2 (M+H)⁺.

[0585] Intermediate- 128:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(pyridin-4-ylmethyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 113 using

1-(pyridin-4-ylmethyl)-1H-benzo[d]imidazol-2(3H)-one in place of Intermediate- 12.

[0586] Intermediate- 129:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(pyridin-2-ylmethyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 113 using

1-(pyridin-2-ylmethyl)-1H-benzo[d]imidazol-2(3H)-one in place of Intermediate- 12.

MS (ESI) m/z: 337.2 (M+H)⁺.

[0587] Intermediate- 130:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(pyridin-3-ylmethyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 113 using

1-(pyridin-3-ylmethyl)-1H-benzo[d]imidazol-2(3H)-one in place of Intermediate- 12.

MS (ESI) m/z: 337.2 (M+H)⁺.

[0588] Intermediate- 131:

1-(((1r,4r)-4-aminocyclohexyl)methyl)-3-(2-oxo-2-phenylethyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (white solid) is prepared in 46% yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 113 using

1-(2-oxo-2-phenylethyl)-1H-benzo[d]imidazol-2(3H)-one in place of Intermediate- 12.

[0589] Intermediate- 132:

5-chloro-N-(((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

The title compound (solid) is prepared in 61% yield in 2 steps by the similar manner to Step-1 and Step-2 of Example 9 using Mesylate-3 in place of Mesylate- 1.

¹H -NMR (400 MHz, DMSO-d₆) delta 10.76 (1H, s), 8.79 (1H, d, J = 1.8 Hz), 8.51 (1H, d, J = 7.8 Hz), 8.16 (1H, d, J = 2.3 Hz), 7.12-7.03 (1H, m), 6.97-6.87 (3H, m), 3.67-3.51 (1H, m), 3.57 (2H, d, J = 6.9 Hz), 1.89-1.76 (2H, m), 1.76-1.51 (3H, m), 1.20-1.00 (4H, m).

MS (ESI) m/z: 453.2 (M+H)⁺.

[0590] Intermediate- 133:

5-bromo-2-ethyl-3-methyl-2H-pyrazolo[3,4-b]pyridine

To a solution of 5-bromo-3-methyl-1H-pyrazolo[3,4-b]pyridine (100 mg, 0.472 mmol) in THF (2 mL) is added 1.9 M solution of sodium bis(trimethylsilyl)amide in THF (0.37 mL, 0.707 mmol) at 0 °C and stirred for 5 min. To this is added iodoethane (0.057 mL) at 0 °C and stirred for 30 min then at rt for 4 hrs. The reaction is quenched by adding saturated aqueous ammonium chloride solution. The resultant mixture is extracted with EtOAc. The organic phase is washed with brine, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-90% EtOAc in n-hexane to give 94 mg (83%) of the title compound as a brown gum.

¹H -NMR (400 MHz, CDCl₃) delta 8.63 (1H, d, J = 2.3 Hz), 8.07 (1H, d, J = 2.3 Hz), 4.42 (2H, q, J = 7.3 Hz), 2.59 (3H, s), 1.58 (3H, t, J = 7.3 Hz).

[0591] Intermediate- 134:

1-(5-(methylamino)pyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 1-(5-chloropyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one (50 mg, 0.20 mmol, Step-1 of Intermediate- 57), methanamine hydrochloride (68 mg, 1.01 mmol), DIEA (262 mg, 2.03 mmol) and DBU (154 mg, 1.01 mmol) in NMP (2 mL) is irradiated with micro-wave at 220 °C for 30 min, and the mixture is diluted with saturated aqueous sodium bicarbonate, extracted with EtOAc. The organic layer is concentrated in vacuo. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 48 mg (99% yield) of the title compound as a solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.57 (1H, d, J = 1.8 Hz), 7.89 (1H, d, J = 1.4 Hz), 7.44-7.41 (1H, m), 7.15-7.08 (3H, m), 4.84 (1H, br s), 3.07 (3H, d, J = 5.5 Hz).

MS (ESI) m/z: 256.5 (M+H)⁺.

[0592] Intermediate- 135:

(S)-l-(6-((tetrahydrofuran-3-yl)amino)pyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

<Step-1>: l-(6-fluoropyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

A mixture of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-lH-benzo[d]imidazole-l-carboxylate (840 mg, 2.55 mmol, step-1 of Intermediate- 15) in 4 M HCl-dioxane (30 mL) is stirred at room temperature for 3 hrs. The mixture is concentrated. The residue is suspended in diisopropyl ether and the precipitate is collected by filtration. This solid is washed with diisopropyl ether, dried in vacuo to give 350 mg (60% yield) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.10 (1H, br s), 8.47 (1H, dd, J = 2.7, 0.9 Hz), 8.22 (1H, ddd, J = 8.6, 6.8, 2.7 Hz), 7.41 (1H, dd, J = 8.6, 3.2 Hz), 7.11-7.07 (2H, m), 7.06-7.02 (2H, m).

MS (ESI) m/z: 230.2 (M+H)⁺.

[0593] <Step-2>:

(S)-l-(6-((tetrahydrofuran-3-yl)amino)pyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

A mixture of l-(6-fluoropyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one (35 mg, 0.15 mmol, Step-1 of Intermediate- 135), (S)-tetrahydrofuran-3-amine hydrochloride (189 mg, 1.53 mmol), DIEA (197 mg, 1.53 mmol) and DBU (116 mg, 0.76 mmol) in 2-propanol (1 mL) is stirred at 120 °C overnight. The mixture is diluted with H₂O, extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated in vacuo. The resultant residue is purified by column chromatography on amine-gel eluting with 50-100% EtOAc in n-hexane to give 22 mg (48% yield) of the title compound.

¹H -NMR (400 MHz, CDCl₃) delta 8.93 (1H, br s), 8.28 (1H, d, J = 2.7 Hz), 7.59 (1H, dd, J = 8.6, 2.7 Hz), 7.14-7.06 (3H, m), 6.97 (1H, d, J = 7.3 Hz), 6.56 (1H, d, J = 9.1 Hz), 4.91 (1H, d, J = 7.3 Hz), 4.53-4.49 (1H, m), 4.06-4.00 (2H, m), 3.91 (1H, td, J = 8.7, 5.5 Hz), 3.79 (1H, dd, J = 9.1, 2.7 Hz), 2.42-2.33 (1H, m), 1.97-1.94 (1H, m).

MS (ESI) m/z: 297.4 (M+H)⁺.

[0594] Intermediate- 136:

(R)-l-(6-((tetrahydrofuran-3-yl)amino)pyridin-3-yl)-lH-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 50% yield (23 mg) by the similar manner to Step-2 of Intermediate- 135 using (R)-tetrahydrofuran-3-amine hydrochloride (189 mg, 1.53 mmol) in place of (S)-tetrahydrofuran-3-amine hydrochloride.

¹H -NMR (400 MHz, CDCl₃) delta 9.21 (1H, br s), 8.28 (1H, d, J = 2.3 Hz), 7.59 (1H,

dd, $J = 8.7, 2.3$ Hz), 7.14-7.06 (3H, m), 6.97 (1H, d, $J = 7.3$ Hz), 6.56 (1H, d, $J = 8.7$ Hz), 4.93 (1H, d, $J = 7.3$ Hz), 4.55-4.46 (1H, m), 4.05-4.01 (2H, m), 3.91 (1H, td, $J = 8.2, 5.5$ Hz), 3.79 (1H, dd, $J = 9.1, 2.7$ Hz), 2.42-2.33 (1H, m), 1.97-1.94 (1H, m).

MS (ESI) m/z : 297.4 (M+H)⁺.

[0595] Intermediate- 137:

3-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)isonicotinonitrile

A mixture of 1H-benzo[d]imidazol-2(3H)-one (50 mg, 0.37 mmol), 3-fluoroisonicotinonitrile (46 mg, 0.37 mmol), and Cs₂CO₃ (364 mg, 1.12 mmol) in DMSO (1 mL) is stirred at rt for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 24 mg (27% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, DMSO-d₆) δ 11.44 (1H, br s), 9.04 (1H, s), 8.95 (1H, d, $J = 5.0$ Hz), 8.16 (1H, d, $J = 5.0$ Hz), 7.14 (2H, d, $J = 4.1$ Hz), 7.09-7.01 (1H, m), 6.98 (1H, d, $J = 7.8$ Hz).

MS (ESI) m/z : 237.4 (M+H)⁺.

[0596] Intermediate- 138:

2-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)nicotinonitrile

The title compound is prepared in 36% yield (32 mg, pale yellow solid) by the similar manner to Intermediate- 137 using 2-chloronicotinonitrile (52 mg, 0.37 mmol) in place of 3-fluoroisonicotinonitrile.

¹H-NMR (400 MHz, DMSO-d₆) δ 11.40 (1H, br s), 8.92 (1H, dd, $J = 5.0, 1.8$ Hz), 8.60 (1H, dd, $J = 7.7, 1.8$ Hz), 7.73 (1H, dd, $J = 7.7, 5.0$ Hz), 7.20-7.10 (3H, m), 7.08-7.02 (1H, m).

MS (ESI) m/z : 237.4 (M+H)⁺.

[0597] Intermediate- 139:

1-(thiazol-4-ylmethyl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound (pale yellow solid) is prepared in quantitative yield in 2 steps by the similar manner to Step- 1 and Step-2 of Intermediate- 1 using 4-(chloromethyl)thiazole in place of 4-(iodomethyl)tetrahydro-2H-pyran.

MS (ESI) m/z : 232.2 (M+H)⁺.

[0598] Intermediate- 140:

1-(2-(trifluoromethyl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step- 1>: N¹-(2-nitrophenyl)-2-(trifluoromethyl)pyridin-3-amine

The title compound is prepared in 95% yield (200 mg, yellow solid) by the similar manner to Step-1 of Intermediate- 101 using 1-bromo-2-nitrobenzene (150 mg, 0.74 mmol) and 2-(trifluoromethyl)pyridin-3-amine (120 mg, 0.74 mmol) in place of

2-bromo-1-methyl-3-nitrobenzene and methyl 5-aminopicolinate.

¹H-NMR (400 MHz, CDCl₃) delta 9.58 (1H, br s), 8.52 (1H, d, J = 4.6 Hz), 8.26 (1H, dd, J = 8.2, 1.4 Hz), 7.91 (1H, d, J = 8.7 Hz), 7.52 (1H, dd, J = 8.2, 4.6 Hz), 7.46 (1H, td, J = 8.2, 1.4 Hz), 7.12 (1H, dd, J = 8.7, 0.9 Hz), 6.97 (1H, ddd, J = 8.7, 8.2, 1.4 Hz). MS (ESI) m/z: 284.2 (M+H)⁺.

[0599] <Step-2>: N¹-(2-(trifluoromethyl)pyridin-3-yl)benzene-1,2-diamine

The title compound is prepared in quantitative yield (181 mg, brown solid) by the similar manner to Step-2 of Intermediate- 88 using N-(2-nitrophenyl)-2-(trifluoromethyl)pyridin-3-amine (200 mg, 0.71 mmol, Step-1 of Intermediate- 140) in place of N-(2-nitrophenyl)chroman-3-amine.

¹H-NMR (400 MHz, CDCl₃) delta 8.09 (1H, d, J = 4.1 Hz), 7.23 (1H, dd, J = 8.2, 4.1 Hz), 7.15 (1H, td, J = 7.8, 1.4 Hz), 7.08 (1H, d, J = 7.8 Hz), 6.96 (1H, d, J = 8.2 Hz), 6.83 (1H, dd, J = 6.8, 1.4 Hz), 6.78 (1H, td, J = 7.8, 1.4 Hz), 5.82 (1H, br s), 3.80 (2H, br s).

MS (ESI) m/z: 254.1 (M+H)⁺.

[0600] <Step-3>: 1-(2-(trifluoromethyl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a solution of N¹-(2-(trifluoromethyl)pyridin-3-yl)benzene-1,2-diamine (100 mg, 0.40 mmol) in THF is added CDI (192 mg, 1.19 mmol) at room temperature. The mixture is stirred overnight. The mixture is diluted with 2 M aqueous sodium hydroxide solution, extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated in vacuo. The resultant residue is purified by column chromatography on silica-gel eluting with 40-100% EtOAc in n-hexane to give 89 mg (81% yield) of the title compound as a brown solid.

¹H-NMR (400 MHz, CDCl₃) delta 9.37 (1H, br s), 8.90 (1H, d, J = 4.5 Hz), 7.90 (1H, d, J = 7.8 Hz), 7.75 (1H, dd, J = 7.8, 4.5 Hz), 7.14 (2H, d, J = 4.1 Hz), 7.08-7.01 (1H, m), 6.62 (1H, d, J = 7.87 Hz).

MS (ESI) m/z: 280.0 (M+H)⁺.

[0601] Intermediate- 141:

5-chloro-2-(2-methoxyethyl)nicotinic acid

<Step-1>: benzyl 2-bromo-5-chloronicotinate

A mixture of 2,5-dichloronicotinic acid (500 mg, 2.60 mmol), (bromomethyl)benzene (534 mg, 3.13 mmol), and K₂CO₃ (1.08 g, 7.81 mmol) in MeCN (10 mL) is stirred at rt for 1 day. The mixture is concentrated. The residue is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-5% EtOAc in n-hexane to give 409 mg (48% yield) of the title compound as a pale yellow oil.

¹H-NMR (400 MHz, CDCl₃) delta 8.44 (1H, d, J = 2.3 Hz), 8.05 (1H, d, J = 2.7 Hz),

7.49-7.45 (2H, m), 7.45-7.36 (3H, m), 5.39 (2H, s).

MS (ESI) m/z : 328.25(M+H)⁺.

[0602] <Step-2>: benzyl 5-chloro-2-(2-methoxyethyl)nicotinate

A mixture of benzyl 2-bromo-5-chloronicotinate (100 mg, 0.31 mmol, Step-1 of Intermediate- 141), 1-bromo-2-methoxyethane (213 mg, 1.53 mmol), nickel(II) chloride ethylene glycol dimethyl ether complex (7 mg, 0.031 mmol), Ir[dF(CF₃)ppy]₂ (dtbbpy)PF₆ (3 mg, 0.0031 mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (8 mg, 0.031 mmol), tris(trimethylsilyl)silane (228 mg, 0.92 mmol), and 2,6-lutidine (66 mg, 0.61 mmol) in DME (4 mL) is stirred under blue FED irradiation for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-10% EtOAc in n-hexane to give 46 mg (49% yield) of the title compound as a pale yellow gum.

¹H-NMR (400 MHz, CDCl₃) δ 8.61 (1H, d, J = 2.3 Hz), 8.14 (1H, d, J = 2.3 Hz), 7.48-7.35 (5H, m), 5.36 (2H, s), 3.73 (2H, t, J = 6.8 Hz), 3.46 (2H, t, J = 6.8 Hz), 3.29 (3H, s).

MS (ESI) m/z : 306.4 (M+H)⁺.

[0603] <Step-3>: 5-chloro-2-(2-methoxyethyl)nicotinic acid

The title compound is prepared in 71% yield (23 mg, pale yellow gum) by the similar manner to Step-4 of Intermediate-2 using benzyl

5-chloro-2-(2-methoxyethyl)nicotinate (46 mg, 0.15 mmol, Step-2 of Intermediate- 141) in place of methyl

3-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z : 216.4 (M+H)⁺.

[0604] Intermediate- 142:

5-chloro-2-cyclobutylnicotinic acid

The title compound (pale yellow gum) is prepared in 35% yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 141 using bromocyclobutane in place of 1-bromo-2-methoxyethane.

MS (ESI) m/z : 212.4 (M+H)⁺.

[0605] Intermediate- 143:

5-chloro-2-(methoxymethyl)nicotinic acid

<Step-1>: 5-chloro-2-(hydroxymethyl)nicotinic acid

A mixture of 3-chlorofuro[3,4-b]pyridin-5(7H)-one (100 mg, 0.59 mmol, Step-1 of Intermediate- 143) and 2 M aqueous sodium hydroxide solution (0.60 mL, 1.20 mmol) in MeOH (3 mL) is stirred at 60 °C for 1 hr. The mixture is concentrated, diluted with 2 M hydrochloric acid (0.60 mL, 1.20 mmol) and water to afford pale yellow solid.

The precipitate is collected by filtration, washed with water, and dried in vacuo at 50° C to give 51 mg (46% yield) of the title compound as a yellow solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.50 (1H, d, J = 2.3 Hz), 8.20 (1H, d, J = 2.3 Hz), 4.81 (2H, s).

MS (ESI) m/z: 188.0 (M+H)⁺.

[0606] <Step-2>: 5-chloro-2-(methoxymethyl)nicotinic acid

To a solution of 5-chloro-2-(hydroxymethyl)nicotinic acid (30 mg, 0.16 mmol) in DMF (0.5 mL) is added sodium hydride (60% dispersion in mineral oil, 18 mg, 0.40 mmol) at 0 °C. The mixture is stirred at room temperature for 10 min. Then, to the mixture is added iodomethane (0.025 mL, 0.40 mmol) and stirred for 3 days. The mixture is diluted with saturated aqueous ammonium chloride, extracted with EtOAc, concentrated. To the residue in THF (1 mL) and methanol (1 mL) is added 2 M aqueous sodium hydroxide solution (0.16 mL, 0.32 mmol). The mixture is stirred at 60 °C for 1 hr. The mixture is neutralized with 2 M hydrochloric acid, concentrated. The residue is diluted with water, extracted with EtOAc, concentrated, purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) PE-AX, 1 g/6 mL, Biotage) to give 30 mg (93% yield) of the title compound as a yellow solid.

MS (ESI) m/z: 202.4 (M+H)⁺.

[0607] Intermediate- 144:

1-(4,6-dimethylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step- 1>: 4,6-dimethyl-N-(2-nitrophenyl)pyridin-3-amine

The title compound is prepared in quantitative yield (301 mg, orange gum) by the similar manner to Step-1 of Intermediate- 101 using 4,6-dimethylpyridin-3-amine (151 mg, 1.24 mmol) and 1-bromo-2-nitrobenzene (300 mg, 1.49 mmol) in place of methyl 5-aminopicolinate and 2-bromo-1-methyl-3-nitrobenzene.

¹H -NMR (400 MHz, CDCl₃) delta 9.20 (1H, br s), 8.39 (1H, s), 8.23 (1H, d, J = 8.7 Hz), 7.34 (1H, dd, J = 8.7, 7.3 Hz), 7.14 (1H, s), 6.78 (1H, dd, J = 8.7, 7.3 Hz), 6.68 (1H, d, J = 8.7 Hz), 2.57 (3H, s), 2.32 (3H, s).

MS (ESI) m/z: 244.5 (M+H)⁺.

[0608] <Step-2>: N¹-(4,6-dimethylpyridin-3-yl)benzene-1, 2-diamine

The title compound is prepared in 95% yield (252 mg, pale yellow gum) by the similar manner to Step-2 of Intermediate- 88 using 4,6-dimethyl-N-(2-nitrophenyl)pyridin-3-amine (306 mg, 1.24 mmol, Step-1 of Intermediate- 144) in place of N-(2-nitrophenyl)chroman-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 7.93 (1H, s), 6.99-6.92 (1H, m), 6.96 (1H, s), 6.86-6.79 (2H, m), 6.73 (1H, ddd, J = 7.8, 7.3, 1.8 Hz), 4.87 (1H, br s), 3.70 (2H, br s), 2.46 (3H, s), 2.20 (3H, s).

MS (ESI) m/z: 214.4 (M+H)⁺.

[0609] <Step-3>: methyl

5-(6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

To a mixture of N'-O-dimethylpyridin-S-yObenzene-l, 2-diamine (252 mg, 1.18 mmol, Step-2 of Intermediate- 144), pyridine (0.48 mL, 5.91 mmol) in THF (2 mL) is added triphosgene (438 mg, 1.48 mmol) at 0 °C. The mixture is stirred at rt for 1 hr. The mixture is quenched with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 246 mg (87% yield) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.17 (1H, br s), 8.36 (1H, s), 7.37 (1H, s), 7.10-7.02 (2H, m), 6.97 (1H, dd, J = 7.8, 1.8 Hz), 6.64 (1H, d, J = 7.8 Hz), 2.52 (3H, s), 2.07 (3H, s).

MS (ESI) m/z: 240.5 (M+H)⁺.

[0610] Intermediate- 145:

1-(2,3-dimethylpyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (pale yellow solid) is prepared in 44% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 144 using 2,3-dimethylpyridin-4-amine (243 mg, 1.24 mmol) in place of 4,6-dimethylpyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.21 (1H, br s), 8.43 (1H, d, J = 5.5 Hz), 7.26 (1H, d, J = 5.0 Hz), 7.13-7.04 (2H, m), 6.98 (1H, dd, J = 6.8, 1.8 Hz), 6.68 (1H, d, J = 7.8 Hz), 2.56 (3H, s), 2.03 (3H, s).

MS (ESI) m/z: 240.5 (M+H)⁺.

[0611] Intermediate- 146:

1-(6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 80% yield (21 mg) by the similar manner to Step-2 of Intermediate- 135 (25 mg, 0.11 mmol) using 2 M methanamine in methanol (0.55 mL, 1.09 mmol) in place of (S)-tetrahydrofuran-3-amine hydrochloride.

MS (ESI) m/z: 241.4 (M+H)⁺.

[0612] Intermediate- 147:

1-(3-chloropyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: ethyl 2-((3-chloropyridin-4-yl)amino)benzoate

The title compound is prepared in quantitative yield (orange gum) by the similar manner to Step-1 of Intermediate- 101 using 3-chloropyridin-4-amine and ethyl 2-iodobenzoate in place of methyl 5-aminopicolinate and 2-bromo-1-methyl-3-nitrobenzene.

¹H -NMR (400 MHz, CDCl₃) delta 9.89 (1H, br s), 8.48 (1H, s), 8.24 (1H, d, J = 5.5

Hz), 8.08 (1H, dd, J = 7.8, 1.4 Hz), 7.59-7.48 (2H, m), 7.36 (1H, d, J = 5.5 Hz), 7.06 (1H, ddd, J = 8.2, 6.9, 1.4 Hz), 4.41 (2H, q, J = 7.3 Hz), 1.42 (3H, t, J = 7.3 Hz).

MS (ESI) m/z: 277.5 (M+H)⁺.

[0613] <Step-2>: 2-((3-chloropyridin-4-yl)amino)benzoic acid

The title compound is quantitative yield (pale yellow solid) by the similar manner to Step-4 of Intermediate-2 using ethyl 2-((3-chloropyridin-4-yl)amino)benzoate (Step-1 of Intermediate- 147) in place of methyl

3-(((3-((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 249.5 (M+H)⁺.

[0614] <Step-3> : 1-(3-chloropyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 31% yield (pale yellow solid) by the similar manner to Step-2 of Intermediate-98 using 2-((3-chloropyridin-4-yl)amino)benzoic acid (Step-2 of Intermediate- 147) in place of

2-((2,3-dihydro-1H-inden-5-yl)amino)nicotinic acid.

¹H -NMR (400 MHz, CDCl₃) delta 9.40-9.18 (1H, m), 8.69 (1H, s), 8.71 (1H, d, J = 5.0 Hz), 7.51 (1H, d, J = 5.0 Hz), 7.16 (2H, d, J = 4.1 Hz), 7.12-7.06 (1H, m), 6.77 (1H, d, J = 7.8 Hz).

MS (ESI) m/z: 246.3 (M+H)⁺.

[0615] Intermediate- 148:

1-(2,5-dimethylpyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (pale yellow gum) is prepared in 46% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 144 using 2,5-dimethylpyridin-4-amine in place of 4,6-dimethylpyridin-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 10.15 (1H, br s), 8.60 (1H, s), 7.20 (1H, s), 7.19-7.11 (2H, m), 7.06 (1H, td, J = 7.2, 1.4 Hz), 6.74 (1H, d, J = 7.8 Hz), 2.62 (3H, s), 2.22 (3H, s).

MS (ESI) m/z: 240.4 (M+H)⁺.

[0616] Intermediate- 149:

1-(quinolin-8-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (pale yellow solid) is prepared in 25% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 144 using quinolin-8-amine in place of 4,6-dimethylpyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.08 (1H, br s), 8.82 (1H, dd, J = 4.1, 1.8 Hz), 8.53 (1H, dd, J = 8.2, 1.4 Hz), 8.18 (1H, dd, J = 8.2, 1.4 Hz), 7.93 (1H, dd, J = 7.3, 1.4 Hz), 7.80 (1H, t, J = 7.8 Hz), 7.62 (1H, dd, J = 8.2, 4.1 Hz), 7.09 (1H, d, 7.8 Hz), 7.02 (1H, td, J = 7.8, 0.9 Hz), 6.87 (1H, td, J = 7.8, 0.9 Hz), 6.40 (1H, d, J = 7.8 Hz).

MS (ESI) m/z: 262.4 (M+H)⁺.

[0617] Intermediate- 150:

1-(isoquinolin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (pale yellow solid) is prepared in 25% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 144 using isoquinolin-4-amine in place of 4,6-dimethylpyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.33 (1H, br s), 9.51 (1H, s), 8.64 (1H, s), 8.33 (1H, dd, J = 5.9, 2.7 Hz), 7.85-7.76 (2H, m), 7.52 (1H, dd, J = 6.9, 2.7 Hz), 7.16 (1H, d, J = 7.8 Hz), 7.93 (1H, td, J = 7.8, 1.4 Hz), 6.94 (1H, td, J = 7.8, 1.4 Hz), 6.57 (1H, d, J = 7.8 Hz).

MS (ESI) m/z: 262.4 (M+H)⁺.

[0618] Intermediate- 151:

N,4-dimethyl-5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

<Step- 1>: methyl 4-methyl-5-((2-methyl-6-nitrophenyl)amino)picolinate

The title compound is prepared in 34% yield (61 mg, brown gum) by the similar manner to Step-1 of Intermediate- 101 using methyl 5-amino-4-methylpicolinate (100 mg, 0.602 mmol) in place of methyl 5-aminopicolinate.

MS (ESI) m/z: 302.4 (M+H)⁺.

[0619] <Step-2>: methyl 5-((2-amino-6-methylphenyl)amino)-4-methylpicolinate

A mixture of methyl 4-methyl-5-((2-methyl-6-nitrophenyl)amino)picolinate (61 mg, 0.20 mmol, Step-1 of Intermediate- 151), tin(II) chloride (347 mg, 1.83 mmol) in MeOH (1 mL) is stirred for 1 hr at rt. The mixture is purified by column chromatography on amino-functional silica gel eluting with 100% MeOH to give 60 mg (quantitative yield) of the title compound as a brown solid.

MS (ESI) m/z: 272.5 (M+H)⁺.

[0620] <Step-3>: methyl

4-methyl-5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

The title compound is prepared in 59% yield (39 mg, yellow solid) by the similar manner to Step-3 of Intermediate- 105 using methyl 5-((2-amino-6-methylphenyl)amino)-4-methylpicolinate (60 mg, 0.22 mmol, Step-2 of Intermediate- 151) in place of methyl 5-((2-aminophenyl)amino)-4-methylpicolinate.

MS (ESI) m/z: 298.4 (M+H)⁺.

[0621] <Step-4>:

N,4-dimethyl-5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in quantitative yield (43 mg, brown solid) by the similar manner to Intermediate- 87 using methyl

4-methyl-5-(7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (39 mg, 0.13 mmol, Step-3 of Intermediate- 151) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

MS (ESI) m/z: 297.4 (M+H)⁺.

[0622] Intermediate- 152:

2-(oxetan-3-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2H-benzo[d][1,2,3]triazole

<Step-1>:

5-bromo-2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazole and

5-bromo-1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazole

A mixture of 5-bromo-1H-benzo[d][1,2,3]triazole (100 mg, 0.505 mmol), 3-iodooxetane (111 mg, 0.606 mmol), cesium carbonate (247 mg, 0.757 mmol) in DMF (1 mL) is stirred overnight at 100 °C. The mixture is added with saturated aqueous ammonium chloride. The resultant mixture is extracted with DCM and concentrated. The mixture is purified by column chromatography on silica-gel eluting with 4-66% EtOAc in n-hexane to give 22 mg (17% yield, more polar) of 5-bromo-2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazole as a pale yellow solid and 61 mg (48% yield, less polar) of 5-bromo-1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazole as a colorless gum.

5-bromo-2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazole: ¹H-NMR (400 MHz, CDCl₃) delta 8.32-8.25 (1H, m), 7.74 (1H, dd, J = 8.9, 1.0 Hz), 7.65 (1H, dd, J = 8.9, 1.6 Hz), 6.11-5.99 (1H, m), 5.33-5.22 (4H, m).

MS (ESI) m/z: 254.3 (M+H)⁺.

5-bromo-1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazole: ¹H-NMR (400 MHz, CDCl₃) delta 8.11-8.05 (1H, m), 7.78 (1H, d, J = 8.7 Hz), 7.54-7.46 (1H, m), 6.10-5.95 (1H, m), 5.31 (2H, t, J = 7.0 Hz), 5.19 (2H, t, J = 7.0 Hz).

[0623] <Step-2>:

2-(oxetan-3-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2H-benzo[d][1,2,3]triazole

To a mixture of 5-bromo-2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazole (21 mg, 0.083 mmol, Step-1 of Intermediate- 152),

4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (25 mg, 0.099 mmol),

Pd(dppf)Cl₂ (7 mg, 0.00827 mmol) and potassium acetate (24 mg, 0.248 mmol) in

1,4-dioxane (1.5 mL) is stirred at 80 °C for 1 hr. The mixture is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 17 mg (65% yield) of the title compound as pale yellow oil.

MS (ESI) m/z: 302.4 (M+H)⁺.

[0624] Intermediate- 153:

1-(oxetan-3-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo[d][1,2,3]triazole

The title compound is prepared in 69 % yield (36 mg, pale yellow solid) by the similar manner to Step-2 of Intermediate- 152 using 5-bromo-1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazole (44 mg, 0.173 mmol, Step-1 of Intermediate- 152) in place of 5-bromo-2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazole. MS (ESI) m/z: 302.4 (M+H)⁺.

[0625] Intermediate- 154:

1-(isoquinolin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 80% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using isoquinolin-5-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

MS (ESI) m/z: 262.4 (M+H)⁺.

[0626] Intermediate- 155:

1-(quinolin-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 84% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using quinolin-6-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

MS (ESI) m/z: 262.3 (M+H)⁺.

[0627] Intermediate- 156:

1-(quinolin-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in 82% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using quinolin-5-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

MS (ESI) m/z: 262.3 (M+H)⁺.

[0628] Intermediate- 157:

1-(quinolin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using quinolin-3-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

MS (ESI) m/z: 262.4 (M+H)⁺.

[0629] Intermediate- 158:

1-(1-methyl- 1H-indazol-4-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using 1-methyl-1H-indazol-4-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

¹H -NMR (400 MHz, CDCl₃) delta 7.56 (1H, d, J = 0.9 Hz), 7.73 (1H, d, J = 8.7 Hz), 7.54 (1H, dd, J = 8.7, 7.3 Hz), 7.23 (1H, d, J = 7.3 Hz), 7.08 (1H, td, J = 7.8, 0.9 Hz), 7.04 (1H, dd, J = 7.8, 0.9 Hz), 6.95 (1H, dd, J = 7.8, 1.8 Hz), 6.78 (1H, d, J = 7.8 Hz), 4.09 (3H, s). A signal due to NH is not observed.

MS (ESI) m/z: 265.4 (M+H)⁺.

[0630] Intermediate- 159:

5-chloro-2-(2,2-difluoroethyl)nicotinic acid

The title compound (pale yellow gum) is prepared in 47% yield in 2 steps by the similar manner to Step-2 and Step-3 of Intermediate- 141 using 1,1-difluoro-2-iodoethane in place of 1-bromo-2-methoxyethane.

MS (ESI) m/z: 222.3 (M+H)⁺.

[0631] Intermediate- 160:

1-(imidazo[1,2-a]pyridin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (pale brown solid) is prepared in 36% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 144 using imidazo[1,2-a]pyridin-5-amine in place of 4,6-dimethylpyridin-3-amine.

MS (ESI) m/z: 251.3 (M+H)⁺.

[0632] Intermediate- 161:

1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 63% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 112 using 3-bromo-2-nitropyridine and quinolin-6-amine in place of 4-(pyridin-4-yloxy)aniline and 1-bromo-2-nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.97 (1H, br s), 8.97 (1H, dd, J = 4.1, 1.8 Hz), 8.48 (1H, dd, J = 8.7, 1.4 Hz), 8.22 (1H, d, J = 2.3 Hz), 8.18 (1H, d, J = 9.1 Hz), 8.04 (1H, dd, J = 5.0, 1.4 Hz), 7.97 (1H, dd, J = 8.7, 2.3 Hz), 7.62 (1H, dd, J = 8.2, 1.4 Hz), 7.49 (1H, dd, J = 7.8, 1.4 Hz), 7.07 (1H, dd, J = 7.8, 5.0 Hz).

MS (ESI) m/z: 263.3 (M+H)⁺.

[0633] Intermediate- 162:

1-(quinolin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 63% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 112 using 3-bromo-2-nitropyridine and quinolin-3-amine in place of 4-(pyridin-4-yloxy)aniline and 1-bromo-2-nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 12.00 (1H, br s), 9.12 (1H, d, J = 2.3 Hz), 8.63 (1H, d, J = 2.7 Hz), 8.10 (2H, t, J = 6.8 Hz), 8.05 (1H, dd, J = 5.5, 1.4 Hz), 7.85 (1H, ddd, J = 8.3, 6.8, 1.4 Hz), 7.71 (1H, ddd, J = 8.3, 7.8, 0.9 Hz), 7.53 (1H, dd, J = 8.3, 1.4 Hz), 7.08 (1H, dd, J = 8.3, 5.5 Hz).

MS (ESI) m/z: 263.3 (M+H)⁺.

[0634] Intermediate- 163:

3-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in quantitative yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-99 using quinolin-6-amine in place of 4-methoxyaniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 9.26 (1H, d, J = 2.7 Hz), 8.71 (1H, d, J = 2.3 Hz), 8.10 (1H, dd, J = 5.1, 1.4 Hz), 8.08 (1H, d, J = 4.1 Hz), 7.94 (1H, dd, J = 5.1, 1.4 Hz), 7.82 (1H, ddd, J = 8.2, 6.9, 1.4 Hz), 7.68 (1H, ddd, J = 8.2, 7.3, 1.4 Hz), 7.41 (1H, dd, J = 7.3, 1.4 Hz), 7.11 (1H, dd, J = 7.3, 5.5 Hz). A signal due to NH is not observed.
MS (ESI) m/z: 263.3 (M+H)⁺.

[0635] Intermediate- 164:

1-(2-chlorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 48% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-chloroaniline and 4-chloronicotinic acid in place of 2,3-dihydro-1H-inden-5-amine and 2-chloronicotinic acid.

¹H -NMR (400 MHz, CDCl₃) delta 9.33 (1H br s), 8.44 (1H, s), 8.31 (1H, d, J = 5.0 Hz), 7.69-7.62 (1H, m), 7.55-7.50 (3H, m), 6.71 (1H, dd, J = 5.5, 0.9 Hz).

MS (ESI) m/z: 246.3 (M+H)⁺.

[0636] Intermediate- 165:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound (pale yellow solid) is prepared in 86% yield in 2 steps by the similar manner to Step-1 and Step-2 of Example 9 using Mesylate-4 in place of Mesylate- 1.

¹H -NMR (400 MHz, DMSO-d₆) delta 10.81 (1H, s), 8.82 (1H, d, J = 2.3 Hz), 8.63 (1H, d, J = 7.8 Hz), 8.14 (1H, s), 7.30-6.90 (4H, m), 3.75-3.61 (3H, m), 1.95-1.85 (2H, m), 2.82-2.70 (1H, m), 2.70-2.60 (2H, m), 1.20-1.10 (4H, m). A signal due to NH is not observed.

MS (ESI) m/z: 435.3 (M+H)⁺.

[0637] Intermediate- 166:

1-(quinolin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 98% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using quinolin-4-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 9.10 (1H, d, J = 4.6 Hz), 8.19 (1H, d, J = 8.2 Hz), 7.86 (1H, ddd, J = 8.2, 5.9, 1.8 Hz), 7.71 (1H, d, J = 4.6 Hz), 7.65-7.60 (2H, m), 7.18-7.07 (2H, m), 6.96 (1H, td, J = 7.8, 1.4 Hz), 6.65 (1H, d, J = 7.8 Hz). A signal due to NH is not observed.

MS (ESI) m/z: 262.3 (M+H)⁺.

[0638] Intermediate- 167:

1-(isoquinolin-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 20% yield in 3 steps by the similar manner to Step-

1, Step-2, and Step-3 of Intermediate- 140 using isoquinolin-6-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

MS (ESI) m/z: 262.3 (M+H)⁺.

[0639] Intermediate- 168:

1-(4-(hydroxymethyl)phenyl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (off-white solid) is prepared in 13% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-4 using (4-(hydroxymethyl)phenyl)boronic acid in place of (4-fluorophenyl)boronic acid.

MS (ESI) m/z: 241.0 (M+H)⁺.

[0640] Intermediate- 169:

3-(p-tolyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 78% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using p-toluidine in place of 2,3-dihydro- 1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.35 (1H, s), 7.92 (1H, dd, J = 5.0, 1.4 Hz), 7.52 (2H, d, J = 8.2 Hz), 7.39 (1H, dd, J = 7.8, 1.4 Hz), 7.33 (2H, d, J = 8.2 Hz), 7.08 (1H, dd, J = 7.8, 5.0 Hz), 2.38 (3H, s).

MS (ESI) m/z: 226.3 (M+H)⁺.

[0641] Intermediate- 170:

1-(1,8-naphthyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step- 1>: N-(2-nitrophenyl)-1,8-naphthyridin-3 -amine

The title compound is prepared in 8% yield (20 mg) by the similar manner to Step-1 of Intermediate- 112 using 1,8-naphthyridin-3-amine (144 mg, 0.99 mmol) in place of 4-(pyridin-4-yloxy)aniline.

MS (ESI) m/z: 267.3 (M+H)⁺.

[0642] <Step-2>: N¹-(1,8-naphthyridin-3-yl)benzene- 1,2-diamine

The title compound is prepared in quantitative yield (44 mg) by the similar manner to Step-2 of Intermediate-88 using methyl N-(2-nitrophenyl)-1,8-naphthyridin-3-amine (20 mg, 0.075 mmol, Step-1 of Intermediate- 170) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 237.3 (M+H)⁺.

[0643] <Step-3>: methyl

4-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

To a solution of N¹-1,8-naphthyridin-3-ylbenzene-1, 2-diamine (50 mg, 0.21 mmol) in THF (2 mL) is added di(1H-1,2,4-triazol-1-yl)methanone (104 mg, 0.64 mmol) at room temperature. The mixture is stirred overnight. To the mixture is added saturated aqueous sodium bicarbonate, extracted with EtOAc, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel

eluting with 50-90% EtOAc in n-hexane to give 20 mg (36% yield) of the title compound.

MS (ESI) m/z: 266.3 (M+H)⁺.

[0644] Intermediate- 171:

1-(quinazolin-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 17% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 170 using quinazolin-6-amine in place of 1,8-naphthyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 9.28 (1H, d, J = 2.8 Hz), 9.12 (1H, d, J = 2.8 Hz), 8.71 (1H, d, J = 2.8 Hz), 8.57 (1H, dd, J = 8.2, 1.8 Hz), 7.71 (1H, d, J = 7.8 Hz), 7.21 (1H, d, J = 7.8 Hz), 7.11 (2H, d, J = 4.1 Hz), 7.07-7.02 (1H, m). A signal due to NH is not observed.

MS (ESI) m/z: 263.3 (M+H)⁺.

[0645] Intermediate- 172:

1-(quinolin-7-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 87% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using quinolin-7-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 9.73 (1H, br s), 8.89 (1H, dd, J = 4.6, 1.4 Hz), 8.32 (1H, d, J = 2.3 Hz), 8.25 (1H, dd, J = 8.2, 0.9 Hz), 8.01 (1H, d, J = 8.7 Hz), 7.86 (1H, dd, J = 8.7, 2.3 Hz), 7.49 (1H, dd, J = 8.2, 4.1 Hz), 7.24 (1H, dd, J = 7.3, 1.4 Hz), 7.18-7.06 (3H, m).

MS (ESI) m/z: 262.0 (M+H)⁺.

[0646] Intermediate- 173:

1-(isoquinolin-7-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 30% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using isoquinolin-7-amine in place of 2-(trifluoromethyl)pyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 9.40 (1H, s), 8.55 (1H, d, J = 5.5 Hz), 8.32 (1H, d, J = 1.8 Hz), 8.13 (1H, d, J = 8.7 Hz), 7.96 (1H, dd, J = 8.7, 1.8 Hz), 7.90 (1H, d, J = 5.5 Hz), 7.14 (1H, d, J = 7.8 Hz), 7.12-7.08 (2H, m), 7.05-7.00 (1H, m). A signal due to NH is not observed.

MS (ESI) m/z: 262.0 (M+H)⁺.

[0647] Intermediate- 174:

3-(4-fluoro-3-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in quantitative yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-99 using 4-fluoro-3-methoxyaniline in place of 4-methoxyaniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.40 (1H, br s), 7.94 (1H, dd, J = 5.5, 1.4 Hz), 7.47 (1H, dd, J = 7.7, 2.3 Hz), 7.42-7.33 (2H, m), 7.26-7.18 (1H, m), 7.09 (1H, dd, J = 7.7, 5.5 Hz), 3.84 (3H, s).

MS (ESI) m/z: 260.3 (M+H)⁺.

[0648] Intermediate- 175:

3-(4-acetylphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 83% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-99 using 1-(4-aminophenyl)ethanone in place of 4-methoxyaniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.53 (1H, br s), 8.12 (2H, d, J = 8.9Hz), 7.98 (1H, dd, J = 5.0, 1.4 Hz), 7.95 (2H, d, J = 8.9 Hz), 7.44 (1H, dd, J = 7.8, 1.4 Hz), 7.14 (1H, dd, J = 7.8, 5.0 Hz), 2.63 (3H, s).

MS (ESI) m/z: 254.2 (M+H)⁺.

[0649] Intermediate- 176:

3-(3-(cyclopentyloxy)-4-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 8% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 3-(cyclopentyloxy)-4-methoxyaniline in place of 2,3-dihydro- 1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.30 (1H, s), 7.92 (1H, dd, J = 5.5, 1.4 Hz), 7.37 (1H, dd, J = 7.8, 1.4 Hz), 7.19 (1H, d, J = 2.3 Hz), 7.13 (1H, dd, J = 7.8, 2.7 Hz), 7.09-7.04 (2H, m), 4.75 (1H, br s), 3.80 (3H, s), 2.92-2.80 (2H, m), 2.80-2.68 (4H, m), 2.62-2.52 (2H, m).

MS (ESI) m/z: 326.3 (M+H)⁺.

[0650] Intermediate- 177:

3-(4-ethoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 16% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 4-ethoxyaniline in place of 2,3-dihydro- 1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.30 (1H, br s), 7.91 (1H, dd, J = 5.5, 1.4 Hz), 7.50 (2H, d, J = 9.2 Hz), 7.37 (1H, dd, J = 7.3, 1.4 Hz), 7.10-7.03 (3H, m), 4.08 (2H, q, J = 6.9 Hz), 1.36 (3H, t, J = 6.9 Hz).

MS (ESI) m/z:256.3 (M+H)⁺.

[0651] Intermediate- 178:

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-methyl-1H-indole-2-carboxylic acid

<Step-1>: ethyl

1-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1H-indole-2-carboxylate

The title compound (black solid) is prepared in 26% yield in 3 steps by the similar

manner to Step-1, Step-2, and Step-3 of Intermediate- 179 using ethyl 6-amino-1-methyl-1H-indole-2-carboxylate (336 mg, 1.54 mmol) in place of quinoxalin-6-amine.

MS (ESI) m/z: 336.4 (M+H)⁺.

[0652] <Step-2>:

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-methyl-1H-indole-2-carboxylic acid

The title compound (off-white solid) is prepared in quantitative yield in 2 steps by the similar manner to Step-3 and Step-4 of Intermediate- 3 using ethyl 1-methyl-5-(2-oxo-2,3-dihydro- 1H-benzo [d]imidazol- 1-yl)- 1H-indole-2-carboxylate (93 mg, 0.28 mmol, Step-1 of Intermediate- 178) in place of methyl 2-((2-oxo-2, 3-dihydro- 1H-benzo [d]imidazol- 1-yl)methyl)benzoate.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.53 (1H, d, J = 2.7 Hz), 8.40 (1H, d, J = 8.2 Hz), 7.

82 (1H, d, J = 1.8 Hz), 7.79 (1H, d, J = 2.7 Hz), 7.75 (1H, d, J = 9.1 Hz), 7.43 (1H, dd, J = 9.1, 1.8 Hz), 7.33 (1H, d, J = 8.2 Hz), 7.33 (1H, d, J = 8.2 Hz), 7.31 (1H, s), 7.13 (1H, td, J = 7.8, 0.9 Hz), 7.04 (1H, td, J = 7.8, 0.9 Hz), 6.94 (1H, d, J = 7.3 Hz), 4.09 (3H, s), 3.79 (2H, d, J = 6.9 Hz), 3.71 (1H, br s), 2.47 (3H, s), 1.95-1.73 (5H, m), 1.28-1.17 (4H, m).

MS (ESI) m/z: 572.0 (M+H)⁺.

[0653] Intermediate- 179:

1-(quinoxalin-6-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: N-(2-nitrophenyl)quinoxalin-6-amine

The title compound is prepared in 93% yield (244 mg, red solid) by the similar manner to Step-1 of Intermediate- 101 using 1-bromo-2-nitrobenzene (200 mg, 0.99 mmol) and quinoxalin-6-amine (144 mg, 0.99 mmol) in place of 2-bromo-1-methyl-3-nitrobenzene and methyl 5-aminopicolinate.

MS (ESI) m/z: 267.4 (M+H)⁺.

[0654] <Step-2>: N¹-(quinoxalin-6-yl)benzene-1, 2-diamine

The title compound is prepared in quantitative yield (230 mg, black solid) by the similar manner to Step-2 of Intermediate- 88 using N-(2-nitrophenyl)quinoxalin-6-amine (244 mg, 0.92 mmol, Step-1 of Intermediate- 179) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 239.3 (M+H)⁺.

[0655] <Step-3>: 1-(quinoxalin-6-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield (255 mg, off-white solid) by the similar manner to Step-3 of Intermediate-20 using N¹-(quinoxalin-6-yl)benzene-1, 2-diamine (230 mg, 0.97 mmol, Step-2 of Intermediate-

179) in place of N¹,N¹-difluorophenylbenzene-1, 2-diamine.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.34 (1H, br s), 9.03 (1H, d, J = 4.1 Hz), 9.02 (1H, d, J = 4.1 Hz), 8.28 (1H, d, J = 9.1 Hz), 8.27 (1H, d, J = 2.3 Hz), 8.11 (1H, dd, J = 9.1, 2.3 Hz), 7.22 (1H, d, J = 7.8 Hz), 7.15-7.12 (2H, m), 7.09-7.04 (1H, m).

MS (ESI) m/z: 263.0 (M+H)⁺.

[0656] Intermediate- 180:

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinic acid

The title compound is prepared in 90% yield (solid) by the similar manner to Step-4 of Intermediate-36 using Mesylate-3 in place of Mesylate- 1.

¹H-NMR (400 MHz, DMSO-d₆) delta 8.98 (1H, br), 8.87 (1H, d, J = 1.8 Hz), 8.58 (1H, d, J = 7.8 Hz), 8.30-8.18 (3H, m), 7.39 (1H, d, J = 7.8 Hz), 7.31-7.17 (2H, m), 7.12 (1H, t, J = 7.5 Hz), 3.80 (2H, d, J = 6.4 Hz), 3.75-3.60 (1H, br), 2.00-1.60 (5H, m), 1.33-1.05 (4H, m).

MS (ESI) m/z: 573.9 (M+H)⁺.

[0657] Intermediate- 181:

3-(2,4-dichlorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 11% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2,4-dichloroaniline in place of 2,3-dihydro-1H-inden-5-amine.

MS (ESI) m/z: 280.2 (M+H)⁺.

[0658] Intermediate- 182:

1-(imidazo[1,5-a]pyridin-7-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield (138 mg, green solid) by the similar manner to Step-2 of Intermediate-95 using 7-bromoimidazo[1,5-a]pyridine (98 mg, 0.50 mmol) in place of 5-bromo-2,3-dimethyl-2H-indazole.

MS (ESI) m/z: 251.3 (M+H)⁺.

[0659] Intermediate- 183:

1-(6-(2-methoxyethoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of 1-(6-fluoropyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (60 mg, 0.26 mmol, Step-1 of intermediate- 135), 2-methoxyethanol (60 mg, 0.79 mmol) in DMF (2 mL) is added potassium tert-butoxide (88 mg, 0.79 mmol) at room temperature. The mixture is stirred at 80 °C overnight. The mixture is diluted with H₂O, extracted with EtOAc, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 40-100% EtOAc in n-hexane to give 37 mg (50% yield) of the title compound.

MS (ESI) m/z: 286.0 (M+H)⁺.

[0660] Intermediate- 184:

1-(2-methyl-2H-indazol-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 80% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 140 using 2-methyl-2H-indazol-4-amine (109 mg, 0.74 mmol) in place of 2-(trifluoromethyl)pyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.13 (1H, s), 7.67 (1H, dd, J = 8.7, 0.9 Hz), 7.36 (1H, dd, J = 8.7, 7.3 Hz), 7.12 (1H, 1H, d, J = 7.6 Hz), 7.09-7.02 (2H, m), 6.95 (1H, ddd, J = 8.7, 7.3, 1.4 Hz), 6.77 (1H, d, J = 7.6 Hz), 4.12 (3H, s). A signal due to NH is not observed.

MS (ESI) m/z: 265.4 (M+H)⁺.

[0661] Intermediate- 185:

1-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 80% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 179 using

1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine in place of quinoxalin-6-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.23 (1H, br s), 8.48 (1H, d, J = 2.3 Hz), 8.07 (1H, d, J = 2.3 Hz), 7.47 (1H, d, J = 2.3 Hz), 7.16-7.04 (3H, m), 6.96 (1H, d, J = 7.8 Hz), 6.60 (1H, d, J = 3.7 Hz), 5.73 (2H, s), 3.60 (2H, t, J = 8.2 Hz), 0.95 (2H, t, J = 8.2 Hz), -0.03 (9H, s).

MS (ESI) m/z: 381.3 (M+H)⁺.

[0662] Intermediate- 186:

1-(3-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 85% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 179 using

3-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine in place of quinoxalin-6-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.63 (1H, br s), 8.44 (1H, d, J = 2.3 Hz), 8.01 (1H, d, J = 2.3 Hz), 7.23 (1H, d, J = 0.9 Hz), 7.17-7.04 (3H, m), 6.94 (1H, d, J = 7.8 Hz), 5.67 (2H, s), 3.57 (2H, t, J = 8.2 Hz), 2.33 (3H, d, J = 0.9 Hz), 0.95 (2H, t, J = 8.2 Hz), 0.03 (9H, s).

MS (ESI) m/z: 395.3 (M+H)⁺.

[0663] Intermediate- 187:

3-(3-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

[0664] <Step-1>:

3-methyl-N-(3-nitropyridin-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-

b]pyridin-5-amine

The title compound is prepared in 68% yield (175 mg) by the similar manner to Step-1 of Intermediate- 101 using

3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine (190 mg, 1.11 mmol, Step-2 of Intermediate-229) and 2-bromo-3-nitropyridine (132 mg, 0.65 mmol) in place of 2-bromo-1-methyl-3-nitrobenzene and methyl 5-aminopicolinate.

MS (ESI) m/z: 400.3 (M+H)⁺.

[0665] <Step-2>: N² -

(3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridine -2,3-diamine

The title compound is prepared in quantitative yield (204 mg) by the similar manner to Step-2 of Intermediate- 88 using

3-methyl-N-(3-nitropyridin-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine (175 mg, 0.79 mmol, Step-1 of Intermediate- 187) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 370.0 (M+H)⁺.

[0666] <Step-3>:

3-(3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)- 1H-pyrrolo[2,3-b]pyridin-5-yl)- 1H-i midazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in quantitative yield (188 mg) by the similar manner to Step-3 of Intermediate- 170 using N² -

(3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridine -2,3-diamine (176 mg, 0.48 mmol, Step-2 of Intermediate- 187) in place of N¹ - (1,8-naphthyridin-3-yl)benzene- 1,2-diamine.

¹H -NMR (400 MHz, CDCl₃) delta 10.28 (1H, br s), 8.55 (1H, d, J = 2.3 Hz), 8.09 (1H, d, J = 2.3 Hz), 8.06 (1H, dd, J = 5.0, 1.4 Hz), 7.37 (1H, dd, J = 7.8, 1.4 Hz), 7.21 (1H, d, J = 1.4 Hz), 7.06 (1H, dd, J = 7.8, 5.0 Hz), 5.65 (2H, s), 3.56 (2H, dd, J = 8.2, 7.8 Hz), 2.34 (3H, d, J = 1.4 Hz), 0.94 (2H, dd, J = 8.2, 7.8 Hz), -0.02 (9H, s).

MS (ESI) m/z: 395.9 (M+H)⁺.

[0667] Intermediate- 188:

(R)-1-(6-((tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 85% yield (55 mg) by the similar manner to Intermediate-24 using (R)-tetrahydrofuran-3-ol (38 mg, 0.44 mmol) in place of 2-((tetrahydro-2H-pyran-2-yl)oxy)ethanol.

MS (ESI) m/z: 298.3 (M+H)⁺.

[0668] Intermediate- 189:

1-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 69% yield (45 mg) by the similar manner to Intermediate-24 using 2-methylpropane-1,2-diol (39 mg, 0.44 mmol) in place of 2-((tetrahydro-2H-pyran-2-yl)oxy)ethanol.

MS (ESI) m/z: 300.3 (M+H)⁺.

[0669] Intermediate- 190:

(S)-1-(6-((tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 80% yield (52 mg) by the similar manner to Intermediate-24 using (S)-tetrahydrofuran-3-ol (38 mg, 0.44 mmol) in place of 2-((tetrahydro-2H-pyran-2-yl)oxy)ethanol.

MS (ESI) m/z: 298.2 (M+H)⁺.

[0670] Intermediate- 191:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 96% yield (solid) by the similar manner to Intermediate-54 using Mesylate-4 in place of Mesylate- 1.

¹H -NMR (400 MHz, CDCl₃) delta 8.64 (1H, d, J = 2.3 Hz), 8.46 (1H, br d, J = 1.6 Hz), 8.04 (1H, ddd, J = 8.8, 6.6, 2.8 Hz), 7.91 (1H, d, J = 2.3 Hz), 7.20 (1H, td, J = 7.7, 1.1 Hz), 7.17-7.04 (4H, m), 6.86 (1H, t, J = 54.8 Hz), 6.01 (1H, d, J = 7.3 Hz), 4.06-3.88 (1H, m), 3.81 (2H, d, J = 7.3 Hz), 2.15 (2H, d, J = 9.6 Hz), 2.04-1.81 (3H, m), 1.41-1.11 (4H, m).

MS (ESI) m/z: 529.9 (M+H)⁺.

[0671] Intermediate- 192:

5-chloro-N-((1r,4r)-4-((3-(6-fluoro-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

<Step- 1>: 6-fluoro-4-methyl-N-(2-nitrophenyl)pyridin-3-amine

A mixture of 1-fluoro-2-nitrobenzene (100 mg, 0.505 mmol), 6-fluoro-4-methylpyridin-3-amine (111 mg, 0.606 mmol), potassium t-butoxide (247 mg, 0.757 mmol) in THF (1 mL) is stirred for 1 hr at rt. The mixture is added with saturated aqueous ammonium chloride. The resultant mixture is extracted with EtOAc. The organic layer is dried over MgSO₄, filtered and concentrated in vacuo to give 390 mg of the title compound as a crude. The compound is used for the next reaction without further purification.

MS (ESI) m/z: 248.3 (M+H)⁺.

[0672] <Step-2>: N¹-(6-fluoro-4-methylpyridin-3-yl)benzene-1, 2-diamine

The title compound is prepared in 82% yield (256 mg, brown solid) by the similar manner to Step-2 of Intermediate- 151 using 6-fluoro-4-methyl-N-(2-nitrophenyl)pyridin-3-amine (354 mg, Step-1 of Intermediate- 192) in place of methyl 4-methyl-5-((2-methyl-6-nitrophenyl)amino)picolinate.

MS (ESI) m/z: 218.3 (M+H)⁺.

- [0673] <Step-3>: 1-(6-fluoro-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one
The title compound is prepared in 21% yield (60 mg, brown solid) by the similar manner to Step-3 of Intermediate- 105 using N¹-(6-fluoro-4-methylpyridin-3-yl)benzene-1, 2-diamine (256 mg, 1.18 mmol, Step-2 of Intermediate- 192) in place of methyl 5-((2-aminophenyl)amino)-4-methylpicolinate.

MS (ESI) m/z: 244.3 (M+H)⁺.

- [0674] <Step-4>:
5-chloro-N-((1r,4r)-4-((3-(6-fluoro-4-methylpyridin-3-yl)-2-oxo-2, 3-dihydro- 1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (20 mg, 0.055 mmol, Mesylate- 1), 1-(6-fluoro-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (14 mg, 0.055 mmol, Step-3 of Intermediate- 192), and cesium carbonate (45 mg, 0.139 mmol) in DMSO (1 mL) is stirred overnight at 80 °C. The mixture is diluted with saturated aqueous sodium chloride. The mixture is extracted with THF. The organic layer is concentrated. The resultant mixture is washed with water followed by diisopropyl ether to give 30 mg (quantitative yield) of the title compound as a brown gum.

MS (ESI) m/z: 508.2 (M+H)⁺.

- [0675] Intermediate- 193:
1-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one
<Step-1>: N⁵-(2-nitrophenyl)-N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine
The title compound is prepared in 52% yield (134 mg, brown solid) by the similar manner to Step-1 of Intermediate-73 using N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine (157 mg, 0.821 mmol) in place of 1-methyl- 1H-indazol-5-amine.

¹H -NMR (400 MHz, CDCl₃) delta 9.25 (1H, s), 8.20 (1H, dd, J = 8.7, 2.5 Hz), 8.08 (1H, d, J = 2.5 Hz), 7.44-7.30 (2H, m), 6.88 (1H, dd, J = 8.5, 1.1 Hz), 6.82-6.67 (1H, m), 6.59 (1H, d, J = 8.7 Hz), 4.26-3.99 (2H, m).

MS (ESI) m/z: 313.2 (M+H)⁺.

- [0676] <Step-2>: N⁵-(2-aminophenyl)-N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine
The title compound is prepared in 73% yield (88 mg, brown gum) by the similar manner to Step-2 of Intermediate- 151 using N⁵-(2-nitrophenyl)-N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine (134 mg, 0.429 mmol, Step-1 of Intermediate- 193) in place of methyl 4-methyl-5-((2-methyl-6-nitrophenyl)amino)picolinate.

MS (ESI) m/z: 283.3 (M+H)⁺.

- [0677] <Step-3>:

1-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of N⁵-(2-aminophenyl)-N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine (88 mg, 0.31 mmol, Step-2 of Intermediate- 193) and CDI (76 mg, 0.47 mmol) in MeCN (1 mL) is stirred overnight at rt. After the reaction mixture is concentrated, the resultant mixture is washed with water followed by diisopropyl ether to give 37 mg (39% yield) of the title compound as a brown solid.

MS (ESI) m/z: 309.2 (M+H)⁺.

[0678] Intermediate- 194:

1-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 28% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 193 using N² - (2,2-difluoroethyl)pyridine-2, 5-diamine in place of N² - (2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

MS (ESI) m/z: 291.2 (M+H)⁺.

[0679] Intermediate- 195:

1-(1,5-naphthyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 51% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 102 using 1,5-naphthyridin-3-amine and 1-bromo-2-nitrobenzene in place of 2-bromo-4-fluoro-1 -nitrobenzene and methyl 5-aminopicolinate.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.40 (1H, br s), 9.25 (1H, d, J = 2.7 Hz), 9.09 (1H, dd, J = 4.1, 1.8 Hz), 8.61 (1H, d, J = 1.8 Hz), 8.53 (1H, d, J = 8.2 Hz), 7.87 (1H, dd, J = 8.2, 4.1 Hz), 7.23 (1H, d, J = 7.8 Hz), 7.15-7.13 (2H, m), 7.09-7.03 (1H, m).

MS (ESI) m/z: 263.0 (M+H)⁺.

[0680] Intermediate- 196:

1-(quinazolin-7-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 76% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 102 using quinazolin-7-amine and 1-bromo-2-nitrobenzene in place of 2-bromo-4-fluoro-1 -nitrobenzene and methyl 5-aminopicolinate.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.34 (1H, br s), 9.68 (1H, s), 9.35 (1H, s), 8.37 (1H, d, J = 8.7 Hz), 8.17 (1H, d, J = 2.3 Hz), 8.04 (1H, dd, J = 8.7, 2.3 Hz), 7.27-7.24 (1H, m), 7.15-7.13 (2H, m), 7.09-7.05 (1H, m).

MS (ESI) m/z: 263.0 (M+H)⁺.

[0681] Intermediate- 197:

3-(2-fluorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 65% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-fluoroaniline in place

of 2,3-dihydro-1H-inden-5-amine.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.44 (1H, s), 7.90 (1H, dd, J = 5.0, 1.4 Hz), 7.62-7.53 (2H, m), 7.50-7.35 (3H, m), 7.09 (1H, dd, J = 7.8, 5.0 Hz).

MS (ESI) m/z: 230.3 (M+H)⁺.

[0682] Intermediate- 198:

3-(2-chloro-4-methylphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step- 1>: N-(2-chloro-4-methylphenyl)-3-nitropyridin-2-amine

The title compound is prepared in 73% yield (135 mg) by the similar manner to Step-1 of Intermediate- 112 using 2-bromo-3-nitropyridine (150 mg, 0.74 mmol) and 2-chloro-4-methylaniline (105 mg, 0.74 mmol) in place of 1-bromo-2-nitrobenzene and 4-(pyridin-4-yloxy)aniline.

MS (ESI) m/z: 264.0 (M+H)⁺.

[0683] <Step-2>: N²-(2-chloro-4-methylphenyl)pyridine-2, 3-diamine

The title compound is prepared in 73% yield (135 mg) by the similar manner to Step-2 of Intermediate-43 using N-(2-chloro-4-methylphenyl)-3-nitropyridin-2-amine (194 mg, 0.94 mmol, Step-1 of Intermediate- 198) in place of 2-bromo-N-(2-nitrophenyl)pyridin-4-amine.

MS (ESI) m/z: 233.9 (M+H)⁺.

[0684] <Step-3>: 3-(2-chloro-4-methylphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 50% yield (89 mg) by the similar manner to Step-3 of Intermediate-20 using N²-(2-chloro-4-methylphenyl)pyridine-2, 3-diamine (135 mg, 0.84 mmol, Step-2 of Intermediate- 198) in place of N¹-(2,4-difluorophenyl)benzene- 1,2-diamine.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.37 (1H, br s), 7.85 (1H, dd, J = 5.5, 1.4 Hz), 7.52 (1H, d, J = 1.4 Hz), 7.45 (1H, d, J = 7.8 Hz), 7.28 (1H, dd, J = 7.3, 1.4 Hz), 7.32 (1H, dd, J = 7.3, 1.4 Hz), 7.06 (1H, dd, J = 7.3, 5.5), 2.40 (3H, s).

MS (ESI) m/z: 259.9 (M+H)⁺.

[0685] Intermediate- 199:

3-(2-chloro-5-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 6% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 198 using 2-chloro-5-methoxy aniline in place of 2-chloro-4-methylaniline.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.39 (1H, br s), 7.86 (1H, d, J = 5.0, 1.4 Hz), 7.58 (1H, d, J = 8.7 Hz), 7.39 (1H, dd, J = 7.8, 1.4 Hz), 7.23 (1H, dd, J = 3.2 Hz), 7.14 (1H, dd, J = 8.7, 3.2 Hz), 7.07 (1H, dd, J = 7.8, 5.0 Hz), 3.79 (3H, s).

MS (ESI) m/z: 275.9 (M+H)⁺.

[0686] Intermediate-200:

3-(2-chloro-5-fluorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 24% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 198 using 2-chloro-5-fluoroaniline in place of 2-chloro-4-methylaniline.

¹H -NMR (400 MHz, CDCl₃) delta 11.46 (1H, br s), 7.88 (1H, dd, J = 7.8, 5.5 Hz), 7.77 (1H, dd, J = 8.7, 5.5 Hz), 7.67 (1H, ddd, J = 9.1, 5.5, 2.7 Hz), 7.48 (1H, ddd, J = 9.1, 5.5, 2.7 Hz), 7.41 (1H, dd, J = 7.8, 1.4 Hz), 7.09 (1H, dd, J = 7.8, 5.5 Hz).

MS (ESI) m/z: 263.8 (M+H)⁺.

[0687] Intermediate-20 1:

3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 85% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 187 using

1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine in place of 3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine.

MS (ESI) m/z: 381.9 (M+H)⁺.

[0688] Intermediate-202:

3-(2-phenoxyethyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step- 1>: 3-nitro-N-(2-phenoxyethyl)pyridin-2-amine

A mixture of 2-chloro-3-nitropyridine (150 mg, 0.95 mmol), 2-phenoxyethanamine (130 mg, 0.95 mmol), and DIEA (0.50 mL, 2.84 mmol) is stirred at 70 °C for 3 hrs. The mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-40% EtOAc in n-hexane to give 181 mg (74% yield) of the title compound as a yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 8.55 (1H, br s), 8.45-8.40 (2H, m), 7.32-7.25 (2H, m), 7.00-6.91 (3H, m), 6.68 (1H, dd, J = 8.2, 5.0 Hz), 4.22 (2H, t, J = 5.5 Hz), 4.07 (2H, q, J = 5.5 Hz).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0689] <Step-2>: N²-(2-phenoxyethyl)pyridine-2, 3-diamine

The title compound is prepared in quantitative yield (160 mg, pale brown gum) by the similar manner to Step-2 of Intermediate- 88 using

3-nitro-N-(2-phenoxyethyl)pyridin-2-amine (181 mg, 0.70 mmol, Step-1 of Intermediate-202) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 230.3 (M+H)⁺.

[0690] <Step-3>: 3-(2-phenoxyethyl)- 1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 16% yield (32 mg, pale yellow solid) by the similar manner to Step-3 of Intermediate- 170 using N² - (2-phenoxyethyl)pyridine-2, 3-diamine (160 mg, 0.70 mmol, Step-2 of Intermediate-

202) in place of N¹-1^Λ-naphthyridin-S-yObenzene-l, 2-diamine.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.15 (1H, s), 7.93 (1H, d, J = 5.0 Hz), 7.30-7.21 (3H, m), 7.00 (1H, dd, J = 7.8, 5.0 Hz), 6.95-6.85 (3H, m), 4.32 (2H, t, J = 5.5 Hz), 4.20 (2H, t, J = 5.5 Hz).

MS (ESI) m/z: 256.3 (M+H)⁺.

[0691] Intermediate-203:

1-(6-(isopropylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 19% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 193 using N² - isopropylpyridine-2, 5-diamine in place of N² - (2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

MS (ESI) m/z: 269.3 (M+H)⁺.

[0692] Intermediate-204:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-fluoro-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of ((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate (20 mg, 0.050 mmol, Mesylate-4), methyl 1-(6-fluoro-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (12 mg, 0.050 mmol, Step-3 of Intermediate- 192), and cesium carbonate (32 mg, 0.097 mmol) in DMSO (1 mL) is stirred for 4.5 hrs at 100 °C. The mixture is diluted with saturated aqueous sodium chloride. The mixture is extracted with THF. The organic layer is concentrated. The resultant mixture is dissolved in DCM and washed with water. The organic layer is dried over MgSO₄, filtered and concentrated in vacuo to give 31 mg of the title compound as a crude. The compound is used for the next reaction without further purification.

MS (ESI) m/z: 544.2 (M+H)⁺.

[0693] Intermediate-205:

1-(6-((3,3-difluoropropyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: N²-(3,3-difluoropropyl)-N⁵-(2-nitrophenyl)pyridine-2, 5-diamine

The title compound is prepared in 94% yield (37 mg, brown gum) by the similar manner to Step-1 of Intermediate-73 using N² - (3,3-difluoropropyl)pyridine-2, 5-diamine (24 mg, 0.13 mmol) in place of 1-methyl- 1H-indazol-5-amine.

MS (ESI) m/z: 309.2 (M+H)⁺.

[0694] <Step-2>: N⁵-(2-aminophenyl)-N²-(3,3-difluoropropyl)pyridine-2, 5-diamine

The title compound is prepared in 92% yield (31 mg, brown gum) by the similar manner to Step-2 of Intermediate- 151 using N²-(3,3-difluoropropyl)-N⁵ - (2-nitrophenyl)pyridine-2, 5-diamine (37 mg, 0.12 mmol) in place of methyl

4-methyl-5-((2-methyl-6-nitrophenyl)amino)picolinate.

MS (ESI) m/z: 279.3 (M+H)⁺.

[0695] <Step-3>:

1-(6-((3,3-difluoropropyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of N⁵-(2-aminophenyl)-N²-(3,3-difluoropropyl)pyridine-2, 5-diamine (31 mg, 0.11 mmol, Step-2 of Intermediate-205) and CDI (27 mg, 0.17 mmol) in MeCN (1 mL) is stirred for 1 hr at rt. After the reaction mixture is concentrated, the residue is added with water. The resultant mixture is extracted with EtOAc and concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 24-100% EtOAc in n-hexane to give 14 mg (42% yield) of the title compound as a brown gum.

MS (ESI) m/z: 305.2 (M+H)⁺.

[0696] Intermediate-206:

3-(3-chloropyridin-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step-1>: N-(3-chloropyridin-4-yl)-3-nitropyridin-2-amine

The title compound is prepared in 76% yield (141 mg) by the similar manner to Step-1 of Intermediate-101 using 2-bromo-3-nitropyridine (150 mg, 0.74 mmol) and 3-chloropyridin-4-amine (95 mg, 0.74 mmol) in place of methyl 5-aminopicolinate and 2-bromo-1-methyl-3-nitrobenzene.

¹H-NMR (400 MHz, CDCl₃) delta 10.9 (1H, br s), 8.78 (1H, d, J = 5.5 Hz), 8.65 - 8.59 (3H, m), 8.44 (1H, d, J = 5.5 Hz), 7.11-7.05 (1H, m).

MS (ESI) m/z: 250.9 (M+H)⁺.

[0697] <Step-2>: N²-(3-chloropyridin-4-yl)pyridine-2, 3-diamine

The title compound is prepared in 33% yield (41 mg) by the similar manner to Step-2 of Intermediate-43 using N-(3-chloropyridin-4-yl)-3-nitropyridin-2-amine (141 mg, 0.56 mmol, Step-1 of Intermediate-206) in place of 2-bromo-N-(2-nitrophenyl)pyridin-4-amine.

MS (ESI) m/z: 220.9 (M+H)⁺.

[0698] <Step-3>: 3-(3-chloropyridin-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in quantitative yield (46 mg) by the similar manner to Step-3 of Intermediate-170 using N²-(3-chloropyridin-4-yl)pyridine-2, 3-diamine (41 mg, 0.19 mmol, Step-2 of Intermediate-206) in place of N¹-(1,8-naphthyridin-3-yl)benzene-1,2-diamine.

MS (ESI) m/z: 246.9 (M+H)⁺.

[0699] Intermediate-207 :

N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

The title compound is prepared in 86% yield (solid) by the similar manner to In-

intermediate-54 using Mesylate-4 in place of Mesylate- 1, and Intermediate-39 in place of tert-butyl

3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate, re-spectively.

¹H -NMR (400 MHz, CDCl₃) delta 8.68-8.61 (2H, m), 7.92 (1H, d, J = 2.3 Hz), 7.84 (1H, dd, J = 8.7, 2.7 Hz), 7.66 (1H, d, J = 8.2 Hz), 7.25-7.16 (1H, m), 7.12 (2H, d, J = 4.0 Hz), 7.08 (1H, d, J = 7.3 Hz), 6.86 (1H, t, J = 54.7 Hz), 5.97 (1H, d, J = 7.8 Hz), 4.04-3.88 (1H, m), 3.81 (2H, d, J = 6.9 Hz), 2.21-2.09 (2H, m), 2.02-1.80 (3H, m), 1.41-1.14 (4H, m).

MS (ESI) m/z: 591.9 (M+H)⁺.

[0700] Intermediate-208:

4-methoxy-2-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)benzonitrile

<Step- 1>: 4-methoxy-2-((3-nitropyridin-2-yl)amino)benzonitrile

A mixture of 2-fluoro-3-nitropyridine (90 mg, 0.63 mmol), 2-amino-4-methoxybenzonitrile (94 mg, 0.63 mmol), and Cs₂CO₃ (619 mg, 1.90 mmol) in DMSO (3 mL) is stirred at rt for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 62 mg (36% yield) of the title compound as an orange solid.

MS (ESI) m/z: 271.3 (M+H)⁺.

[0701] <Step-2>: 2-((3-aminopyridin-2-yl)amino)-4-methoxybenzonitrile

The title compound is prepared in quantitative yield (55 mg, pale yellow gum) by the similar manner to Step-2 of Intermediate- 88 using 4-methoxy-2-((3-nitropyridin-2-yl)amino)benzonitrile (62 mg, 0.23 mmol, Step-1 of Intermediate-208) in place of N-(2-nitrophenyl)chroman-3-amine.

MS (ESI) m/z: 241.3 (M+H)⁺.

[0702] <Step-3>: 4-methoxy-2-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)benzonitrile

The title compound is prepared in quantitative yield (61 mg, pale yellow gum) by the similar manner to Step-3 of Intermediate-20 using

2-((3-aminopyridin-2-yl)amino)-4-methoxybenzonitrile (55 mg, 0.23 mmol, Step-2 of Intermediate-208) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.52 (1H, s), 7.99 (1H, d, J = 8.7 Hz), 7.92 (1H, dd, J = 5.0, 1.4 Hz), 7.45 (1H, dd, J = 7.8, 1.4 Hz), 7.34 (1H, d, J = 2.7 Hz), 7.26 (1H, dd, J = 8.7, 2.7 Hz), 7.13 (1H, dd, J = 7.8, 5.0 Hz), 3.88 (3H, s).

MS (ESI) m/z: 267.3 (M+H)⁺.

[0703] Intermediate-209:

1-(1-(pyridin-3-yl)piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 1-(piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one (200 mg, 0.921 mmol), 3-iodopyridine (189 mg, 0.921 mmol), potassium t-butoxide (207 mg, 1.84 mmol), palladium (II) acetate (41 mg, 0.18 mmol), and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (107 mg, 0.184 mmol) in 1,4-dioxane (2 mL) is stirred for 1 day at 100 °C. The reaction mixture is concentrated and the resultant residue is purified by column chromatography on amino-functional silica gel eluting with 0-30% MeOH in EtOAc to give 27 mg (10% yield) of the title compound as a brown gum.

MS (ESI) m/z: 295.3 (M+H)⁺.

[0704] Intermediate-210:

1-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 38% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 193 using N² -

(2,2-difluoropropyl)pyridine-2, 5-diamine in place of N² -

(2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

MS (ESI) m/z: 305.2 (M+H)⁺.

[0705] Intermediate-2 11:

5-(4-bromopyridin-2-yl)oxazole

To a solution of 4-bromopicolinaldehyde (0.25 g, 1.34 mmol) in MeOH (20 mL) is added potassium carbonate (0.557 g, 4.03 mmol) and TosMIC (0.315 g, 1.61 mmol). The resulting mixture is stirred at room temperature for 3 hrs. The reaction mixture is evaporated to dryness, diluted with water and extracted with EtOAc twice. The combined organics are washed with water and brine, dried over sodium sulfate, filtered and evaporated. The residue is purified by column chromatography on silica-gel eluting with 30% EtOAc in n-hexane to give 196 mg (65% yield) of the title compound.

¹H -NMR (400 MHz, CDCl₃) delta 8.45 (1H, d, J = 5.5 Hz), 7.99 (1H, s), 7.85 (1H, d, J = 1.8 Hz), 7.73 (1H, s), 7.41 (1H, dd, J = 5.5, 1.8 Hz).

[0706] Intermediate-212:

1-(5-chloro-6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: tert-butyl

3-(5-chloro-6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 11% yield (17 mg, pale yellow gum) by the similar manner to Step-1 of Intermediate-4 using (5-chloro-6-fluoropyridin-3-yl)boronic acid (75 mg, 0.43 mmol) in place of (4-fluorophenyl)boronic acid.

¹H -NMR (400 MHz, CDCl₃) delta 8.31 (1H, dd, J = 2.5, 1.6 Hz), 8.08 (1H, dd, J = 7.8, 2.5 Hz), 7.96 (1H, dd, J = 7.3, 1.8 Hz), 7.25-7.18 (2H, m), 6.98 (1H, dd, J = 6.4,

2.7 Hz), 1.69 (9H, s).

[0707] <Step-2>:

1-(5-chloro-6-(methylanino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of tert-butyl

3-(5-chloro-6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (17 mg, 0.046 mmol, Step-1 of Intermediate-2 12), methylamine hydrochloride (39 mg, 0.58 mmol), and DIEA (0.101 mL, 0.581 mmol) in NMP (0.5 mL) is stirred for 35 min at 220 °C under microwave irradiation. The reaction mixture is added with water. The resultant mixture is extracted with EtOAc/THF (50:50) and concentrated. The resultant residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 11 mg (85% yield) of the title compound as a brown solid.

MS (ESI) m/z: 275.1 (M+H)⁺.

[0708] Intermediate- 213

1-(1,3-dimethyl- 1H-pyrrolo [2,3-b]pyridin-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound is prepared in 72% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 179 using 1,3-dimethyl- 1H-pyrrolo[2,3-b]pyridin-5-amine in place of quinoxalin-6-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.15 (1H, br s), 8.30 (1H, d, J = 2.3 Hz), 8.06 (1H, d, J = 2.3 Hz), 7.41 (1H, d, J = 0.9 Hz), 7.10-7.03 (2H, m), 6.98 (1H, td, J = 7.8, 1.8 Hz), 6.85 (1H, d, J = 7.8 Hz), 3.82 (3H, s), 2.27 (3H, d, J = 0.9 Hz).

MS (ESI) m/z: 279.3 (M+H)⁺.

[0709] Intermediate-214:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of ((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate (500 mg, 1.26 mmol, Mesylate-4), 3-(2,4-dimethoxybenzyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one (359 mg, 1.26 mmol, Intermediate- 122) and cesium carbonate (1.23 g, 3.78 mmol) in DMSO (5 mL) is stirred at 80 °C overnight. The mixture is diluted with water (30 mL) to afford suspension. The precipitate is collected by filtration, washed with diisopropyl ether (10 mL) and dried in vacuo. The solid in TFA (20 mL) is stirred at 75 °C overnight. The mixture is concentrated, purified by column chromatography on amino-functional silica-gel eluting with 50-85% EtOAc in n-hexane to give 420 mg (76% yield) of the title compound as a brown solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.51 (1H, br s), 8.80 (1H, d, J = 2.3 Hz), 8.62 (1H, br d, J = 7.8 Hz), 8.12 (1H, d, J = 2.3 Hz), 7.87 (1H, dd, J = 5.1, 1.4 Hz), 7.46 (1H, dd, J = 7.8, 1.4 Hz), 7.11 (1H, t, J = 53 Hz), 6.98 (1H, dd, J = 5.1, 2.7 Hz),

3.70-3.62 (1H, m), 3.63 (2H, d, J = 6.9 Hz), 1.91-1.84 (2H, m), 1.80-1.69 (1H, m), 1.69-1.59 (2H, m), 1.23-1.04 (4H, m).

MS (ESI) m/z: 435.8 (M+H)⁺.

[0710] Intermediate-215:

N-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyrazine-2-carboxamide
<Step-1>: tert-butyl

3-(5-(methoxycarbonyl)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

A mixture of methyl 5-chloropyrazine-2-carboxylate (100 mg, 0.58 mmol), tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (136 mg, 0.58 mmol), and Cs₂CO₃ (283 mg, 0.87 mmol) in DMSO (3 mL) is stirred at rt for 1 day. The mixture is diluted with 10% aqueous citric acid solution. The precipitate is collected and washed with diisopropyl ether to give 178 mg (83% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 371.2 (M+H)⁺.

[0711] <Step-2>: N-

methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyrazine-2-carboxamide

The title compound is prepared in 57% yield (74 mg, pale pink solid) by the similar manner to Intermediate-87 using tert-butyl

3-(5-(methoxycarbonyl)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (178 mg, 0.48 mmol, Step-1 of Intermediate-215) in place of methyl 5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

¹H-NMR (400 MHz, DMSO-d₆) delta 9.51 (1H, d, J = 1.4 Hz), 9.12 (1H, d, J = 1.4 Hz), 8.88 (1H, q, J = 5.0 Hz), 8.09 (1H, dd, J = 7.8, 1.4 Hz), 7.19 (1H, dd, J = 7.8, 1.4 Hz), 7.11 (2H, d, J = 7.8 Hz), 2.85 (3H, d, J = 5.0 Hz). A signal due to NH is not observed.

MS (ESI) m/z: 270.2 (M+H)⁺.

[0712] Intermediate-216:

1-(6-(cyclopropylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 30% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-193 using N²-cyclopropylpyridine-2,5-diamine in place of N²-(2,2,2-trifluoroethyl)pyridine-2,5-diamine.

MS (ESI) m/z: 267.2 (M+H)⁺.

[0713] Intermediate-217:

1-(4-methyl-6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 52% yield (26 mg, brown gum) by the similar manner to Step-2 of Intermediate-212 using

1-(6-fluoro-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (13 mg, 0.053 mmol, Step-3 of Intermediate- 192) in place of tert-butyl 3-(5-chloro-6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate.

MS (ESI) m/z: 255.2 (M+H)⁺.

[0714] Intermediate-218:

3-(1-methyl-1H-indazol-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (off-white solid) is prepared in 74% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 1-methyl-1H-indazol-5-amine in place of 2,3-dihydro-1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.30 (1H, br s), 8.12 (1H, s), 7.94 (1H, d, J = 1.4 Hz), 7.89 (1H, dd, J = 5.1, 1.4 Hz), 7.74 (1H, d, J = 8.7 Hz), 7.57 (1H, dd, J = 8.7, 1.8 Hz), 7.37 (1H, dd, J = 7.8, 1.4 Hz), 7.06 (1H, dd, J = 7.8, 2.3 Hz), 4.08 (3H, s).

MS (ESI) m/z: 265.9 (M+H)⁺.

[0715] Intermediate-219:

5-(4-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound is prepared in 52% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3 and Step-4 of Intermediate- 101 using 1-bromo-3-fluoro-2-nitrobenzene in place of 2-bromo-1-methyl-3-nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.91 (1H, br s), 8.86 (1H, t, J = 1.4 Hz), 8.84 (1H, br d, J = 5.0 Hz), 8.20 (2H, d, J = 1.4 Hz), 7.08-6.97 (3H, m), 2.85 (3H, d, J = 5.0 Hz).

MS (ESI) m/z: 287.3 (M+H)⁺.

[0716] Intermediate-220:

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinic acid

[0717] <Step-1>:

methyl

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

The title compound (solid) is prepared in 75% yield by the similar manner to Step-3 and Step-4 of Intermediate- 3 using Mesylate-4 and methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (102 mg, 0.38 mmol, Step-3 of Intermediate-36) in place of Mesylate- 1 and methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

¹H -NMR (400 MHz, CDCl₃) delta 9.04 (1H, d, J = 2.3 Hz), 8.64 (1H, d, J = 2.3 Hz), 8.33 (1H, d, J = 8.7 Hz), 8.18 (1H, dd, J = 8.5, 2.5 Hz), 7.92 (1H, d, J = 2.3 Hz), 7.26-7.19 (2H, m), 7.19-7.06 (2H, m), 6.85 (1H, t, J = 54.7 Hz), 5.89 (1H, d, J = 7.3

Hz), 4.06 (3H, s), 4.03-3.90 (1H, m), 3.83 (2H, d, J = 6.9 Hz), 2.17 (2H, br d, J = 11.9 Hz), 2.05-1.82 (3H, m), 1.42-1.16 (4H, m).

MS (ESI) m/z: 569.8 (M+H)⁺.

[0718] <Step-2>:

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinic acid

A mixture of Step-1 of Intermediate-220 (162 mg, 0.28 mmol) in MeOH (3 mL) is added 2 M aqueous sodium hydroxide solution (2 mL) and stirred at rt for 2 hr. The mixture is added 2 M hydrochloric acid, the solid is precipitated. The precipitated solid is collected and washed with water, the title compound is prepared in 84% yield (133 mg, solid).

¹H -NMR (400 MHz, DMSO-d₆) delta 8.98 (1H, t, J = 1.6 Hz), 8.83 (1H, d, J = 2.3 Hz), 8.68 (1H, d, J = 7.8 Hz), 8.25 (2H, d, J = 1.4 Hz), 8.16 (1H, d, J = 2.3 Hz), 7.40 (1H, d, J = 7.8 Hz), 7.35 (1H, br), 7.28-7.17 (2H, m), 7.15 (1H, t, J = 54.0 Hz), 7.15-7.07 (1H, m), 3.80 (2H, d, J = 7.3 Hz), 3.77-3.65 (1H, m), 2.02-1.68 (5H, m), 1.37-1.11 (4H, m).

MS (ESI) m/z: 555.8 (M+H)⁺.

[0719] Intermediate-22 1:

3-chloro-N-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

<Step-1>: methyl 3-chloro-5-((2-nitrophenyl)amino)picolinate

A mixture of 1-bromo-2-nitrobenzene (50 mg, 0.248 mmol), methyl 5-amino-3-chloropicolinate (46 mg, 0.248 mmol), Pd₂(dba)₃ (11 mg, 0.012 mmol), Xantphos (14 mg, 0.025 mmol) and K₃P0₄ (105 mg, 0.495 mmol) in 1,4-dioxane (3 mL) is stirred at 80 °C for 1 hr. The reaction mixture is poured into water and extracted EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-33 % EtOAc in n-hexane to give 58 mg (76% yield) of the title compound as a yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.38 (1H, br s), 8.53 (1H, d, J = 2.4 Hz), 8.26 (1H, dd, J = 8.4, 1.6 Hz), 7.71 (1H, d, J = 2.4 Hz), 7.60-7.52 (1H, m), 7.47-7.42 (1H, m), 7.09-7.03 (1H, m), 4.02 (3H, s). MS (ESI) m/z: 308.1 (M+H)⁺.

[0720] <Step-2>: methyl 5-((2-aminophenyl)amino)-3-chloropicolinate

A mixture of methyl 3-chloro-5-((2-nitrophenyl)amino)picolinate (58 mg, 0.189 mmol, Step-1 of Intermediate-22 1) in MeOH (3 mL) is evacuated and backfilled with N₂ gas. To this is added 5% platinum on alumina (10 mg). The mixture is evacuated and backfilled with H₂ gas and stirred at rt under H₂ atmosphere. After 2.5 hrs, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 52 mg (99% yield) of the title compound as red brown oil.

¹H -NMR (400 MHz, CDCl₃) delta 8.12 (1H, d, J = 2.4 Hz), 7.19-7.09 (2H, m), 6.91 (1H, d, J = 2.4 Hz), 6.88-6.78 (2H, m), 5.77 (1H, br s), 3.95 (3H, s), 3.78 (2H, br s). MS (ESI) m/z: 278.2 (M+H)⁺.

[0721] <Step-3>: methyl

3-chloro-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

A mixture of methyl 5-((2-aminophenyl)amino)-3-chloropicolinate (52 mg, 0.189 mmol, Step-2 of Intermediate-22 1), CDI (91 mg, 0.562 mmol) in THF (3 mL) is stirred at rt for 14 hrs. The mixture is concentrated. The residual solid is suspended with IPE (10 mL). The precipitate is collected by filtration, washed with IPE to give 25 mg (44% yield) of the title compound as a beige solid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.43 (1H, br s), 8.87 (1H, d, J = 1.8 Hz), 8.39 (1H, d, J = 1.8 Hz), 7.57 (1H, s), 7.25 (1H, d, J = 7.6 Hz), 7.18-7.03 (2H, m), 3.93 (3H, s). MS (ESI) m/z: 304.1 (M+H)⁺.

[0722] <Step-4>:

3-chloro-N-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in 99 % yield (24 mg, pale orange solid) by the similar manner to Intermediate- 87 using methyl

3-chloro-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (25 mg, 0.082 mmol, Step-3 of Intermediate-22 1) in place of methyl 5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.81 (1H, d, J = 2.0 Hz), 8.74-8.66 (1H, m), 8.32 (1H, d, J = 2.0 Hz), 7.21-7.02 (4H, m), 2.81 (3H, d, J = 4.8 Hz). MS (ESI) m/z: 303.1 (M+H)⁺. A signal due to NH is not observed.

[0723] Intermediate-222:

N,6-dimethyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

<Step-1>: methyl 6-methyl-5-((2-nitrophenyl)amino)picolinate

A mixture of 1-bromo-2-nitrobenzene (50 mg, 0.248 mmol), methyl 5-amino-6-methylpicolinate (41 mg, 0.248 mmol), Pd₂(dba)₃ (11 mg, 0.012 mmol), Xantphos (14 mg, 0.025 mmol) and K₃P0₄ (105 mg, 0.495 mmol) in 1,4-dioxane (3 mL) is stirred at 100 °C for 1.5 hrs. The reaction mixture is poured into water and extracted EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50 % EtOAc in n-hexane to give 53 mg (75 % yield) of the title compound as an orange solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.40 (1H, br s), 8.26 (1H, dd, J = 8.4, 1.2 Hz), 8.05 (1H, d, J = 8.0 Hz), 7.78 (1H, d, J = 8.4 Hz), 7.53-7.46 (1H, m), 7.19 (1H, dd, J = 8.4, 1.2 Hz), 7.01-6.93 (1H, m), 4.02 (3H, s), 2.68 (3H, s). MS (ESI) m/z: 288.2 (M+H)⁺.

[0724] <Step-2>: methyl 5-((2-aminophenyl)amino)-6-methylpicolinate

A solution of methyl 6-methyl-5-((2-nitrophenyl)amino)picolinate (53 mg, 0.184 mmol, Step-1 of Intermediate-222) in MeOH (3 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (10 mg). The mixture is evacuated and backfilled with H₂ gas and stirred at rt under H₂ atmosphere. After 2 hrs, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 47 mg (99% yield) of the title compound.

¹H-NMR (400 MHz, CDCl₃) delta 7.87 (1H, d, J = 8.8 Hz), 7.17-7.07 (2H, m), 6.87-6.75 (3H, m), 5.45 (1H, br s), 3.96 (3H, s), 3.75 (2H, br s), 2.64 (3H, s). MS (ESI) m/z: 258.2 (M+H)⁺.

[0725] <Step-3>: methyl

6-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate

A mixture of methyl 5-((2-aminophenyl)amino)-6-methylpicolinate (47 mg, 0.184 mmol, Step-2 of Intermediate-222), CDI (89 mg, 0.548 mmol) in THF (3 mL) is stirred at rt for 16 hrs. The mixture is concentrated. The residue is poured into IPE (3 mL) and THF (3 mL). The mixture is concentrated. The residual solid is suspended with IPE (10 mL). The obtained solid is washed with IPE to give 51 mg (99% yield) of the title compound as a beige solid.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.30 (1H, br s), 8.11-8.04 (2H, m), 7.14-7.07 (2H, m), 7.03-6.96 (1H, s), 6.73 (1H, d, J = 7.6 Hz), 3.93 (3H, s), 2.37 (3H, s). MS (ESI) m/z: 284.2 (M+H)⁺.

[0726] <Step-4>:

N,6-dimethyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in 99% yield (51 mg, red brown oil) by the similar manner to Intermediate-87 using methyl

6-methyl-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate (51 mg, 0.180 mmol, Step-3 of Intermediate-222) in place of methyl

5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinate.

¹H-NMR (400 MHz, DMSO-d₆) delta 12.01 (1H, br s), 8.78-8.73 (1H, m), 8.05-7.98 (2H, m), 7.17-7.07 (2H, m), 7.03-6.97 (1H, m), 6.72 (1H, d, J = 7.6 Hz), 2.86 (3H, d, J = 4.8 Hz), 2.38 (3H, s). MS (ESI) m/z: 283.2 (M+H)⁺.

[0727] Intermediate-223:

2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxylic acid

<Step-1>: methyl 2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxylate

A mixture of methyl 1H-indazole-3-carboxylate (260 mg, 1.45 mmol), 2,2,2-trifluoroethyl trifluoromethanesulfonate (411 mg, 1.77 mmol) and K₂CO₃ (408 mg, 2.95 mmol) in DMF (4 mL) is stirred at 60 °C for 3 hrs. The reaction mixture is diluted with water, extracted with EtOAc. The organic layer is dried over MgSO₄,

filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 10% EtOAc in n-hexane to give the title compound as an off-white solid (229 mg, 60% yield).

MS (ESI) m/z: 259.1 (M+H)⁺.

[0728] <Step-2>: 2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxylic acid

The title compound is prepared in quantitative yield (110 mg, off-white solid) by the similar manner to Step-4 of Intermediate-2 using methyl

2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxylate (113 mg, 0.44 mmol, Step-1 of Intermediate-223) in place of methyl

3-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate

3-methyl-5-nitro-1H-pyrrolo[2,3-b]pyridine.

MS (ESI) m/z: 245.1 (M+H)⁺.

[0729] Intermediate-224:

N-(((1r,4r)-4-((3-(6-bromo-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

<Step-1>: 6-bromo-4-methyl-N-(2-nitrophenyl)pyridin-3-amine

To a mixture of 6-bromo-4-methylpyridin-3-amine (1.0 g, 5.4 mmol), 1-fluoro-2-nitrobenzene (777 mg, 5.5 mmol) in THF (30 mL) is added potassium tert-butoxide (1.2 g, 10.7 mmol) at 0 °C, and stirred at rt overnight. The solvent is removed under vacuum, the mixture is added saturated aqueous ammonium chloride and extracted with EtOAc, and passed through sodium sulfate. The solvent is removed under vacuum, the solid is triturated with isopropyl ether and filtered, the title compound is prepared in 81% yield (1.33 g, solid).

¹H-NMR (400 MHz, CDCl₃) delta 9.17 (1H, s), 8.32 (1H, s), 8.24 (1H, dd, J = 7.2, 1.2 Hz), 7.48 (1H, s), 7.41 (1H, ddd, J = 8.4, 6.8, 1.6 Hz), 6.86 (1H, ddd, J = 8.8, 6.8, 0.8 Hz), 6.78 (1H, dd, J = 8.7, 1.4 Hz), 2.27 (3H, s).

MS (ESI) m/z: 307.8 (M+H)⁺.

[0730] <Step-2>: N¹-(6-bromo-4-methylpyridin-3-yl)benzene-1, 2-diamine

A mixture of 6-bromo-4-methyl-N-(2-nitrophenyl)pyridin-3-amine (1.33 g, 4.3 mmol, Step-1 of Intermediate-224), Fe (723 mg, 13.0 mmol), ammonium chloride (693 mg, 13.0 mmol) in ethanol (30 mL) and H₂O (10 mL) is stirred at 90 °C overnight. The mixture is passed through celite and washed with DCM. The solvent is added water and extracted with DCM, and passed through sodium sulfate. The solvent are removed under vacuum, the crude product is triturated with isopropyl ether and filtered, the title compound is prepared in 84% yield (1.01 g, solid).

¹H-NMR (400 MHz, CDCl₃) delta 7.66 (1H, s), 7.22 (1H, s), 7.17-6.89 (2H, m), 6.86-6.67 (2H, m), 4.97 (1H, s), 3.63 (2H, br), 2.23 (3H, s).

MS (ESI) m/z: 277.9 (M+H)⁺.

[0731] <Step-3>: 1-(6-bromo-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

To a mixture of N'-ib-bromo-d-methylpyridin-S-yObenzene-l, 2-diamine (1.01 g, 3.6 mmol) in THF (20 mL) is added CDI (942 mg, 5.8 mmol) and stirred at rt for 2 days. The solvent is removed under vacuum, the mixture is added saturated aqueous ammonium chloride, extracted with DCM and passed through sodium sulfate. The solvent is removed under vacuum, the residue is washed with isopropyl ether and filtered, the title compound is prepared in 75% yield (826 mg, solid).

¹H -NMR (400 MHz, CDCl₃) delta 10.50 (1H, s), 8.38 (1H, s), 7.60 (1H, s), 7.20-7.11 (2H, m), 7.11-7.03 (1H, td, J = 7.3, 1.8 Hz), 6.72 (1H, d, J = 7.8 Hz), 2.26 (3H, s).

MS (ESI) m/z: 303.8 (M+H)⁺.

[0732] <Step-4>: N-

((1r,4r)-4-((3-(6-bromo-4-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazo 1-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

The title compound (solid) is prepared in 80% yield by the similar manner to Intermediate-207 using

1-(6-bromo-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (Step-3 of Intermediate-224) in place of Intermediate-39.

¹H -NMR (400 MHz, CDCl₃) delta 8.64 (1H, d, J = 2.3 Hz), 8.33 (1H, s), 7.92 (1H, d, J = 2.3 Hz), 7.56 (1H, s), 7.22-7.14 (1H, m), 7.12-7.04 (2H, m), 6.86 (1H, t, J = 54.8 Hz), 6.78-6.72 (1H, m), 5.97 (1H, d, J = 8.2 Hz), 4.05-3.88 (1H, m), 3.83 (2H, d, J = 6.9 Hz), 2.21 (3H, s), 2.20-2.08 (2H, m), 2.05-1.81 (3H, m), 1.42-1.16 (4H, m).

MS (ESI) m/z: 605.8 (M+H)⁺.

[0733] Intermediate-225:

1-(5-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in quantitative yield (pale yellow solid) by the similar manner to Intermediate-42 using

1-(5-chloropyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one (Step-1 of Intermediate-57) in place of 1-(6-chloropyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one.

MS (ESI) m/z: 357.1 (M+H)⁺.

[0734] Intermediate-226:

5-chloro-N-((1r,4r)-4-((3-(2-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[0735] <Step-1>: tert-butyl

3-(2-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

A mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (28 mg, 0.12 mmol), copper (II) acetate (54 mg, 0.30 mmol), pyridine (0.029 mL, 0.36

mmol), and (2-chloropyridin-4-yl)boronic acid (47 mg, 0.30 mmol) in 1,2-dichloroethane (2 mL) is stirred overnight at 60 °C. The reaction mixture is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 4-100% EtOAc in n-hexane to give 5.2 mg (13% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 346.1 (M+H)⁺.

[0736] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(2-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (14 mg, 0.038 mmol, Mesylate-1), tert-butyl

3-(2-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (5.2 mg, 0.14 mmol, Step-1 of Intermediate-226), and cesium carbonate (24 mg, 0.074 mmol) in DMSO (1 mL) is stirred for 2 hrs at 100 °C. The mixture is diluted with saturated aqueous sodium chloride. The mixture is extracted with THF. After the organic layer is concentrated, the resultant residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 17 mg of the title compound as a crude. The compound is used for the next reaction without further purification.

MS (ESI) m/z: 510.0 (M+H)⁺.

[0737] Intermediate-227:

3-methyl-1-(tetrahydro-2H-pyran-2-yl)-6-(4, 4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole

A mixture of 6-bromo-3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (136 mg, 0.46 mmol), bis(pinacolato)diboron (234 mg, 0.92 mmol), potassium acetate (90 mg, 0.92 mmol), palladium (II) acetate (10 mg, 0.046 mmol) and 2-(dicyclohexylphosphino)biphenyl (32 mg, 0.092 mmol) in 1,4-dioxane (0.5 mL) is stirred overnight at 80 °C. The reaction mixture is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 6-50% EtOAc in n-hexane to give 127 mg (81% yield) of the title compound as a colorless syrup.

MS (ESI) m/z: 342.9 (M+H)⁺.

[0738] Intermediate-228:

N-methyl-5-(4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in 36% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3 and Step-4 of Intermediate-101 using 1-bromo-3-methyl-2-nitrobenzene in place of 2-bromo-1-methyl-3-nitrobenzene.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.41 (1H, br s), 8.86 (1H, t, J = 5.0 Hz), 8.83 (1H, br s), 8.19 (2H, d, J = 1.8 Hz), 6.97-6.92 (3H, m), 2.85 (3H, d, J = 5.0 Hz), 2.35

(3H, s).

MS (ESI) m/z: 283.3 (M+H)⁺.

[0739] Intermediate-229:

1-(3-methyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

[0740] <Step-1>:

3-methyl-5-nitro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine

To a solution of 3-methyl-5-nitro-1H-pyrrolo[2,3-b]pyridine (300 mg, 1.84 mmol) in DMF (7 mL) is added sodium hydride (60% dispersion in mineral oil, 73.6 mg, 1.84 mmol) at 0 °C and stirred. After 30 min, to the mixture is added

2-(trimethylsilyl)ethoxymethyl chloride (0.49 mL, 2.76 mmol) and stirred at room temperature for 2 hrs. The reaction is quenched with saturated aqueous ammonium chloride (10 mL), extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 40-100% EtOAc in n-hexane to give 400 mg (70% yield) of the title compound.

¹H -NMR (400 MHz, CDCl₃) delta 9.21 (1H, d, J = 2.3 Hz), 8.71 (1H, d, J = 2.3 Hz), 7.23 (1H, s), 5.66 (2H, s), 3.54-3.50 (2H, m), 2.37 (3H, s), 0.94-0.89 (2H, m), -0.07 (9H, s).

MS (ESI) m/z: 308.3 (M+H)⁺.

[0741] <Step-2>:

3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine

A mixture of

3-methyl-5-nitro- 1-((2-(trimethylsilyl)ethoxy)methyl)- 1H-pyrrolo[2,3-b]pyridine (400 mg, 1.30 mmol, Step-1 of Intermediate-229) and 10% Pd/C (143 mg) in MeOH (2 mL) is stirred under H₂ atmosphere for 4 hrs. The mixture is filtered through a pad of celite, and the filtrate is concentrated to give 350 mg (97% yield) of the title compound.

MS (ESI) m/z: 278.3 (M+H)⁺.

[0742] <Step-3>:

1-(3-methyl- 1-((2-(trimethylsilyl)ethoxy)methyl)- 1H-pyrrolo[2,3-b]pyridin-5-yl)- 1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 33% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 187 using 3-bromo-2-nitropyridine in place of 2-bromo-3-nitropyridine.

MS (ESI) m/z: 395.9 (M+H)⁺.

[0743] Intermediate-230:

4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole

The title compound is prepared in 65% yield (205 mg, pale yellow oil) by the similar

manner to Step-1 of Intermediate-229 using 4-(4-bromophenyl)-1H-pyrazole (100 mg, 0.45 mmol) in place of 3-methyl-5-nitro-1H-pyrrolo[2,3-b]pyridine.

¹H-NMR (400 MHz, CDCl₃) delta 7.77 (2H, d, J = 3.7 Hz), 7.47 (2H, d, J = 6.4 Hz), 7.34 (2H, d, J = 6.4 Hz), 5.43 (2H, s), 3.78 (2H, dd, J = 9.1, 8.2 Hz), 0.90 (2H, dd, J = 9.1, 8.2 Hz), -0.03 (9H, s).

MS (ESI) m/z: 354.8 (M+H)⁺.

[0744] Intermediate-23 1:

5-chloro-2-(fluoromethyl)nicotinic acid

[0745] <Step-1>: benzyl 5-chloro-2-(hydroxymethyl)nicotinate

A mixture of 3-chlorofuro[3,4-b]pyridin-5(7H)-one (113 mg, 0.67 mmol) and 2 M aqueous sodium hydroxide solution (0.18 mL, 0.36 mmol) in water (0.18 mL) is stirred at 80 °C for 2 hrs. After cooling, the mixture is concentrated. To the residue in DMF (1 mL) is added benzyl bromide (0.050 mL, 0.42 mmol) at 0 °C. The mixture is stirred at room temperature overnight. The mixture is neutralized with 2 M hydrochloric acid, diluted with water, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 50-100% EtOAc in n-hexane to give 50 mg (27% yield) of the title compound as a brown solid.

MS (ESI) m/z: 277.9 (M+H)⁺.

[0746] <Step-2>: benzyl 5-chloro-2-(fluoromethyl)nicotinate

To a solution of benzyl 5-chloro-2-(hydroxymethyl)nicotinate (10 mg, 0.022 mmol, Step-1 of Intermediate-23 1) in DCM (1 mL) is added bis(2-methoxyethyl)aminosulfur trifluoride (0.012 mL, 0.067 mmol) at 0 °C, stirred for 0.5 hr. The mixture is diluted with saturated aqueous sodium bicarbonate, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated to give 11 mg (quantitative yield) of the title compound as a brown solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.74 (1H, d, J = 2.3 Hz), 8.28 (1H, dd, J = 2.3, 0.9 Hz), 7.47 - 7.38 (5H, m), 5.81 (2H, d, J = 46.7 Hz), 5.39 (2H, s).

MS (ESI) m/z: 279.9 (M+H)⁺.

[0747] <Step-3>: 5-chloro-2-(fluoromethyl)nicotinic acid

The title compound is prepared in quantitative yield (8.5 mg, off-white solid) by the similar manner to Step-4 of Intermediate-2 using benzyl 5-chloro-2-(fluoromethyl)nicotinate (10 mg, 0.023 mmol, Step-2 of Intermediate-23 1) in place of methyl

3-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate
3-methyl-5-nitro-1H-pyrrolo[2,3-b]pyridine.

MS (ESI) m/z: 189.9 (M+H)⁺.

[0748] Intermediate-232:

1-(3-methylbenzo [d]isoxazol-5-yl)- 1H-benzo [d]imidazol-2(3H)-one

The title compound (solid) is prepared in 85% yield in 3 steps by the similar manner to Step-3, Step-4 and Step-5 of Intermediate- 116 using 3-methylbenzo[d]isoxazol-5-amine in place of 1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-amine (Step-2 of Intermediate - 116).

¹H -NMR (400 MHz, CDCl₃) delta 8.22 (1H, brd, J = 5.5 Hz), 7.86-7.83 (1H, m), 7.73-7.70 (1H, m), 7.19-7.02 (3H, m), 6.98 (1H, d, J = 7.3 Hz), 6.51 (1H, dd, J = 5.0, 1.4 Hz), 2.62 (3H, s).

MS (ESI) m/z: 266.3 (M+H)⁺.

[0749] Intermediate-233:

3-(6-methoxypyridin-3-yl)-3,4-dihydroquinazolin-2(1H)-one

<Step-1>: 6-methoxy-N-(2-nitrobenzyl)pyridin-3-amine

To a mixture of 2-nitrobenzaldehyde (50 mg, 0.329 mmol), 6-methoxypyridin-3-amine (49 mg, 0.394 mmol) and acetic acid (0.019 mL, 0.329 mmol) in DCM (2 mL) is added sodium triacetoxyborohydride (105 mg, 0.493 mmol) and stirred at rt overnight. The reaction mixture is washed with 2 M aqueous sodium hydroxide solution, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-80% EtOAc in n-hexane to give 67 mg (79% yield) of the title compound as a brown viscous oil.

¹H -NMR (400 MHz, CDCl₃) delta 8.06 (1H, dd, J = 8.2, 1.4 Hz), 7.64 (1H, dd, J = 7.5, 1.1 Hz), 7.58 (1H, td, J = 7.5, 1.4 Hz), 7.51 (1H, d, J = 3.2 Hz), 7.47-7.41 (1H, m), 6.95 (1H, dd, J = 8.7, 3.2 Hz), 6.60 (1H, d, J = 9.6 Hz), 4.67 (2H, s), 4.08 (1H, br s), 3.84 (3H, s).

[0750] <Step-2>: N-(2-aminobenzyl)-6-methoxypyridin-3-amine

A solution of the product of Step-1 of Intermediate-233 (42 mg, 0.162 mmol) in EtOAc is evacuated and backfilled with N₂ gas (three times). To this is added Pt-alumina (5%) (10 mg). Then the mixture is evacuated and backfilled with H₂ gas and stirred vigorously at rt for 1 hr. After the reaction mixture is evacuated and backfilled with N₂ gas, the mixture is filtered through celite pad. The filtrate is concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 0-10% MeOH in EtOAc to give 37 mg (quantitative yield) of the title compound as a yellow gum.

¹H -NMR (400 MHz, CDCl₃) delta 7.69 (1H, d, J = 2.7 Hz), 7.18-7.12 (2H, m), 7.07 (1H, dd, J = 8.7, 3.2 Hz), 6.78-6.70 (2H, m), 6.65 (1H, d, J = 8.7 Hz), 4.22-4.15 (4H, m), 3.88 (3H, s), 3.41 (1H, s).

[0751] <Step-3>: 3-(6-methoxypyridin-3-yl)-3,4-dihydroquinazolin-2(1H)-one

To a solution of the product of Step-2 of Intermediate-233 (37 mg, 0.161 mmol) in THF (1 mL) is added CDI (49 mg, 0.302 mmol) and stirred at rt overnight. To the reaction mixture is added CDI (92 mg, 0.568 mmol) and stirred at rt for 1 hr. To this is added CDI (102 mg, 0.629 mmol) and stirred at rt for 30 min. To this is added further CDI (102 mg, 0.629 mmol) and stirred at rt for 30 min. The mixture is diluted with saturated sodium hydrogen carbonate aqueous solution. The mixture is extracted with EtOAc. The organic layer is dried over MgSO_4 , filtered and concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 15-50% EtOAc in n-hexane to give 30 mg (73%) of the title compound as an ivory solid. ^1H -NMR (400 MHz, CDCl_3) δ 8.18 (1H, d, J = 2.7 Hz), 7.63 (1H, dd, J = 8.9, 3.0 Hz), 7.26-7.20 (1H, m), 7.10-7.08 (2H, m), 7.03-6.97 (1H, m), 6.79 (1H, d, J = 8.2 Hz), 6.74 (1H, d, J = 7.3 Hz), 4.81 (2H, s), 3.95 (3H, s).

[0752] Intermediate-234:

3-(4-chlorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 66% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 4-chloroaniline in place of 2,3-dihydro-1H-inden-5-amine.

MS (ESI) m/z : 246.2 ($\text{M}+\text{H}$) $^+$.

[0753] Intermediate-235:

tert-butyl

7-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate

<Step-1>: tert-butyl

7-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate

The title compound is prepared in 52% yield (188 mg, pale yellow solid) by the similar manner to Step-2 of Intermediate-95 using tert-butyl

7-bromo-3,4-dihydroisoquinoline-2(1H)-carboxylate (310 mg, 0.99 mmol) in place of 5-bromo-2,3-dimethyl-2H-indazole.

^1H -NMR (400 MHz, CDCl_3) δ 7.38-7.30 (3H, m), 7.18-6.97 (4H, m), 4.67 (2H, br s), 3.70 (2H, br s), 2.91 (2H, br s), 1.51 (9H, s). A signal due to NH is not observed.

MS (ESI) m/z : 367.2 ($\text{M}+\text{H}$) $^+$.

[0754] <Step-2>:

tert-butyl

7-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate

The title compound is prepared in 97% yield (138 mg, pale yellow solid) by the similar manner to Step-2 of Intermediate-57 using Mesylate-4 (85 mg, 0.21 mmol) and

tert-butyl

7-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (78 mg, 0.21 mmol, Step-1 of Intermediate-235) in place of Mesylate- 1 and 1-(5-chloropyrazin-2-yl)- 1H-benzo[d]imidazol-2(3H)-one.

MS (ESI) m/z: 666.4 (M+H)⁺.

[0755] Intermediate-236:

3-(6-methylquinolin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (gray solid) is prepared in 83% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 6-methylquinolin-3-amine in place of 2,3-dihydro- 1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) 9.14 (1H, d, J = 2.3 Hz), 8.58 (1H, d, J = 2.3 Hz), 8.01-7.97 (2H, m), 7.85 (1H, s), 7.66 (1H, dd, J = 8.7, 1.8 Hz), 7.46 (1H, dd, J = 7.8, 1.4 Hz), 7.15 (1H, dd, J = 7.8, 5.0 Hz), 2.54 (3H, s). A signal due to NH is not observed.

MS (ESI) m/z: 277.0 (M+H)⁺.

[0756] Intermediate-237:

3-(2-chloro-4-fluorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 29% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 198 using 2-chloro-4-fluoroaniline in place of 2-chloro-4-methylaniline.

¹H -NMR (400 MHz, CDCl₃) delta 11.42 (1H, br s), 7.87 (1H, dd, J = 5.5, 1.4 Hz), 7.74 (1H, dd, J = 8.7, 3.2 Hz), 7.70 (1H, dd, J = 8.6, 5.9 Hz), 7.44 (1H, dd, J = 8.7, 3.2 Hz), 7.41 (1H, dd, J = 8.7, 3.2 Hz), 7.08 (1H, dd, J = 7.8, 2.3 Hz).

MS (ESI) m/z: 263.8 (M+H)⁺.

[0757] Intermediate-238:

3-(3-chloro-4-methylphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 97% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 3-chloro-4-methylaniline in place of 2,3-dihydro- 1H-inden-5-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.47 (1H, br s), 7.96 (1H, dd, J = 5.0, 1.4 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.61 (1H, dd, J = 8.2, 2.3 Hz), 7.50 (1H, d, J = 8.2 Hz), 7.41 (1H, dd, J = 8.7, 1.4 Hz), 7.11 (1H, dd, J = 7.8, 5.0 Hz), 2.40 (3H, s).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0758] Intermediate-239:

2-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)benzonitrile

The title compound (pale yellow solid) is prepared in 29% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-208 using 2-aminobenzonitrile in place of 2-amino-4-methoxybenzonitrile.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.55 (1H, br s), 8.09 (1H, dd, J = 7.8, 1.4 Hz), 7.95-7.88 (2H, m), 7.76 (1H, dd, J = 7.3, 1.4 Hz), 7.71 (1H, td, J = 7.8, 1.4 Hz), 7.46 (1H, dd, J = 7.8, 1.4 Hz), 7.14 (1H, dd, J = 7.8, 5.0 Hz).

MS (ESI) m/z: 237.4 (M+H)⁺.

[0759] Intermediate-240:

5-fluoro-1-(6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 70% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 193 using 1-bromo-4-fluoro-2-nitrobenzene in place of 1-bromo-2-nitrobenzene and N²-methylpyridine-2, 5-diamine in place of N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

MS (ESI) m/z: 259.2 (M+H)⁺.

[0760] Intermediate-24 1:

6-fluoro-1-(6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 49% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 193 using 2-bromo-4-fluoro-1 -nitrobenzene in place of 1-bromo-2-nitrobenzene and N²-methylpyridine-2, 5-diamine in place of N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

MS (ESI) m/z: 259.2 (M+H)⁺.

[0761] Intermediate-242:

5-(7-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide

The title compound is prepared in 30% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3 and Step-4 of Intermediate- 118 using 2-fluoro-1-methoxy-3-nitrobenzene in place of 1,2-difluoro-3-nitrobenzene.

MS (ESI) m/z: 299.1 (M+H)⁺.

[0762] Intermediate-243:

1-(2-chloro-5-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow gum) is prepared in 29% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-chloro-5-methoxy aniline and 4-chloronicotinic acid in place of 2,3-dihydro- 1H-inden-5-amine and 2-chloronicotinic acid.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.47 (1H, br s), 8.31 (1H, s), 8.17 (1H, d, J = 5.5 Hz), 7.63 (1H, d, J = 9.1 Hz), 7.28 (1H, d, J = 3.2 Hz), 7.18 (1H, dd, J = 9.1, 3.2 Hz), 6.75 (1H, d, J = 5.5 Hz), 3.81 (3H, s).

MS (ESI) m/z: 276.2 (M+H)⁺.

[0763] Intermediate-244:

1-(2-chloro-5-fluorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 47% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-chloro-5-fluoroaniline

and 4-chloronicotinic acid in place of 2,3-dihydro-1H-inden-5-amine and 2-chloronicotinic acid.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.54 (1H, br s), 8.33 (1H, s), 8.18 (1H, d, J = 5.5 Hz), 7.82 (1H, dd, J = 9.1, 5.5 Hz), 7.74 (1H, dd, J = 9.1, 3.2 Hz), 7.52 (1H, ddd, J = 9.1, 8.2, 3.2 Hz), 6.81 (1H, dd, J = 5.5, 0.9 Hz).

MS (ESI) m/z: 264.2 (M+H)⁺.

[0764] Intermediate-245:

N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(trifluoromethyl)nicotinamide

The title compound is prepared in 87% yield (solid) by the similar manner to Step-2 of Intermediate-57 using Intermediate-39 and Mesylate-3 in place of 1-(5-chloropyrazin-2-yl)-1H-benzo[d]imidazol-2(3H)-one and Mesylate-1.

¹H-NMR (400 MHz, CDCl₃) delta 8.67 (1H, d, J = 2.3 Hz), 8.64 (1H, d, J = 2.7 Hz), 7.88 (1H, d, J = 2.4 Hz), 7.84 (1H, dd, J = 8.7, 2.7 Hz), 7.66 (1H, d, J = 8.4 Hz), 7.24-7.16 (1H, m), 7.14-7.10 (2H, m), 7.08 (1H, d, J = 7.6 Hz), 5.69 (1H, d, J = 8.2 Hz), 4.02-3.88 (1H, m), 3.81 (2H, d, J = 6.9 Hz), 2.15 (2H, br d, J = 9.6 Hz), 2.00-1.82 (3H, m), 1.41-1.12 (4H, m).

MS (ESI) m/z: 609.7 (M+H)⁺.

[0765] Intermediate-246:

5-chloro-N-((1r,4r)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

The title compound is prepared in 85% yield (112 mg, yellow solid) by the similar manner to Intermediate-54 using Mesylate-3 (100 mg, 0.241 mmol) in place of Mesylate-1.

¹H-NMR (400 MHz, DMSO-d₆) delta 8.66 (1H, d, J = 2.3 Hz), 8.37 (1H, d, J = 7.8 Hz), 8.28 (1H, d, J = 2.3 Hz), 8.07-8.00 (2H, m), 7.22 (1H, dd, J = 8.7, 3.2 Hz), 7.15 (1H, d, J = 7.8 Hz), 7.01-6.93 (1H, m), 6.91-6.85 (2H, m), 3.57 (2H, d, J = 6.9 Hz), 3.54-3.38 (1H, m), 1.75-1.66 (2H, m), 1.66-1.50 (3H, m), 1.11-0.88 (4H, m).

MS (ESI) m/z: 548.2 (M+H)⁺.

[0766] Intermediate-247 :

4-fluoro-1-(6-(methylamino)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound (brown solid) is prepared in 57% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-193 using 1-bromo-3-fluoro-2-nitrobenzene in place of 1-bromo-2-nitrobenzene and N²-methylpyridine-2,5-diamine in place of N²-(2,2,2-trifluoroethyl)pyridine-2,5-diamine.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.42 (1H, s), 7.86 (1H, d, J = 2.6 Hz), 7.27 (1H, dd, J = 8.8, 2.6 Hz), 6.84-6.71 (2H, m), 6.68-6.60 (1H, m), 6.47 (1H, dd, J = 7.3, 1.4 Hz), 6.39 (1H, d, J = 8.8 Hz), 2.62 (3H, d, J = 4.6 Hz).

MS (ESI) m/z: 259.2 (M+H)⁺.

[0767] Intermediate-248:

2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxymethyl)-1H-pyrrolo[2,3-b]pyridine

<Step-1>:

5-bromo-2-methyl-1-((2-(trimethylsilyl)ethoxymethyl)-1H-pyrrolo[2,3-b]pyridine

To a solution of 5-bromo-2-methyl-1H-pyrrolo[2,3-b]pyridine (100 mg, 0.47 mmol) in THF (1 mL) and DMF (1 mL) is added sodium hydride (60% dispersion in mineral oil, 20 mg, 0.50 mmol) at 0 °C. The mixture is stirred at room temperature for 30 min. To the mixture is added 2-(trimethylsilyl)ethoxymethyl chloride (0.10 mL, 0.57 mmol) at 0 °C. The mixture is stirred at room temperature for 30 min. The reaction is diluted with water at 0 °C, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-15% EtOAc in n-hexane to give 161 mg (quantitative yield) of the title compound.

MS (ESI) m/z: 342.8 (M+H)⁺.

[0768] <Step-2>:

2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxymethyl)-1H-pyrrolo[2,3-b]pyridine

A solution of

5-bromo-2-methyl-1-((2-(trimethylsilyl)ethoxymethyl)-1H-pyrrolo[2,3-b]pyridine (72 mg, 0.19 mmol, Step-1 of Intermediate-248), bis(pinacolato)diboron (57 mg, 0.22 mmol), potassium acetate (55 mg, 0.56 mmol) and

[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride dichloromethane adduct (15 mg, 0.019 mmol) in 1,4-dioxane (2.5 mL) is stirred at 80 °C overnight. The mixture is concentrated. The residue is purified by column chromatography on amine-gel eluting with 0-20% EtOAc in n-hexane to give 13 mg (16% yield) of the title compound as a pale yellow syrup.

[0769] Intermediate-249:

1-(2-chloro-5-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

<Step-1>: N-(2-chloro-5-methoxyphenyl)-2-nitropyridin-3-amine

The title compound is prepared in 79% yield (228 mg, pale yellow solid) by the similar manner to Step-1 of Intermediate-101 using 3-bromo-2-nitropyridine (250 mg, 1.23 mmol) and 2-chloro-5-methoxyaniline (162 mg, 1.03 mmol) in place of 2-bromo-1-methyl-3-nitrobenzene and methyl 5-aminopicolinate.

¹H-NMR (400 MHz, CDCl₃) δ 9.16 (1H, br s), 8.07 (1H, dd, J = 4.1, 1.4 Hz), 7.63 (1H, dd, J = 8.7, 1.4 Hz), 7.43 (1H, d, J = 8.7, 4.1 Hz), 7.42 (1H, d, J = 9.2 Hz), 6.93 (1H, d, J = 2.7 Hz), 6.78 (1H, dd, J = 9.2, 2.7 Hz), 3.81 (3H, s).

MS (ESI) m/z: 280.2 (M+H)⁺.

[0770] <Step-2>: N³-(2-chloro-5-methoxyphenyl)pyridine-2, 3-diamine

The title compound is prepared in quantitative yield (204 mg, brown gum) by the similar manner to Step-2 of Intermediate-20 using methyl N-(2-chloro-5-methoxyphenyl)-2-nitropyridin-3-amine (228 mg, 0.82 mmol, Step-1 of Intermediate-249) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

MS (ESI) m/z: 250.2 (M+H)⁺.

[0771] <Step-3>: 1-(2-chloro-5-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

A mixture of N³-(2-chloro-5-methoxyphenyl)pyridine-2, 3-diamine (204 mg, 0.82 mmol, Step-2 of Intermediate-249) and CDI (331 mg, 2.04 mmol) in THF (3 mL) is stirred at room temperature for 1 day. The mixture is quenched with 10% aqueous citric acid solution. The precipitate is collected and washed with diisopropyl ether to give 194 mg (96% yield) of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.88 (1H, s), 7.99 (1H, dd, J = 4.1, 2.3 Hz), 7.62 (1H, d, J = 8.7 Hz), 7.29 (1H, d, J = 2.7 Hz), 7.16 (1H, dd, J = 8.7, 2.7 Hz), 7.01 (1H, s), 7.00 (1H, d, J = 2.3 Hz), 3.80 (3H, s).

MS (ESI) m/z: 276.2 (M+H)⁺.

[0772] Intermediate-250:

1-(2-chloro-5-fluorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 82% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 2-chloro-5-fluoroaniline in place of 2-chloro-5-methoxyaniline.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.95 (1H, s), 8.01 (1H, dd, J = 5.0, 1.4 Hz), 7.81 (1H, dd, J = 9.1, 5.5 Hz), 7.73 (1H, dd, J = 9.1, 3.2 Hz), 7.51 (1H, ddd, J = 9.1, 7.8, 3.2 Hz), 7.09 (1H, dd, J = 7.8, 1.4 Hz), 7.02 (1H, dd, J = 7.8, 5.0 Hz).

MS (ESI) m/z: 264.2 (M+H)⁺.

[0773] Intermediate-251:

1-(4-fluoro-3-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 76% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 4-fluoro-3-methoxyaniline in place of 2-chloro-5-methoxy aniline.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.85 (1H, br s), 7.99 (1H, dd, J = 5.0, 1.4 Hz), 7.42-7.31 (3H, m), 7.14-7.10 (1H, m), 7.03 (1H, dd, J = 7.8, 5.0 Hz), 3.87 (3H, s).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0774] Intermediate-252:

N-((1*r*,4*r*)-4-((3-(2-bromopyridin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

<Step-1>: 2-bromo-N-(2-nitrophenyl)pyridin-4-amine

The title compound is prepared in 50% yield (208 mg, brown solid) by the similar manner to Step-1 of Intermediate-20 using 2-bromopyridin-4-amine (200 mg, 1.42 mmol) in place of 2,4-difluoroaniline.

¹H -NMR (400 MHz, CDCl₃) delta 9.20 (1H, s), 8.28-8.19 (2H, m), 7.64-7.56 (2H, m), 7.32 (1H, d, J = 2.4 Hz), 7.15-7.07 (1H, m), 7.05 (1H, dd, J = 5.7, 2.4 Hz).

MS (ESI) m/z: 296.0 (M+H)⁺.

[0775] <Step-2>: N¹-(2-bromopyridin-4-yl)benzene-1, 2-diamine

The title compound is prepared in 99% yield (185 mg, orange solid) by the similar manner to Step-2 of Intermediate- 151 using

2-bromo-N-(2-nitrophenyl)pyridin-4-amine (208 mg, 0.707 mmol, Step-1 of Intermediate-252) in place of methyl

4-methyl-5-((2-methyl-6-nitrophenyl)amino)picolinate.

MS (ESI) m/z: 264.0 (M+H)⁺.

[0776] <Step-3>: 1-(2-bromopyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 88% yield (178 mg, pale yellow solid) by the similar manner to Step-3 of Intermediate- 193 using N¹-

(2-bromopyridin-4-yl)benzene-1, 2-diamine (185 mg, 0.700 mmol, Step-2 of Intermediate-252) in place of N⁵-(2-aminophenyl)-N²-

(2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.24 (1H, s), 8.33 (1H, d, J = 5.3 Hz), 7.75 (1H, d, J = 1.8 Hz), 7.56 (1H, dd, J = 5.3, 1.8 Hz), 7.12 (1H, d, J = 8.2 Hz), 7.01-6.79 (3H, m).

MS (ESI) m/z: 292.1 (M+H)⁺.

[0777] <Step-4>: N-

((1r,4r)-4-((3-(2-bromopyridin-4-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound is prepared in 94% yield (160 mg, pale yellow solid) by the similar manner to Step-3 of Intermediate- 3 using

1-(2-bromopyridin-4-yl)-1H-benzo[d]imidazol-2(3H)-one (89 mg, 0.31 mmol, Step-3 of Intermediate-252) in place of methyl

2-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol- 1-yl)methyl)benzoate.

¹H -NMR (400 MHz, CDCl₃) delta 8.52 (1H, d, J = 5.4 Hz), 8.49 (1H, d, J = 2.3 Hz), 7.88 (1H, d, J = 2.0 Hz), 7.64 (1H, dd, J = 5.4, 2.0 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.32 (1H, d, J = 7.8 Hz), 7.25-7.20 (1H, m), 7.16 (1H, t, J = 7.8 Hz), 7.09 (1H, d, J = 7.8 Hz), 5.54 (1H, d, J = 8.2 Hz), 4.01-3.89 (1H, m), 3.81 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.24-2.10 (2H, m), 1.98-1.86 (3H, m), 1.39-1.12 (4H, m).

MS (ESI) m/z: 556.0 (M+H)⁺.

[0778] Intermediate-253:

3-(2-chloro-5-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 82% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 3-bromo-4-nitropyridine in place of 3-bromo-2-nitropyridine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.72 (1H, br s), 8.23 (1H, d, J = 5.5 Hz), 7.87 (1H, s), 7.63 (1H, d, J = 8.7 Hz), 7.43 (1H, d, J = 8.2 Hz), 7.20-7.13 (2H, m), 3.81 (3H, s).

MS (ESI) m/z: 276.2 (M+H)⁺.

[0779] Intermediate-254:

3-(3-fluorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 82% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 2-chloro-5-fluoroaniline and 3-bromo-4-nitropyridine in place of 2-chloro-5-methoxy aniline and 3-bromo-2-nitropyridine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.78 (1H, br s), 8.30 (1H, s), 8.26 (1H, d, J = 5.0 Hz), 7.66-7.59 (1H, m), 7.53 (1H, dt, J = 10.1, 2.3 Hz), 7.50-7.47 (1H, m), 7.31 (1H, td, J = 10.1, 2.7 Hz), 7.16 (1H, d, J = 4.6 Hz).

MS (ESI) m/z: 230.3 (M+H)⁺.

[0780] Intermediate-255:

5-bromo-2-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazol-2-yl)pyridine

Under an atmosphere of nitrogen at 0 °C, a solution of 5-bromo-2-(1H-imidazol-2-yl)pyridine (100 mg, 0.446 mmol) in THF (2 mL) is treated with portionwise addition of sodium hydride (60% dispersion in mineral oil, 20 mg, 0.491 mmol). After stirring for 30 min at 0 °C, 2-(trimethylsilyl)ethoxymethyl chloride (0.103 mL, 0.580 mmol) is added and the mixture is stirred for 1 hr at 0 °C. The reaction mixture is poured into water and is extracted with EtOAc. The organic layers are dried over sodium sulfate, filtered and concentrated under vacuum to afford crude product. The crude product is purified by column chromatography on silica gel eluting with 0-100 % EtOAc in n-hexane to give 137 mg (87% yield) of the title compound.

¹H -NMR (400 MHz, CDCl₃) delta 8.63 (1H, d, J = 2.3 Hz), 8.11 (1H, d, J = 8.7 Hz), 7.89 (1H, dd, J = 8.7, 2.3 Hz), 7.22 (1H, d, J = 1.4 Hz), 7.17 (1H, d, J = 1.4 Hz), 6.00 (2H, s), 3.56-3.52 (2H, m), 0.91-0.86 (2H, m), -0.07 (9H, s).

[0781] Intermediate-256:

4-(3-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole

The title compound is prepared in 64% yield (67 mg) by the similar manner to Intermediate-255 using 4-(3-bromophenyl)-1H-pyrazole (66 mg, 0.291 mmol) in place of 5-bromo-2-(1H-imidazol-2-yl)pyridine.

¹H -NMR (400 MHz, CDCl₃) delta 7.82 (1H, d, J = 0.9 Hz), 7.80 (1H, br), 7.65 (1H,

dd, J = 1.8, 1.8 Hz), 7.44-7.41 (1H, m), 7.38-7.35 (1H, m), 7.26-7.22 (1H, m), 5.46 (2H, s), 3.62-3.58 (2H, m), 0.95-0.91 (2H, m), -0.01 (9H, s).

[0782] Intermediate-257 :

tert-butyl 4-(4-bromopyridin-2-yl)-1H-pyrazole-1-carboxylate

A mixture of tert-butyl

4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole-1-carboxylate (100 mg, 0.340 mmol), 2,4-dibromopyridine (81 mg, 0.340 mmol), Pd(PPh₃)₄ (39 mg, 0.034 mmol) and Cs₂CO₃ (332 mg, 1.020 mmol) in 1,4-dioxane (3 mL) is stirred at 80 °C for 1 hr. The reaction mixture is poured into water and extracted EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50 % EtOAc in n-hexane to give 23 mg (21% yield) of the title compound as colorless oil.

¹H-NMR (400 MHz, CDCl₃) delta 8.59 (1H, d, J = 0.7 Hz), 8.44-8.41 (1H, m), 8.20 (1H, d, J = 0.7 Hz), 7.72-7.69 (1H, m), 7.36 (1H, dd, J = 5.3, 1.8 Hz), 1.68 (9H, s). MS (ESI) m/z: 324.0 (M+H)⁺.

[0783] Intermediate-258:

4-bromo-2-(1-methyl-1H-pyrazol-3-yl)pyridine

A mixture of 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (44 mg, 0.211 mmol), 2,4-dibromopyridine (50 mg, 0.211 mmol), Pd(PPh₃)₄ (24 mg, 0.021 mmol) and Cs₂CO₃ (206 mg, 0.633 mmol) in 1,4-dioxane (2 mL) is stirred at 80 °C for 1 hr. The reaction mixture is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50 % EtOAc in n-hexane to give 33 mg (66% yield) of the title compound as pale yellow oil.

¹H-NMR (400 MHz, CDCl₃) delta 8.42 (1H, d, J = 5.2 Hz), 8.11 (1H, d, J = 1.6 Hz), 7.42 (1H, d, J = 2.2 Hz), 7.35 (1H, dd, J = 5.2, 1.6 Hz), 6.86 (1H, d, J = 2.2 Hz), 3.99 (3H, s). MS (ESI) m/z: 238.0 (M+H)⁺.

[0784] Intermediate-259:

N-((1r,4r)-4-((3-(2-bromopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

The title compound is prepared in 91% yield (165 mg, brown solid) by the similar manner to Step-4 of Intermediate-252 using ((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate (122 mg, 0.307 mmol, Mesylate-4) in place of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methanesulfonate.

¹H-NMR (400 MHz, CDCl₃) delta 8.64 (1H, d, J = 2.3 Hz), 8.51 (1H, d, J = 5.4 Hz), 7.92 (1H, d, J = 2.3 Hz), 7.87 (1H, d, J = 2.0 Hz), 7.64 (1H, dd, J = 5.4, 2.0 Hz), 7.32 (1H, d, J = 7.8 Hz), 7.25-7.21 (1H, m), 7.16 (1H, t, J = 7.8 Hz), 7.08 (1H, d, J = 6.9 Hz), 6.84 (1H, t, J = 54.7 Hz), 5.86 (1H, d, J = 7.3 Hz), 4.04-3.88 (1H, m), 3.80 (2H, d,

$J = 6.9$ Hz), 2.16 (2H, d, $J = 11.0$ Hz), 2.00-1.83 (3H, m), 1.39-1.10 (4H, m).

MS (ESI) m/z : 592.0 (M+H)⁺.

[0785] Intermediate-260:

3-(3-fluoro-4-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in quantitative yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-99 using 3-fluoro-4-methoxyaniline in place of 4-methoxyaniline.

¹H-NMR (400 MHz, DMSO- d_6) δ 7.73 (1H, dd, $J = 13.3, 2.3$ Hz), 7.67-7.63 (2H, m), 7.24 (1H, t, $J = 9.6$ Hz), 7.11 (1H, dd, $J = 7.3, 1.4$ Hz), 6.86 (1H, dd, $J = 7.3, 5.0$ Hz), 3.87 (3H, s). A signal due to NH is not observed.

MS (ESI) m/z : 260.1 (M+H)⁺.

[0786] Intermediate-261:

1-(6-(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

<Step-1>: 1-(6-(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-yn-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 1-(6-bromopyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (50 mg, 0.17 mmol, Intermediate-39), 2-(prop-2-yn-1-yloxy)tetrahydro-2H-pyran (48 mg, 0.35 mmol), CuI (7 mg, 0.034 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride dichloromethane adduct (28 mg, 0.034 mmol) and TEA (0.096 mL, 0.69 mmol) in DMF (3 mL) is stirred at 65 °C for 1 day. The mixture is diluted with water, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated to give the title compound as a crude. The crude is used next step without purification.

MS (ESI) m/z : 349.8 (M+H)⁺.

[0787] <Step-2>:

1-(6-(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of

1-(6-(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-yn-1-yl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (crude, 0.17 mmol, Step-1 of Intermediate-261) and 10% Pd/C (37 mg) in MeOH (1 mL) and THF (0.5 mL) is stirred under H₂ atmosphere for 3 hrs. The mixture is filtered through a pad of celite and the filtrate is concentrated to give the title compound as a crude. The crude is used next step without purification.

MS (ESI) m/z : 353.9 (M+H)⁺.

[0788] Intermediate-262:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((6-fluoro-3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 31% in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate-224 using 6-fluoropyridin-3-amine and 1,4-difluoro-2-nitrobenzene in place of 6-bromo-4-methylpyridin-3-amine and 1-fluoro-2-nitrobenzene.

¹H -NMR (400 MHz, CDCl₃) delta 8.64 (1H, d, J = 2.3 Hz), 8.44 (1H, br d, J = 1.4 Hz), 8.02 (1H, ddd, J = 8.4, 6.8, 2.8 Hz), 7.92 (1H, d, J = 1.8 Hz), 7.13 (1H, dd, J = 8.7, 3.2 Hz), 6.98 (1H, dd, J = 9.1, 4.1 Hz), 6.89-6.77 (2H, m), 6.85 (1H, t, J = 54.4 Hz), 5.97 (1H, d, J = 7.3 Hz), 4.09-3.88 (1H, m), 3.78 (2H, d, J = 6.9 Hz), 2.17 (2H, d, J = 10.5 Hz), 2.04-1.80 (3H, m), 1.43-1.11 (4H, m).

MS (ESI) m/z: 547.8 (M+H)⁺.

[0789] Intermediate-263:

5-chloro-N-((1r,4r)-4-((3-(2-chloropyridin-4-yl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide

<Step-1>: 1-(2-chloropyridin-4-yl)-5-fluoro-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 37% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 193 using 2-chloropyridin-4-amine and 1-bromo-4-fluoro-2-nitrobenzene in place of N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine and 1-bromo-2-nitrobenzene.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.43 (1H, s), 8.36 (1H, d, J = 5.5 Hz), 7.62 (1H, d, J = 1.6 Hz), 7.53 (1H, dd, J = 5.5, 1.6 Hz), 7.15 (1H, dd, J = 8.7, 4.6 Hz), 6.79 (1H, dd, J = 8.7, 2.3 Hz), 6.76-6.66 (1H, m).

MS (ESI) m/z: 264.1 (M+H)⁺.

[0790] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(2-chloropyridin-4-yl)-6-fluoro-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide

The title compound is prepared in 97% yield by the similar manner to Step-3 of Intermediate-3 using 1-(2-chloropyridin-4-yl)-5-fluoro- 1H-benzo[d]imidazol-2(3H)-one (Step-1 of Intermediate-263) and Mesylate-4 in place of methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate and Mesylate- 1.

MS (ESI) m/z: 564.0 (M+H)⁺.

[0791] Intermediate-264:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol- 1-yl)methyl)cyclohexyl)nicotinamide

<Step-1>: tert-butyl

5-fluoro-2-oxo-2, 3-dihydro- 1H-benzo[d] imidazole- 1-carboxylate

The title compound is prepared by the similar manner to Step-3 of Intermediate- 193 using tert-butyl (2-amino-4-fluorophenyl)carbamate in place of N⁵-(2-aminophenyl)-N²-(2,2,2-trifluoroethyl)pyridine-2, 5-diamine.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.21 (1H, s), 7.42 (1H, dd, J = 8.8, 4.8 Hz), 6.73-6.68 (1H, m), 6.65 (1H, dd, J = 8.8, 2.3 Hz), 1.38 (9H, s).

MS (ESI) m/z: 251.2 (M-H)⁻.

[0792] <Step-2>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 2 steps by the similar manner to Step-1 and Step-2 of Example 9 using tert-butyl

5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (Step-1 of Intermediate-264) and Masylate-4 in place of tert-butyl

2-oxo-2, 3-dihydro- 1H-benzo[d] imidazole- 1-carboxylate and Mesylate- 1.

MS (ESI) m/z: 551.1 (M-H)⁻.

[0793] Intermediate-265:

N-((1r,4r)-4-((3-(5-bromopyridin-2-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

The title compound (pale yellow solid) is prepared in in 29% yield 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate-224 using 5-bromopyridin-2-amine in place of 6-bromo-4-methylpyridin-3-amine.

MS (ESI) m/z: 592.0 (M+H)⁺.

[0794] Intermediate-266:

3-(2-chloro-5-fluorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 11% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 198 using 2-chloro-5-fluoroaniline and 3-bromo-4-nitropyridine in place of 2-chloro-4-methylaniline and 2-bromo-3-nitropyridine.

MS (ESI) m/z: 264.1 (M+H)⁺.

[0795] Intermediate-267:

3-(3-fluoro-4-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 72% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 3-bromo-4-nitropyridine and 3-fluoro-4-methoxyaniline in place of 3-bromo-2-nitropyridine and 2-chloro-5-methoxyaniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.64 (1H, br s), 8.24 (1H, d, J = 5.0 Hz), 8.18 (1H, s), 7.53 (1H, dd, J = 12.4, 1.8 Hz), 7.41-7.31 (2H, m), 7.13 (1H, d, J = 5.5 Hz), 3.92 (3H, s).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0796] Intermediate-268:

1-(2-fluoro-5-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 31% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 2-fluoro-5-methoxyaniline in place of 2-chloro-5-methoxy aniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.43 (1H, br s), 7.90 (1H, dd, J = 5.0, 1.4 Hz), 7.43-7.34 (2H, m), 7.17 (1H, dd, J = 5.9, 3.2 Hz), 7.13-7.07 (2H, m), 3.78 (3H, s).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0797] Intermediate-269:

3-(2-chlorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 14% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 198 using 2-chloroaniline and 3-bromo-4-nitropyridine in place of 2-chloro-4-methylaniline and 2-bromo-3-nitropyridine.

MS (ESI) m/z: 246.1 (M+H)⁺.

[0798] Intermediate-270:

1-(3-fluoro-4-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 49% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 3-fluoro-4-methoxyaniline in place of 2-chloro-5-methoxy aniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.39 (1H, br s), 7.94 (1H, dd, J = 5.1, 1.4 Hz), 7.58 (1H, dd, J = 12.6, 2.4 Hz), 7.49-7.45 (1H, m), 7.39 (1H, dd, J = 7.7, 1.4 Hz), 7.31 (1H, J = 9.1 Hz), 7.09 (1H, dd, J = 7.7, 5.3 Hz), 3.90 (3H, s).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0799] Intermediate-271:

3-(2-fluoro-5-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 55% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 3-bromo-4-nitropyridine and 2-fluoro-5-methoxyaniline in place of 3-bromo-2-nitropyridine and 2-chloro-5-methoxyaniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.72 (1H, br s), 8.24 (1H, d, J = 5.0 Hz), 8.02 (1H, s), 7.43 (1H, t, J = 9.6 Hz), 7.24 (1H, dd, J = 6.4, 3.2 Hz), 7.17-7.08 (2H, m), 3.79 (3H, s).

MS (ESI) m/z: 260.2 (M+H)⁺.

[0800] Intermediate-272:

1-(3-fluoro-4-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in quantitative yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 3-fluoro-4-methoxyaniline and 4-chloronicotinic acid in place of 2,3-dihydro- 1H-inden-5-amine and 2-chloronicotinic acid.

MS (ESI) m/z: 260.2 (M+H)⁺.

[0801] Intermediate-273:

3-(2-fluoro-5-methoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 85% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-fluoro-5-methoxyaniline in place of 2,3-dihydro-1H-inden-5-amine.

MS (ESI) m/z: 260.2 (M+H)⁺.

[0802] Intermediate-274:

1-(2-fluoro-5-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

The title compound (pale yellow solid) is prepared in 89% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-98 using 2-fluoro-5-methoxyaniline and 4-chloronicotinic acid in place of 2,3-dihydro-1H-inden-5-amine and 2-chloronicotinic acid.

MS (ESI) m/z: 260.2 (M+H)⁺.

[0803] Intermediate-275:

N-methyl-4-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide

The title compound is prepared in 29% yield by the similar manner to Intermediate-137 using 4-chloro-N-methylpicolinamide in place of 3-fluoroisonicotinonitrile. The reaction is carried out at 120 °C.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.43 (1H, s), 8.89 (1H, br dd, J = 9.2, 4.0 Hz), 8.78 (1H, d, J = 5.5 Hz), 8.29 (1H, d, J = 1.8 Hz), 7.89 (1H, dd, J = 5.3, 2.1 Hz), 7.32 (1H, d, J = 7.8 Hz), 7.21-7.06 (3H, m), 2.86 (3H, d, J = 4.6 Hz).

MS (ESI) m/z: 269.0 (M+H)⁺.

[0804] Intermediate-276:

1-(3-fluorophenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

The title compound is prepared in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 3-fluoroaniline in place of 2-chloro-5-methoxyaniline.

MS (ESI) m/z: 230.2 (M+H)⁺.

[0805] Intermediate-277:

N-((1r,4r)-4-((3-(5-bromopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound (pale yellow solid) is prepared in 16% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate-252 using 5-bromopyridin-2-amine in place of 2-bromopyridin-4-amine.

¹H-NMR (400 MHz, DMSO-d₆) delta 8.52 (1H, d, J = 2.3 Hz), 8.32 (1H, d, J = 2.6 Hz), 8.19 (1H, d, J = 7.8 Hz), 8.05 (1H, dd, J = 8.8, 2.6 Hz), 7.91 (1H, d, J = 8.8 Hz), 7.78 (1H, d, J = 6.9 Hz), 7.57 (1H, d, J = 2.3 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.04-6.96

(1H, m), 6.96-6.84 (1H, m), 3.58 (2H, d, J = 6.9 Hz), 3.50 (1H, s), 2.25 (3H, s), 1.77-1.47 (5H, m), 1.09-0.91 (4H, m).

MS (ESI) m/z: 556.0 (M+H)⁺.

[0806] Intermediate-278:

N-((1*r*,4*r*)-4-((3-(6-bromopyridin-2-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound (pale yellow solid) is prepared in 31% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate-252 using 6-bromopyridin-2-amine in place of 2-bromopyridin-4-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.33 (1H, d, J = 2.7 Hz), 8.20 (1H, d, J = 8.2 Hz), 8.01 (1H, d, J = 8.2 Hz), 7.83-7.77 (1H, m), 7.76 (1H, d, J = 7.8 Hz), 7.59 (1H, d, J = 2.3 Hz), 7.43 (1H, d, J = 7.8 Hz), 7.18 (1H, d, J = 6.9 Hz), 7.04 (1H, td, J = 7.8, 1.4 Hz), 6.98 (1H, td, J = 7.7, 1.2 Hz), 3.60 (2H, d, J = 7.3 Hz), 3.56-3.42 (1H, m), 2.26 (3H, s), 1.77-1.46 (5H, m), 1.10-0.93 (4H, m).

MS (ESI) m/z: 556.0 (M+H)⁺.

[0807] Intermediate-279:

N-((1*r*,4*r*)-4-((3-(6-bromopyridin-2-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

The title compound (brown solid) is prepared in 46% yield in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Intermediate-224 using 6-bromopyridin-2-amine in place of 6-bromo-4-methylpyridin-3-amine.

¹H -NMR (400 MHz, DMSO-d₆) delta 8.62 (1H, d, J = 2.3 Hz), 8.44 (1H, d, J = 7.8 Hz), 8.01 (1H, d, J = 8.2 Hz), 7.94 (1H, d, J = 2.3 Hz), 7.83-7.70 (2H, m), 7.42 (1H, d, J = 7.3 Hz), 7.17 (1H, d, J = 6.9 Hz), 7.11-6.75 (3H, m), 3.59 (2H, d, J = 7.3 Hz), 3.54-3.42 (1H, m), 1.76-1.45 (5H, m), 1.11-0.90 (4H, m).

MS (ESI) m/z: 592.0 (M+H)⁺.

[0808] Intermediate-280:

5-chloro-N-((1*r*,4*r*)-4-((3-(5-chloropyrazin-2-yl)-6-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide

The title compound is prepared by the similar manner to Step-1 of Intermediate-57 using

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((6-fluoro-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (Intermediate-264) in place of 1*H*-benzo[d]imidazol-2(3*H*)-one.

[0809] Example synthesis part

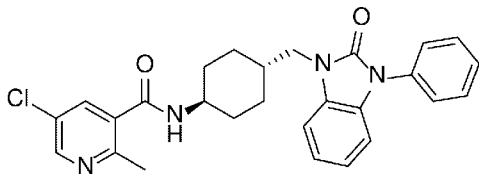
Each chemical structure of Example synthesis part is described as a free-base.

[0810] Representative procedure for Method A1

The following preparation of Example 1 represents the Method A1.

[0811] Example 1:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenyl-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.18]



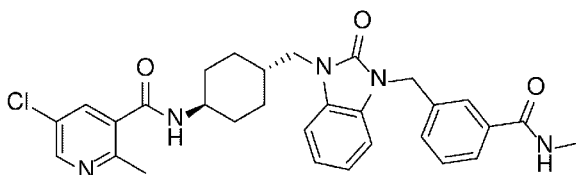
[0812] A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (25 mg, 0.069 mmol, Mesylate- 1), 1-phenyl- 1H-benzo[d]imidazol-2(3H)-one (15 mg, 0.069 mmol), and cesium carbonate (45 mg, 0.14 mmol) in DMSO (0.5 mL) is stirred at 80 °C for 5 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 7.4 mg (22% yield) of the title compound.

[0813] Representative procedure for Method B

The following preparation of Example 4 represents the Method B.

[0814] Example 4:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(methylcarbamoyl)benzyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.19]



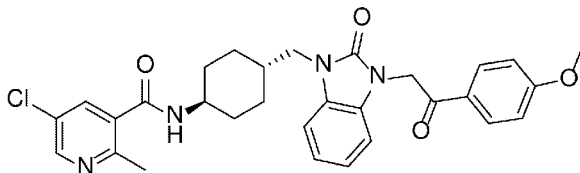
[0815] A mixture of 3-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid (22 mg, 0.041 mmol, Intermediate-2), 2 M methanamine in THF (0.5 mL), HBTU (31 mg, 0.083 mmol), and TEA (0.029 mL, 0.21 mmol) in DCM (2 mL) is stirred at room temperature for 1 day. The mixture is diluted with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by amino-functional silica gel column chromatography and then purified by preparative LC-MS to give 2.2 mg (10% yield) of the title compound.

[0816] Representative procedure for Method C1

The following preparation of Example 9 represents the Method C1.

[0817] Example 9:

5-chloro-N-((1*r*,4*r*)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.20]



[0818] <Step-1>: tert-butyl

3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazole-1-carboxylate

A mixture of ((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (500 mg, 1.39 mmol, Mesylate-1), tert-butyl 2-oxo-2,3-dihydro-1*H*-benzo[d]imidazole-1-carboxylate (325 mg, 1.39 mmol), and cesium carbonate (903 mg, 2.77 mmol) in DMSO (1 mL) is stirred at 80 °C for 6 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 487 mg (70% yield) of the title compound as a yellow gum.

¹H-NMR (400 MHz, CDCl₃) delta 8.47 (1H, d, J = 2.3 Hz), 7.84 (1H, dd, J = 7.8, 0.9 Hz), 7.60 (1H, d, J = 2.3 Hz), 7.21 (1H, td, J = 7.8, 0.9 Hz), 7.13 (1H, td, J = 7.8, 1.4 Hz), 6.96 (1H, dd, J = 7.8, 0.9 Hz), 5.66 (1H, d, J = 8.2 Hz), 4.00-3.88 (1H, m), 3.71 (2H, d, J = 6.9 Hz), 2.60 (3H, s), 2.17-2.09 (2H, m), 1.98-1.80 (3H, m), 1.68 (9H, s), 1.37-1.12 (4H, m). MS (ESI) m/z: 499.2 (M+H)⁺.

[0819] <Step-2>:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in quantitative yield (477 mg, a pale yellow solid) by the similar manner to Step-2 of Intermediate- 1 using tert-butyl 3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazole-1-carboxylate (487 mg, 0.98 mmol, Step-1 of Example 9).

MS (ESI) m/z: 399.1 (M+H)⁺.

[0820] <Step-3>:

5-chloro-N-((1*r*,4*r*)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[0821] A mixture of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl

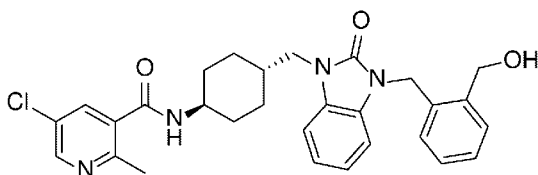
)cyclohexyl)nicotinamide (25 mg, 0.057 mmol, Step-2 of Example 9), 2-bromo-1-(4-methoxyphenyl)ethanone (13 mg, 0.057 mmol), and cesium carbonate (37 mg, 0.12 mmol) in DMSO (0.5 mL) is stirred at rt for 2 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 5.6 mg (18% yield) of the title compound.

[0822] Representative procedure for Method D

The following preparation of Example 11 represents the Method D.

[0823] Example 11:

5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.21]



[0824] A mixture of

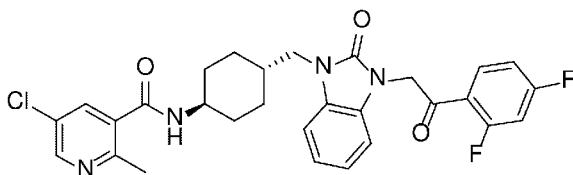
2-((3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoic acid (34 mg, 0.064 mmol, Intermediate-3) and CDI (16 mg, 0.096 mmol) in THF (1 mL) is stirred at room temperature for 5 hrs. Then, to the mixture is added sodium borohydride (10 mg, 0.26mmol) in water (0.5 mL) at rt. The mixture is stirred at rt for 1 hr. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by amino-functional silica gel column chromatography and then purified by preparative LC-MS to give 7 mg (21% yield) of the title compound.

[0825] Representative procedure for Method C2

The following preparation of Example 12 represents the Method C2.

[0826] Example 12:

5-chloro-N-((1r,4r)-4-((3-(2-(2,4-difluorophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.22]



[0827] A mixture of 5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (25 mg, 0.057 mmol, Step-2 of Example 9), 2-bromo-1-(2,4-difluorophenyl)ethanone (19 mg, 0.069 mmol) and potassium carbonate (16 mg, 0.12 mmol) in DMF (0.5 mL) is stirred at rt for 5 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.2 mg (10% yield) of the title compound.

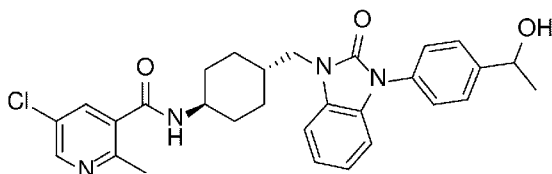
[0828] Representative procedure for Method E

The following preparation of Example 19 represents the Method E.

[0829] Example 19:

5-chloro-N-((1*r*,4*r*)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.23]



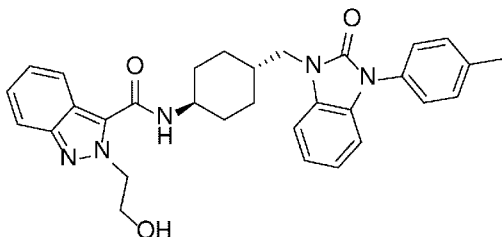
[0830] A mixture of N-

((1*r*,4*r*)-4-((3-(4-acetylphenyl)-2-oxo-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (20 mg, 0.039 mmol, Example 18) in MeOH (1 mL) is added sodium borohydride (3 mg, 0.077 mmol) at rt. The mixture is stirred at rt for 30 min. The mixture is diluted with water. The mixture is extracted with DCM. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by preparative LC-MS to give 4.5 mg (22% yield) of the title compound.

[0831] Example 40:

2-(2-hydroxyethyl)-N-((1*r*, 4*r*)-4-((2-oxo-3-(*p*-tolyl)-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2*H*-indazole-3-carboxamide

[Chem.24]



[0832] <Step-1>: methyl

2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2H-indazole-3-carboxylate

A mixture of methyl 1H-indazole-3-carboxylate (300 mg, 1.70 mmol), (2-bromoethoxy)(tert-butyl)dimethylsilane (489 mg, 2.04 mmol) in DMSO (5 mL) is stirred at 80 °C for 5 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc:m-hexane (1:1). The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-25% EtOAc in n-hexane to give 163 mg (29% yield) of the title compound as a pale yellow oil.

¹H-NMR (400 MHz, CDCl₃) δ 8.02 (1H, dt, J = 8.7, 0.9 Hz), 7.78 (1H, dt, J = 8.7, 0.9 Hz), 7.38-7.33 (1H, m), 7.30-7.25 (1H, m), 5.08 (2H, t, J = 5.9 Hz), 4.09 (2H, t, J = 5.9 Hz), 4.03 (3H, s), 0.78 (9H, s), -0.13 (6H, s). MS (ESI) m/z: 335.3 (M+H)⁺.

[0833] <Step-2>: 2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2H-indazole-3-carboxylic acid

A mixture of methyl

2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2H-indazole-3-carboxylate (163 mg, 0.49 mmol, Step-1 of Example 40) and 2 M aqueous sodium hydroxide solution (2 mL) in THF (1 mL) and MeOH (1 mL) is stirred at 50 °C for 2 hrs. The mixture is acidified with 2 M hydrochloric acid. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 141 mg (90% yield) of the title compound as a yellow solid.

MS (ESI) m/z: 321.3 (M+H)⁺.

[0834] <Step-3>: (1r,4r)-methyl

4-(2-(2-hydroxyethyl)-2H-indazole-3-carboxamido)cyclohexanecarboxylate

To a mixture of 2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2H-indazole-3-carboxylic acid (167 mg, 0.52 mmol, Step-2 of Example 40), (1r,4r)-methyl

4-aminocyclohexanecarboxylate hydrochloride (101 mg, 0.52 mmol), and TEA (0.29 mL, 2.01 mmol) in DCM (2 mL) is added 1.7 M T3P (registered trademark) in EtOAc (0.61 mL, 1.04 mmol) at rt. The mixture is stirred at rt for 1 hr. The mixture is quenched with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-80% EtOAc in n-hexane to give 70 mg (39% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 346.3 (M+H)⁺.

[0835] <Step-4>: (1r,4r)-methyl

4-(2-(2-((tert-butyldiphenylsilyl)oxy)ethyl)-2H-indazole-3-carboxamido)cyclohexanecarboxylate

[0836] To a solution of (1r,4r)-methyl

4-(2-(2-hydroxyethyl)-2H-indazole-3-carboxamido)cyclohexanecarboxylate (70 mg, 0.20 mmol, Step-3 of Example 40), DIEA (0.11 mL, 0.61 mmol) and DMAP (2 mg,

0.02 mmol) in DCM (1 mL) is added tert-butylchlorodiphenylsilane (0.08 mL, 0.30 mmol) at rt. The mixture is stirred at rt for 3 days. The mixture is quenched with saturated aqueous sodium bicarbonate. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-50% EtOAc in n-hexane to give 111 mg (94% yield) of the title compound as a pale yellow solid.

[0837] <Step-5>:

2-(2-((tert-butyldiphenylsilyl)oxy)ethyl)-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2H-indazole-3-carboxamide

To a mixture of (1r,4r)-methyl 4-(2-(2-((tert-butyldiphenylsilyl)oxy)ethyl)-2H-indazole-3-carboxamido)cyclohexanecarboxylate (111 mg, 0.19 mmol, Step-4 of Example 40) in THF (4 mL) is added lithium aluminum hydride (11 mg, 0.29 mmol) at 0 °C. The mixture is stirred at 0 °C for 1 hr. The mixture is acidified with 2 M hydrochloric acid and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 101 mg (96% yield) of the title compound as a pale yellow solid.

¹H -NMR (400 MHz, CDCl₃) delta 7.78 (1H, d, J = 8.7 Hz), 7.66 (1H, d, J = 8.2 Hz), 7.40-7.31 (7H, m), 7.28-7.17 (5H, m), 5.94 (1H, d, J = 5.5 Hz), 5.06 (2H, t, J = 5.5 Hz), 4.19 (2H, t, J = 5.5 Hz), 3.95-3.82 (1H, m), 3.49 (2H, d, J = 6.4 Hz), 2.11-2.00 (2H, m), 1.90-1.80 (2H, m), 1.52-1.40 (1H, m), 1.20-1.08 (4H, m), 0.93 (9H, s). A signal due to OH is not observed. MS (ESI) m/z: 556.4 (M+H)⁺.

[0838] <Step-6>:

((1r,4r)-4-(2-(2-((tert-butyldiphenylsilyl)oxy)ethyl)-2H-indazole-3-carboxamido)cyclohexyl)methyl methanesulfonate

To a mixture of 2-(2-((tert-butyldiphenylsilyl)oxy)ethyl)-N-((1r,4r)-4-(hydroxymethyl)cyclohexyl)-2H-indazole-3-carboxamide (101 mg, 0.18 mmol, Step-5 of Example 40), and TEA (0.05 mL, 0.36 mmol) in DCM (3 mL) is added methanesulfonic anhydride (48 mg, 0.27 mmol) at rt. The mixture is stirred at rt for 1 hr. The mixture is quenched with saturated aqueous sodium bicarbonate. The mixture is extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 122 mg (quantitative yield) of the title compound as a pale orange solid.

MS (ESI) m/z: 634.5 (M+H)⁺.

[0839] <Step-7>:

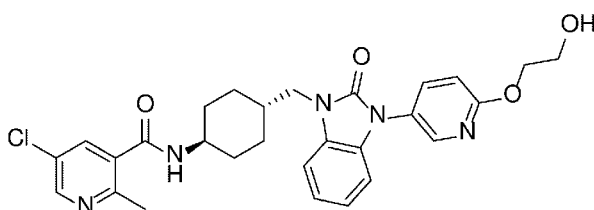
2-(2-hydroxyethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide

A mixture of ((1r,4r)-4-(2-(2-((tert-butyldiphenylsilyl)oxy)ethyl)-2H-indazole-3-carboxamido)cyclo

hexyl)methyl methanesulfonate (30 mg, 0.047 mmol, Step-6 of Example 40), 1-(p-tolyl)-1H-benzo[d]imidazol-2(3H)-one (11 mg, 0.047 mmol), and cesium carbonate (31 mg, 0.095 mmol) in DMSO (0.5 mL) is stirred at 80 °C for 3 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 4.3 mg (17% yield) of the title compound.

[0840] Example 50:

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.25]



[0841] <Step-1>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methanesulfonate (249 mg, 0.69 mmol, Mesylate-1), 1-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (245 mg, 0.69 mmol, Intermediate-24), and cesium carbonate (449 mg, 1.38 mmol) in DMF (2 mL) is stirred at 80 °C for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-100% EtOAc in n-hexane to give 395 mg (92% yield) of the title compound as a brown solid.

MS (ESI) m/z: 620.4 (M+H)⁺.

[0842] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

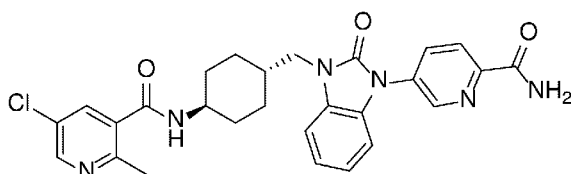
A mixture of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (395 mg, 0.64 mmol, Step-1 of Example 50) and p-toluenesulfonic acid (20 mg, 0.11 mmol) in MeOH (3 mL) and water (1 mL) is stirred at 70 °C for 3 hrs. The mixture is

diluted with saturated sodium hydrogen carbonate aqueous solution. The mixture is extracted with DCM. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-90% EtOAc in DCM to give 207 mg (61% yield) of the title compound as a pale yellow solid.

[0843] Example 62:

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)picolinamide

[Chem.26]



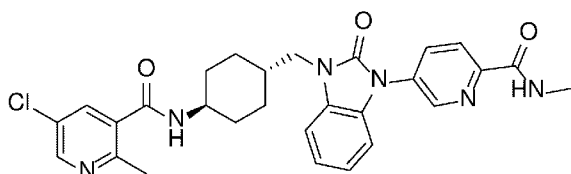
[0844] A mixture of

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)picolinic acid (25 mg, 0.048 mmol, Intermediate-36), ammonia hydrochloride (13 mg, 0.24 mmol), HBTU (55 mg, 0.14 mmol), and TEA (0.034 mL, 0.24 mmol) in DMF (2 mL) is stirred at room temperature for 1 day. The mixture is diluted with saturated sodium hydrogen carbonate aqueous solution. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 7.4 mg (30% yield) of the title compound.

[0845] Example 63:

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-*N*-methylpicolinamide

[Chem.27]



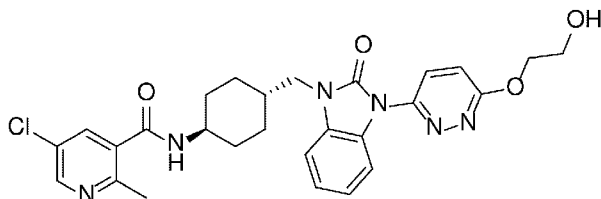
[0846] A mixture of

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)picolinic acid (25 mg, 0.048 mmol, Intermediate-36), methanamine hydrochloride (16 mg, 0.24 mmol), HBTU (55 mg, 0.14 mmol), and TEA (0.034 mL, 0.24 mmol) in DMF (2 mL) is stirred at room temperature for 1 day. The mixture is diluted with saturated sodium hydrogen carbonate aqueous solution.

The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.3 mg (13% yield) of the title compound.

[0847] Example 69:

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.28]



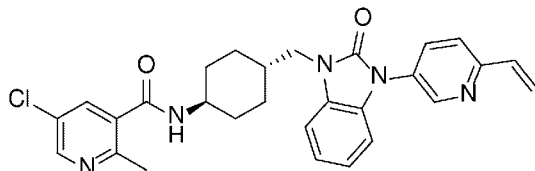
[0848] A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (25 mg, 0.069 mmol, Mesylate- 1), 1-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (15 mg, 0.069 mmol, Intermediate-42), and cesium carbonate (68 mg, 0.21 mmol) in DMSO (0.5 mL) is stirred at 90 °C for 5 hrs. The mixture is diluted with water and extracted with EtOAc. The organic layer is concentrated. The residual oil and p-toluenesulfonic acid (25 mg) in MeOH (1 mL) and water (1 mL) is stirred at 80 °C for 1 hr. The mixture is diluted with saturated sodium hydrogen carbonate aqueous solution. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 12 mg (32% yield) of the title compound.

[0849] Representative procedure for Method F

The following preparation of Example 70 represents the Method L.

[0850] Example 70:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2, 3-dihydro- 1H-benzo[d]imidazol- 1-yl)methyl)cyclohexyl)nicotinamide
[Chem.29]



[0851] A microwave vial equipped with a stirrer bar is charged with N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d] imidazol- 1-yl)met hyl)cyclohexyl)-5-chloro-2-methylnicotinamide (100 mg, 0.18 mmol, Example 66),

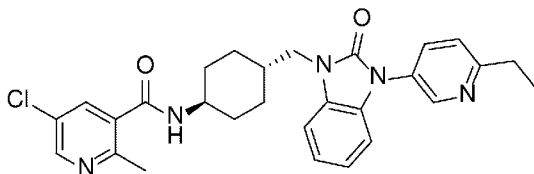
cesium carbonate (176 mg, 0.541 mmol), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (36.1 mg, 0.234 mmol), palladium(II)acetate (2.0 mg, 0.009 mmol) and XPhos (8.59 mg, 0.018 mmol), then sealed with a cap lined with a disposable septum. The vial is then evacuated under vacuum and purged with nitrogen atmosphere. Anhydrous THF (1 mL) and water (0.1 mL) are added by syringe and the resulting mixture is stirred and heated at 80 °C for overnight. The reaction mixture is extracted with EtOAc and water. The organic layer is dried (sodium sulfate) and concentrated in vacuo. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 85 mg (94% yield) of the title compound.

[0852] Representative procedure for Method G

The following preparation of Example 72 represents the Method G.

[0853] Example 72:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-ethylpyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.30]

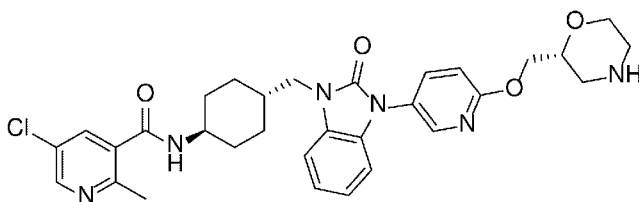


[0854] To an ethanol (1 mL) solution of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (13 mg, 0.026 mmol) is added 5% platinum on alumina (1 mg) and the resulting mixture is stirred at room temperature under hydrogen atmosphere for 3 hrs. The catalyst is filtered off and the filtrate is concentrated. The resulting crude product is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 5.7 mg (44% yield) of the title compound.

[0855] Example 74:

5-chloro-2-methyl-N-((1*R*,4*r*)-4-((3-(6-((*R*)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.31]



[0856] <Step-1>: (*R*)-tert-butyl

2-(((5-(3-(((1*r*,4*R*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate

The title compound is prepared in 46% yield (68 mg, a pale yellow gum) by the similar manner to Step-3 of Intermediate-2 using (R)-tert-butyl

2-(((5-(2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate (46 mg, 0.11 mmol, Intermediate-45) in place of methyl

3-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) *m/z*: 691.8 (M+H)⁺.

[0857] <Step-2>:

5-chloro-2-methyl-N-((1*R*,4*r*)-4-((3-(6-((R)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A solution of (R)-tert-butyl

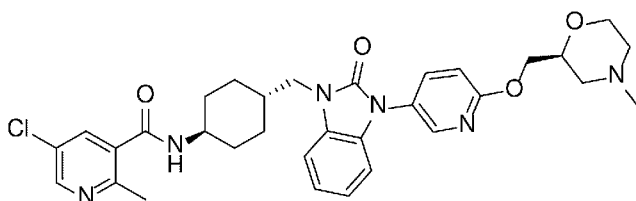
2-(((5-(3-(((1*r*,4*R*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate (28 mg, 0.041 mmol, Step-1 of Example 74) in DCM (1 mL) and TFA (1 mL) is stirred at rt for 1 hr. The mixture is concentrated. The residue is basified with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by preparative LC-MS to give 6.2 mg (11% yield) of the title compound.

[0858] Representative procedure for Method H

The following preparation of Example 75 represents the Method H.

[0859] Example 75:

5-chloro-2-methyl-N-((1*S*,4*r*)-4-((3-(6-(((S)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide [Chem.32]



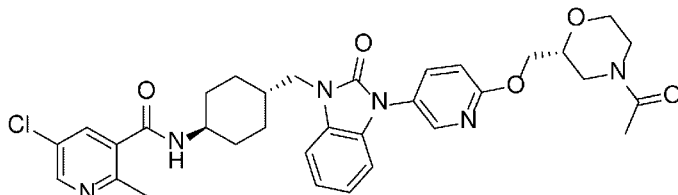
[0860] To a mixture of

5-chloro-2-methyl-N-((1*S*,4*r*)-4-((3-(6-(((S)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (10 mg, 0.017 mmol, Intermediate-46), paraformaldehyde (5 mg) in DCM (2 mL) is added sodium triacetoxyborohydride (18 mg, 0.085 mmol) at rt. The mixture is stirred at rt for 1 day. The mixture is basified with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by preparative LC-MS to give 6.8 mg

(66% yield) of the title compound.

[0861] Example 77: N-

((1*R*,4*r*)-4-((3-(6-(((*R*)-4-acetylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.33]

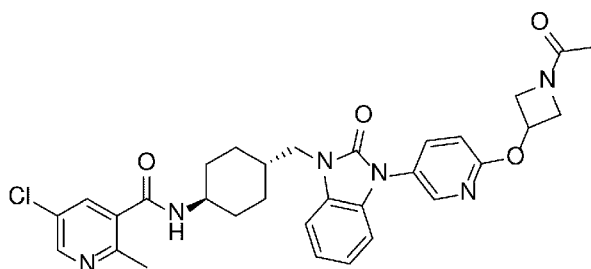


[0862] To a mixture of

5-chloro-2-methyl-N-((1*R*,4*r*)-4-((3-(6-((*R*)-morpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (22 mg, 0.037 mmol, Step-2 of Example 74) and TEA (0.025 mL, 0.18 mmol) in DCM (1 mL) is added acetic anhydride (0.01 mL, 0.11 mmol). The mixture is stirred at rt for 1 day. The mixture is basified with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by preparative LC-MS to give 8.1 mg (35% yield) of the title compound.

[0863] Example 78: N-

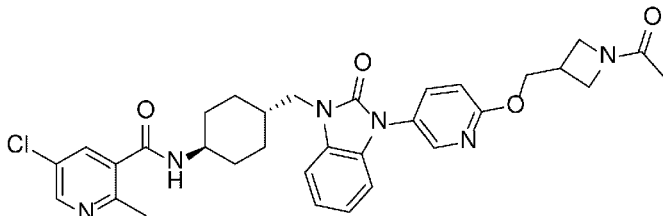
((1*r*,4*r*)-4-((3-(6-((1-acetylazetidin-3-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.34]



[0864] To a mixture of N-

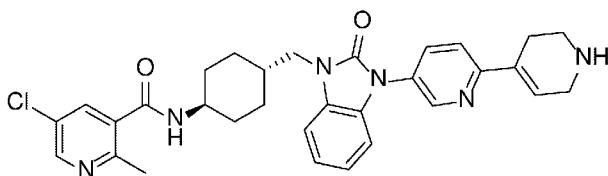
((1*r*,4*r*)-4-((3-(6-(azetidin-3-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (20 mg, 0.037 mmol, Intermediate-47) and TEA (0.025 mL, 0.18 mmol) in DCM (1 mL) is added acetic anhydride (0.01 mL, 0.11 mmol). The mixture is stirred at rt for 1 day. The mixture is basified with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by preparative LC-MS to give 6.2 mg (29% yield) of the title compound.

- [0865] Example 79: N-((1*r*,4*r*)-4-((3-(6-((1-acetylazetidin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide [Chem.35]



- [0866] To a mixture of N-((1*r*,4*r*)-4-((3-(6-(azetidin-3-ylmethoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (21 mg, 0.037 mmol, Intermediate-48) and TEA (0.025 mL, 0.18 mmol) in DCM (1 mL) is added acetic anhydride (0.01 mL, 0.11 mmol). The mixture is stirred at rt for 1 day. The mixture is basified with saturated aqueous sodium bicarbonate and extracted with DCM. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by preparative LC-MS to give 3.9 mg (18% yield) of the title compound.

- [0867] Example 85: 5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(*r*,2',3',6'-tetrahydro-[2,4'-bipyridin]-5-yl)-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide [Chem.36]



- [0868] A microwave vial equipped with a stirrer bar is charged with N-((1*r*,4*r*)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (20 mg, 0.036 mmol, Example 66), cesium carbonate (35.2 mg, 0.108 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2*H*)-carboxylate (14.5 mg, 0.047 mmol), palladium(II)acetate (0.41 mg, 0.0018 mmol) and XPhos (1.72 mg, 0.0036 mmol), then sealed with a cap lined with a disposable septum. The vial is then evacuated under vacuum and purged with nitrogen atmosphere. Anhydrous THF (1 mL) and water (0.1 mL) are added by syringe and the resulting mixture is stirred and heated at 90 °C for over night. The reaction mixture is extracted with EtOAc and water. The organic layer is dried (sodium sulfate) and concentrated in

vacuo. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give tert-butyl 5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-5',6'-dihydro-[2,4'-bipyridine]-*r*(2'-*H*)-carboxylate (22 mg, 0.033 mmol, 93% yield). Then, a solution of tert-butyl 5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-5',6'-dihydro-[2,4'-bipyridine]-*r*(2'-*H*)-carboxylate (22 mg, 0.033 mmol) in 4 M hydrochloric acid in 1,4-dioxane (1 mL) is stirred at rt for 1 hr. The reaction mixture is concentrated and extracted with ethyl acetate - saturated aqueous sodium bicarbonate. The organic layer is washed with brine, dried (sodium sulfate) and concentrated to give the title compound (18 mg, 97% yield).

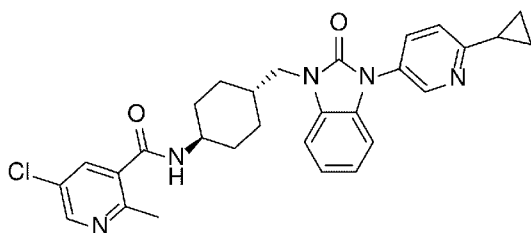
[0869] Representative procedure for Method A2

The following preparation of Example 86 represents the Method A2.

[0870] Example 86:

5-chloro-*N*-(((1*r*,4*r*)-4-((3-(6-cyclopropylpyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.37]



[0871] A mixture of Mesylate-1 (4.3 mg, 0.012 mmol), Intermediate-51 (3 mg, 0.012 mmol), cesium carbonate (9.7 mg, 0.030 mmol) in NMP (0.2 mL) is stirred at 80 °C for 4 hrs. After cooled to rt, the mixture is diluted with water and extracted with EtOAc. The organic layer is dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 2.2 mg (36% yield) of the title compound.

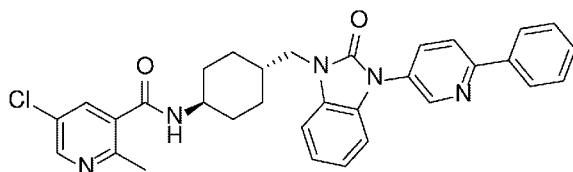
[0872] Representative procedure for Method I

The following preparation of Example 89 represents the Method I.

[0873] Example 89:

5-chloro-2-methyl-*N*-(((1*r*,4*r*)-4-((2-oxo-3-(6-phenylpyridin-3-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.38]



[0874] A mixture of N-((1*r*,4*r*)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (25 mg, 0.045 mmol, Example 66), phenylboronic acid (11 mg, 0.09 mmol), and [1,1'-bis(diphenylphosphino)ferrocene] dichloropalladium(II), complex with dichloromethane (4 mg, 0.004 mmol) in 1,4-dioxane (0.7 mL) and saturated aqueous sodium bicarbonate (0.7 mL) is stirred at 80 °C for 3 hrs. The mixture is diluted with water. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 9.6 mg (39% yield) of the title compound.

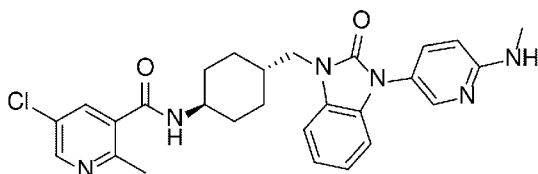
[0875] Representative procedure for Method J

The following preparation of Example 91 represents the Method J.

[0876] Example 91:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.39]



[0877] A mixture of

5-chloro-N-((1*r*,4*r*)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (25 mg, 0.051 mmol, Intermediate-54), dimethylamine hydrochloride (27 mg, 0.51 mmol), and DIEA (0.088 mL, 0.51 mmol) in NMP (2 mL) is irradiated with microwave at 220 °C for 30 min. The mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 10 mg (40% yield) of the title compound.

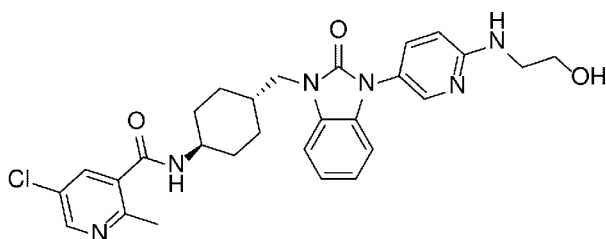
[0878] Representative procedure for Method K

The following preparation of Example 93 represents the Method K.

[0879] Example 93:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.40]

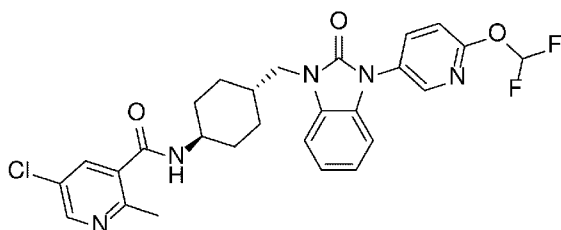


[0880] A mixture of Example 66 (15 mg, 0.027 mmol), 2-aminoethanol (5.0 mg, 0.081 mmol) and TEA (0.02 mL, 0.14 mmol) in 2-propanol (0.5 mL) is stirred at 100 °C for 20 min then 150 °C for 3.5 hrs under microwave irradiation. After cooled to rt, the mixture is diluted with EtOAc, washed with water, dried over MgSO_4 , filtered and concentrated in vacuo. The residue is purified by preparative LC-MS to give 6.8 mg (47% yield) of the title compound.

[0881] Example 97:

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.41]



[0882] <Step-1>: N-

((1r,4r)-4-((3-(6-(tert-butoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of Example 66 (40 mg, 0.072 mmol) and potassium tert-butoxide (24.3 mg, 0.216 mmol) in 1-methyl-2-pyrrolidone (0.5 mL) is stirred at 80 °C overnight. To the mixture is added potassium tert-butoxide (24.3 mg, 0.216 mmol) and stirred at 90 °C. After starting material is completely consumed, the reaction mixture is cooled to rt. The mixture is diluted with EtOAc, washed with 1 M hydrochloric acid, dried over MgSO_4 , filtered and concentrated in vacuo. The residue is purified by column chromatography on silica-gel eluting with 20-90% EtOAc in n-hexane to give 10 mg (25% yield) of the title compound.

MS (ESI) m/z: 548.5 (M+H)⁺.

[0883] <Step-2>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-oxo-1,6-dihydropyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A solution of N-

((1r,4r)-4-((3-(6-(tert-butoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (10 mg, 0.018 mmol) in DCM (0.2 mL) and TFA (0.5 mL) is stirred at rt for 30min. The reaction mixture is concentrated and the residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give the title compound as a crude product (11 mg). It is used for the next Step-3 without further purification. MS (ESI) m/z: 492.3 (M+H)⁺.

[0884] <Step-3>:

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

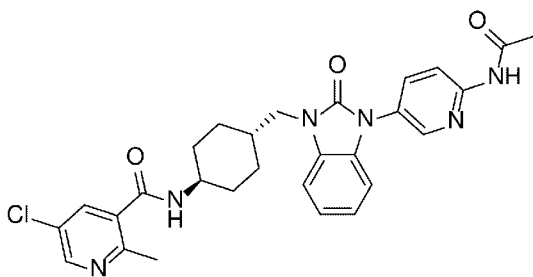
A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-oxo-1,6-dihydropyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (10 mg, 0.020 mmol) and sodium chlorodifluoroacetate (4.7 mg, 0.030 mmol) in acetonitrile (1 mL) is stirred at 85 °C overnight. After cooled to rt, the mixture is diluted with EtOAc, washed with water. The organic layer is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.0 mg (27% yield) of the title compound.

[0885] Example 98: N-

((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.42]



[0886] A mixture of Example 66 (20 mg, 0.036 mmol), acetamide (3.2 mg, 0.054 mmol), Xantphos (2 mg, 0.0036 mmol), palladium (II) acetate (1 mg, 0.0044 mmol) and cesium carbonate (23 mg, 0.072 mmol) in 1,4-dioxane (0.5 mL) is stirred at 100 °C overnight. To the mixture are added XPhos (4 mg, 0.0084 mmol) and palladium (II) acetate (1 mg, 0.0044 mmol) and stirred at 100 °C overnight. After cooled to rt, the mixture is diluted with EtOAc and water. The insoluble material is filtered off through celite pad. The filtrate is extracted with EtOAc. The organic layer is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.0 mg (16% yield) of the

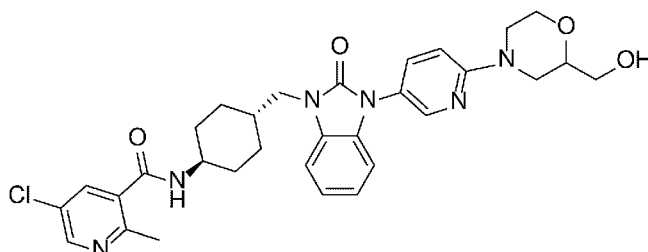
title compound.

[0887] Representative procedure for Method L

The following preparation of Example 99 represents the Method L.

[0888] Example 99:

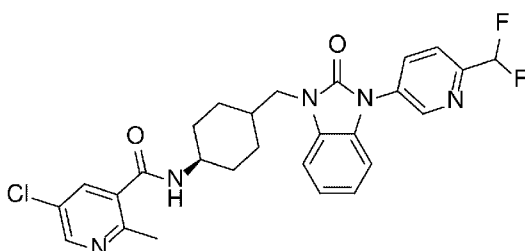
5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)morpholino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.43]



[0889] A mixture of morpholin-2-ylmethanol (22 mg, 0.184 mmol), Intermediate- 54 (18 mg, 0.036 mmol), and TEA (0.102 mL, 0.729 mmol) in 2-propanol (0.5 mL) is stirred at 160 °C for 3 hrs under microwave irradiation. After cooled to rt, the mixture is concentrated. The residue is diluted with EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 10.4 mg (48% yield) of the title compound.

[0890] Example 100:

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.44]



[0891] <Step-1>:

5-chloro-N-((1r,4r)-4-((3-(6-formylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

Ozone is bubbled in a solution of Example 70 (100 mg, 0.199 mmol) in DCM (2 mL) at -78 °C until reaction solution turned to pale blue solution. N₂ is bubbled to dissipate blue color, and dimethylsulfane (0.087 mL, 1.20 mmol) is added to the reaction mixture and stirred for 20 min at -78 °C, then stirred over night at room temperature. After removal of solvent, the residue is extracted with ethyl acetate-water. The organic layer is washed with brine, dried over sodium sulfate filtered and concentrated. The

residue is purified by column chromatography on silica-gel eluting with 30-100% EtOAc in n-hexane followed by 0-10% MeOH in EtOAc to give 65 mg (65% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z : 504.5 (M+H)⁺.

[0892] <Step-2>:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-(difluoromethyl)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

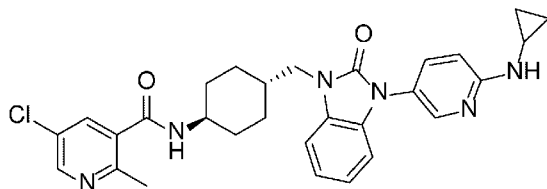
To a solution of

5-chloro-N-((1*r*,4*r*)-4-((3-(6-formylpyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (20 mg, 0.040 mmol) in DCM (0.5 mL) is added deoxofluor (40 microL, 0.217 mmol) at -50 °C and stirred at 0 °C for 30 min then rt overnight. After cooling to 0 °C, the reaction is quenched with saturated aqueous sodium bicarbonate. The resulting mixture is extracted with EtOAc. The organic phase is dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 5.8 mg (28% yield) of the title compound.

[0893] Example 101:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.45]



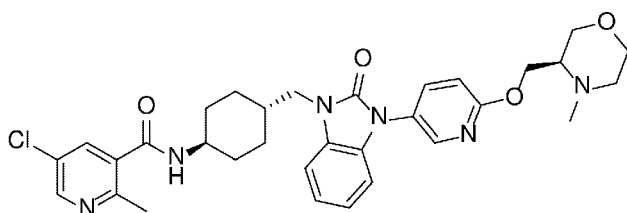
[0894] To a mixture of

5-chloro-N-((1*r*,4*r*)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (25 mg, 0.051 mmol, Intermediate-54), and cyclopropylamine (29 mg, 0.51 mmol) in NMP (2 mL) is added sodium hydride (60% dispersion in mineral oil, 22 mg, 0.15 mmol) at room temperature. The mixture is stirred at room temperature for 1 day. The mixture is diluted with water and extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.1 mg (8% yield) of the title compound.

[0895] Example 102:

5-chloro-2-methyl-N-((1*R*,4*r*)-4-((3-(6-(((*R*)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.46]



[0896] <Step-1>: (R)-tert-butyl

3-(((5-(3-(((1*R*,4*R*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate

To a mixture of

5-chloro-*N*-((1*R*,4*r*)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (25 mg, 0.051 mmol, Intermediate-54), and (S)-tert-butyl 3-(hydroxymethyl)morpholine-4-carboxylate (11 mg, 0.51 mmol) in DMF (2 mL) is added sodium hydride (60% dispersion in mineral oil, 8 mg, 0.20 mmol) at room temperature. The mixture is stirred at room temperature for 1 hr. The mixture is diluted with water and extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 23 mg (66% yield) of the title compound as a pale yellow gum.

MS (ESI) *m/z*: 691.6 (M+H)⁺.

[0897] <Step-2>:

5-chloro-2-methyl-*N*-((1*R*,4*r*)-4-((3-(6-((*R*)-morpholin-3-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide hydrochloride

The title compound is prepared in quantitative yield (21 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using (R)-tert-butyl

3-(((5-(3-(((1*R*,4*R*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate (23 mg, 0.033 mmol, Step-1 of Example 102).

MS (ESI) *m/z*: 591.5 (M+H)⁺.

[0898] <Step-3>:

5-chloro-2-methyl-*N*-((1*R*,4*r*)-4-((3-(6-(((*R*)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

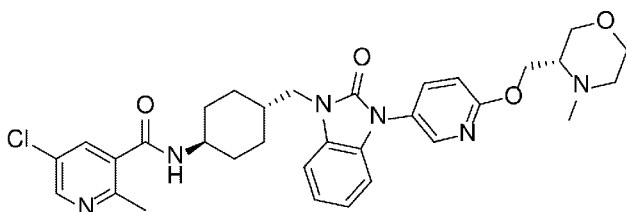
[0899] To a mixture of

5-chloro-2-methyl-*N*-((1*R*,4*r*)-4-((3-(6-((*R*)-morpholin-3-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide hydrochloride (21 mg, 0.033 mmol, Step-2 of Example 102), paraformaldehyde (10 mg) in DCM (2 mL) is added sodium triacetoxyborohydride (18 mg, 0.085 mmol) at rt. The

mixture is stirred at rt for 3 hrs. The mixture is basified with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 1.9 mg (9% yield) of the title compound.

[0900] Example 103:

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide [Chem.47]



[0901] <Step-1>: (S)-tert-butyl

3-(((5-(3-(((1r,4S)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate

[0902] To a mixture of

5-chloro-N-((1r,4r)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (25 mg, 0.051 mmol, Intermediate-54), and (R)-tert-butyl 3-(hydroxymethyl)morpholine-4-carboxylate (11 mg, 0.51 mmol) in DMF (2 mL) is added sodium hydride (60% dispersion in mineral oil, 8 mg, 0.20 mmol) at room temperature. The mixture is stirred at room temperature for 1 hr. The mixture is diluted with water and extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 23 mg (66% yield) of the title compound as a pale yellow gum.

MS (ESI) m/z: 691.6 (M+H)⁺.

[0903] <Step-2>:

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-morpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide hydrochloride

The title compound is prepared in quantitative yield (21 mg, a pale yellow gum) by the similar manner to Step-2 of Intermediate- 1 using (S)-tert-butyl 3-(((5-(3-(((1r,4S)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)methyl)morpholine-4-carboxylate (23 mg, 0.033 mmol, Step-1 of Example 103).

MS (ESI) m/z: 591.5 (M+H)⁺.

[0904] <Step-3>:

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

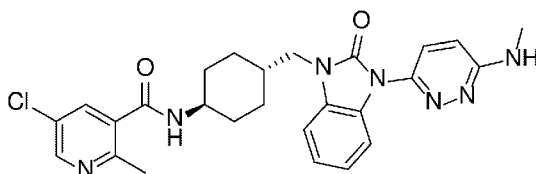
To a mixture of

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-((S)-morpholin-3-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide hydrochloride (21 mg, 0.033 mmol, Step-2 of Example 103), paraformaldehyde (10 mg) in DCM (2 mL) is added sodium triacetoxyborohydride (18 mg, 0.085 mmol) at rt. The mixture is stirred at rt for 3 hrs. The mixture is basified with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.8 mg (14% yield) of the title compound.

[0905] Example 104:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.48]



[0906] A mixture of

5-chloro-N-((1r,4r)-4-((3-(6-chloropyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (23 mg, 0.045 mmol, Intermediate-55), methanamine hydrochloride (30 mg, 0.45 mmol) and DIEA (0.079 mL, 0.45 mmol) in NMP (2 mL) is irradiated with microwave at 200 °C for 30 min. The mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.2 mg (14% yield) of the title compound.

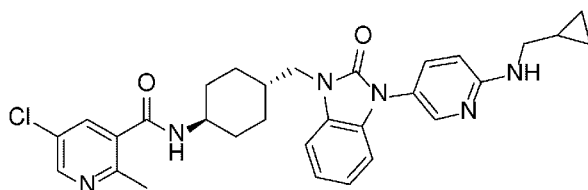
[0907] Representative procedure for Method M

The following preparation of Example 105 represents the Method M.

[0908] Example 105:

5-chloro-N-((1r,4r)-4-((3-(6-((cyclopropylmethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.49]

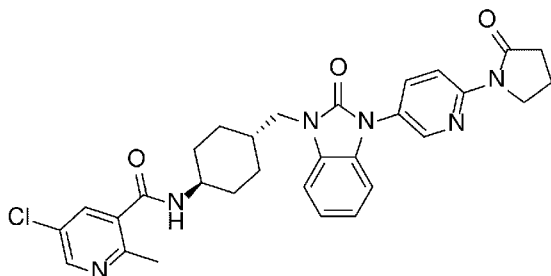


[0909] A mixture of 5-chloro-N-((1r,4r)-4-((3-(6-fluoropyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (25 mg, 0.051 mmol, Intermediate-54), cyclopropylmethanamine (36 mg, 0.51 mmol), DIEA (0.088 mL, 0.51 mmol), and DBU (0.038 mL, 0.25 mmol) in NMP (2 mL) is irradiated with microwave at 220 °C for 30 min. The mixture is diluted with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 5.1 mg (18% yield) of the title compound.

[0910] Example 111:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.50]



[0911] A mixture of Example 66 (20 mg, 0.036 mmol), pyrrolidin-2-one (6.1 mg, 0.072 mmol), XPhos (5.2 mg, 0.011 mmol), tris(dibenzylideneacetone)dipalladium(0) (5.0 mg, 0.0054 mmol) and sodium tert-pentoxide (7.9 mg, 0.072 mmol) in 1,4-dioxane (0.5 mL) is stirred at 100 °C overnight. After cooled to rt, the mixture is diluted with EtOAc and water followed by extraction with EtOAc. The organic layer is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 10.4 mg (52% yield) of the title compound.

[0912] Representative procedure for Method N

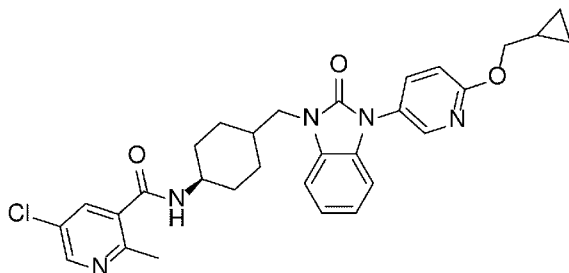
The following preparation of Example 112 represents the Method N.

[0913] Example 112:

5-chloro-N-(4-((3-(6-(cyclopropylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo

[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.51]

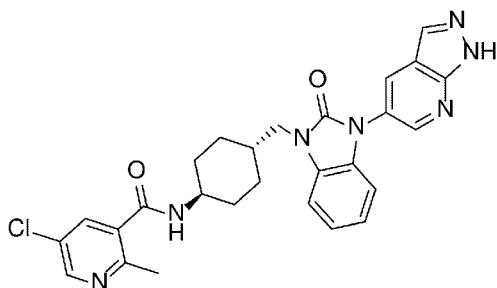


[0914] A mixture of Intermediate- 54 (20 mg, 0.040 mmol), cyclopropylmethanol (20 mg, 0.277 mmol) and sodium tert-pentoxide (14 mg, 0.127 mmol) in THF is stirred at 90 ° C for 11 hrs. After cooled to rt, the mixture is diluted with EtOAc, washed with water and brine, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 11.1 mg (50% yield) of the title compound.

[0915] Example 128:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.52]



[0916] <Step-1>: 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine

A mixture of 5-bromo-1H-pyrazolo[3,4-b]pyridine (202 mg, 1.02 mmol), 3,4-dihydro-2H-pyran (0.187 mL, 2.04 mmol) and p-toluenesulfonic acid (19 mg, 0.10 mmol) in toluene (2 mL) is stirred at 100 °C for 4 hrs. After cooling to rt, the mixture is directly purified by column chromatography on silica-gel eluting with 10-60% EtOAc in n-hexane to give 281 mg (98% yield) of the title compound as a pale yellow oil.

¹H-NMR (400 MHz, CDCl₃) delta 8.61 (1H, d, J = 1.8 Hz), 8.21 (1H, d, J = 0.9 Hz), 8.17 (1H, dd, J = 1.8, 0.9 Hz), 5.70 (1H, dd, J = 8.5, 2.5 Hz), 4.04-3.96 (1H, m), 3.81-3.71 (1H, m), 2.54-2.38 (1H, m), 2.22-2.07 (2H, m), 1.88-1.65 (3H, m).

[0917] <Step-2>:

1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine

After degassed with N₂ gas, a mixture of 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine (230 mg, 0.815

mmol), bis(pinacolato)diboron (621 mg, 2.45 mmol), Pd(dppf)Cl₂ (60 mg, 0.082 mmol) and potassium acetate (240 mg, 2.45 mmol) in 1,4-dioxane (3 mL) is stirred at 100 °C for 3 hrs. After cooled to rt, the mixture is directly purified by column chromatography on silica-gel eluting with 10-60% EtOAc in n-hexane to give 200 mg (75% yield) of the title compound as a brown oil.

¹H-NMR (400 MHz, CDCl₃) delta 8.89 (1H, d, J = 1.4 Hz), 8.51 (1H, d, J = 1.4 Hz), 8.08 (1H, d, J = 0.9 Hz), 6.18 (1H, dd, J = 10.7, 2.5 Hz), 4.17-4.09 (1H, m), 3.89-3.81 (1H, m), 2.75-2.53 (1H, m), 2.20-2.09 (1H, m), 2.02-1.94 (1H, m), 1.88-1.72 (2H, m), 1.69-1.59 (1H, m), 1.37 (12H, s). MS (ESI) m/z: 330.3 (M+H)⁺.

[0918] <Step-3>: tert-butyl

2-oxo-3-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2, 3-dihydro- 1H-benzo [d]imidazole- 1-carboxylate

A mixture of tert-butyl 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (100 mg, 0.427 mmol), copper (II) acetate (116 mg, 0.640 mmol), TEA (0.089 mL, 0.640 mmol),

1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine (200 mg, 0.608 mmol) and MS 4A (100 mg) in DCM (3 mL) is stirred at rt for 4 days. To the reaction mixture are added copper (II) acetate (116 mg, 0.640 mmol) and TEA (0.089 mL, 0.640 mmol) and stirred at rt overnight. The mixture is directly purified by column chromatography on amino-functional silica-gel eluting with 5-60% EtOAc in n-hexane to give 127 mg (68% yield) of the title compound as a white solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.67 (1H, d, J = 2.3 Hz), 8.20 (1H, d, J = 2.3 Hz), 8.16 (1H, s), 7.95 (1H, dd, J = 7.5, 1.8 Hz), 7.24-7.14 (2H, m), 6.89 (1H, dd, J = 7.3, 1.8 Hz), 6.18 (1H, dd, J = 10.5, 2.3 Hz), 4.20-4.10 (1H, m), 3.92-3.79 (1H, m), 2.75-2.60 (1H, m), 2.26-2.11 (1H, m), 2.09-2.00 (1H, m), 1.88-1.77 (2H, m), 1.73-1.61 (10H, m). MS (ESI) m/z: 436.2 (M+H)⁺.

[0919] <Step-4>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of Mesylate- 1 (100 mg, 0.277 mmol), tert-butyl 2-oxo-3-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2, 3-dihydro- 1H-benzo [d]imidazole- 1-carboxylate (127 mg, 0.292 mmol), cesium carbonate (226 mg, 0.693 mmol) in NMP (1 mL) is stirred at 80 °C overnight. To the mixture is added Mesylate- 1 (22 mg, 0.061 mmol) and stirred at 80 °C for 16 hrs. After cooled to rt, the mixture is diluted with EtOAc and washed with water. The organic layer is dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography

on silica-gel eluting with 30-100% EtOAc in n-hexane followed by 0-10% MeOH in EtOAc to give 103 mg (62% yield) of the title compound.

¹H-NMR (400 MHz, CDCl₃) delta 8.73 (1H, d, J = 2.3 Hz), 8.49 (1H, d, J = 2.3 Hz), 8.24 (1H, d, J = 2.3 Hz), 8.16 (1H, s), 7.61 (1H, d, J = 2.3 Hz), 7.22-7.17 (1H, m), 7.13-7.07 (2H, m), 7.04-7.00 (1H, m), 6.18 (1H, dd, J = 10.5, 2.7 Hz), 5.57 (1H, d, J = 7.8 Hz), 4.20-4.12 (1H, m), 4.04-3.80 (4H, m), 2.80-2.52 (4H, m), 2.25-2.12 (3H, m), 2.10-1.76 (6H, m), 1.73-1.62 (1H, m), 1.44-1.07 (4H, m). MS (ESI) m/z: 600.4 (M+H)⁺.

[0920] <Step-5>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A solution of

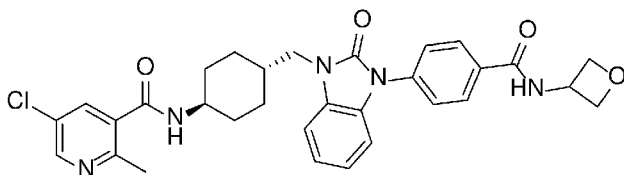
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (103 mg, 0.172 mmol) in DCM (0.5 mL) and TFA (1 mL) is stirred at rt for 1.5 hrs. After the reaction mixture is concentrated, the residue is dissolved into DCM, washed with saturated aqueous sodium bicarbonate, dried over MgSO₄, filtered and concentrated. One third of the resultant residue is purified by preparative LC-MS to give 8.8 mg (29% yield) of the title compound.

[0921] Representative procedure for Method O

The following preparation of Example 130 represents the Method O.

[0922] Example 130:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxetan-3-ylcarbamoyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.53]



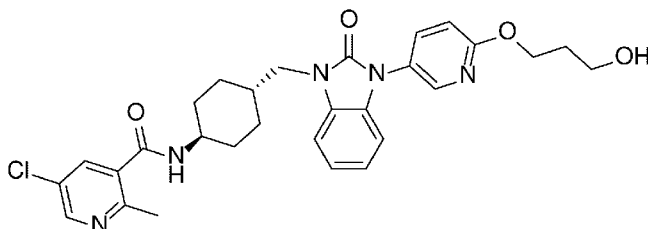
[0923] A mixture of

4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoic acid (25 mg, 0.048 mmol, Intermediate-9), oxetan-3-amine (7 mg, 0.096 mmol), HBTU (37 mg, 0.096 mmol), and TEA (0.034 mL, 0.24 mmol) in DMF (1 mL) is stirred at room temperature for 3 hrs. The mixture is diluted with saturated sodium hydrogen carbonate aqueous solution. The mixture is extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE

(registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 5.9 mg (21% yield) of the title compound.

[0924] Example 134:

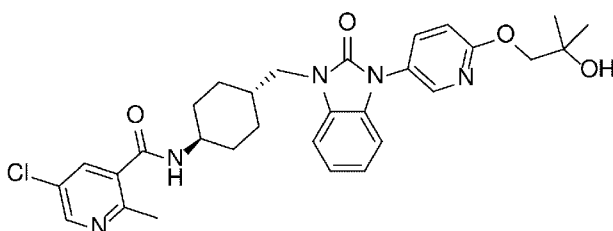
5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.54]



[0925] A mixture of Intermediate- 54 (15 mg, 0.030 mmol), propane- 1,3-diol (3.5 mg, 0.046 mmol) and sodium tert-pentoxide (8.4 mg, 0.076 mmol) in THF (0.5 mL) is stirred at 120 °C for 30 min under microwave irradiation. After cooled to rt, to the reaction mixture is added MeOH to dissolve precipitate. The resulting solution is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 6.0 mg (36% yield) of the title compound.

[0926] Example 135:

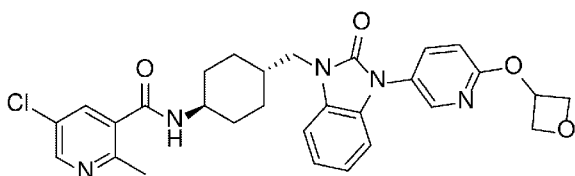
5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.55]



[0927] The title compound is prepared in 26% yield (4.3 mg) by the similar manner to Example 134 using 2-methylpropane-1,2-diol (4.1 mg, 0.046 mmol) in place of propane- 1,3-diol.

[0928] Example 140:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.56]

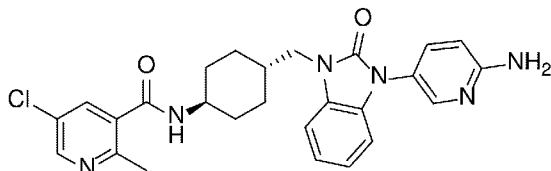


[0929] The title compound is prepared in 65% yield (10.8 mg) by the similar manner to Example 134 using oxetan-3-ol (3.4 mg, 0.046 mmol) in place of propane- 1,3-diol.

[0930] Example 143:

N-((1*r*,4*r*)-4-((3-(6-aminopyridin-3-yl)-2-oxo-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.57]



[0931] <Step-1>: N-

((1*r*,4*r*)-4-((3-(6-azidopyridin-3-yl)-2-oxo-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of Intermediate- 54 (15 mg, 0.030 mmol) and sodium azide (4.0 mg, 0.061 mmol) in DMSO is stirred at 100 °C overnight. After cooled to rt, the mixture is diluted with EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 30-100% EtOAc in n-hexane to give 10 mg (64% yield) of the title compound as a beige solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.22-9.20 (1H, m), 8.49 (1H, d, J = 2.7 Hz), 8.20 (1H, dd, J = 9.6, 0.9 Hz), 8.00 (1H, dd, J = 9.6, 1.8 Hz), 7.62 (1H, d, J = 2.7 Hz), 7.31-7.24 (1H, m), 7.21-7.17 (2H, m), 7.14 (1H, d, J = 7.8 Hz), 5.63 (1H, d, J = 7.8 Hz), 4.06-3.90 (1H, m), 3.85 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.23-2.12 (2H, m), 2.04-1.82 (3H, m), 1.47-1.11 (4H, m).

[0932] <Step-2>: N-

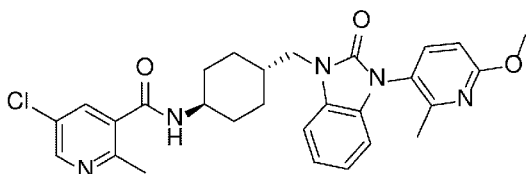
((1*r*,4*r*)-4-((3-(6-aminopyridin-3-yl)-2-oxo-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of triphenylphosphine (6.1 mg, 0.023 mmol) and N-((1*r*,4*r*)-4-((3-(6-azidopyridin-3-yl)-2-oxo-2, 3-dihydro- 1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (10 mg, 0.019 mmol) in THF (1 mL) and water (0.1 mL) is stirred at rt overnight. To this is added 2 M hydrochloric acid and stirred at rt for 5 hrs. To the reaction mixture is added 2 M aqueous sodium hydroxide solution to neutralize the mixture. The resultant mixture is extracted with EtOAc. The organic phase is dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 4.6 mg (48% yield) of the title compound.

[0933] Example 149:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.58]



[0934] <Step-1>: 6-fluoro-2-methyl-N-(2-nitrophenyl)pyridin-3-amine

The title compound is prepared in 64% yield (562 mg, an orange solid) by the similar manner to Step-1 of Intermediate-20 using 6-fluoro-2-methylpyridin-3-amine (500 mg, 3.96 mmol) in place of 2,4-difluoroaniline.

¹H-NMR (400 MHz, CDCl₃) delta 9.20 (1H, s), 8.25 (1H, dd, J = 8.5, 1.6 Hz), 7.68 (1H, t, J = 7.8 Hz), 7.42-7.36 (1H, m), 6.88 (1H, dd, J = 7.8, 3.7 Hz), 6.85-6.80 (1H, m), 6.65 (1H, dd, J = 8.7, 1.4 Hz), 2.45 (3H, s).

[0935] <Step-2>: N¹-(6-fluoro-2-methylpyridin-3-yl)benzene-1, 2-diamine

The title compound is prepared in quantitative yield (494 mg) by the similar manner to Step-2 of Intermediate-20 using 4-fluoro-2-methyl-N-(2-nitrophenyl)aniline (562 mg, 2.27 mmol, Step-1 of Example 149) in place of 2,4-difluoro-N-(2-nitrophenyl)aniline.

¹H-NMR (400 MHz, CDCl₃) delta 7.03 (1H, td, J = 7.5, 1.4 Hz), 6.98 (1H, dd, J = 8.7, 6.9 Hz), 6.91 (1H, dd, J = 7.5, 1.4 Hz), 6.82 (1H, dd, J = 7.5, 1.4 Hz), 6.76 (1H, td, J = 7.5, 1.4 Hz), 6.63 (1H, dd, J = 8.7, 3.7 Hz), 4.92 (1H, s), 3.73 (2H, s), 2.46 (3H, s).

[0936] <Step-3>: 1-(6-fluoro-2-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 92% yield (511 mg, an off-white powder) by the similar manner to Step-3 of Intermediate-20 using N¹-(6-fluoro-2-methylpyridin-3-yl)benzene-1, 2-diamine (494 mg, 2.27 mmol, Step-2 of Example 149) in place of N¹-(2,4-difluorophenyl)benzene-1, 2-diamine.

¹H-NMR (400 MHz, CDCl₃) delta 9.19 (1H, s), 7.78 (1H, dd, J = 8.5, 7.3 Hz), 7.18-7.12 (2H, m), 7.10-7.05 (1H, m), 6.97 (1H, dd, J = 8.5, 3.2 Hz), 6.67 (1H, d, J = 7.3 Hz), 2.40 (3H, s).

[0937] <Step-4>:

5-chloro-N-((1r,4r)-4-((3-(6-fluoro-2-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of Mesylate- 1 (50 mg, 0.139 mmol), 1-(6-fluoro-2-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (40 mg, 0.166 mmol), cesium carbonate (113 mg, 0.346 mmol) in NMP (0.5 mL) is stirred at 80 °C for 5 hrs. After cooled to rt, the mixture is diluted with water and extracted with EtOAc. The organic layer is dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 30-100% EtOAc in n-hexane followed by 0-10% MeOH in EtOAc to give 42 mg (60% yield) of the title

compound as a beige solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.49 (1H, d, J = 2.3 Hz), 7.75 (1H, t, J = 7.8 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.21-7.16 (1H, m), 7.12-7.05 (2H, m), 6.95 (1H, dd, J = 7.8, 3.4 Hz), 6.71-6.67 (1H, m), 5.56 (1H, d, J = 7.8 Hz), 4.05-3.89 (1H, m), 3.84 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.36 (3H, s), 2.22-2.10 (2H, m), 2.03-1.82 (3H, m), 1.43-1.14 (4H, m).

[0938] <Step-5>:

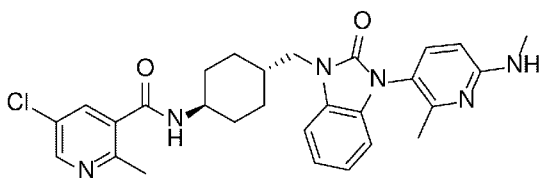
5-chloro-N-((1r,4r)-4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of

5-chloro-N-((1r,4r)-4-((3-(6-fluoro-2-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (20 mg, 0.039 mmol) and sodium methoxide (4.3 mg, 0.079 mmol) in MeOH is stirred at 120 °C for 30 min then 150 °C for 30 min. After cooled to rt, the mixture is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 9.1 mg (44% yield) of the title compound.

[0939] Example 150:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.59]



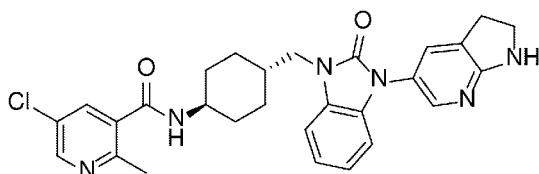
[0940] A mixture of

5-chloro-N-((1r,4r)-4-((3-(6-fluoro-2-methylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (20 mg, 0.039 mmol, Step-4 of Example 149), 2 M methylamine in THF (0.039 mL, 0.079 mmol), DBU (0.030 mL, 0.197 mmol), TEA (0.027 mL, 0.197 mmol) in 2-propanol (0.5 mL) is stirred at 160 °C for 3 hrs under microwave irradiation. After cooled to rt, the mixture is concentrated. The residue is dissolved into EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 5.1 mg (25% yield) of the title compound.

[0941] Example 152:

5-chloro-N-((1r, 4r)-4-((3-(2, 3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.60]



[0942] <Step-1>: tert-butyl

3-(1-(tert-butoxycarbonyl)-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

The title compound is prepared in 31% yield (60 mg, a colorless viscous oil) by the similar manner to Intermediate- 58 using tert-butyl

5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (222 mg, 0.640 mmol) in place of 2,3-dimethoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine.

¹H-NMR (400 MHz, CDCl₃) delta 8.32 (1H, d, J = 2.3 Hz), 7.93-7.89 (1H, m), 7.59-7.56 (1H, m), 7.21-7.08 (2H, m), 6.96-6.91 (1H, m), 4.15-4.08 (2H, m), 3.13 (2H, t, J = 8.5 Hz), 1.69 (9H, s), 1.58 (9H, s).

[0943] <Step-2>: tert-butyl

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-2, 3-dihydro- 1H-pyrrolo[2,3-b]pyridine- 1-carboxylate

The title compound is prepared in 49% yield (40 mg, a beige solid) by the similar manner to the Step-4 of Example- 149 using

3-(1-(tert-butoxycarbonyl)-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (60 mg, 0.133 mmol) in place of 1-(6-fluoro-2-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one.

MS (ESI) m/z: 617.2 (M+H)⁺.

[0944] <Step-3>:

5-chloro-N-(((1r,4r)-4-((3-(2, 3-dihydro- 1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

After a solution of tert-butyl

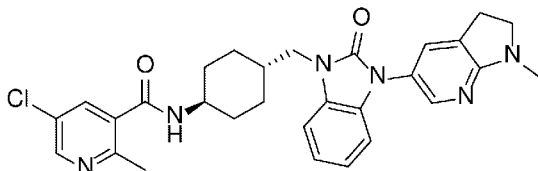
5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-2, 3-dihydro- 1H-pyrrolo[2,3-b]pyridine- 1-carboxylate (40 mg, 0.065 mmol) in DCM (0.5 mL) and TFA (1 mL) is stirred at rt for 30 min, the reaction mixture is concentrated. The residual oil is purified by column chromatography on silica-gel eluting with 50-100% EtOAc in n-hexane followed by 0-10% MeOH in EtOAc to give 19 mg (57% yield) of the title compound as a white solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.48 (1H, d, J = 2.3 Hz), 7.93 (1H, d, J = 2.3 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.36 (1H, d, J = 2.3 Hz), 7.14 (1H, td, J = 7.7, 0.9 Hz), 7.10-7.02 (2H, m), 6.98 (1H, dd, J = 7.7, 0.9 Hz), 5.67 (1H, d, J = 8.2 Hz), 4.68 (1H,

s), 4.05-3.87 (1H, m), 3.79 (2H, d, J = 6.9 Hz), 3.72 (2H, t, J = 8.5 Hz), 3.14 (2H, t, J = 8.5 Hz), 2.22-2.09 (2H, m), 2.03-1.83 (3H, m), 1.44-1.12 (4H, m).

[0945] Example 154:

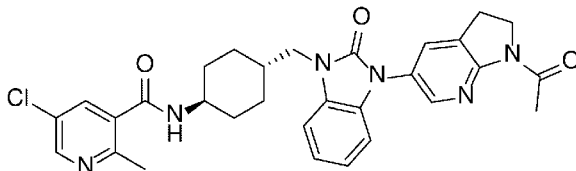
5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.61]



[0946] A mixture of Example 152 (10 mg, 0.019 mmol), formic acid (0.2 mL) and 37% formaline (0.2 mL) is stirred at 80 °C overnight. After cooled to rt, the mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 6.9 mg (67% yield) of the title compound.

[0947] Example 155:

N-((1r,4r)-4-((3-(1-acetyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.62]



[0948] A mixture of Example 152 (7 mg, 0.014 mmol), acetic anhydride (0.010 mL, 0.106 mmol) and DMAP (0.5 mg, 0.004 mmol) in pyridine is stirred at rt overnight. After the reaction mixture is concentrated, the resultant residue is dissolved into EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 5.1 mg (67% yield) of the title compound.

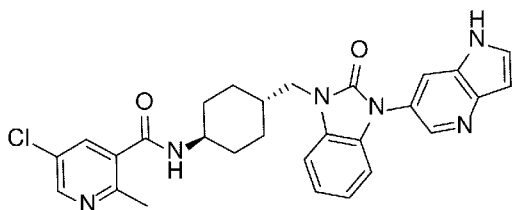
[0949] Representative procedure for Method O

The following preparation of Example 158 represents the Method O.

[0950] Example 158:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.63]



[0951] <Step-1>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of Mesylate- 1 (8.3 mg, 0.023 mmol), Intermediate- 82 (30 mg, 0.062 mmol) and Cs_2CO_3 (16 mg, 0.048 mmol) in DMSO (0.5 mL) is stirred at 80 °C for 5 hrs. After cooled to rt, the mixture is diluted with EtOAc, washed with water, dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-10% MeOH in EtOAc to give 40 mg (quantitative yield) of the title compound.

MS (ESI) m/z: 645.2 (M+H)⁺.

[0952] <Step-2>:

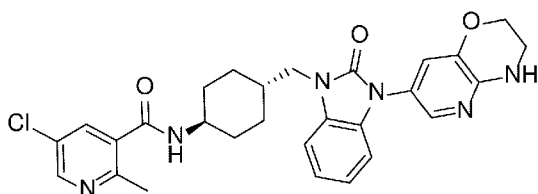
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

To a solution of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (30 mg, 0.046 mmol) in DCM (0.5 mL) is added TFA (1 mL) at rt and stirred. After 30min the reaction mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 7.8 mg (33% yield) of the title compound.

[0953] Example 159:

5-chloro-N-((1r,4r)-4-((3-(3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.64]



[0954] The title compound is prepared in 37% yield for 2 steps by the similar manner to

Step-1 and Step-2 of Example 158 using Intermediate- 83 in place of Intermediate-82.

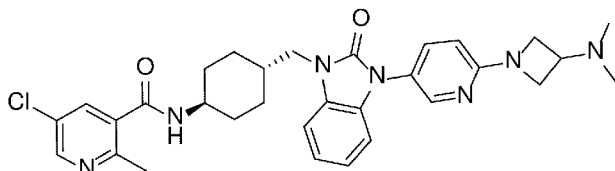
[0955] Representative procedure for Method P

The following preparation of Example 161 represents the Method P.

[0956] Example 161:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.65]

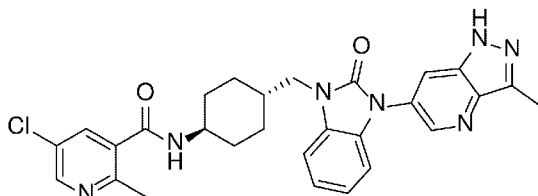


[0957] A mixture of Intermediate- 54 (15 mg, 0.030 mmol), N,N-dimethylazetidin-3-amine dihydrochloride (7.9 mg, 0.046 mmol), DBU (0.014 mL, 0.091 mmol) and DIEA (0.016 mL, 0.091 mmol) in 2-propanol (0.5 mL) is stirred at 120 °C for 1 hr under microwave irradiation. To this are added N,N-dimethylazetidin-3-amine dihydrochloride (2.0 mg, 0.012 mmol), DBU (0.014 mL, 0.091 mmol) and DIEA (0.016 mL, 0.091 mmol) and stirred at 120 °C for 1 hr under microwave irradiation. To this are added N,N-dimethylazetidin-3-amine dihydrochloride (2.0 mg, 0.012 mmol), DBU (0.014 mL, 0.091 mmol) and DIEA (0.016 mL, 0.091 mmol) and stirred at 120 °C for 30 min under microwave irradiation. The resultant mixture is diluted with EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 8.1 mg (46% yield) of the title compound.

[0958] Example 172:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(3-methyl-1*H*-pyrazolo[4,3-*b*]pyridin-6-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.66]



[0959] The title compound is prepared in 43% yield for 2 steps by the similar manner to Step-1 and Step-2 of Example 158 using Intermediate-93 in place of Intermediate-82.

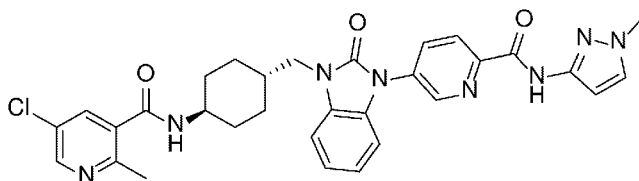
[0960] Representative procedure for Method Q

The following preparation of Example 173 represents the Method Q.

[0961] Example 173:

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-N-(1-methyl-1*H*-pyrazol-3-yl)picolinamide

[Chem.67]



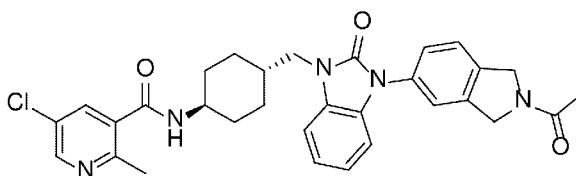
[0962] To a mixture of 5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinic acid (20 mg, 0.038 mmol, Intermediate-36), 1-methyl-1H-pyrazol-3-amine (5.6 mg, 0.058 mmol) and DIEA (0.027 mL, 0.15 mmol) in DMF (1 mL) is added HATU (29 mg, 0.077 mmol). The mixture is stirred at room temperature overnight. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 7.8 mg (33% yield) of the title compound.

MS (ESI) m/z: 599.2 (M+H)⁺.

[0963] Example 188:

N-(((1r,4r)-4-((3-(2-acetylisoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.68]



[0964] <Step-1>: 5-bromo-2-((2-nitrophenyl) sulfonyl)isoindoline

A mixture of 5-bromoisoindoline hydrochloride (500 mg, 2.13 mmol), 2-nitrobenzenesulfonyl chloride (709 mg, 3.20 mmol) and potassium carbonate (884 mg, 6.40 mmol) in MeCN (3 mL) is stirred for 1 hr at rt. After the reaction mixture is concentrated, the residue is added with saturated aqueous ammonium chloride. The resultant mixture is washed with water to give 996 mg of the title compound as a pale yellow solid. The compound is used for the next reaction without further purification.

MS (ESI) m/z: 382.9 (M+H)⁺.

[0965] <Step-2>:

2-((2-nitrophenyl)sulfonyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoindoline

The title compound is prepared in 72% yield in 2 steps (663 mg, brown solid) by the similar manner to Step-1 of Intermediate- 107 using

5-bromo-2-((2-nitrophenyl)sulfonyl)isoindoline (Step-1 of Example 188) in place of

6-bromo-3-methyl- 1-(tetrahydro-2H-pyran-2-yl)- 1H-indazole.

¹H -NMR (400 MHz, CDCl₃) delta 8.05-8.00 (1H, m), 7.73 (1H, d, J = 8.0 Hz), 7.71-7.66 (3H, m), 7.64-7.60 (1H, m), 7.24 (1H, d, J = 8.0 Hz), 4.85-4.79 (4H, m), 1.34 (12H, s).

MS (ESI) m/z: 431.1 (M+H)⁺.

[0966] <Step-3>:

1-(2-((2-nitrophenyl)sulfonyl)isoindolin-5-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 31% yield (205 mg, brown gum) by the similar manner to Intermediate- 84 using

2-((2-nitrophenyl)sulfonyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoindoline (361 mg, 1.51 mmol, Step-2 of Example 188) in place of

1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-b]pyridine.

MS (ESI) m/z: 437.0 (M+H)⁺.

[0967] <Step-4>:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-((2-nitrophenyl)sulfonyl)isoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 38% yield (64 mg, brown gum) by the similar manner to Step-3 of Intermediate- 3 using

1-(2-((2-nitrophenyl)sulfonyl)isoindolin-5-yl)-1H-benzo[d]imidazol-2(3H)-one (104 mg, 0.074 mmol, Step-3 of Example 188) in place of methyl

2-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol- 1-yl)methyl)benzoate.

MS (ESI) m/z: 701.3 (M+H)⁺.

[0968] <Step-5>:

5-chloro-N-((1r,4r)-4-((3-(isoindolin-5-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-((2-nitrophenyl)sulfonyl)isoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (48 mg, 0.068 mmol, Step-4 of Example 188), 1-dodecanethiol (0.033 mL, 0.14 mmol) and DBU (0.021 mL, 0.14 mmol) in MeCN (0.5 mL) is stirred for 2 hrs at rt. The mixture is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 26 mg (75% yield) of the title compound as a brown solid.

MS (ESI) m/z: 516.3 (M+H)⁺.

[0969] <Step-6>: N-

((1r,4r)-4-((3-(2-acetylisoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of

5-chloro-N-((1*r*,4*r*)-4-((3-(isoindolin-5-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (57 mg, 0.11 mmol, Step-5 of Example 188), acetic anhydride (0.016 mL, 0.17 mmol) and TEA (0.023 mL, 0.17 mmol) in DCM is stirred for 2 hrs at rt. After the reaction mixture is concentrated, the resultant residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and column chromatography on amino-functional silica gel eluting with 2-100% MeOH in DCM. The residue is purified by preparative LC-MS to give 3.5 mg (6% yield) of the title compound.

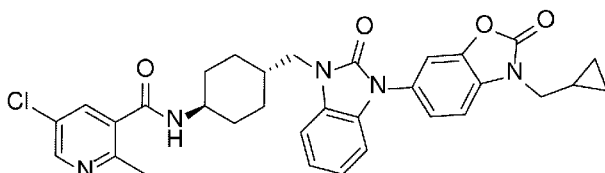
[0970] Representative procedure for Method R

The following preparation of Example 195 represents the Method R.

[0971] Example 195:

5-chloro-N-((1*r*,4*r*)-4-((3-(3-(cyclopropylmethyl)-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.69]

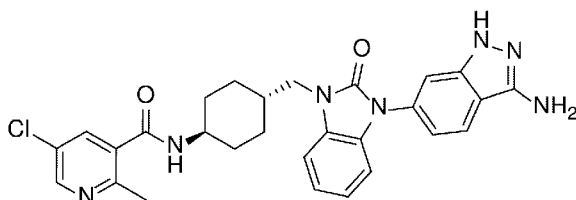


[0972] A mixture of Intermediate- 104 (15 mg, 0.056 mmol), the product of Step-2 of Example 9 (15 mg, 0.038 mmol), copper(I) iodide (11 mg, 0.056 mmol), N',N'-dimethylethane-1, 2-diamine (0.012 mL, 0.113 mmol) and Cs₂CO₃ (49 mg, 0.150 mmol) in DMA (0.3 mL) is stirred at 100 °C overnight. After cooled to rt, the reaction mixture is diluted with EtOAc, washed with 28% ammonia aqueous solution, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 6.2 mg (28% yield) of the title compound.

[0973] Example 197:

N-((1*r*,4*r*)-4-((3-(3-amino-1*H*-indazol-6-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.70]



[0974] <Step-1>:

5-chloro-N-((1*r*,4*r*)-4-((3-(4-cyano-3-fluorophenyl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in 72% yield (47 mg) by the similar manner to Example 195 using 4-bromo-2-fluorobenzonitrile (38 mg, 0.188 mmol) in place of Intermediate-104. In addition, the purification is carried out by column chromatography on silica gel eluting with 20-100% EtOAc in n-hexane instead of preparative LC-MS. ¹H-NMR (400 MHz, CDCl₃) delta 8.49 (1H, d, J = 2.3 Hz), 7.79 (1H, dd, J = 8.5, 7.1 Hz), 7.64-7.58 (2H, m), 7.28-7.07 (5H, m), 5.57 (1H, d, J = 7.8 Hz), 4.01-3.88 (1H, m), 3.81 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.16 (2H, d, J = 10.1 Hz), 2.01-1.85 (3H, m), 1.40-1.10 (4H, m).

MS (ESI) m/z: 518.3 (M+H)⁺.

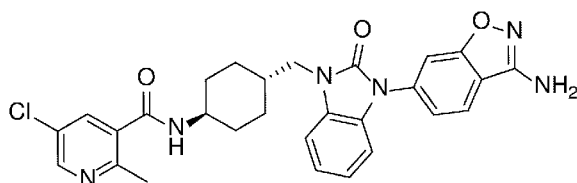
[0975] <Step-2>: N-

((1*r*,4*r*)-4-((3-(3-amino-1*H*-indazol-6-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of 5-chloro-N-((1*r*,4*r*)-4-((3-(4-cyano-3-fluorophenyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (20 mg, 0.039 mmol) and hydrazine hydrate (0.010 mL, 0.193 mmol) in EtOH (0.5 mL) is stirred at 150 °C for 20 min under microwave irradiation. To this is added hydrazine hydrate (0.010 mL, 0.193 mmol) stirred at 150 °C for 20 min under microwave irradiation. After cooled to rt, water is added to it and stirred for 1 min. The precipitate is collected by filtration, dried in vacuo, and purified by preparative LC-MS to give 4.6 mg (22% yield) of the title compound.

[0976] Example 198:

N-((1*r*,4*r*)-4-((3-(3-aminobenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.71]

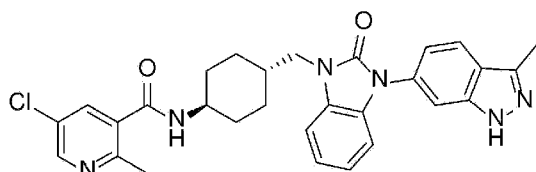


[0977] A mixture of the product of Step-1 of Example 197 (20 mg, 0.039 mmol), N-hydroxyacetamide (8.7 mg, 0.116 mmol) and K₂CO₃ in DMF (0.5 mL) and water (0.1 mL) is stirred at 80 °C for 2 hrs. After cooled to rt, the mixture is diluted with EtOAc, washed with water, dried over MgSO₄, filtered and concentrated. The residue is purified by preparative LC-MS to give 5.9 mg (29% yield) of the title compound.

[0978] Example 205:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(3-methyl-1*H*-indazol-6-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.72]



[0979] <Step-1>:

5-chloro-2-methyl-N-((1r,4r)-4-(((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 75% yield (83 mg, yellow gum) by the similar manner to Step-3 of Intermediate- 3 using

1-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-6-yl)-1H-benzo[d]imidazol-2(3H)-one (85 mg, 0.18 mmol, Step-2 of Intermediate- 107) in place of methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 613.3 (M+H)⁺.

[0980] <Step-2>:

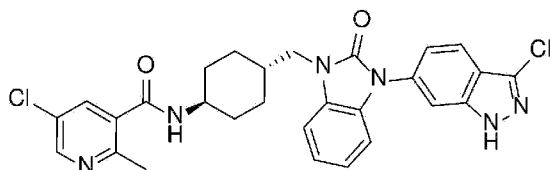
5-chloro-2-methyl-N-((1r,4r)-4-(((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

5-chloro-2-methyl-N-((1r,4r)-4-(((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (28 mg, 0.045 mmol, Step-1 of Example 205) in TFA (1 mL) is stirred overnight at rt. After the reaction mixture is concentrated, the resultant residue is purified by preparative LC-MS to give 4.8 mg (20% yield) of the title compound.

[0981] Example 210:

5-chloro-N-((1r,4r)-4-(((3-(3-chloro-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.73]



[0982] <Step-1>: 6-bromo-3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole

A mixture of 6-bromo-3-chloro-1H-indazole (100 mg, 0.432 mmol), 4-methylbenzenesulfonic acid hydrate (3.6 mg, 0.019 mmol) and 3,4-dihydro-2H-pyran (0.028 mL, 0.302 mmol) in toluene (2 mL) is stirred at 80 °C for 2 hrs. After cooled to rt, the mixture is purified by column chromatography on silica-gel eluting with 0-70% EtOAc in n-hexane to give 104 mg (76%) of the title compound as a white solid.

¹H -NMR (400 MHz, CDCl₃) delta 7.77 (1H, d, J = 1.4 Hz), 7.52 (1H, d, J = 8.7 Hz), 7.33 (1H, dd, J = 8.7, 1.4 Hz), 5.61 (1H, dd, J = 9.1, 2.7 Hz), 4.06-3.97 (1H, m), 3.80-3.68 (1H, m), 2.57-2.41 (1H, m), 2.20-2.01 (2H, m), 1.83-1.62 (3H, m).

[0983] <Step-2>:

5-chloro-N-((1*r*,4*r*)-4-((3-(3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in 42% yield (10 mg) by the similar manner to Example 195 using 6-bromo-3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (24 mg, 0.075 mmol) in place of Intermediate- 104. In addition, the purification is carried out by column chromatography on silica gel eluting with 0-10% MeOH in EtOAc instead of preparative LC-MS.

¹H -NMR (400 MHz, CDCl₃) delta 8.48 (1H, d, J = 2.3 Hz), 7.87-7.75 (2H, m), 7.61 (1H, d, J = 2.3 Hz), 7.40 (1H, dd, J = 8.7, 1.4 Hz), 7.25-7.05 (4H, m), 5.69 (1H, dd, J = 9.1, 2.7 Hz), 5.63 (1H, d, J = 8.2 Hz), 4.08-3.65 (5H, m), 2.70-2.48 (4H, m), 2.23-1.90 (7H, m), 1.84-1.55 (3H, m), 1.50-1.15 (4H, m).

MS (ESI) m/z: 631.3 (M-H)⁻.

[0984] <Step-3>:

5-chloro-N-((1*r*,4*r*)-4-((3-(3-chloro-1H-indazol-6-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

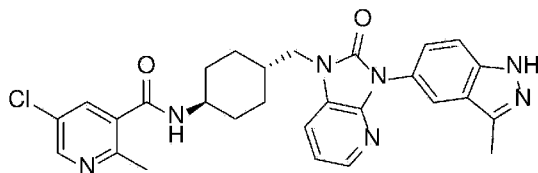
The title compound is prepared in 92% yield (8 mg) by the similar manner to Step-2 of Example 158 using the product of Step-2 of Example 210 (10 mg, 0.016 mmol) in place of the product of Step-1 of Example 158.

[0985] Representative procedure for Method S

The following preparation of Example 212 represents the Method S.

[0986] Example 212:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(3-methyl- 1H-indazol-5-yl)-2-oxo-2, 3-dihydro- 1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.74]



[0987] <Step-1>:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 18% yield (15 mg, brown solid) by the similar

manner to Step-3 of Intermediate- 3 using

3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one (48 mg, 0.13 mmol, Intermediate- 111) in place of methyl 2-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol- 1-yl)methyl)benzoate.

MS (ESI) m/z: 614.3 (M+H)⁺.

[0988] <Step-2>:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2, 3-dihydro- 1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide

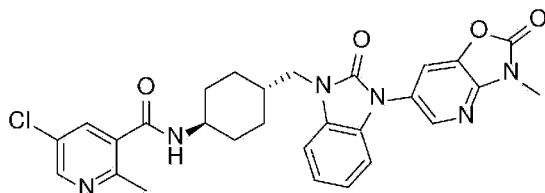
5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.024 mmol, Step-1 of Example 212) in TFA (1 mL) is stirred for 2 hrs at rt. After the reaction mixture is concentrated, the resultant residue is purified by preparative LC-MS to give 5.1 mg (40% yield) of the title compound.

[0989] Representative procedure for Method T

The following preparation of Example 215 represents the Method T.

[0990] Example 215:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrooxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide [Chem.75]



[0991] A mixture of

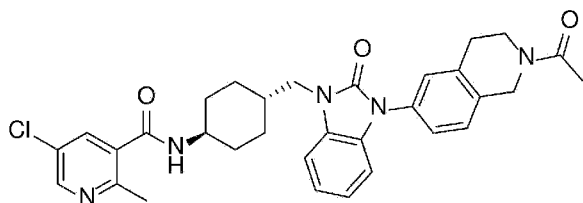
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9), 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxazolo[4,5-b]pyridin-2(3H)-one (10 mg, 0.038 mmol), copper acetate (17 mg, 0.094 mmol) and TEA (0.016 mL, 0.113 mmol) in MeCN (2 mL) is stirred at 100 °C for 2 hrs. The mixture is filtered through celite pad. The filtrate is concentrated in vacuo. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 6.2 mg (30% yield) of the title compound.

MS (ESI) m/z: 547.2 (M+H)⁺.

[0992] Example 218:

N-((1r,4r)-4-((3-(2-acetyl- 1,2,3,4-tetrahydroisoquinolin-6-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.76]



[0993] <Step-1>: tert-butyl

6-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate

The title compound is prepared in 84% yield in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate- 112 using tert-butyl 6-amino-3,4-dihydroisoquinoline-2(1H)-carboxylate in place of 4-(pyridin-4-yloxy)aniline.

¹H -NMR (400 MHz, DMSO-d₆) delta 11.12 (1H, br s), 7.37-7.31 (3H, m), 7.07-7.04 (2H, m), 7.00-6.97 (2H, m), 4.57 (2H, s), 3.59 (2H, t, J = 5.9 Hz), 2.85 (2H, t, J = 5.9 Hz), 1.44 (9H, s).

MS (ESI) m/z: 365.9 (M+H)⁺.

[0994] <Step-2>: tert-butyl

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate

The title compound is prepared in 87% yield (151 mg) by the similar manner to Step-3 of Intermediate- 3 using tert-butyl 6-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (101 mg, 0.28 mmol, Step-1 of Example 218) in place of methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 630.1 (M+H)⁺.

[0995] <Step-3>:

5-chloro-2-methyl-N-(((1r,4r)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

To a solution of tert-butyl 6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (164 mg, 0.25 mmol, Step-2 of Example 218) in 1,4-dioxane (1 mL) is added 4 M HCl in 1,4-dioxane (5 mL) at room temperature. The mixture is stirred at room temperature for 1 hr. The mixture is concentrated to give 142 mg (quantitative yield) of the title compound.

MS (ESI) m/z: 530.0 (M+H)⁺.

[0996] <Step-4>: N-

((1r,4r)-4-((3-(2-acetyl- 1,2,3,4-tetrahydroisoquinolin-6-yl)-2-oxo-2, 3-dihydro-1H-benz o[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

To a mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (25 mg, 0.042 mmol, Step-3 of Example 218) and TEA (0.035 mL, 0.25 mmol) in dichloromethane (2 mL) is added acetic anhydride (0.012 mL, 0.13 mmol) at room temperature. The mixture is stirred at room temperature overnight. The mixture is quenched with saturated aqueous sodium bicarbonate, extracted with EtOAc. The organic layer is concentrated. The residue is purified by preparative LC-MS to give 8.3 mg (33% yield) of the title compound.

MS (ESI) m/z: 572.2 (M+H)⁺.

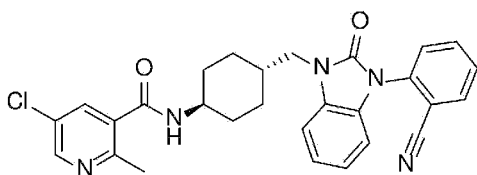
[0997] Representative procedure for Method U

The following preparation of Example 219 represents the Method U.

[0998] Example 219:

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.77]



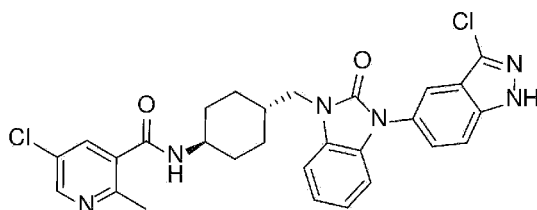
[0999] A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (25 mg, 0.063 mmol, Step-2 of Ex 9), 2-fluorobenzonitrile (11 mg, 0.094 mmol) and Cs₂CO₃ (41 mg, 0.125 mmol) in DMSO (1 mL) is stirred at 100 °C for 4 hr. The mixture is added water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The solvent is removed under vacuum, the crude product is purified by preparative LC-MS to give 7.9 mg (25% yield) of the title compound.

[1000] Example 222:

5-chloro-N-((1r,4r)-4-((3-(3-chloro- 1H-indazol-5-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.78]



[1001] <Step-1>: 5-bromo-3-chloro- 1-(tetrahydro-2H-pyran-2-yl)- 1H-indazole

The title compound is prepared in 84% yield (115 mg, colorless oil) by the similar manner to Step-1 of Example 210 using 5-bromo-3-chloro-1H-indazole (100 mg, 0.432 mmol) in place of 6-bromo-3-chloro-1H-indazole.

¹H -NMR (400 MHz, CDCl₃) delta 7.82 (1H, dd, J = 1.8, 0.9 Hz), 7.51 (1H, dd, J = 9.1, 1.8 Hz), 7.46 (1H, dd, J = 9.1, 0.9 Hz), 5.64 (1H, dd, J = 8.7, 2.7 Hz), 4.01-3.95 (1H, m), 3.76-3.68 (1H, m), 2.55-2.44 (1H, m), 2.20-2.02 (2H, m), 1.82-1.60 (3H, m).

[1002] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in 43% yield (32 mg, beige gum) by the similar manner to Step-2 of Example 210 using

5-bromo-3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (59 mg, 0.188 mmol) and N,N,N',N'-tetramethylethane-1, 2-diamine (0.066 mL, 0.439 mmol) in place of 6-bromo-3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole and N',N'-dimethylethane- 1,2-diamine, respectively.

¹H -NMR (400 MHz, CDCl₃) delta 8.49 (1H, d, J = 2.3 Hz), 7.84 (1H, d, J = 1.8 Hz), 7.73 (1H, d, J = 8.2 Hz), 7.63-7.58 (2H, m), 7.17 (1H, td, J = 7.5, 1.4 Hz), 7.12-7.02 (3H, m), 5.72 (1H, dd, J = 8.9, 2.5 Hz), 5.57 (1H, d, J = 8.2 Hz), 4.06-3.90 (2H, m), 3.84 (2H, d, J = 6.9 Hz), 3.80-3.70 (1H, m), 2.67-2.45 (4H, m), 2.22-2.08 (4H, m), 2.02-1.88 (3H, m), 1.83-1.63 (3H, m), 1.44-1.15 (4H, m).

MS (ESI) m/z: 631.3 (M-H)⁺.

[1003] <Step-3>:

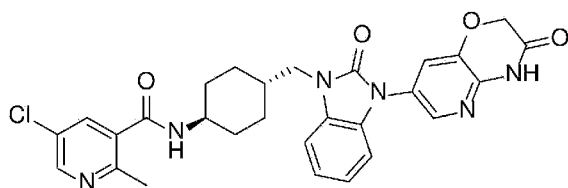
5-chloro-N-((1r,4r)-4-((3-(3-chloro-1H-indazol-5-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in 27% yield (3.5 mg) by the similar manner to Step-3 of Example 210 using the product of Step-2 of Example 222 in place of the product of Step-2 of Example 210.

[1004] Example 224:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.79]



[1005] <Step-1>:

7-bromo-4-((2-(trimethylsilyl)ethoxy)methyl)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one

A mixture of 7-bromo-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one (300 mg, 1.31 mmol), (2-(chloromethoxy)ethyl)trimethylsilane (0.279 mL, 1.57 mmol) and Cs_2CO_3 (854 mg, 2.62 mmol) in DMF (4 mL) is stirred at 70 °C for 2 hrs. After cooled to rt, the reaction mixture is diluted with EtOAc, washed with water, dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-100% EtOAc in n-hexane to give 215 mg (46%) of the title compound as a colorless oil.

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.12 (1H, d, $J = 2.1$ Hz), 7.41 (1H, d, $J = 2.1$ Hz), 5.56 (2H, s), 4.70 (2H, s), 3.72-3.67 (2H, m), 1.00-0.94 (2H, m), -0.02 (9H, s).

[1006] <Step-2>:

7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-((2-(trimethylsilyl)ethoxy)methyl)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one

A mixture of 7-bromo-4-((2-(trimethylsilyl)ethoxy)methyl)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one (100 mg, 0.278 mmol, Step-1 of Example 224), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (85 mg, 0.334 mmol), $\text{Pd}(\text{dppf})\text{Cl}_2\text{-DCM}$ adduct (23 mg, 0.028 mmol) and potassium acetate (82 mg, 0.835 mmol) in 1,4-dioxane (2 mL) is stirred at 120 °C for 20 min under microwave irradiation. The mixture is concentrated in vacuo. The residue is purified by column chromatography on silica-gel eluting with 0-33% EtOAc in n-hexane to give 99 mg (88% yield) of the title compound as yellow oil.

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.40 (1H, d, $J = 1.4$ Hz), 7.59 (1H, d, $J = 1.4$ Hz), 5.62 (2H, s), 4.66 (2H, s), 3.75-3.66 (2H, m), 1.34 (12H, s), 0.99-0.93 (2H, m), 0.02 (9H, s). MS (ESI) m/z : 407.4 ($\text{M}+\text{H}$) $^+$.

[1007] <Step-3>:

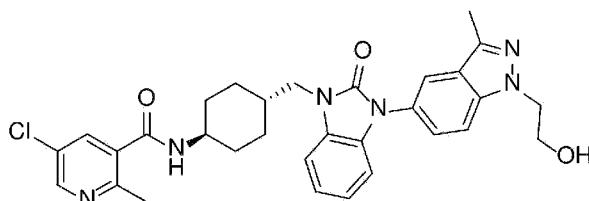
5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of 5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9),

7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-((2-(trimethylsilyl)ethoxy)methyl)-2-H-pyrido[3,2-b][1,4]oxazin-3(4H)-one (23 mg, 0.056 mmol, Step-2 of Example 224), copper(II) acetate (17 mg, 0.094 mmol) and TEA (0.016 mL, 0.113 mmol) in DMA (2 mL) is stirred at 100 °C for 2 hrs. To the mixture is added copper acetate (17 mg, 0.094 mmol) and TEA (0.016 mL, 0.113 mmol) and the mixture is stirred at 100 °C for 2 hrs. The mixture is filtered through celite pad. The filtrate is concentrated in vacuo. The residue is purified by column chromatography on silica-gel eluting with 0-66% EtOAc in n-hexane to give 14 mg of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-oxo-4-((2-(trimethylsilyl)ethoxy)methyl)-3,4-dihydro-2H-pyrido [3,2-b][1,4]oxazin-7-yl)-2,3-dihydro-1H-benzo [d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide. This is dissolved in DCM (1.5 mL). To the mixture is added TFA (0.5 mL) and the mixture is stirred at rt for 1.5 hrs. The mixture is concentrated. The residue is dissolved in DCM (3 mL). The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated and then purified by preparative LC-MS to give 3.3 mg (16 % yield) of the title compound. MS (ESI) m/z: 547.3 (M+H)⁺.

[1008] Example 230:

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.80]



[1009] <Step-1>:

5-chloro-N-((1r,4r)-4-((3-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in 92% yield (oil) by the similar manner to Step-3 of Intermediate-3 using

1-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-1H-benzo[d]imidazol-2(3H)-one (Intermediate- 116) in place of methyl

2-((2-oxo-2, 3-dihydro- 1H-benzo [d]imidazol- 1-yl)methyl)benzoate.

¹H -NMR (400 MHz, CDCl₃) delta 8.39 (1H, d, J = 2.3 Hz), 7.75 (1H, d, J = 1.4 Hz), 7.55 (1H, d, J = 2.3 Hz), 7.52 (1H, d, J = 8.2 Hz), 7.41 (1H, dd, J = 8.7, 1.8 Hz), 7.16 (1H, td, J = 7.5, 1.5 Hz), 7.10-7.04 (2H, m), 7.03-6.98 (1H, m), 6.36 (1H, d, J = 8.2 Hz), 4.56-4.51 (4H, m), 3.98 (2H, t, J = 5.5 Hz), 3.98-3.86 (1H, m), 3.81 (2H, d, J = 6.9 Hz), 3.22 (3H, s), 2.56 (3H, s), 2.53 (3H, s), 2.16-2.04 (2H, m), 2.01-1.82 (3H, m),

1.40-1.14 (4H, m)

MS (ESI) m/z: 617.1 (M+H)⁺.

[1010] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

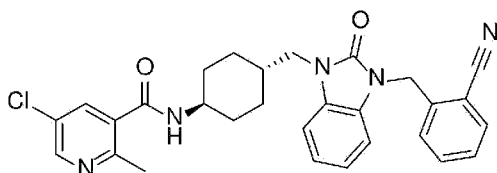
A mixture of

5-chloro-N-((1r,4r)-4-((3-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (30 mg, 0.049 mmol, Step-1 of Ex 230) in 4 M HCl/1,4-dioxane (1 mL) is stirred at rt for 1 hr. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative LC-MS to give 8.8 mg (32% yield) of the title compound.

[1011] Example 241:

5-chloro-N-((1r,4r)-4-((3-(2-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.81]



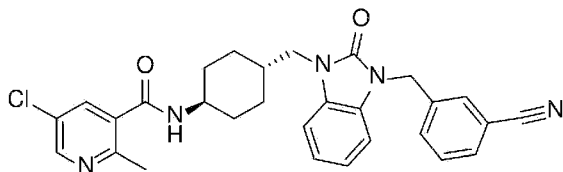
[1012] A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.050 mmol, Step-2 of Ex 9), 2-(bromomethyl)benzonitrile (11 mg, 0.055 mmol) and Cs₂CO₃ (33 mg, 0.10 mmol) in DMSO (1 mL) is stirred at 80 °C for 6 hr. The mixture is added water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The solvent is removed under vacuum, the crude product is purified by preparative LC-MS to give 7.6 mg (30% yield, solid) of the title compound.

[1013] Example 242:

5-chloro-N-((1r,4r)-4-((3-(3-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

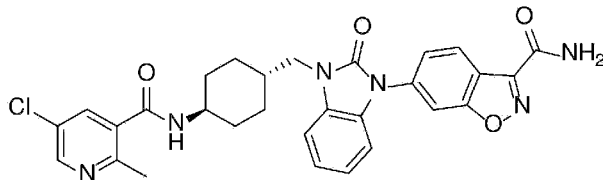
[Chem.82]



[1014] The title compound is prepared in 33% yield (solid) by the similar manner to Ex 241 using 3-(bromomethyl)benzonitrile in place of 2-(bromomethyl)benzonitrile.

[1015] Example 243:

6-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxamide
[Chem.83]



[1016] <Step-1>: methyl

6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d]isoxazole-3-carboxylate

The title compound is prepared in 54% yield (1.15 g, yellow solid) by the similar manner to Step-1 of Intermediate- 107 using methyl

6-bromobenzo[d]isoxazole-3-carboxylate (716 mg) in place of 6-bromo-3-methyl-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazole.

¹H -NMR (400 MHz, CDCl₃) delta 8.14-8.09 (2H, m), 7.84 (1H, d, J = 8.2 Hz), 4.10 (3H, s), 1.38 (12H, s).

MS (ESI) m/z: 304.3 (M+H)⁺.

[1017] <Step-2>: methyl

6-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxylate

A mixture of

5-chloro-2-methyl-N-(((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (137 mg, 0.345 mmol, Step-2 of Example 9), copper(II) acetate (125 mg, 0.689 mmol), TEA (0.096 mL, 0.69 mmol) and methyl

6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d]isoxazole-3-carboxylate (288 mg, 0.517 mmol, Step-1 of Example 243) in MeCN (3.4 mL) is stirred overnight at 60 °C. The reaction mixture is concentrated and the resultant residue is purified by column chromatography on silica-gel eluting with 24-100% EtOAc in n-hexane to give 80 mg (40% yield) of the title compound as a brown gum.

¹H -NMR (400 MHz, CDCl₃) delta 8.49 (1H, d, J = 2.5 Hz), 8.27 (1H, d, J = 8.7 Hz), 7.95 (1H, d, J = 1.8 Hz), 7.73 (1H, dd, J = 8.7, 1.8 Hz), 7.61 (1H, d, J = 2.5 Hz), 7.25-7.18 (2H, m), 7.17-7.07 (2H, m), 5.57 (1H, d, J = 7.8 Hz), 4.12 (3H, s), 4.02-3.90 (1H, m), 3.84 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.21-2.12 (2H, m), 1.99-1.87 (3H, m), 1.44-1.15 (4H, m).

MS (ESI) m/z: 574.4 (M+H)⁺.

[1018] <Step-3>:

6-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-

o-lH-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxamide

A mixture of methyl

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydr

o-lH-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxylate (10 mg, 0.017 mmol,

Step-2 of Example 243) and 2 M ammonia in MeOH (0.5 mL) is stirred overnight at rt.

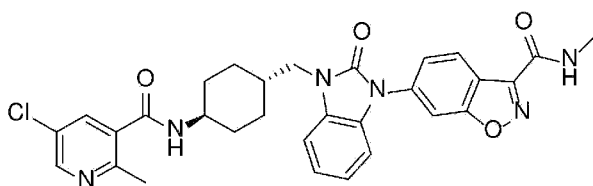
After the reaction mixture is concentrated, the resultant residue is purified by

preparative LC-MS to give 4.8 mg (51% yield) of the title compound.

[1019] Example 244:

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-lH-benzo[d]imidazol-1-yl)-N-methylbenzo[d]isoxazole-3-carboxamide

[Chem.84]

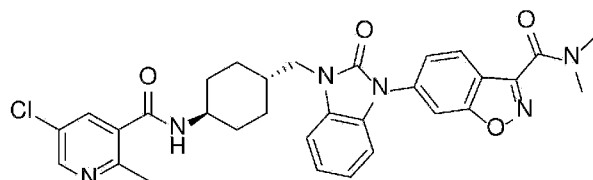


[1020] The title compound is prepared in 36% yield (3.5 mg) by the similar manner to Step-3 of Example 243 using 2 M methylamine in THF (0.5 mL) in place of 2 M ammonia in MeOH.

[1021] Example 245:

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-lH-benzo[d]imidazol-1-yl)-N,N-dimethylbenzo[d]isoxazole-3-carboxamide

[Chem.85]

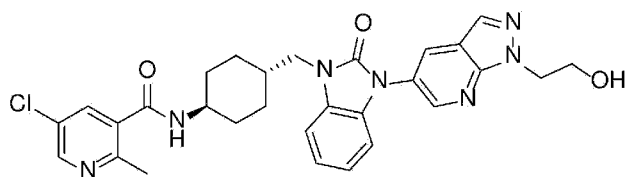


[1022] The title compound is prepared in 54% yield (5.4 mg) by the similar manner to Step-3 of Example 243 using 2 M dimethylamine in THF (0.5 mL) in place of 2 M ammonia in MeOH.

[1023] Example 253:

5-chloro-N-(((1r,4r)-4-((3-(1-(2-hydroxyethyl)-lH-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-lH-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.86]



[1024] <Step-1>:

5-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-pyrazolo[3,4-b]pyridine

A mixture of 5-bromo-1H-pyrazolo[3,4-b]pyridine (100 mg, 0.505 mmol), (2-bromoethoxy)(tert-butyl)dimethylsilane (0.119 mL, 0.555 mmol) and Cs_2CO_3 (411 mg, 1.26 mmol) in DMF (2 mL) is stirred at rt overnight. The reaction mixture is diluted with EtOAc, washed with water, dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-25% EtOAc in n-hexane to give 119 mg (66%) of the title compound as a colorless oil.

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.55 (1H, d, $J = 2.1$ Hz), 8.17 (1H, d, $J = 2.1$ Hz), 7.96 (1H, s), 4.63 (2H, t, $J = 5.7$ Hz), 4.08 (2H, t, $J = 5.7$ Hz), 0.73 (9H, s), -0.15 (6H, s).

[1025] <Step-2>:

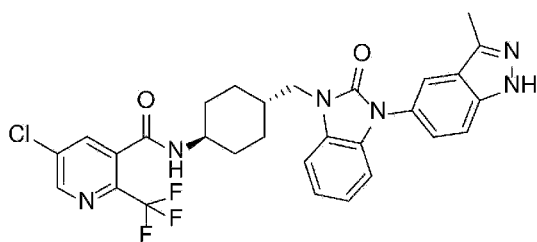
5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.050 mmol, Step-2 of Example 9), 5-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-pyrazolo[3,4-b]pyridine (36 mg, 0.100 mmol, Step-1 of Example 253), $\text{N}^{\wedge}\text{NP}$ -dimethylethane-1,2-diamine (0.030 mL, 0.276 mmol), Cs_2CO_3 (65 mg, 0.201 mmol) and CuI (24 mg, 0.125 mmol) in DMA (1.5 mL) is stirred at 100 °C for 2 hrs. The mixture is poured into 28% aqueous ammonia solution (3 mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-90% EtOAc in n-hexane to give 32 mg of N-((1r,4r)-4-((3-(1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide. This is dissolved in DCM (1.5 mL). To the mixture is added TFA (0.5 mL) and the mixture is stirred at rt for 0.5 hrs. The mixture is concentrated. The residue is dissolved in DCM (5 mL). The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated and then purified by preparative LC-MS to give 9.0 mg (32% yield) of the title compound.

[1026] Example 260:

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

[Chem.87]



[1027] <Step-1>:

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

A mixture of Intermediate- 132 (32 mg, 0.071 mmol), 5-bromo-3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (31 mg, 0.11 mmol), CuI (27 mg, 0.14 mmol), DMEDA (13 mg, 0.14 mmol) and Cs₂CO₃ (45 mg, 0.21 mmol) in DMA (1 mL) is stirred at 130 °C for 6 hrs under N₂ condition. To the mixture is added water, extracted with EtOAc and passed through sodium sulfate/amino-functional silica gel. The solvent is removed under vacuum, the title compound is obtained as a crude solid. The title compound is used next step without further purification.

MS (ESI) m/z: 667.5 (M+H)⁺.

[1028] <Step-2>:

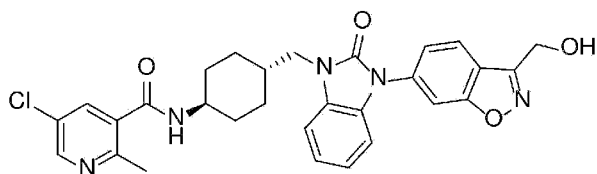
5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

A mixture of 5-chloro-N-((1r,4r)-4-((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide (Step-1 of Ex 260) is added DCM/TFA = 1/1 (1 mL) and stirred at rt for 2 hrs. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative LC-MS to give 6.0 mg (15% yield, total: 2 steps) of the title compound.

[1029] Example 261:

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.88]



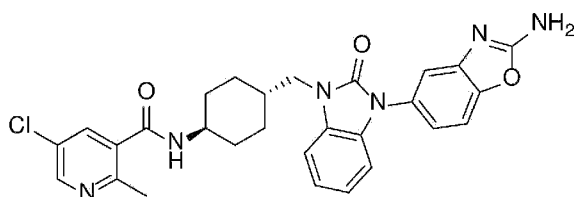
[1030] A mixture of methyl

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)-2-methylnicotinamide

o-1H-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxylate (40 mg, 0.070 mmol, Step-2 of Example 243), sodium borohydride (42 mg, 1.11 mmol) and lithium chloride (71 mg, 1.67 mmol) in THF is stirred for 4 hrs at rt. The reaction mixture is added with saturated aqueous ammonium chloride. The resultant mixture is extracted with EtOAc and concentrated. The resultant residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage). The residue is purified by preparative LC-MS to give 5.1 mg (13% yield) of the title compound.

[1031] Example 263:

N-((1r,4r)-4-((3-(2-aminobenzo[d]oxazol-5-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.89]



[1032] <Step- 1>: 5-bromo-N-(2,4-dimethoxybenzyl)benzo [d]oxazol-2-amine

To a stirred solution of 5-bromo-2-chlorobenzo[d]oxazole (50 mg, 0.215 mmol) in THF (1 mL) are added (2,4-dimethoxyphenyl)methanamine (72 mg, 0.430 mmol) and TEA (0.090 mL, 0.645 mmol) at rt and stirred for 1 hr. The reaction mixture is diluted with water, extracted with EtOAc. The organic phase is dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-50% EtOAc in n-hexane to give 30 mg (38%) of the title compound as an ivory solid.

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 7.46 (1H, d, $J = 1.8$ Hz), 7.26 (1H, d, $J = 8.2$ Hz), 7.12 (1H, dd, $J = 8.2, 1.8$ Hz), 7.07 (1H, d, $J = 8.2$ Hz), 6.48 (1H, d, $J = 2.3$ Hz), 6.44 (1H, dd, $J = 8.2, 2.3$ Hz), 5.46 (1H, t, $J = 5.9$ Hz), 4.56 (2H, d, $J = 5.9$ Hz), 3.85 (3H, s), 3.80 (3H, s).

[1033] <Step-2>: N-

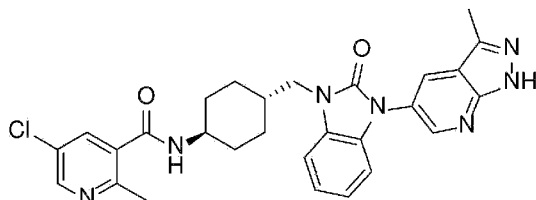
((1r,4r)-4-((3-(2-aminobenzo[d]oxazol-5-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (40 mg, 0.100 mmol, Step-2 of Example 9), 5-bromo-N-(2,4-dimethoxybenzyl)benzo[d]oxazol-2-amine (44 mg, 0.120 mmol, Step-1 of Example 263), NhNP-dimethylethane-1, 2-diamine (0.060 mL, 0.552 mmol), Cs_2CO_3 (131 mg, 0.402 mmol) and CuI (48 mg, 0.250 mmol) in DMA (1.5 mL) is stirred at 110 °C for 21 hrs. The mixture is poured into 28% aqueous ammonia solution (5

mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on amino-functional silica gel eluting with 0-90% EtOAc in n-hexane to give 14 mg of 5-chloro-N-((1r,4r)-4-((3-(2-((2,4-dimethoxybenzyl)amino)benzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide. This is dissolved in DCM (1.5 mL). To the mixture is added TFA (1.5mL) and the mixture is stirred at 45 °C for 1.5 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 4.1 mg (38% yield) of the title compound.

[1034] Example 271:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.90]

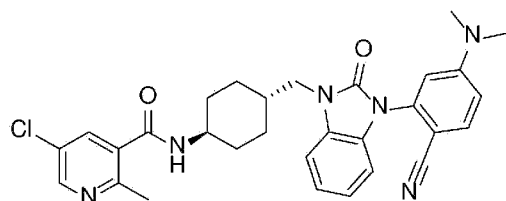


[1035] The title compound is prepared in 21% yield in 2 steps by the similar manner to Step-1 and Step-2 of Example 260 using

5-bromo-3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine and 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (Step-2 of Example 9) in place of 5-bromo-3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole and 5-chloro-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide.

[1036] Example 273:

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.91]

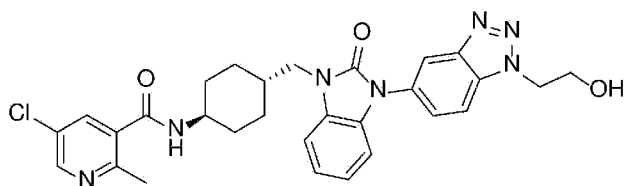


[1037] A solution of Ex 307 (30 mg, 0.052 mmol), dimethylamine hydrochloride (8.5 mg, 0.10 mmol), Pd₂(dba)₃ (2.4 mg, 0.0026 mmol), Xantphos (1.5 mg, 0.0026 mmol) and

Cs_2CO_3 (51 mg, 0.16 mmol) in 1,4-dioxane (1 mL) is stirred at 100 °C for 12 hrs. To the mixture is added water, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed under vacuum, the crude product is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.6 mg (13% yield) of the title compound.

[1038] Example 276:

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.92]



[1039] <Step-1>:

5-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-benzo[d][1,2,3]triazole

Sodium hydride (60%, dispersion in mineral oil) (45 mg, 1.14 mmol) and (2-bromoethoxy)(tert-butyl)dimethylsilane (0.243 mL, 1.14 mmol) is added to the solution of 5-bromo-1H-benzo[d][1,2,3]triazole (150 mg, 0.757 mmol) in DMF at 0 °C. After that the reaction mixture is warmed up to 60 °C and stirred overnight at the same temperature. The reaction mixture is added with saturated aqueous ammonium chloride. The resultant mixture is extracted with DCM and concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 8-50% EtOAc in n-hexane to give 79 mg (29% yield) of the title compound as a pale yellow gum.

¹H-NMR (400 MHz, CDCl_3) δ 8.04 (1H, d, J = 1.8 Hz), 7.74 (1H, d, J = 9.4 Hz), 7.45 (1H, dd, J = 9.4, 1.8 Hz), 4.80 (2H, t, J = 5.7 Hz), 4.25 (2H, t, J = 5.7 Hz), 0.77 (9H, s), -0.09 (6H, s).

MS (ESI) m/z: 356.4 (M+H)⁺.

[1040] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

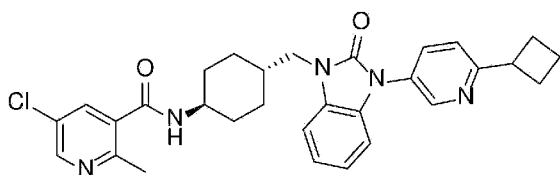
A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9), 5-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-benzo[d][1,2,3]triazole (20 mg, 0.056 mmol, Step-1 of Example 276), NhNP-dimethylethane-1,2-diamine (0.022 mL, 0.207 mmol), Cs_2CO_3 (49 mg, 0.150 mmol) and CuI (18 mg, 0.094 mmol) in DMA

(1.5 mL) is stirred at 100 °C for 4.5 hrs. The mixture is poured into 28% aqueous ammonia solution (3 mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.2 mg (10% yield) of the title compound.

[1041] Example 279:

5-chloro-N-((1*r*,4*r*)-4-((3-(6-cyclobutylpyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.93]

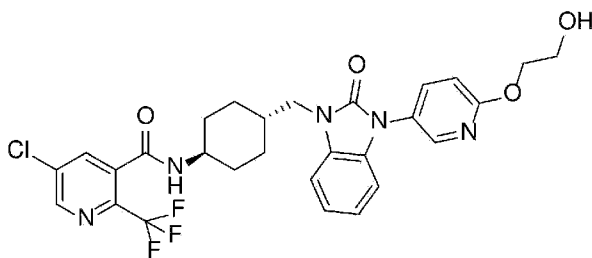


[1042] A mixture of N-

((1*r*,4*r*)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (30 mg, 0.054 mmol, Example 66), bromocyclobutane (37 mg, 0.27 mmol), nickel(II) chloride ethylene glycol dimethyl ether complex (1.2 mg, 0.0054 mmol), Ir[dF(CF₃)ppy]2(dtbbpy)PF₆ (0.6 mg, 0.00054 mmol), 4,4'-di-*tert*-butyl-2,2'-bipyridine (1.5 mg, 0.0054 mmol), tris(trimethylsilyl)silane (40 mg, 0.16 mmol), and 2,6-lutidine (12 mg, 0.11 mmol) in DME (0.3 mL) is stirred under blue LED irradiation for 3 days. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.4 mg (8% yield) of the title compound.

[1043] Example 301:

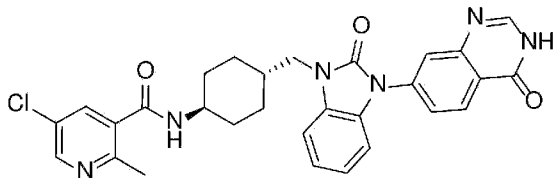
5-chloro-N-((1*r*,4*r*)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide
[Chem.94]



[1044] The title compound is prepared in 25% yield in 2 steps by the similar manner to Step-1 and Step-2 of Example 50 using Mesylate-3 in place of Mesylate-1.

[1045] Example 305:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(4-oxo-3,4-dihydroquinazolin-7-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.95]



[1046] <Step-1>: 7-bromo-4-((4-methoxybenzyl)oxy)quinazoline

A mixture of 7-bromoquinazolin-4-ol (100 mg, 0.444 mmol), Cs₂CO₃ (434 mg, 1.33 mmol) and 1-(chloromethyl)-4-methoxybenzene (0.073 mL, 0.533 mmol) in THF (2 mL) is stirred at rt overnight. To the reaction mixture are added Cs₂CO₃ (200 mg, 0.614 mmol) and 1-(chloromethyl)-4-methoxybenzene (0.073 mL, 0.533 mmol) and stirred at rt for 2 hrs. The reaction mixture is diluted with EtOAc and water, then the resultant mixture is extracted with EtOAc. The organic phase is washed with brine, dried over MgSO₄, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-50% EtOAc in n-hexane to give 145 mg (95%) of the title compound as a white solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.17 (1H, d, J = 8.2 Hz), 8.09 (1H, s), 7.87 (1H, d, J = 1.8 Hz), 7.60 (1H, dd, J = 8.2, 1.8 Hz), 7.30 (2H, d, J = 8.7 Hz), 6.88 (2H, d, J = 8.7 Hz), 5.11 (2H, s), 3.79 (3H, s).

MS (ESI) m/z: 345.3 (M+H)⁺.

[1047] <Step-2>:

5-chloro-N-((1*r*,4*r*)-4-((3-(4-((4-methoxybenzyl)oxy)quinazolin-7-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in quantitative yield (50 mg, yellow gum) by the similar manner to Step-2 of Example 210 using

7-bromo-4-((4-methoxybenzyl)oxy)quinazoline (39 mg, 0.113 mmol, Step-1 of Example 305) in place of

6-bromo-3-chloro-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazole.

¹H-NMR (400 MHz, CDCl₃) delta 8.50-8.44 (2H, m), 8.14 (1H, s), 7.93 (1H, d, J = 2.3 Hz), 7.80 (1H, dd, J = 8.7, 2.3 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.33 (2H, d, J = 8.7 Hz), 7.28-7.23 (1H, m), 7.22-7.16 (1H, m), 7.14-7.04 (2H, m), 6.90 (2H, d, J = 8.7 Hz), 5.58 (1H, d, J = 8.2 Hz), 5.16 (2H, s), 4.02-3.88 (1H, m), 3.83 (2H, d, J = 6.9 Hz), 3.80 (3H, s), 2.61 (3H, s), 2.20-2.10 (2H, m), 2.03-1.82 (3H, m), 1.41-1.15 (4H, m).

MS (ESI) m/z: 633.7 (M+H)⁺.

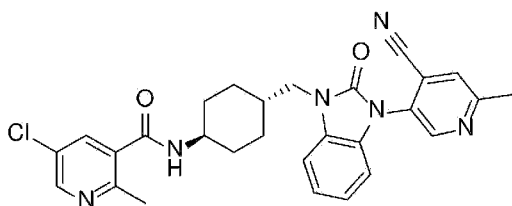
[1048] <Step-3>:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(4-oxo-3,4-dihydroquinazolin-7-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

TFA (1 mL) is added to the product of Step-2 of Example 305 (50 mg, 0.075 mmol) and refluxed for 1.5 hrs. After cooled to rt, the mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 4.6 mg (11% yield) of the title compound.

[1049] Example 308:

5-chloro-N-((1*r*,4*r*)-4-((3-(4-cyano-6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.96]



[1050] <Step-1>: N-

((1*r*,4*r*)-4-((3-(6-bromo-4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound is prepared in 91% yield (132 mg, solid) by the similar manner to Ex 219 using 2-bromo-5-fluoroisonicotinonitrile (66 mg, 0.33 mmol) in place of 2-fluorobenzonitrile.

¹H-NMR (400 MHz, CDCl₃) δ 8.70 (1H, s), 8.48 (1H, d, J = 2.3 Hz), 7.94 (1H, s), 7.60 (1H, d, J = 2.3 Hz), 7.24 (1H, dd, J = 7.8, 1.4 Hz), 7.18-7.08 (2H, m), 6.94 (1H, d, J = 7.3 Hz), 5.70 (1H, d, J = 7.8 Hz), 4.02-3.89 (1H, m), 3.84 (2H, br), 2.60 (3H, s), 2.22-2.08 (2H, m), 2.02-1.83 (3H, m), 1.42-1.15 (4H, m)

MS (ESI) m/z: 581.1 (M+H)⁺.

[1051] <Step-2>:

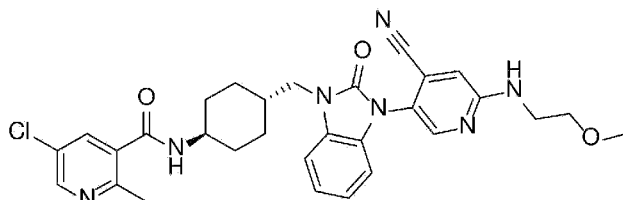
5-chloro-N-((1*r*,4*r*)-4-((3-(4-cyano-6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of N-((1*r*,4*r*)-4-((3-(6-bromo-4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (30 mg, 0.052 mmol, Step-1 of Ex 308), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (10 mg, 0.078 mmol), Pd(PPh₃)₄ (12 mg, 0.010 mmol), K₂CO₃ (14 mg, 0.103 mmol) in 1,4-dioxane/H₂O = 2/1 (3 mL) is stirred at 100 °C overnight. The mixture is added water, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed under vacuum, the crude product is purified by a strong anion exchange cartridge

(ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.8 mg (11% yield) of the title compound.

[1052] Example 310:

5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.97]

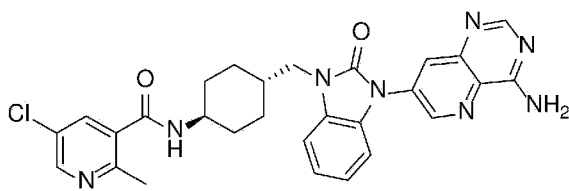


[1053] A mixture of N-

((1r,4r)-4-((3-(6-bromo-4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (30 mg, 0.052 mmol, Step-1 of Ex 308), 2-methoxyethanamine (19 mg, 0.26 mmol), $\text{Pd}_2(\text{dba})_3$ (9.5 mg, 0.010 mmol), Xantphos (6.0 mg, 0.010 mmol) and Cs_2CO_3 (34 mg, 0.10 mmol) in 1,4-dioxane (2 mL) is stirred at 100 °C overnight. The solvent is removed under vacuum, the crude product is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.0 mg (6.7% yield) of the title compound.

[1054] Example 319:

N-((1r,4r)-4-((3-(4-aminopyrido[3,2-d]pyrimidin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.98]



[1055] <Step-1>: 7-bromo-N-(2,4-dimethoxybenzyl)pyrido[3,2-d]pyrimidin-4-amine

A mixture of 7-bromo-4-chloropyrido[3,2-d]pyrimidine (100 mg, 0.409 mmol), (2,4-dimethoxyphenyl)methanamine (103 mg, 0.614 mmol) and K_2CO_3 (170 mg, 1.23 mmol) in DMF (2 mL) is stirred at rt for 2 hrs. The reaction mixture is diluted with EtOAc and water. Insoluble material, which is the title compound, is collected by filtration. Then the filtrate is washed with water and brine, dried over MgSO_4 , filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 5-100% EtOAc in n-hexane to give the title compound as a white solid (66 mg, 43% combined yield).

¹H -NMR (400 MHz, CDCl₃) delta 8.66 (1H, d, J = 2.3 Hz), 8.63 (1H, s), 8.23 (1H, d, J = 1.8 Hz), 7.49 (1H, br s), 7.30 (1H, d, J = 8.2 Hz), 6.50 (1H, d, J = 2.3 Hz), 6.45 (1H, dd, J = 8.2, 2.3 Hz), 4.78 (2H, d, J = 5.9 Hz), 3.88 (3H, s), 3.80 (3H, s).

[1056] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(4-((2,4-dimethoxybenzyl)amino)pyrido[3,2-d]pyrimidin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in 62% yield (30 mg, beige solid) by the similar manner to Step-2 of Example 210 using

7-bromo-N-(2,4-dimethoxybenzyl)pyrido[3,2-d]pyrimidin-4-amine (40 mg, 0.105 mmol), which is the product of Step-1 of Example 319, in place of

6-bromo-3-chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole. In addition, this reaction is carried out at 150°C.

MS (ESI) m/z: 693.7 (M+H)⁺.

[1057] <Step-3>: N-

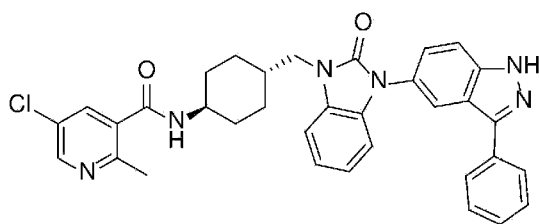
((1r,4r)-4-((3-(4-aminopyrido[3,2-d]pyrimidin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound is prepared in 23% yield (5.5 mg) by the similar manner to Step-3 of Example 305 using the product of Step-2 of Example 319 (30 mg, 0.043 mmol) in place of the product of Step-2 of Example 305.

[1058] Example 348:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-phenyl-1H-indazol-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.99]



[1059] <Step-1>: 5-bromo-3-phenyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole

A mixture of 5-bromo-3-phenyl-1H-indazole (50 mg, 0.18 mmol), 3,4-dihydro-2H-pyran (0.025 mL, 0.28 mmol) and p-toluenesulfonic acid (3 mg, 0.02 mmol) in toluene (1 mL) is stirred for 8 hrs at 80 °C. The reaction mixture is purified by column chromatography on silica-gel eluting with 4-33% EtOAc in n-hexane to give 64 mg (98% yield) of the title compound as a pale yellow gum.

¹H -NMR (400 MHz, CDCl₃) delta 8.13 (1H, d, J = 1.4 Hz), 7.95-7.88 (2H, m), 7.58-7.45 (4H, m), 7.45-7.38 (1H, m), 5.76 (1H, dd, J = 9.1, 2.7 Hz), 4.10-3.99 (1H, m), 3.82-3.70 (1H, m), 2.70-2.53 (1H, m), 2.27-2.08 (2H, m), 1.88-1.60 (3H, m).

MS (ESI) m/z: 357.2 (M+H)⁺.

[1060] <Step-2>:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(3-phenyl-1*H*-indazol-5-yl)-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9),

5-bromo-3-phenyl-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazole (16 mg, 0.045 mmol, Step-1 of Example 348), N,N'-dimethylethane-1, 2-diamine (0.022 mL, 0.207 mmol),

Cs₂CO₃ (49 mg, 0.150 mmol) and CuI (18 mg, 0.094 mmol) in DMA (1.5 mL) is

stirred at 120 °C for 1.5 hrs. The mixture is poured into 28% aqueous ammonia solution (3 mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 12 mg of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-3-(3-phenyl-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazol-5-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide.

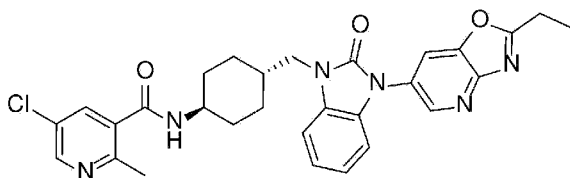
This is dissolved in DCM (1 mL). To the mixture is added TFA (1 mL) and the mixture is stirred at rt for 1.5 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 8.8 mg (40% yield) of the title compound.

MS (ESI) m/z: 591.5 (M+H)⁺.

[1061] Example 355:

5-chloro-N-((1*r*,4*r*)-4-((3-(2-ethyloxazolo[4,5-*b*]pyridin-6-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.100]



[1062] <Step-1>: 5-bromo-N-(4-methoxybenzyl)-3-((4-methoxybenzyl)oxy)pyridin-2-amine

A mixture of 2-amino-5-bromopyridin-3-ol (200 mg, 1.058 mmol), 1-(chloromethyl)-4-methoxybenzene (365 mg, 2.328 mmol) and potassium carbonate (731 mg, 5.29 mmol) in THF (3 mL) is stirred at rt for 3 days. The mixture is stirred at 50 °C for 1 hr. The reaction mixture is poured into water and extracted EtOAc. The organic layer is washed with brine, dried over sodium sulfate, filtered and con-

centrated. The residue is purified by column chromatography on silica-gel eluting with 0-60% EtOAc in n-hexane to give 82 mg (18% yield) of the title compound.

MS (ESI) m/z: 429.3, 431.2 (M+H)⁺.

[1063] <Step-2>:

5-chloro-N-((1r,4r)-4-((3-(6-((4-methoxybenzyl)amino)-5-((4-methoxybenzyl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (55 mg, 0.138 mmol, Step-2 of Example 9), 5-bromo-N-(4-methoxybenzyl)-3-((4-methoxybenzyl)oxy)pyridin-2-amine (77 mg, 0.179 mmol, Step-1 of Example 355), NhNP-dimethylethane-1, 2-diamine (0.037 mL, 0.345 mmol), Cs₂CO₃ (180 mg, 0.552 mmol) and CuI (53 mg, 0.276 mmol) in DMA (1 mL) is stirred at 100 °C for 15 hrs. The mixture is poured into 28% aqueous ammonia solution, extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-90% EtOAc in n-hexane to give 90 mg (87% yield, pale yellow gum) of the title compound.

¹H -NMR (400 MHz, CDCl₃) delta 8.49 (1H, d, J = 2.3 Hz), 7.91 (1H, d, J = 1.8 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.35-7.24 (4H, m), 7.19-6.97 (5H, m), 6.93-6.84 (4H, m), 5.56 (1H, d, J = 7.8 Hz), 5.34 (1H, t, J = 6.0 Hz), 4.99 (2H, s), 4.64 (2H, d, J = 6.0 Hz), 4.01-3.91 (1H, m), 3.85-3.78 (2H, m), 3.82 (3H, s), 3.80 (3H, s), 2.61 (3H, s), 2.21-2.13 (2H, m), 2.01-1.88 (3H, m), 1.41-1.15 (4H, m). MS (ESI) m/z: 747.7 (M+H)⁺.

[1064] <Step-3>: N-

((1r,4r)-4-((3-(6-amino-5-hydroxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of

5-chloro-N-((1r,4r)-4-((3-(6-((4-methoxybenzyl)amino)-5-((4-methoxybenzyl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (90 mg, 0.120 mmol, Step-2 of Example 355) is dissolved in DCM (0.5 mL). To the mixture is added TFA (1.0 mL) and the mixture is stirred at rt for 3 hrs. The reaction mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 50 mg (82 % yield) of the title compound.

¹H -NMR (400 MHz, DMSO-d₆) delta 9.93 (1H, br s), 8.53 (1H, d, J = 2.3 Hz), 8.39 (1H, d, J = 8.2 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.56 (1H, d, J = 2.3 Hz), 7.29 (1H, d, J = 7.8 Hz), 7.10 (1H, td, J = 7.8, 0.9 Hz), 7.03 (1H, td, J = 7.8, 0.9 Hz), 6.94-6.89 (2H,

m), 5.80 (2H, s), 3.78-3.65 (1H, m), 3.75 (2H, d, J = 6.8 Hz), 1.97-1.68 (5H, m), 1.31-1.14 (4H, m). MS (ESI) m/z: 507.4 (M+H)⁺.

[1065] <Step-4>:

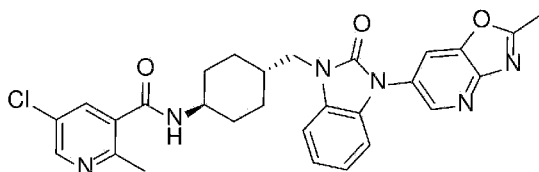
5-chloro-N-((1r,4r)-4-((3-(2-ethyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of N-((1r,4r)-4-((3-(6-amino-5-hydroxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (15 mg, 0.030 mmol, Step-3 of Example 355) and 4-methylbenzenesulfonic acid hydrate (0.6 mg, 0.003 mmol) in 1,1,1-trimethoxypropane (0.5 mL) is stirred at 120 °C for 0.5 hr under microwave irradiation. The mixture is poured into water, extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by preparative LC-MS to give 3.2 mg (20% yield) of the title compound.

[1066] Example 356:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.101]

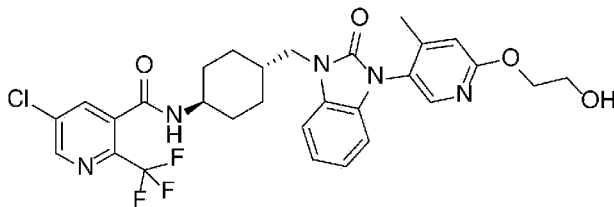


[1067] The title compound is prepared in 26% yield (4.0 mg) by the similar manner to Step-4 of Example 355 using 1,1,1-trimethoxyethane in place of 1,1,1-trimethoxypropane.

[1068] Example 357:

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

[Chem.102]



[1069] <Step-1>:

1-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

A mixture of 1-(6-fluoro-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (80 mg, 0.33 mmol, Step-3 of Intermediate- 192), 2-((tetrahydro-2H-pyran-2-yl)oxy)ethanol (0.134 mL, 0.987 mmol) and potassium tert-butoxide (111 mg, 0.987 mmol) in DMF (1 mL) is stirred for 2 hrs at rt. The reaction

mixture is added with saturated aqueous ammonium chloride. The resultant mixture is extracted with EtOAc. The organic layer is dried over MgSO_4 , filtered and concentrated in vacuo. The resultant residue is purified by column chromatography on silica-gel eluting with 12-100% EtOAc in n-hexane to give 64 mg (69% yield) of the title compound as a pale brown gum.

MS (ESI) m/z: 286.3 (M+H)⁺.

[1070] <Step-2>: tert-butyl

3-(6-(2-((tert-butoxycarbonyl)oxy)ethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate

A mixture of 1-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (64 mg, 0.23 mmol, Step-1 of Example 357), di-tert-butyl dicarbonate (0.465 mL, 2.03 mmol) and potassium tert-butoxide (228 mg, 2.03 mmol) in DMF (1 mL) is stirred for 2 hrs at rt. The reaction mixture is added with saturated aqueous ammonium chloride. The resultant mixture is extracted with EtOAc and the organic layer is concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 4-50% EtOAc in n-hexane to give 35 mg (32% yield) of the title compound as a pale yellow gum.

¹H-NMR (400 MHz, CDCl_3) δ 8.04 (1H, s), 7.90 (1H, dd, J = 7.1, 2.1 Hz), 7.21-7.09 (2H, m), 6.81 (1H, s), 6.67-6.59 (1H, m), 4.64-4.51 (2H, m), 4.46-4.39 (2H, m), 2.13 (3H, s), 1.69 (9H, s), 1.51 (9H, s).

MS (ESI) m/z: 486.5 (M+H)⁺.

[1071] <Step-3>: tert-butyl

2-((5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-4-methylpyridin-2-yl)oxy)ethyl) carbonate

A mixture of ((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate (20 mg, 0.056 mmol, Mesylate-3), tert-butyl 3-(6-(2-((tert-butoxycarbonyl)oxy)ethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-1-carboxylate (11 mg, 0.028 mmol, Step-2 of Example 357) and cesium carbonate (23 mg, 0.069 mmol) in DMSO (1 mL) is stirred overnight at 100 °C. The reaction mixture is added with water. The resultant mixture is extracted with EtOAc and the organic layer is concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 12-100% EtOAc in n-hexane to give 15 mg (61% yield) of the title compound as a pale yellow gum.

MS (ESI) m/z: 704.5 (M+H)⁺.

[1072] <Step-4>:

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihy

dro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide
tert-butyl

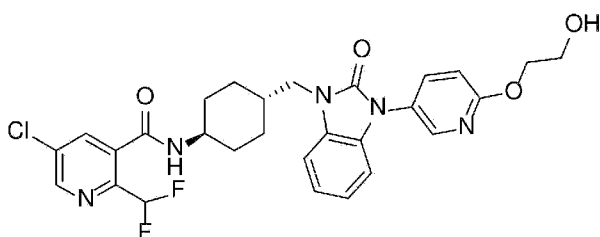
(2-((5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-4-methylpyridin-2-yl)oxy)ethyl)

carbonate (15 mg, 0.022 mmol, Step-3 of Example 357) in TFA (1 mL) is stirred for 1 hr at rt. After the reaction mixture is concentrated, the resultant residue is purified by preparative LC-MS to give 8.3 mg (62% yield) of the title compound.

[1073] Example 365:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.103]



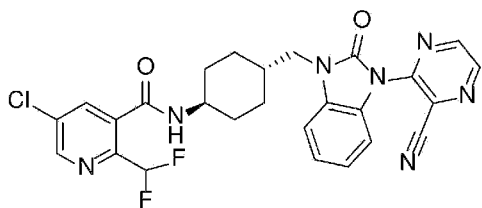
[1074] The title compound is prepared in 30% yield (8.7 mg) by the similar manner to Example 69 using Mesylate-4 (20 mg, 0.050 mmol) and Intermediate-24 (18 mg, 0.050 mmol) in place of Mesylate- 1 and

1-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one.

[1075] Example 369:

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide

[Chem.104]



[1076] A mixture of

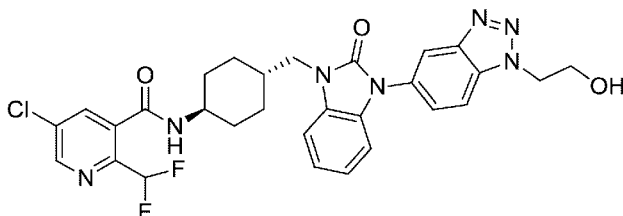
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (25 mg, 0.057 mmol, Intermediate-l65), 3-chloropyrazine-2-carbonitrile (12 mg, 0.086 mmol), and Cs₂CO₃ (56 mg, 0.17 mmol) in DMSO (0.5 mL) is stirred at rt for 3 hrs. The mixture is diluted with water and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by preparative SFC-MS to give 2.6 mg (8% yield) of

the title compound.

[1077] Example 385:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3] triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.105]



[1078] A mixture of

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.034 mmol, Intermediate-l65), 5-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-benzo[d][1,2,3]triazole (15 mg, 0.041 mmol, Step-1 of Example 276), NhNP-dimethylethane-1,2-diamine (0.020 mL, 0.190 mmol), Cs₂CO₃ (45 mg, 0.138 mmol) and CuI (16 mg, 0.086 mmol) in DMA (1.5 mL) is stirred at 100 °C for 15 hrs. The mixture is poured into 28% aqueous ammonia solution (3 mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to remove impurity and then purified by preparative LC-MS to give 4.0 mg (19.47% yield) of the title compound.

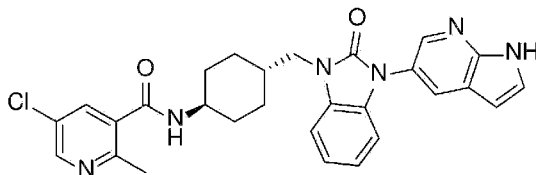
[1079] Representative procedure for Method V

The following preparation of Example 408 represents the Method V.

[1080] Example 408:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.106]



[1081] <Step-1>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 64% yield (24 mg) by the similar manner to Step-3 of Intermediate-3 using

1-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-benzodimidazol-2(3H)-one (21 mg, 0.055 mmol, Intermediate- 185) in place of methyl 2-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol- 1-yl)methyl)benzoate.

MS (ESI) m/z: 645.1 (M+H)⁺.

[1082] <Step-2>:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

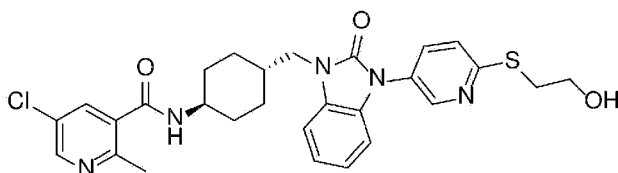
To a solution of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (24 mg, 0.047 mmol, Step-1 of Example 408) in dichloromethane (0.5 mL) is added TFA (1.5 mL). The mixture is stirred at room temperature for 3 hrs. The mixture is concentrated. The residue in 28% aqueous ammonia solution (0.5 mL) and 2 M ammonia in methanol (1.5 mL) is stirred at room temperature overnight. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3 mg (11% yield) of the title compound.

[1083] Example 412:

5-chloro-N-((1r, 4r)-4-((3-(6-((2-hydroxyethyl)thio)pyridin-3-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.107]



[1084] A mixture of Intermediate- 54 (53 mg, 0.11 mmol), 2-mercaptoethanol (25 mg, 0.32 mmol) and Cs₂CO₃ (105 mg, 0.32 mmol) in DMSO (1 mL) is stirred at 50 °C for 2 hrs. To the mixture is added water, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed under vacuum, the crude product is purified by preparative SFC-MS to give 6.7 mg (11% yield) of the title compound.

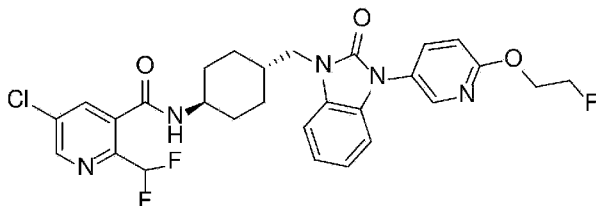
[1085] Representative procedure for Method W

The following preparation of Example 432 represents the Method W.

[1086] Example 432:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-fluoroethoxy)pyridin-3-yl)-2-oxo-

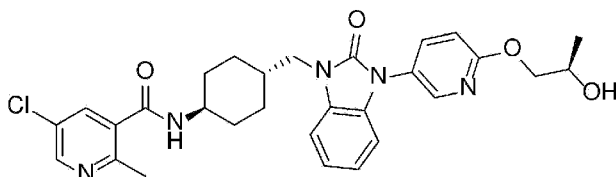
2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.108]



[1087] To a mixture of Intermediate- 191 (15 mg, 0.028 mmol), 2-fluoroethanol (5.4 mg, 0.085 mmol) in DMF (1 mL) is added potassium tert-butoxide (9.5 mg, 0.085 mmol) and stirred at rt overnight. To the mixture is added water, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed under vacuum, the crude product is purified by preparative SFC-MS to give 9.9 mg (61% yield) of the title compound.

[1088] Example 438:

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide
[Chem.109]



[1089] <Step-1>:

(R)-1-(6-(2-(methoxymethoxy)propoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 57% yield (43 mg) by the similar manner to Intermediate- 183 using (R)-2-(methoxymethoxy)propan-1-ol (52 mg, 0.44 mmol) in place of 2-methoxyethanol.

MS (ESI) m/z: 329.9 (M+H)⁺.

[1090] <Step-2>:

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-(methoxymethoxy)propoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

The title compound is prepared in quantitative yield (23 mg) by the similar manner to Step-3 of Intermediate-3 using

(R)-1-(6-(2-(methoxymethoxy)propoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (14 mg, 0.042 mmol, Step-1 of Example 438) in place of methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate.

MS (ESI) m/z: 594.1 (M+H)⁺.

[1091] <Step-3>:

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-

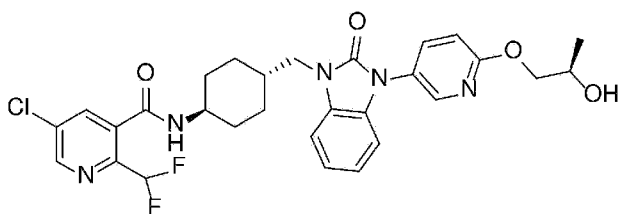
1H-benzo [d]imidazol- 1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-(methoxymethoxy)propoxy)pyridin-3-yl)-2-oxo-2,3-dihydro- 1H-benzo [d]imidazol- 1-yl)methyl)cyclohexyl)-2-methylnicotinamide (23 mg, 0.042 mmol, Step-2 of Example 438) and TFA (1 mL) is stirred at room temperature for 2 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative SFC-MS to give 3.4 mg (32% yield) of the title compound.

[1092] Example 439:

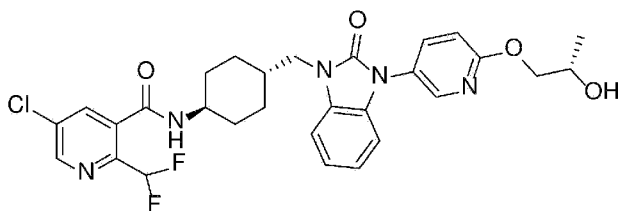
5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.IIO]



[1093] The title compound is prepared in 30% yield in 2 steps by the similar manner to Step-2 and Step-3 of Example 438 using Mesylate-4 in place of Mesylate- 1.

[1094] Example 440:

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.III]



[1095] <Step-1>:

(S)-1-(6-(2-(methoxymethoxy)propoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one

The title compound is prepared in 63% yield (45 mg) by the similar manner to Intermediate- 183 using (S)-2-(methoxymethoxy)propan-1-ol (52 mg, 0.44 mmol) in place of 2-methoxyethanol.

MS (ESI) m/z: 330.0 (M+H)⁺.

[1096] <Step-2>:

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-(methoxymethoxy)propoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinami

de

The title compound is prepared in 41% yield (10 mg) by the similar manner to Step-3 of Intermediate-3 using

(S)-1-(6-(2-(methoxymethoxy)propoxy)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (14 mg, 0.042 mmol, Step-1 of Example 440) and Mesylate-4 (17 mg, 0.042 mmol) in place of methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate and Mesylate- 1.

MS (ESI) m/z: 694.1 (M+H)⁺.

[1097] <Step-3>:5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 55% yield (5.3 mg) by the similar manner to Step-3 of Example 438 using

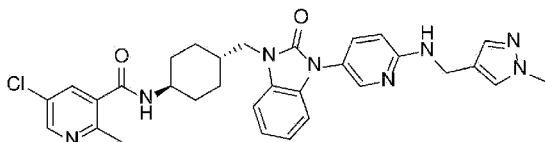
5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-(methoxymethoxy)propoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (10 mg, 0.016 mmol, Step-2 of Example 440) in place of

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-(methoxymethoxy)propoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide.

[1098] Example 441:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(((1-methyl-1H-pyrazol-4-yl)methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.112]



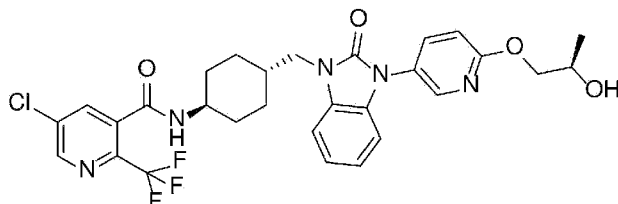
[1099] A mixture of N-

((1r,4r)-4-((3-(6-aminopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (22 mg, 0.045 mmol, Example 143), 1-methyl-1H-pyrazole-4-carbaldehyde (4.93 mg, 0.045 mmol) and acetic acid (0.003 mL, 0.045 mmol) in DCM (5 mL) is stirred at 40 °C for 3 hrs. After cooling to rt, sodium triacetoxy borohydride (18.99 mg, 0.09 mmol) is added. The resulting mixture is stirred at rt for 2 hrs. Then, the mixture is poured onto water, and the aqueous layer is extracted with EtOAc. The combined organic layer is dried over MgSO₄ and concentrated in vacuo to give crude product. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative SFC-MS to give 5.3 mg (20% yield) of the title

compound.

[1100] Example 466:

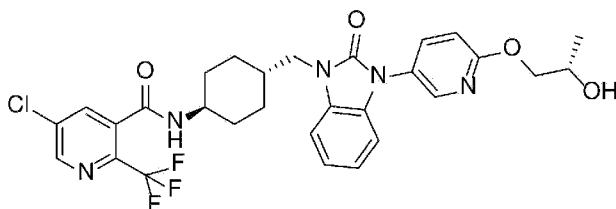
5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide
[Chem.IB]



[1101] The title compound is prepared in 29% yield in 2 steps by the similar manner to Step-2 and Step-3 of Example 438 using Mesylate-3 in place of Mesylate-1.

[1102] Example 467:

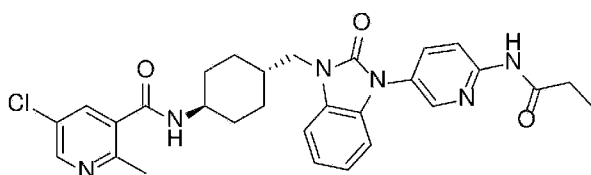
5-chloro-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide
[Chem.IU]



[1103] The title compound is prepared in 23% yield in 2 steps by the similar manner to Step-2 and Step-3 of Example 440 using Mesylate-3 in place of Mesylate-4.

[1104] Example 479:

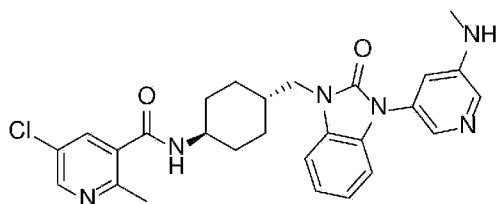
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.II5]



[1105] To a mixture of Ex 143 (20 mg, 0.041 mmol) and DIEA (15.8 mg, 0.12 mmol) in DCM (1 mL) is added propionyl chloride (7.5 mg, 0.081 mmol) and stirred at rt for 1 hr. The solvent is removed under vacuum, the crude product is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 2.5 mg (11% yield) of the title compound.

[1106] Example 487:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(5-(methylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo [d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.116]



[1107] A mixture of 5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo [d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9), tert-butyl (5-bromopyridin-3-yl)(methyl)carbamate (11 mg, 0.038 mmol), *N*',*N*'-dimethylethane-1, 2-diamine (0.022 mL, 0.207 mmol), Cs₂CO₃ (49 mg, 0.150 mmol) and CuI (18 mg, 0.094 mmol) in DMA (1.5 mL) is stirred at 110 °C for 3.5 hrs. The mixture is poured into 28% aqueous ammonia solution (3 mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 22 mg of tert-butyl (5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo [d]imidazol-1-yl)pyridin-3-yl)(methyl)carbamate.

This is dissolved in DCM (1 mL). To the mixture is added TLA (1 mL) and the mixture is stirred at rt for 0.5 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 9.8 mg (52% yield) of the title compound.

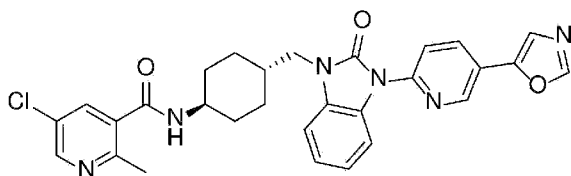
MS (ESI) *m/z*: 505.1 (*M*+*H*)⁺.

[1108] Representative procedure for Method X

The following preparation of Example 489 represents the Method X.

[1109] Example 489:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(5-(oxazol-5-yl)pyridin-2-yl)-2-oxo-2, 3-dihydro-1*H*-benzo [d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.117]



[1110] A mixture of 5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo [d]imidazol-1-yl)methyl

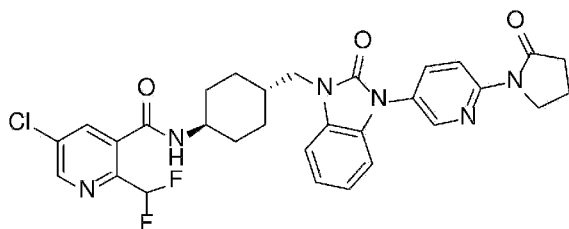
)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9), 5-(6-chloropyridin-3-yl)oxazole (7 mg, 0.038 mmol), Pd₂(dba)₃ (7 mg, 0.0075 mmol), Xantphos (9 mg, 0.015 mmol) and Cs₂CO₃ (25 mg, 0.075 mmol) in 1,4-dioxane (1.5 mL) is stirred at 120 °C for 4.0 hrs. The mixture is stirred at 130 °C for 1.5 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 4.2 mg (21% yield) of the title compound.

[1111] Representative procedure for Method Y

The following preparation of Example 498 represents the Method Y.

[1112] Example 498:

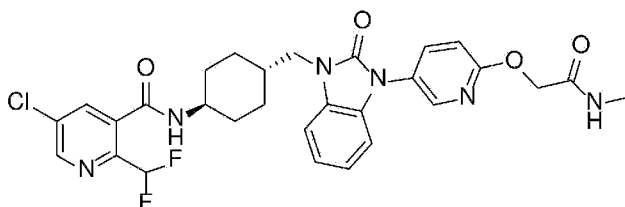
5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.118]



[1113] A mixture of Intermediate-209 (20 mg, 0.034 mmol), pyrrolidin-2-one (8.64 mg, 0.102 mmol), CuI (0.65 mg, 0.0034 mmol), DMEDA (0.60 mg, 0.0068 mmol) and K₂CO₃ (33.1 mg, 0.10 mmol) in 1,4-dioxane (1 mL) is stirred at 100 °C for 4 hrs. To the mixture is added water and extracted with EtOAc, and passed through sodium sulfate/amino-functional silica gel. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative SFC-MS to give 4.0 mg (20% yield) of the title compound.

[1114] Example 500:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(6-(2-(methylamino)-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.119]



[1115] <Step-1>: ethyl

2-((5-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-o

xo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)acetate

A solution of Intermediate- 191 (50 mg, 0.094 mmol), ethyl 2-hydroxyacetate (30 mg 0.28 mmol) and potassium tert-butoxide (32 mg, 0.28 mmol) in THF (2 mL) is stirred at rt for 2 hrs. The solvent is removed by flowing N₂ gas, the title compound is obtained as a crude solid. The title compound is used next step without further purification.

¹H -NMR (400 MHz, CDCl₃) delta 8.62 (1H, d, J = 2.3 Hz), 8.27 (1H, d, J = 2.3 Hz), 7.89 (1H, d, J = 2.3 Hz), 7.78 (1H, dd, J = 8.9, 2.5 Hz), 7.17 (1H, td, J = 7.5, 1.1 Hz), 7.11-6.99 (4H, m), 6.89 (1H, t, J = 54.4 Hz), 6.29 (1H, d, J = 8.2 Hz), 4.93 (2H, s), 4.25 (2H, q, J = 7.2 Hz), 4.00-3.86 (1H, m), 3.79 (2H, d, J = 6.9 Hz), 2.12 (2H, brd, J = 10.1 Hz), 2.01-1.78 (3H, m), 1.37-1.14 (7H, m).

MS (ESI) m/z: 614.0 (M+H)⁺.

[1116] <Step-2>:

2-((5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)acetic acid

To a mixture of ethyl

2-((5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)acetate (Step-1 of Ex 500) in MeOH (2 mL) is added 2 M aqueous sodium hydroxide solution (1 mL) and stirred at rt for 2 hrs. To the mixture is added 2 M hydrochloric acid (1 mL), the solid is precipitated. The precipitated solid is collected, the title compound is prepared in 80% yield (44 mg, solid, total: 2 steps).

¹H -NMR (400 MHz, DMSO-d₆) delta 8.83 (1H, d, J = 2.7 Hz), 8.67 (1H, d, J = 7.8 Hz), 8.33 (1H, d, J = 2.7 Hz), 8.16 (1H, d, J = 2.3 Hz), 7.95 (1H, dd, J = 8.7, 2.7 Hz), 7.34 (1H, d, J = 7.8 Hz), 7.21-6.91 (5H, m), 4.90 (2H, s), 3.78 (2H, d, J = 6.9 Hz), 3.7-3.64 (1H, m), 2.01-1.87 (2H, m), 1.87-1.67 (3H, m), 1.31-1.13 (4H, m).

MS (ESI) m/z: 585.9 (M+H)⁺.

[1117] <Step-3>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-(methylamino)-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of

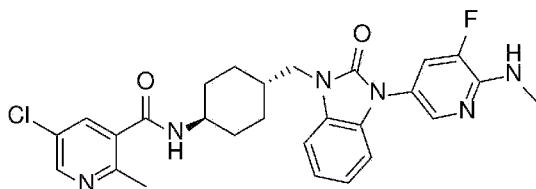
2-((5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)oxy)acetic acid (12 mg, 0.020 mmol, Step-2 of Ex 500), methanamine hydrochloride (4.2 mg, 0.061 mmol), HBTU (12 mg, 0.033 mmol) and DIEA (7.9 mg, 0.061 mmol) in DMF (1 mL) is stirred at rt overnight. To the mixture is added saturated aqueous sodium bicarbonate, extracted with EtOAc and passed through sodium sulfate. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative SFC-MS to give 6.5 mg (53% yield)

of the title compound.

[1118] Example 552:

5-chloro-N-((1*r*,4*r*)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.120]



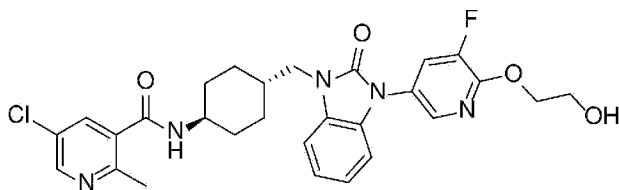
[1119] A mixture of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (25 mg, 0.063 mmol, Step-2 of Example 9), 5-bromo-3-fluoro-N-methylpyridin-2-amine (39 mg, 0.19 mmol), CuI (1.2 mg, 0.0063 mmol), DMEDA (1.1 mg, 0.013 mmol) and K₂CO₃ (26 mg, 0.19 mmol) in 1,4-dioxane (1 mL) is stirred at 100 °C overnight. The mixture is added water and 25% aqueous ammonia solution, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative SFC-MS to give 24 mg (73% yield) of the title compound.

[1120] Example 553:

5-chloro-N-((1*r*,4*r*)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.121]



[1121] <Step-1>:

5-bromo-3-fluoro-2-(2-((tetrahydro-2*H*-pyran-2-yl)oxy)ethoxy)pyridine

A mixture of 5-bromo-2,3-difluoropyridine (200 mg, 1.03 mmol), 2-((tetrahydro-2*H*-pyran-2-yl)oxy)ethanol (166 mg, 1.13 mmol) and Cs₂CO₃ (504 mg, 1.55 mmol) in DMF (2 mL) is stirred at rt overnight. To the mixture is added saturated aqueous ammonium chloride, extracted with EtOAc/n-hexane = 4/1 and passed through sodium sulfate. The solvent is removed under vacuum, the crude product is purified by column chromatography on silica-gel eluting with 0-20% EtOAc in n-hexane, the title compound is prepared in 82% yield (270 mg, oil).

¹H-NMR (400 MHz, CDCl₃) delta 7.97 (1*H*, d, *J* = 1.8 Hz), 7.48 (1*H*, dd, *J* = 9.4, 2.1

Hz), 4.71 (1H, t, J = 3.6 Hz), 4.61-4.49 (2H, m), 4.13-4.02 (1H, m), 3.94-3.77 (2H, m), 3.57-3.47 (1H, m), 1.89-1.67 (2H, m), 1.67-1.44 (4H, m).

MS (ESI) m/z: 319.8 (M+H)⁺.

[1122] <Step-2>:

5-chloro-N-((1*r*,4*r*)-4-((3-(5-fluoro-6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (25 mg, 0.063 mmol, Step-2 of Example 9),

5-bromo-3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridine (30 mg, 0.094 mmol, Step-1 of Ex 553), CuI (1.2 mg, 0.0063 mmol), DMEDA (1.1 mg, 0.013 mmol) and K₂CO₃ (26 mg, 0.19 mmol) in 1,4-dioxane (1 mL) is stirred at 100 °C overnight.

To the mixture is added water and 25% aqueous ammonia solution, extracted with EtOAc and passed through sodium sulfate/amino-functional silica gel. The solvent is removed by flowing N₂ gas, the title compound is prepared as a crude product (38 mg, solid). The product is used next step without further purification.

MS (ESI) m/z: 638.0 (M+H)⁺.

[1123] <Step-3>:

5-chloro-N-((1*r*,4*r*)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

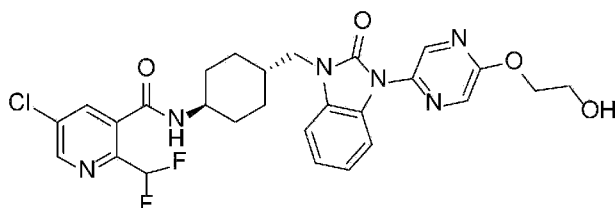
To the mixture of

5-chloro-N-((1*r*,4*r*)-4-((3-(5-fluoro-6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (38 mg, crude, Step-2 of Ex 553) in DCM (1 mL) is added TFA (1 mL) and stirred at rt for 1 hr. The solvent is removed by flowing N₂ gas, the crude product is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative SFC-MS to give 25 mg (72% yield, total: 2 steps) of the title compound.

[1124] Example 563:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

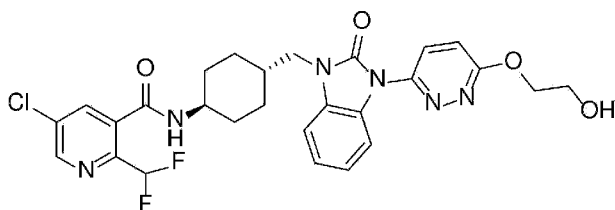
[Chem.122]



[1125] The title compound is prepared in 33% yield (9.4 mg) by the similar manner to Example 69 using Mesylate-4 (20 mg, 0.050 mmol) and Intermediate-225 (18 mg, 0.050 mmol) in place of Mesylate- 1 and 1-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one.

[1126] Example 564:

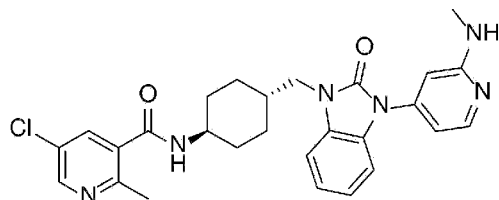
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.123]



[1127] The title compound is prepared in 30% yield (8.6 mg) by the similar manner to Example 69 using Mesylate-4 (20 mg, 0.050 mmol) in place of Mesylate- 1.

[1128] Example 573:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.124]



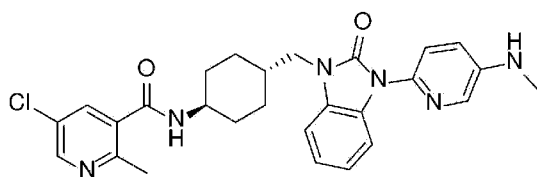
[1129] A mixture of

5-chloro-N-((1r,4r)-4-((3-(2-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (17 mg, Step-2 of Intermediate-226), methylamine hydrochloride (25 mg, 0.37 mmol), and DIEA (0.066 mL, 0.37 mmol) in NMP (0.5 mL) is stirred for 140 min at 220 °C under microwave irradiation. The mixture is diluted with saturated aqueous sodium chloride. The mixture is extracted with THF. The resultant residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage). The resultant residue is purified by preparative LC-MS to give 1.6 mg (8% yield in 2 steps from Step-2 of Intermediate-226) of the title compound.

[1130] Example 574:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.125]



[1131] <Step-1>:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-nitropyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzod[imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (30 mg, 0.075 mmol, Step-2 of Example 9), 2-fluoro-5-nitropyridine (14 mg, 0.098 mmol), and cesium carbonate (49 mg, 0.15 mmol) in DMSO (1 mL) is stirred for 2 hrs at 100 °C. The mixture is diluted with saturated aqueous ammonium chloride. The precipitate is collected and washed with water followed by diisopropyl ether to give 34 mg (86% yield) of the title compound as a pale yellow solid.

MS (ESI) m/z: 521.2 (M+H)⁺.

[1132] <Step-2>: N-

((1r,4r)-4-((3-(5-aminopyridin-2-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

A mixture of

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-nitropyridin-2-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (34 mg, 0.064 mmol, Step-1 of Example 574), tin(II) chloride (110 mg, 0.58 mmol) in MeOH (1 mL) is stirred for 2 days at rt. The mixture is purified by column chromatography on amino-functional silica gel eluting with 100% MeOH to give 37 mg of the title compound as a crude. The compound is used for the next reaction without further purification.

MS (ESI) m/z: 491.1 (M+H)⁺.

[1133] <Step-3>:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

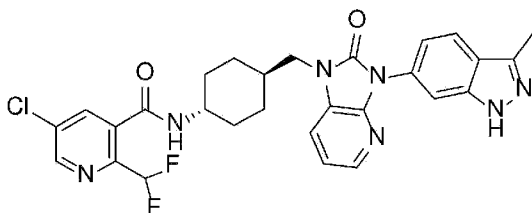
A mixture of N-

((1r,4r)-4-((3-(5-aminopyridin-2-yl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (19 mg, Step-2 of Example 574) and TFA (0.002 mL, 0.003 mmol) in triethyl orthoformate (0.5 mL) is stirred for 6 hrs at 140 °C. After the mixture is concentrated, EtOH (1 mL) and sodium borohydride (7.3 mg, 0.19 mmol) are added to the resultant residue. The reaction mixture is stirred for 2

days at rt. After the mixture is concentrated, the resultant residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage). The resultant residue is purified by preparative LC-MS to give 4.0 mg (25% yield in 2 steps) of the title compound.

[1134] Example 575:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.126]



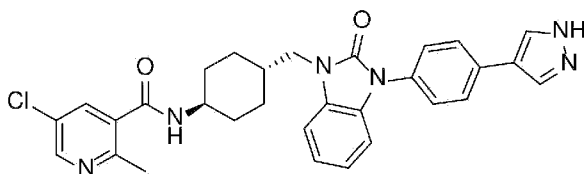
[1135] A solution of

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.046 mmol, Intermediate-214), 3-methyl-1-(tetrahydro-2H-pyran-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (16 mg, 0.046 mmol, Intermediate-227), copper(II) acetate (20 mg, 0.11 mmol) and TEA (0.019 mL, 0.14 mmol) in DMA (1 mL) is stirred at 100 °C overnight. The mixture is filtered through a pad of celite. The filtrate is diluted with water, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered through short column of amino-functional silica gel, concentrated. To the residue in dichloromethane (0.5 mL) is added TFA (1.5 mL). The mixture is stirred at room temperature for 3 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage), concentrated. The residue is purified by preparative LC-MS to give 7.8 mg (26% yield) of the title compound.

MS (ESI) m/z: 566.0 (M+H)⁺.

[1136] Example 581:

N-((1r,4r)-4-((3-(4-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.127]



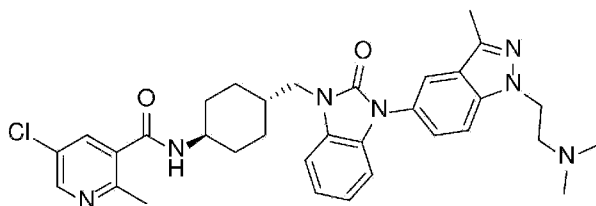
[1137] A mixture of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.050 mmol, Step-2 of Example 9), 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrazole (18 mg, 0.050 mmol, Intermediate-230), NkhP-dimethylethane-1, 2-diamine (0.030 mL, 0.28 mmol), cesium carbonate (65 mg, 0.20 mmol) and CuI (24 mg, 0.13 mmol) in DMA (1.5 mL) is stirred at 120 °C overnight. The reaction is quenched with 28% aqueous ammonia solution, extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. To the residue in DCM (0.5 mL) is added TFA (1 mL) and the mixture is stirred at rt for 2.5 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 7.7 mg (28% yield) of the title compound.

MS (ESI) *m/z*: 541.0 (M+H)⁺.

[1138] Example 588:

5-chloro-N-((1*r*,4*r*)-4-((3-(1-(2-(dimethylamino)ethyl)-3-methyl-1*H*-indazol-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide [Chem.128]



[1139] <Step-1>:

2-(5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-3-methyl-1*H*-indazol-1-yl)ethyl methanesulfonate

To a mixture of Example 230 (226 mg, 0.39 mmol) in DCM (4 mL) is added methanesulfonic anhydride (124 mg, 0.71 mmol) and stirred at rt for 2 hr. The mixture is added water, extracted with DCM and passed through sodium sulfate. The solvent is removed under vacuum, the title compound is prepared in 91 % as a crude product (233 mg, solid). The product is used next step without further purification.

MS (ESI) *m/z*: 651.2 (M+H)⁺.

[1140] <Step-2>:

5-chloro-N-((1*r*,4*r*)-4-((3-(1-(2-(dimethylamino)ethyl)-3-methyl-1*H*-indazol-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

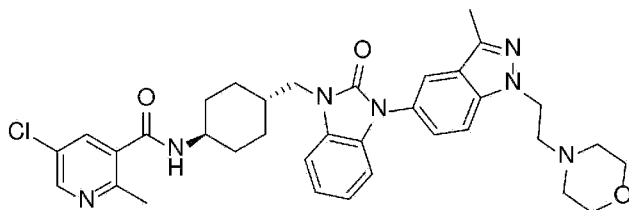
A mixture of

2-(5-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-3-methyl-1*H*-indazol-1-yl)ethyl methanesulfonate (25 mg, 0.038 mmol, Step-1 of Ex 588) and 2 M ammonia in THF (2 mL) is stirred at 80 °

C overnight. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative LC-MS to give 8.5 mg (37% yield) of the title compound.

[1141] Example 589:

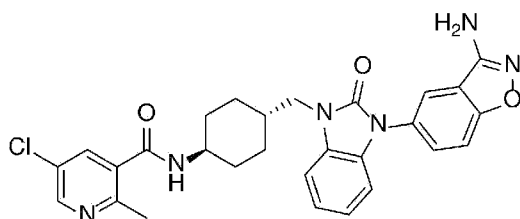
5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(3-methyl-1-(2-morpholinoethyl)-1*H*-indazol-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.129]



[1142] The title compound is prepared in 26% yield (solid) by the similar manner to Step-2 of Example 588 using morpholine in place of dimethylamine.

[1143] Example 591:

N-((1*r*,4*r*)-4-((3-(3-aminobenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.130]



[1144] <Step-1>: 2-fluoro-5-((2-nitrophenyl)amino)benzonitrile

A mixture of 1-bromo-2-nitrobenzene (163 mg, 0.808 mmol), 5-amino-2-fluorobenzonitrile (110 mg, 0.808 mmol), Pd₂(dba)₃ (22 mg, 0.024 mmol), Xantphos (28 mg, 0.048 mmol) and cesium carbonate (527 mg, 1.616 mmol) in 1,4-dioxane (6 mL) is stirred at 100 °C for 1.5 hrs. The reaction mixture is poured into water and extracted EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-33 % EtOAc in n-hexane to give 170 mg (81 % yield) of the title compound as an orange solid.

¹H -NMR (400 MHz, CDCl₃) delta 9.35 (1H, br s), 8.24 (1H, dd, J = 8.6, 1.4 Hz), 7.57-7.42 (3H, m), 7.32-7.21 (1H, m), 7.10 (1H, dd, J = 8.6, 1.4 Hz), 6.93-6.86 (1H, m). MS (ESI) m/z: 256.3 (M-H)⁻.

[1145] <Step-2>: 5-((2-aminophenyl)amino)-2-fluorobenzonitrile

A solution of 2-fluoro-5-((2-nitrophenyl)amino)benzonitrile (170 mg, 0.661 mmol, Step-1 of Example 591) in MeOH (7 mL) and THF (7 mL) is evacuated and backfilled with N₂ gas. To this is added 10% Pd/C (35 mg). The mixture is evacuated and

backfilled with H₂ gas and stirred at rt under H₂ atmosphere. After 1 hr, the reaction mixture is evacuated and backfilled with N₂ gas and the mixture is filtered through celite pad. The filtrate is concentrated in vacuo to give 146 mg (97% yield) of the title compound as a brown solid.

¹H-NMR (400 MHz, CDCl₃) delta 7.12-6.97 (3H, m), 6.92-6.87 (1H, m), 6.85-6.76 (3H, m), 5.26 (1H, br s). A signal due to NH₂ is not observed.

MS (ESI) m/z: 228.3 (M+H)⁺.

[1146] <Step-3>: 2-fluoro-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzonitrile

A mixture of 5-((2-aminophenyl)amino)-2-fluorobenzonitrile (146 mg, 0.643 mmol, Step-2 of Example 591), CDI (208 mg, 1.285 mmol) in THF (5 mL) is stirred at rt for 3.5 hrs. The reaction mixture is poured into water and extracted EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residual solid is suspended with IPE (5 mL). The obtained solid is washed with IPE and EtOAc/n-hexane to give 100 mg (62% yield) of the title compound as a beige solid.

¹H-NMR (400 MHz, CDCl₃) delta 8.85 (1H, br s), 7.91-7.83 (2H, m), 7.42 (1H, t, J = 8.6 Hz), 7.21-7.10 (3H, m), 7.07-7.03 (1H, m). MS (ESI) m/z: 254.3 (M+H)⁺.

[1147] <Step-4>:

5-chloro-N-((1r,4r)-4-((3-(3-cyano-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

A mixture of ((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl methane-sulfonate (114 mg, 0.316 mmol, Mesylate-1),

2-fluoro-5-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzonitrile (80 mg, 0.316 mmol, Step-3 of Example 591), and cesium carbonate (309 mg, 0.948 mmol) in DMSO (6 mL) is stirred at 80 °C for 15 hrs. The reaction mixture is poured into water and extracted EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by column chromatography on silica-gel eluting with 0-80 % EtOAc in n-hexane to give 80 mg (49 % yield) of the title compound as colorless oil.

¹H-NMR (400 MHz, CDCl₃) delta 8.49 (1H, d, J = 2.4 Hz), 7.90-7.82 (2H, m), 7.61 (1H, d, J = 2.4 Hz), 7.40 (1H, t, J = 8.6 Hz), 7.30-7.05 (4H, m), 5.56 (1H, d, J = 8.0 Hz), 4.01-3.90 (1H, m), 3.81 (2H, d, J = 6.8 Hz), 2.61 (3H, s), 2.21-2.13 (2H, m), 2.02-1.87 (3H, m), 1.41-1.15 (4H, m). MS (ESI) m/z: 518.3 (M+H)⁺.

[1148] <Step-5>: N-

((1r,4r)-4-((3-(3-aminobenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

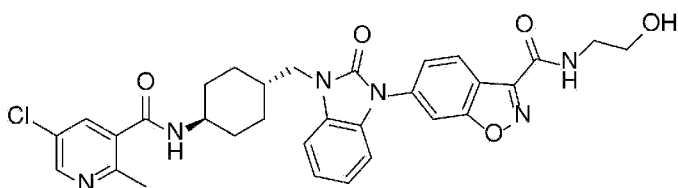
A mixture of

5-chloro-N-((1r,4r)-4-((3-(3-cyano-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide (50 mg, 0.097 mmol, Step-4 of

Example 591), N-hydroxyacetamide (22 mg, 0.290 mmol) and potassium carbonate (80 mg, 0.579 mmol) in DMF/water (5/1, 1.8 mL) is stirred at 80 °C for 2 hrs. The reaction mixture is poured into water and extracted EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by preparative LC-MS to give 8.3 mg (16 % yield) of the title compound.

[1149] Example 594:

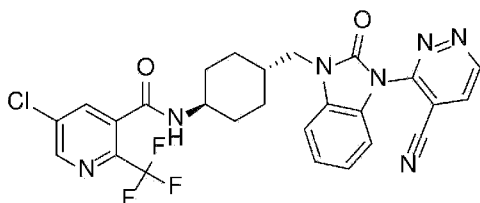
6-(3-(((1*r*,4*r*)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-N-(2-hydroxyethyl)benzo[d]isoxazole-3-carboxamide [Chem.131]



[1150] The title compound is prepared in 48% yield (9.8 mg) by the similar manner to Step-3 of Example 243 using 2-aminoethanol (53 mg, 0.872 mmol) in place of ammonia.

[1151] Example 595:

5-chloro-N-(((1*r*,4*r*)-4-((3-(4-cyanopyridazin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide [Chem.132]

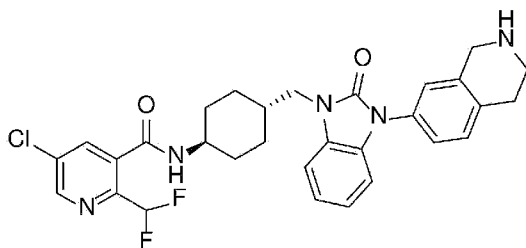


[1152] The title compound is prepared in 24% yield (7.4 mg) by the similar manner to Example 369 using 3-chloropyridazine-4-carbonitrile (12 mg, 0.083 mmol) and 5-chloro-N-(((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide (25 mg, 0.055 mmol, Intermediate- 132) in place of 3-chloropyridazine-2-carbonitrile and Intermediate- 165.

[1153] Example 604:

5-chloro-2-(difluoromethyl)-N-(((1*r*,4*r*)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

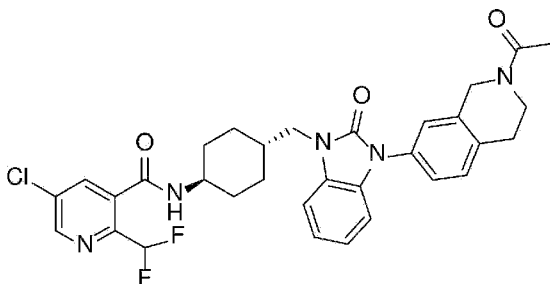
[Chem.133]



[1154] A mixture of tert-butyl 7-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (138 mg, 0.21 mmol, Intermediate-235) and 4 M hydrogen chloride in 1,4-dioxane (2 mL) in MeOH (1 mL) is stirred at rt for 1 hr. The mixture is concentrated to give 125 mg (quantitative yield) of the title compound (HCl salt) as a pale yellow solid. This solid (25 mg) is purified by preparative LC-MS to give 2.3 mg (9% yield) of the title compound.

[1155] Example 605:

N-(((1*r*,4*r*)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide
[Chem.134]

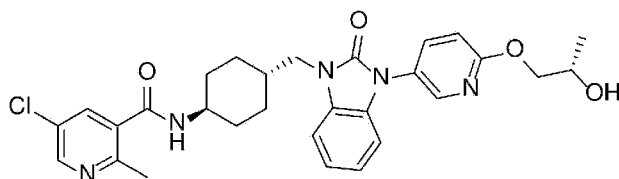


[1156] To a mixture of 5-chloro-2-(difluoromethyl)-N-(((1*r*,4*r*)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (HCl salt, 30 mg, 0.050 mmol, Example 604) and TEA (0.028 mL, 0.20 mmol) in DCM (1 mL) is added acetyl chloride (8 mg, 0.10 mmol) at 0 °C. The mixture is stirred at 0 °C for 30 min. Then, the mixture is quenched with saturated aqueous sodium bicarbonate and extracted with EtOAc. The organic layer is dried over sodium sulfate, filtered and concentrated. The residue is purified by preparative LC-MS to give 8.8 mg (29% yield) of the title compound.

[1157] Example 610:

5-chloro-N-(((1*S*,4*r*)-4-((3-(6-((*S*)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide

[Chem.135]

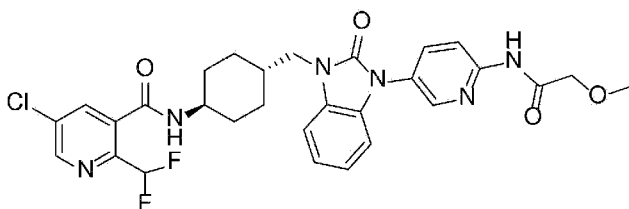


[1158] The title compound is prepared in 53% yield in 2 steps by the similar manner to Step-2 and Step-3 of Example 440 using Mesylate-1 in place of Mesylate-4.

[1159] Example 618:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(6-(2-methoxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.136]

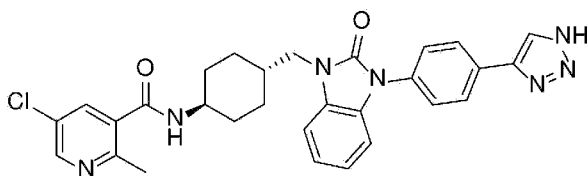


[1160] The title compound is prepared in 15% yield (solid) by the similar manner to Ex 498 using 2-methoxyacetamide in place of pyrrolidin-2-one.

[1161] Example 633:

N-((1*r*,4*r*)-4-((3-(4-(1*H*-1,2,3-triazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.137]



[1162] A mixture of

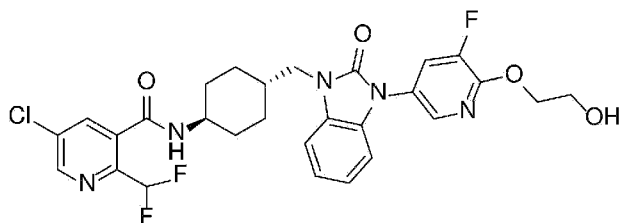
5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.038 mmol, Step-2 of Example 9), 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-1,2,3-triazole (13 mg, 0.038 mmol), NhNP-dimethylethane-1,2-diamine (0.022 mL, 0.207 mmol), cesium carbonate (49 mg, 0.150 mmol) and CuI (18 mg, 0.094 mmol) in DMA (1.5 mL) is stirred at 120 °C for 7.5 hrs. The mixture is poured into 28% aqueous ammonia solution (3 mL), extracted with EtOAc. The organic layer is washed with water, dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE(registered trademark) SCX-2, 1 g/6 mL, Biotage) to give 17 mg of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-1,2,3-triazol-4-yl)phenyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide.

This is dissolved in DCM (1 mL). To the mixture is added TFA (1 mL) and the mixture is stirred at rt for 2.5 hrs. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.8 mg (19% yield) of the title compound.

[1163] Example 638:

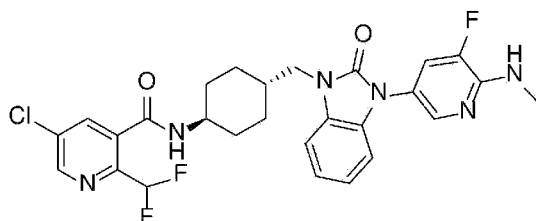
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.138]



[1164] The title compound is prepared in 32% yield (solid, total: 2 steps) by the similar manner to Ex 553 using Intermediate- 165 in place of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (Step-2 of Example 9).

[1165] Example 639:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.139]

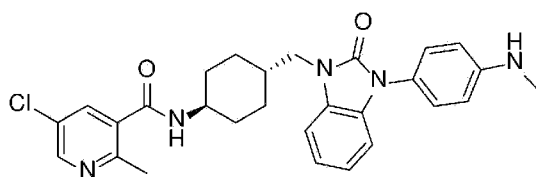


[1166] The title compound is prepared in 34% yield (solid) by the similar manner to Ex 552 using Intermediate- 165 in place of 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (Step-2 of Example 9).

[1167] Example 646:

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(methylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.140]



[1168] <Step-1>:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(4-nitrophenyl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A mixture of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (19 mg, 0.047 mmol, Step-2 of Example 9), 1-bromo-4-nitrobenzene (10 mg, 0.047 mmol), *N,N*-dimethylethane-1, 2-diamine (0.028 mL, 0.26 mmol), cesium carbonate (62 mg, 0.19 mmol) and CuI (23 mg, 0.12 mmol) in DMA (1 mL) is stirred overnight at 100 °C. The mixture is poured into 28% aqueous ammonia solution, extracted with EtOAc. The organic layer is concentrated. The resultant residue is purified by column chromatography on silica-gel eluting with 24-100% EtOAc in *n*-hexane to give 12 mg (50% yield) of the title compound as a yellow solid.

¹H-NMR (400 MHz, CDCl₃) δ 8.49 (1*H*, d, *J* = 2.3 Hz), 8.41 (2*H*, d, *J* = 9.1 Hz), 7.84 (2*H*, d, *J* = 9.1 Hz), 7.61 (1*H*, d, *J* = 2.3 Hz), 7.26-7.20 (2*H*, m), 7.18-7.07 (2*H*, m), 5.55 (1*H*, d, *J* = 8.2 Hz), 4.05-3.88 (1*H*, m), 3.83 (2*H*, d, *J* = 6.9 Hz), 2.61 (3*H*, s), 2.16 (2*H*, m), 2.02-1.86 (3*H*, m), 1.43-1.28 (2*H*, m), 1.27-1.13 (2*H*, m).

MS (ESI) *m/z*: 520.1 (M+H)⁺.

[1169] <Step-2>: N-

((1*r*,4*r*)-4-((3-(4-aminophenyl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

The title compound is prepared as a crude (18 mg) by the similar manner to Step-2 of Example 574 using

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(4-nitrophenyl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (12 mg, 0.024 mmol, Step-1 of Example 646) in place of

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(5-nitropyridin-2-yl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide.

MS (ESI) *m/z*: 490.1 (M+H)⁺.

[1170] <Step-3>:

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(4-(methylamino)phenyl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

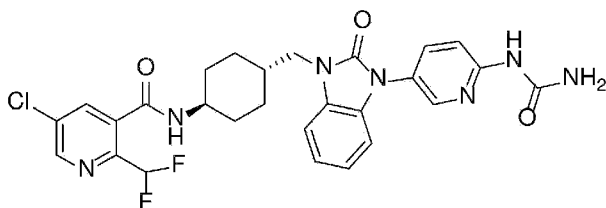
The title compound is prepared in 14% yield in 2 steps (1.7 mg) by the similar manner to Step-3 of Example 574 using N-

((1r,4r)-4-((3-(4-aminophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide (18 mg, Step-2 of Example 646) in place of N-((1r,4r)-4-((3-(5-aminopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide.

[1171] Example 658:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-ureidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.U1]



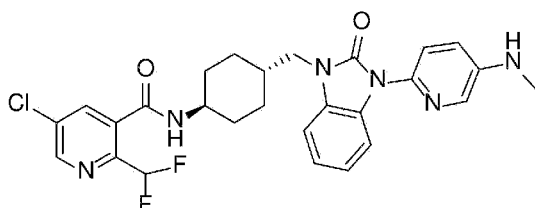
[1172] A mixture of Intermediate-207 (30 mg, 0.051 mmol), ethyl carbamate (14 mg, 0.15 mmol), CuI (1.0 mg, 0.0051 mmol), DMEDA (0.9 mg, 0.010 mmol) and K₂CO₃ (21 mg, 0.15 mmol) in 1,4-dioxane (1 mL) is stirred at 100 °C overnight. The mixture is added 28% aqueous ammonia solution and water, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed by flowing N₂ gas, ethyl

(5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pyridin-2-yl)carbamate is obtained as a crude solid. The mixture is added DMF (1 mL) and NH₄Cl (190 mg, 10.5 mmol), and stirred at 140 °C for 10 hrs. The mixture is added water, extracted with EtOAc and passed through sodium sulfate/ amino-functional silica gel. The solvent is removed by flowing N₂ gas, the crude product is purified by preparative LC-MS to give 4.2 mg (15% yield, total: 2 steps) of the title compound.

[1173] Example 660:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.142]



[1174] <Step-1>: tert-butyl

(6-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-3-yl)(methyl)carbamate

A mixture of

5-chloro-2-(difluoromethyl)-*N*-(((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (16 mg, 0.038 mmol, Intermediate-165), tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate (11 mg, 0.038 mmol), *N*¹,*N*²-dimethylethane-1, 2-diamine (0.022 mL, 0.21 mmol), cesium carbonate (49 mg, 0.15 mmol) and CuI (18 mg, 0.094 mmol) in DMA (1 mL) is stirred overnight at 100 °C.

The mixture is poured into 28% aqueous ammonia solution, extracted with EtOAc. The organic layer is concentrated. The resultant residue is dissolved in DCM and washed with water. The solvent is removed to give 27 mg of the title compound as a crude.

The compound is used for the next reaction without further purification.

MS (ESI) *m/z*: 641.2 (*M*+*H*)⁺.

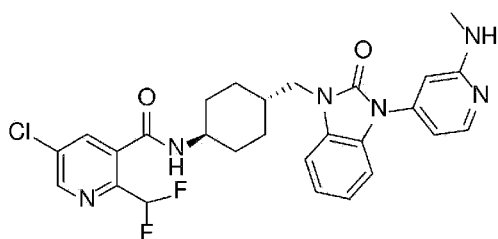
[1175] <Step-2>:

5-chloro-2-(difluoromethyl)-*N*-(((1*r*,4*r*)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
tert-butyl

(6-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)pyridin-3-yl)(methyl)carbamate (27 mg, Step-1 of Example 660) in TFA (1 mL) is stirred for 1 hr at rt. After the reaction mixture is concentrated, the resultant residue is purified by preparative LC-MS to give 5.7 mg (28% yield in 2 steps) of the title compound.

[1176] Example 661:

5-chloro-2-(difluoromethyl)-*N*-(((1*r*,4*r*)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.143]

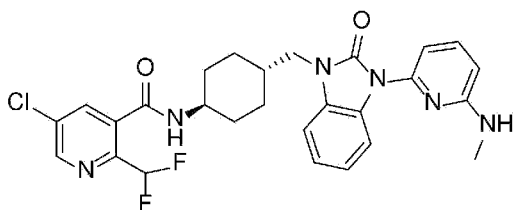


[1177] The title compound is prepared in 24% yield (5.0 mg) by the similar manner to Example 660 using tert-butyl (4-bromopyridin-2-yl)(methyl)carbamate (11 mg, 0.038 mmol) in place of tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate.

[1178] Example 662:

5-chloro-2-(difluoromethyl)-*N*-(((1*r*,4*r*)-4-((3-(6-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.l44]

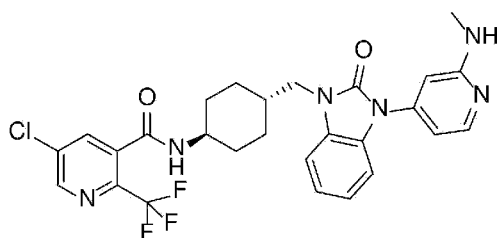


[1179] The title compound is prepared in 33% yield (6.7 mg) by the similar manner to Example 660 using tert-butyl (6-bromopyridin-2-yl)(methyl)carbamate (11 mg, 0.038 mmol) in place of tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate.

[1180] Example 665:

5-chloro-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzod[5,4-b]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

[Chem.l45]

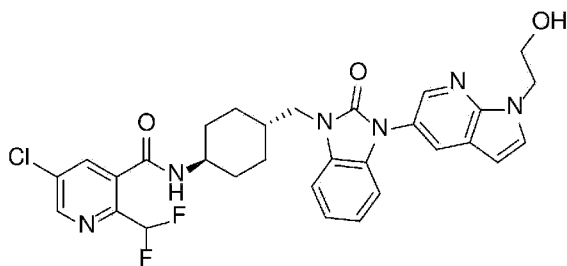


[1181] The title compound is prepared in 20% yield (4.2 mg) by the similar manner to Example 660 using 5-chloro-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzod[5,4-b]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide (17 mg, 0.038 mmol, Intermediate-132) in place of 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-2,3-dihydro-1H-benzod[5,4-b]imidazol-1-yl)methyl)cyclohexyl)nicotinamide and tert-butyl (4-bromopyridin-2-yl)(methyl)carbamate (11 mg, 0.038 mmol) in place of tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate.

[1182] Example 666:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzod[5,4-b]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.l46]



[1183] <Step-1>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 86% yield (74 mg) by the similar manner to Step-3 of Intermediate-3 using

1-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-benzo[d]imidazol-2(3H)-one (48 mg, 0.13 mmol, Intermediate- 185) and Mesylate-4 (50 mg, 0.13 mmol) in place of methyl

2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate and Mesylate- 1.

MS (ESI) m/z: 681.1 (M+H)⁺.

[1184] <Step-2>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

To a solution of

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (60 mg, 0.047 mg, Step-1 of Example 666) in dichloromethane (0.5 mL) is added TFA (1.5 mL). The mixture is stirred at room temperature for 3 hrs. The mixture is concentrated. The residue in 28% aqueous ammonia solution (0.5 mL) and 2 M ammonia in methanol (1.5 mL). The mixture is stirred at room temperature overnight. The mixture is concentrated to give 60 mg (quantitative yield) of the title compound.

MS (ESI) m/z: 550.9 (M+H)⁺.

[1185] <Step-3>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

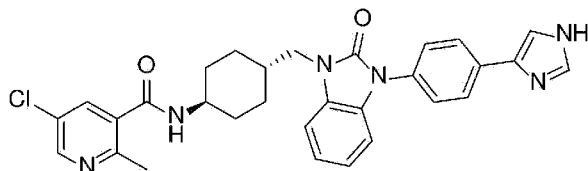
To a solution of

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (15 mg, 0.027 mmol, Step-2 of Example 666) in DMF (1 mL) is added sodium hydride (60% dispersion in mineral oil, 1.1 mg, 0.040 mmol) at 0 °C. The mixture is stirred at room temperature for 30 min. To the mixture is added (2-bromoethoxy)(tert-butyl)dimethylsilane (6.4 mg, 0.027 mmol). The mixture is stirred at room temperature for 2 hrs. The reaction is quenched with saturated aqueous ammonium chloride (10 mL), extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and

then purified by preparative SFC-MS to give 2.2 mg (14% yield) of the title compound.

[1186] Example 667:

N-((1*r*,4*r*)-4-((3-(4-(1*H*-imidazol-4-yl)phenyl)-2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.147]



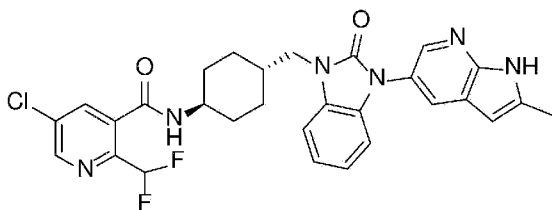
[1187] The title compound is prepared in 22% yield (6.1 mg) by the similar manner to Example 633 using

4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-imidazole (18 mg, 0.050 mmol) in place of

4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*- 1,2,3-triazole.

[1188] Example 673:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(2-methyl-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.148]



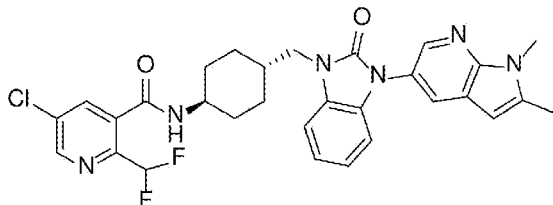
[1189] A solution of

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.046 mmol, Intermediate-165), 2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrrolo[2,3-*b*]pyridine (13 mg, 0.032 mmol, Intermediate-248), copper(II) acetate (20 mg, 0.11 mmol), TEA (0.018 mL, 0.13 mmol) in DMA (1 mL) is stirred at 100 °C overnight. The mixture is filtered through a pad of celite. The filtrate is diluted with water (5 mL), extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered through short column of amino-functional silica gel, concentrated. The residue in dichloromethane (0.5 mL) is added TFA (1.5 mL, 19.5 mmol). The mixture is stirred at room temperature for 3 hrs. The mixture is concentrated. The residue in 28% aqueous ammonia solution (0.5 mL) and 2 M ammonia in methanol (1.5 mL) is stirred at room temperature overnight. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-

2, 1 g/6 mL, Biotage), concentrated. The residue is purified by preparative LC-MS to give 3.2 mg (18% yield) of the title compound.

[1190] Example 674:

5-chloro-2-(difluoromethyl)-N-((1*r*, 4*r*)-4-((3-(1, 2-dimethyl-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)methyl)cyclohexyl)nicotinamide [Chem.149]



[1191] <Step-1>:

1,2-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine

The title compound is prepared in 49% yield (60 mg, pale yellow gum) by the similar manner to Step-1 of Intermediate-81 using 5-bromo-1, 2-dimethyl-1*H*-pyrrolo[2,3-*b*]pyridine (101 mg, 0.45 mmol) in place of 6-bromo-1-methyl-1*H*-pyrrolo[3,2-*b*]pyridine.

[1192] <Step-2>:

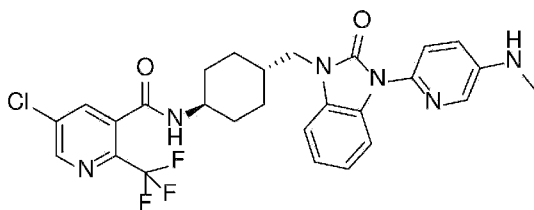
5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(1, 2-dimethyl-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

A solution of 5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((2-oxo-2, 3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.046 mmol, Intermediate-165), 1,2-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (18 mg, 0.046 mmol, Step-1 of Example 674), copper (II) acetate (20 mg, 0.11 mmol), TEA (0.018 mL, 0.13 mmol) in DMA (1 mL) is stirred at 100 °C overnight. The mixture is filtered through a pad of celite. The filtrate is diluted with water, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 3.8 mg (14% yield) of the title compound.

[1193] Example 692:

5-chloro-N-((1*r*,4*r*)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide

[Chem.150]

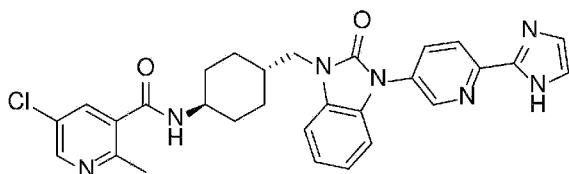


[1194] The title compound is prepared in 26% yield (5.5 mg) by the similar manner to Example 665 using tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate (11 mg, 0.038 mmol) in place of tert-butyl (4-bromopyridin-2-yl)(methyl)carbamate.

[1195] Example 695:

N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.151]

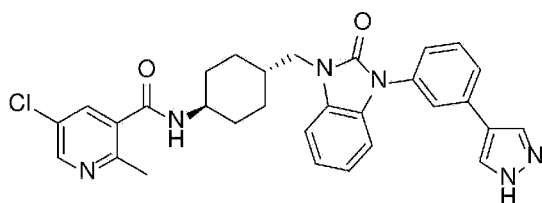


[1196] The title compound is prepared in 23% yield (4.7 mg) by the similar manner to Example 581 using 5-bromo-2-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazol-2-yl)pyridine (13.3 mg, 0.038mmol, Intermediate-255) in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole.

[1197] Example 696:

N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

[Chem.152]

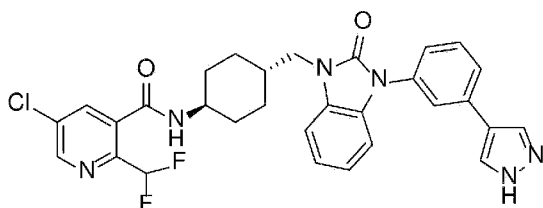


[1198] The title compound is prepared in 10% yield (2.0 mg) by the similar manner to Example 581 using 4-(3-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole (14.6 mg, 41 mmol, Intermediate-256) in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole.

[1199] Example 697:

N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide

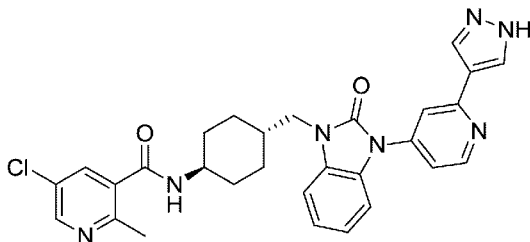
ol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide
[Chem.153]



- [1200] The title compound is prepared in 12% yield (2.5 mg) by the similar manner to Example 581 using 4-(3-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole (14.6 mg, 0.041 mmol, Intermediate-256) and Intermediate-165 in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole and 5-chloro-2-methyl-N-((1R,4R)-4-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide.

[1201] Example 698:

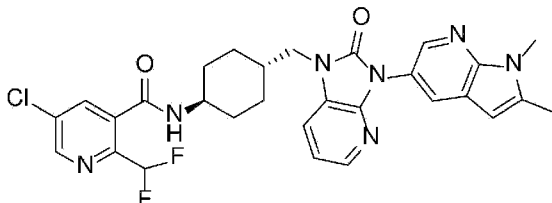
N-((1R,4R)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.154]



- [1202] The title compound is prepared by the similar manner to Example 660 using tert-butyl 4-(4-bromopyridin-2-yl)-1H-pyrazole-1-carboxylate (Intermediate-257) in place of tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate.

[1203] Example 708:

5-chloro-2-(difluoromethyl)-N-((1R,4R)-4-((3-(1,2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.155]



- [1204] The title compound is prepared in 7% yield (1.8 mg) by the similar manner to Step-2

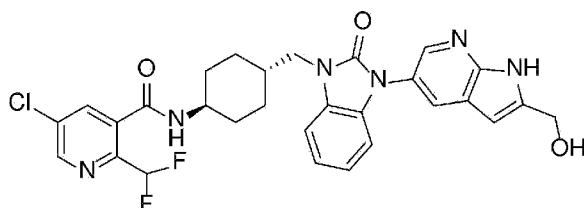
of Example 674 using

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*b*]pyridin-1-yl)methyl)cyclohexyl)nicotinamide (20 mg, 0.046 mmol, Intermediate-2 14) in place of Intermediate- 165.

[1205] Example 709:

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(2-(hydroxymethyl)-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.156]



[1206] <Step-1>: methyl

5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate

The title compound is prepared in 57% yield in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-248 using methyl 5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate in place of 5-bromo-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine.

MS (ESI) *m/z*: 432.9 (*M*+*H*)⁺.

[1207] <Step-2>: methyl

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate

The title compound is prepared in 57% yield (65 mg, brown solid) in by the similar manner to Step-2 of Example 674 using methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate (40 mg, 0.092 mmol, Step-1 of Example 709) in place of 5-bromo-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine.

MS (ESI) *m/z*: 739.0 (*M*+*H*)⁺.

[1208] <Step-3>:

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylic acid

To a mixture of methyl

5-(3-(((1*r*,4*r*)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2

,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine-2-carboxylate (65 mg, 0.088 mmol, Step-2 of Example 709) in MeOH (1.5 mL) and THF (1.5 mL) is added 2 M aqueous sodium hydroxide solution (0.13 mL, 0.26 mmol). The mixture is stirred at 60 °C for 1.5 hrs. The mixture is neutralized with 2 M hydrochloric acid, and concentrated. The residue is diluted water, extracted with EtOAc. The organic layer is dried over sodium sulfate and filtered. The filtrate is concentrated to give 35 mg (55% yield) of the title compound as a brown solid.

MS (ESI) m/z: 725.0 (M+H)⁺.

[1209] <Step-4>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

To a solution of

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid (35 mg, 0.048 mmol, Step-3 of Example 709) in THF (2 mL) is added CDI (31 mg, 0.19 mmol) at room temperature. The mixture is stirred at room temperature for 1 hr. Then, to the mixture is added sodium borohydride (11 mg, 0.29 mmol) in water (0.2 mL) at rt. The mixture is stirred at room temperature for 3 hrs. The mixture is quenched with saturated aqueous ammonium chloride, extracted with EtOAc. The organic layer is concentrated to give 27 mg (78% yield) of the title compound as a brown solid.

MS (ESI) m/z: 711.0 (M+H)⁺.

[1210] <Step-5>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 6% yield (1.7 mg) by the similar manner to Step-2 of Example 408 using

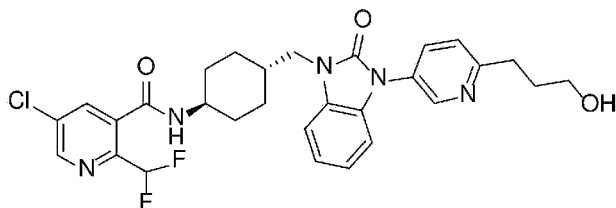
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (27 mg, 0.038 mmol, Step-4 of Example 709) in place of

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide.

[1211] Example 711:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-hydroxypropyl)pyridin-3-yl)-2-ox

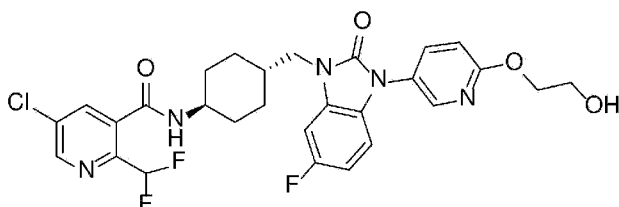
o-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.157]



[1212] A mixture of ((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl methanesulfonate (20 mg, 0.050 mmol, Mesylate-4), 1-(6-(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)pyridin-3-yl)-1H-benzo[d]imidazol-2(3H)-one (18 mg, 0.050 mmol, Intermediate-26 1) and cesium carbonate (49 mg, 0.15 mmol) in DMSO (1 mL) is stirred at 80 °C for 1 day. The mixture is diluted with water, extracted with EtOAc. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue in TFA (2 mL) is stirred at room temperature for 1 hr. The mixture is concentrated. The residue is purified by a strong anion exchange cartridge (ISOLUTE (registered trademark) SCX-2, 1 g/6 mL, Biotage) and then purified by preparative LC-MS to give 4.9 mg (17% yield) of the title compound.

[1213] Example 712:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.158]



[1214] <Step-1>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-2-oxo-3-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared by the similar manner to Step-1 of Intermediate-42 using Intermediate-262 in place of

1-(6-chloropyridazin-3-yl)-1H-benzo[d]imidazol-2(3H)-one.

MS (ESI) m/z: 674.0 (M+H)⁺.

[1215] <Step-2>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 37% yield by the similar manner to Step-2 of

Example 260 using

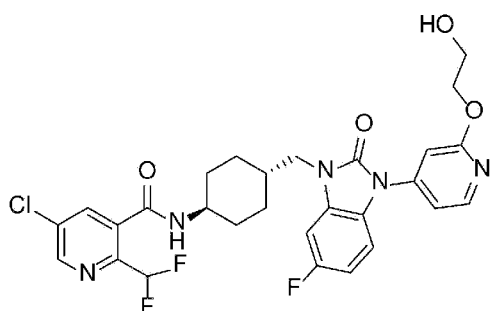
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-2-oxo-3-(6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide (Step-1 of Example 712) in place of

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide.

[1216] Example 714:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(2-(2-hydroxyethoxy)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.159]

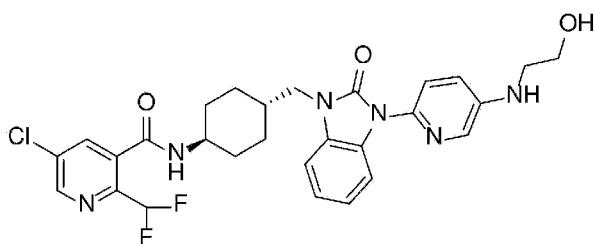


[1217] The title compound is prepared in 2 steps by the similar manner to Step-1 and Step-2 of Example 712 using Intermediate-263 in place of Intermediate-262.

[1218] Example 715:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-((2-hydroxyethyl)amino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.160]



[1219] <Step-1>: tert-butyl

(6-bromopyridin-3-yl)(2-((tert-butyldimethylsilyl)oxy)ethyl)carbamate

The title compound is prepared in 52% yield (41 mg, colorless gum) by the similar manner to Step-1 of Example 276 using tert-butyl (6-bromopyridin-3-yl)carbamate (50 mg, 0.18 mmol) in place of 5-bromo-1H-benzo[d][1,2,3]triazole.

¹H-NMR (400 MHz, CDCl₃) delta 8.35 (1H, d, J = 2.7 Hz), 7.61-7.53 (1H, m), 7.41 (1H, d, J = 9.1 Hz), 3.80 (2H, t, J = 5.3 Hz), 3.71 (2H, t, J = 5.3 Hz), 1.44 (9H, s), 0.86 (9H, s), 0.03 (6H, s).

MS (ESI) m/z: 433.0 (M+H)⁺.

[1220] <Step-2>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-((2-hydroxyethyl)amino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

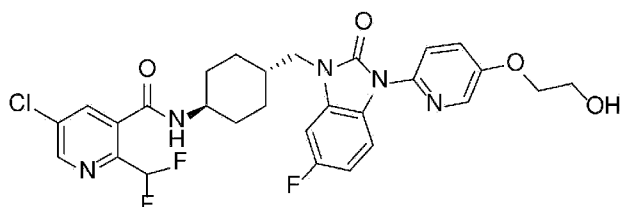
The title compound is prepared in 2 steps by the similar manner to Step-1 and Step-2 of Example 660 using tert-butyl

(6-bromopyridin-3-yl)(2-((tert-butyldimethylsilyl)oxy)ethyl)carbamate (Step-1 of Example 715) in place of tert-butyl (6-bromopyridin-3-yl)(methyl)carbamate.

[1221] Example 716:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.161]



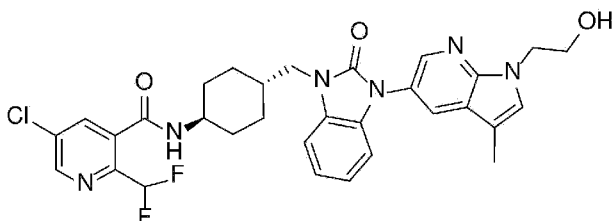
[1222] The title compound is prepared in 2 steps by the similar manner to Step-1 and Step-2 of Example 260 using Intermediate-264 and

2-bromo-5-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)pyridine in place of Intermediate-132 and 5-bromo-3-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole.

[1223] Example 731:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.162]



[1224] The title compound is prepared by the similar manner to Step-3 of Example 666 using Example 456 in place of

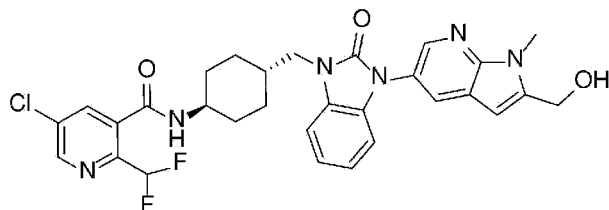
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide.

[1225] Example 732:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide

l)nicotinamide

[Chem.163]

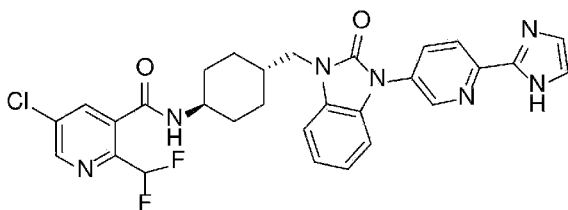


- [1226] The title compound is prepared in 4 steps by the similar manner to Step-1, Step-2, Step-3, and Step-4 of Example 709 using methyl 5-bromo-1-methyl-1H-pyrrolo[2,3-b]pyridine-2-carboxylate in place of methyl 5-bromo-1H-pyrrolo[2,3-b]pyridine-2-carboxylate.

- [1227] Example 733:

N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide

[Chem.164]

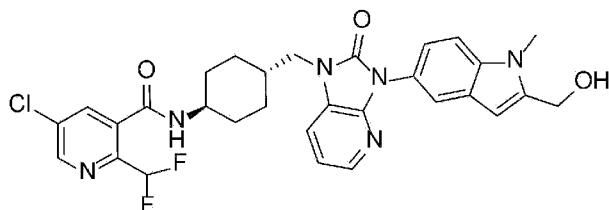


- [1228] The title compound is prepared by the similar manner to Example 581 using 5-bromo-2-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazol-2-yl)pyridine (Intermediate-255) and Intermediate-165 in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole and Step-2 of Example 9.

- [1229] Example 734:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide

[Chem.165]



- [1230] <Step-1>: ethyl

1-methyl-5-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1H-indole-2-carboxylate

The title compound is prepared in 3 steps by the similar manner to Step-1, Step-2,

and Step-3 of Intermediate-249 using 2-bromo-3-nitropyridine and ethyl 5-amino-1-methyl-1H-indole-2-carboxylate in place of 3-bromo-2-nitropyridine and 2-chloro-5-methoxyaniline.

¹H-NMR (400 MHz, DMSO-d₆) delta 11.36 (1H, br s), 7.91 (1H, dd, J = 5.0, 1.8 Hz), 7.89 (1H, d, J = 1.8 Hz), 7.73 (1H, d, J = 8.7 Hz), 7.53 (1H, dd, J = 8.7, 1.8 Hz), 7.39 (1H, dd, J = 7.8, 1.4 Hz), 7.36 (1H, s), 7.08 (1H, dd, J = 7.8, 5.0 Hz), 4.35 (2H, q, J = 7.3 Hz), 4.09 (3H, s), 1.36 (3H, t, J = 7.3 Hz).

MS (ESI) m/z: 336.9 (M+H)⁺.

[1231] <Step-2>: ethyl

5-(1-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1-methyl-1H-indole-2-carboxylate

The title compound is prepared by the similar manner to Step-3 of Intermediate-3 using ethyl

1-methyl-5-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1H-indole-2-carboxylate (Step-1 of Example 734) and Mesylate-4 in place of methyl

2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate and Mesylate-1.

[1232] <Step-3>:

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide

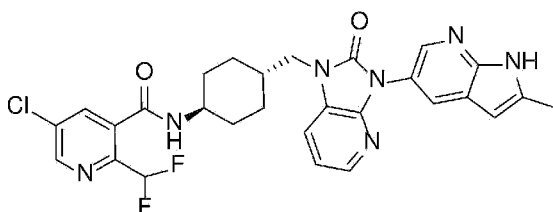
The title compound is prepared in 2 steps by the similar manner to Step-3 and Step-4 of Example 709 using ethyl

5-(1-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1-methyl-1H-indole-2-carboxylate (Step-2 of Example 734) in place of methyl

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine-2-carboxylate.

[1233] Example 738:

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide [Chem.166]

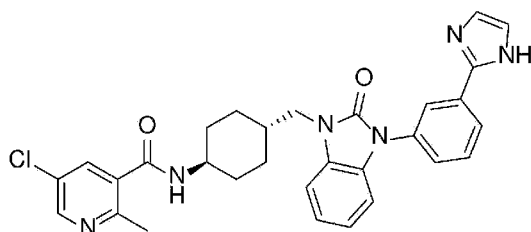


[1234] The title compound is prepared by the similar manner to Example 673 using In-

intermediate-214 in place of Intermediate- 165.

[1235] Example 740:

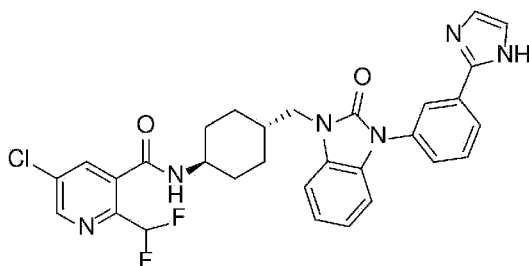
N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.167]



[1236] The title compound is prepared by the similar manner to Example 581 using 2-(3-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazole in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole.

[1237] Example 741:

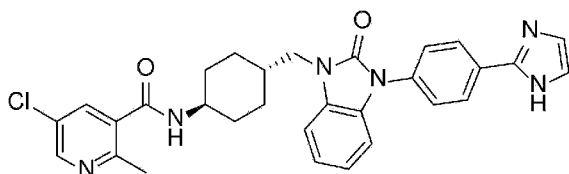
N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide
[Chem.168]



[1238] The title compound is prepared by the similar manner to Example 581 using 2-(3-bromophenyl)- 1-((2-(trimethylsilyl)ethoxy)methyl)- 1H-imidazole and Intermediate- 165 in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole and Step-2 of Example 9.

[1239] Example 742:

N-((1r,4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2, 3-dihydro- 1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide
[Chem.169]

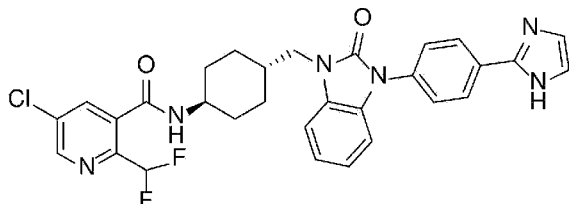


[1240] The title compound is prepared by the similar manner to Example 581 using

2-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazole in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole.

[1241] Example 743:

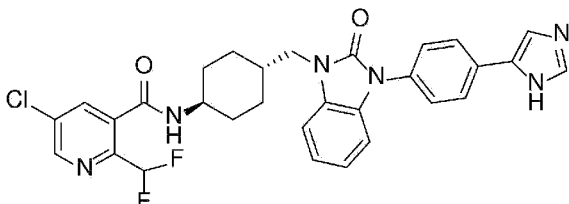
N-((1r,4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide
[Chem.170]



[1242] The title compound is prepared by the similar manner to Example 581 using 2-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazole and In-termediate- 165 in place of 4-(4-bromophenyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole and Step-2 of Example 9.

[1243] Example 769:

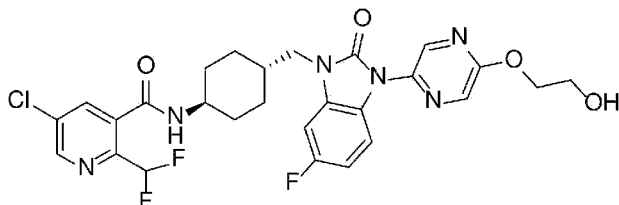
N-((1r,4r)-4-((3-(4-(1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide
[Chem.171]



[1244] The title compound is prepared by the similar manner to Example 667 using In-termediate- 165 in place of Step-2 of Example 9.

[1245] Example 778:

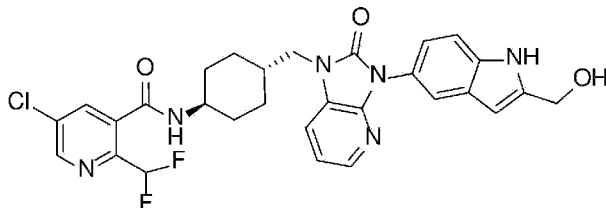
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.172]



[1246] The title compound is prepared in 2 steps by the similar manner to Step-1 and Step-2 of Example 712 using Intermediate-280 in place of Intermediate-262.

[1247] Example 779:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide
[Chem.173]



[1248] <Step-1>: ethyl

5-amino-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indole-2-carboxylate

The title compound is prepared in 2 steps by the similar manner to Step-1 and Step-2 of Intermediate-229 using ethyl 5-nitro-1H-indole-2-carboxylate in place of 3-methyl-5-nitro-1H-pyrrolo[2,3-b]pyridine.

MS (ESI) m/z: 452.8 (M+H)⁺.

[1249] <Step-2>: ethyl

5-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indole-2-carboxylate

The title compound is prepared in 3 steps by the similar manner to Step-1, Step-2, and Step-3 of Intermediate-249 using 2-bromo-3-nitropyridine and ethyl 5-amino-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indole-2-carboxylate (Step-1 of Example 779) in place of 3-bromo-2-nitropyridine and 2-chloro-5-methoxyaniline.

[1250] <Step-3>: ethyl

5-(1-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indole-2-carboxylate

The title compound is prepared by the similar manner to Step-3 of Intermediate-3 using ethyl

5-(2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indole-2-carboxylate (Step-2 of Example 779) and Mesylate-4 in place of methyl 2-((2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzoate and Mesylate-1.

[1251] <Step-4>:

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide

The title compound is prepared in 3 steps by the similar manner to Step-3, Step-4, and Step-5 of Example 709 using ethyl

5-(1-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indole-2-c

arboxylate (Step-3 of Example 779) in place of methyl 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine-2-carboxylate.

[1252] The other examples in Table 2 are prepared according to the representative procedure (Method A to Y) described in the example synthesis part using reactants shown in Table 2. The reactants are commercially available materials or obtained by conventional methods known to those skilled in the art, unless otherwise noted in the synthesis part. Each chemical structure of Example is described as a free-base in Table 2.

The observed MS (positive or negative mode) and retention time by LC-MS of all examples are described in Tables 3-1 to 3-12.

The ¹H-NMR data of selected examples are described in Tables 4-1 to 4-2.

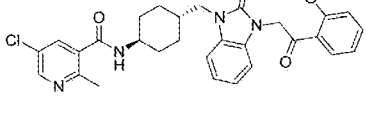
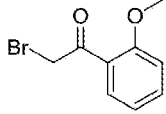
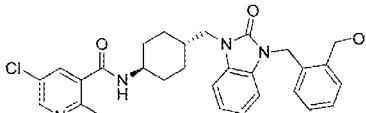
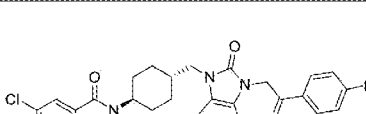
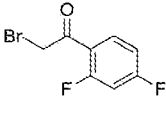
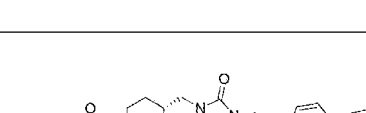
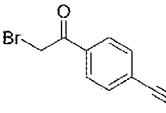
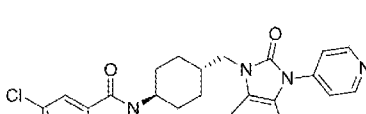
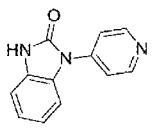
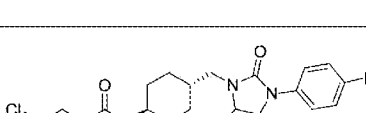
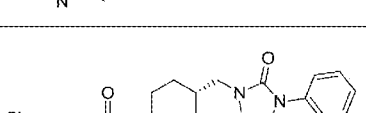
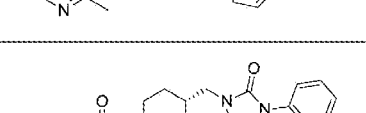
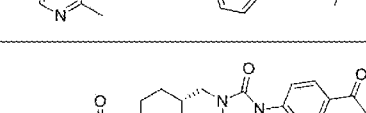
[1253]

[Table 2-1]

Ex.	Structure	Name	Reactants	Method
1		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenyl-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
2		N-((1r,4r)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Mesylate-1	A1
3		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-1, Mesylate-1	A1
4		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(methylcarbamoyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-2, 2 M methanamine in THF	B
5		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
6		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
7		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
8		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
9		5-chloro-N-((1r,4r)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	C1

[1254]

[Table 2-2]

10		5-chloro-N-((1r,4r)-4-((3-(2-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		C1
11		5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-3	D
12		5-chloro-N-((1r,4r)-4-((3-(2-(2,4-difluorophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		C2
13		5-chloro-N-((1r,4r)-4-((3-(2-(4-cyanophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		C2
14		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
15		5-chloro-N-((1r,4r)-4-((3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-4, Mesylate-1	A1
16		5-chloro-N-((1r,4r)-4-((3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-5, Mesylate-1	A1
17		N-((1r,4r)-4-((3-(3-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-6, Mesylate-1	A1
18		N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-7, Mesylate-1	A1

[1255]

[Table 2-3]

19		5-chloro-N-((1r,4r)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Example 18	E
20		5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-8	D
21		5-chloro-N-((1r,4r)-4-((3-(4-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-9	D
22		5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-2	D
23		5-chloro-N-((1r,4r)-4-((3-(4-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-10	D
24		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
25		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
26		5-chloro-N-((1r,4r)-4-((3-(4-chlorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Mesylate-1	A1
27		5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Mesylate-1	A1

[1256]

[Table 2-4]

28		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		A1
29		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-11, Mesylate-1	A1
30		5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-12, Mesylate-1	A1
31		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-13, Mesylate-1	A1
32		5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-14, Mesylate-1	A1
33		5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		A1
34		5-chloro-N-((1r,4r)-4-((3-(2-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		A1
35		5-chloro-N-((1r,4r)-4-((3-(6-(2,2-difluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-15, Mesylate-1	A1
36		5-chloro-N-((1r,4r)-4-((3-(6-ethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-16, Mesylate-1	A1

[1257]

[Table 2-5]

37		2-ethyl-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide		A1
38		2-ethyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide	Intermediate-13, Mesylate-2	A1
39		2-ethyl-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide	Intermediate-12, Mesylate-2	A1
40		2-(2-hydroxyethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide	see Example synthesis part	
41		N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-ethyl-2H-indazole-3-carboxamide	Intermediate-7, Mesylate-2	A1
42		2-ethyl-N-((1r,4r)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide	Example 41,	E
43		5-chloro-N-((1r,4r)-4-((3-(2-methoxypyrimidin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-17, Mesylate-1	A1
44		5-chloro-N-((1r,4r)-4-((3-(3,4-dimethoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-18, Mesylate-1	A1
45		5-chloro-N-((1r,4r)-4-((3-(2-methoxypyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-19, Mesylate-1	A1

[1258]

[Table 2-6]

46		5-chloro-N-((1r,4r)-4-((3-(2,4-difluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-20, Mesylate-1	A1
47		5-chloro-N-((1r,4r)-4-((3-(4-fluoro-2-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-21, Mesylate-1	A1
48		5-chloro-N-((1r,4r)-4-((3-(4-fluoro-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-22, Mesylate-1	A1
49		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-23, Mesylate-1	A1
50		5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
51		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-25, Mesylate-1	A1
52		5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-26, Mesylate-1	A1
53		5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-27, Mesylate-1	A1
54		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-28, Mesylate-1	A1

[1259]

[Table 2-7]

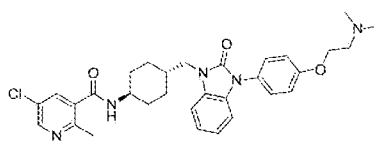
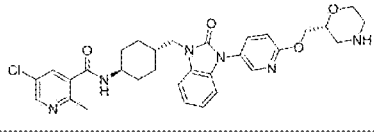
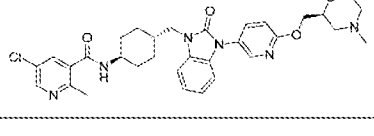
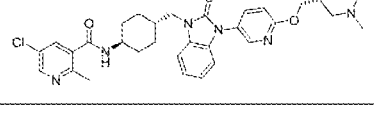
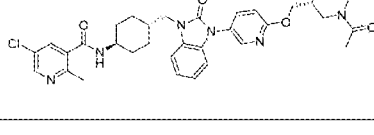
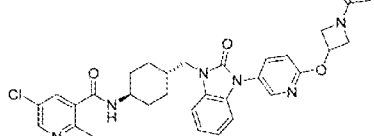
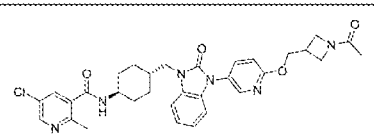
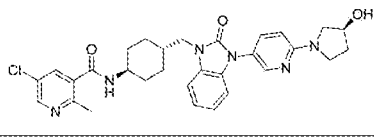
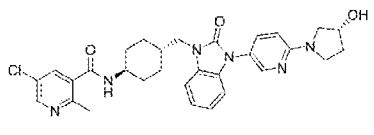
55		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-29, Mesylate-1	A1
56		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-30, Mesylate-1	A1
57		5-chloro-2-methyl-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-31, Mesylate-1	A1
58		5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-32, Mesylate-1	A1
59		5-chloro-N-((1r,4r)-4-((3-(6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-33, Mesylate-1	A1
60		5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-34, Mesylate-1	A1
61		5-chloro-N-((1S,4r)-4-((3-(6-((S)-3-(dimethylamino)pyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-35, Mesylate-1	A1
62		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide	see Example synthesis part	
63		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	see Example synthesis part	

[1260]

[Table 2-8]

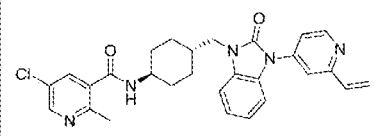
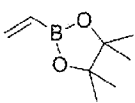
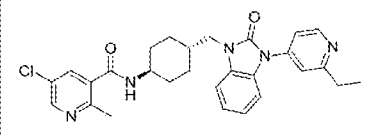
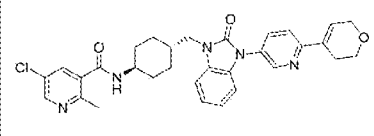
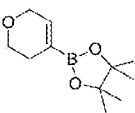
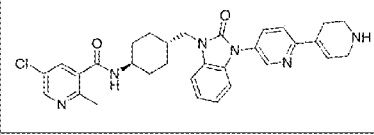
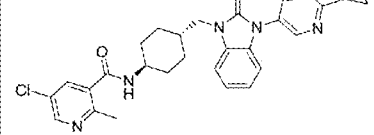
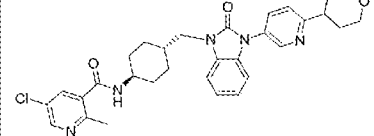
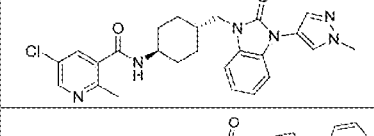
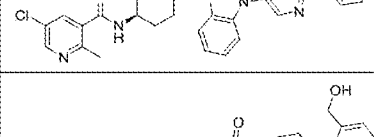
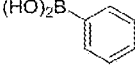
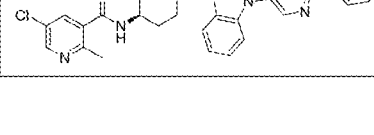
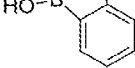
64		5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-37, Mesylate-1	A1
65		5-chloro-N-((1r,4r)-4-((3-(6-(4-(2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-38, Mesylate-1	A1
66		N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-39, Mesylate-1	A1
67		5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-40, Mesylate-1	A1
68		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-41, Mesylate-1	A1
69		5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
70		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex 66,	F
71		N-((1r,4r)-4-((3-(2-bromopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-43, Mesylate-1	A1
72		5-chloro-N-((1r,4r)-4-((3-(6-ethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 70	G

[Table 2-9]

73		5-chloro-N-((1R,4R)-4-((3-(4-(2-(dimethylamino)ethoxy)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-44, Mesylate-1	A1
74		5-chloro-2-methyl-N-((1R,4R)-4-((3-(6-((R)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
75		5-chloro-2-methyl-N-((1S,4R)-4-((3-(6-(((S)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-46	H
76		5-chloro-2-methyl-N-((1R,4R)-4-((3-(6-(((R)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex74	H
77		N-((1R,4R)-4-((3-(6-(((R)-4-acetylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
78		N-((1R,4R)-4-((3-(6-(((1-acetylazetidin-3-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
79		N-((1R,4R)-4-((3-(6-(((1-acetylazetidin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
80		5-chloro-N-((1S,4R)-4-((3-(6-(((S)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-49, Mesylate-1	A1
81		5-chloro-N-((1R,4R)-4-((3-(6-(((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-50, Mesylate-1	A1

[1262]

[Table 2-10]

82		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-vinylpyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex 71, 	F
83		5-chloro-N-((1r,4r)-4-((3-(2-ethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 82	G
84		5-chloro-N-((1r,4r)-4-((3-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 66, 	F
85		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1',2',3',6'-tetrahydro-[2,4'-bipyridin]-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
86		5-chloro-N-((1r,4r)-4-((3-(6-cyclopropylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-51, Mesylate-1	A2
87		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(tetrahydro-2H-pyran-4-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-52, Mesylate-1	A2
88		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-53, Mesylate-1	A1
89		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-phenylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex 66, 	I
90		5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)phenyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 66, 	I

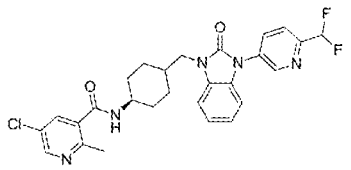
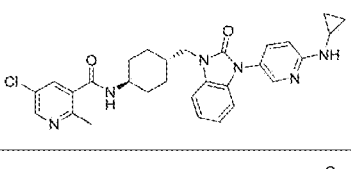
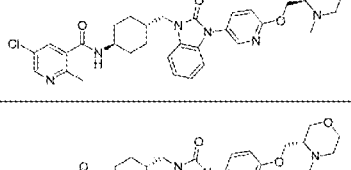
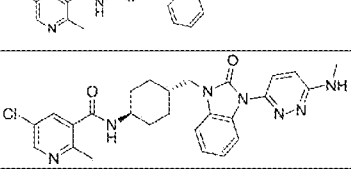
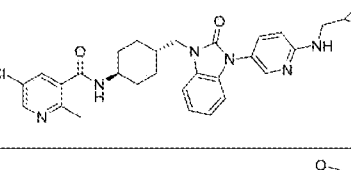
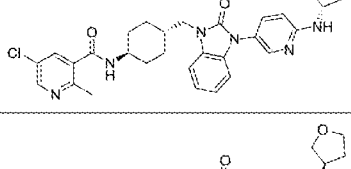
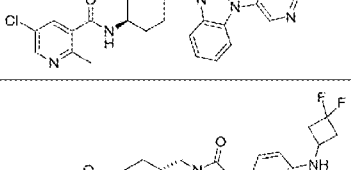
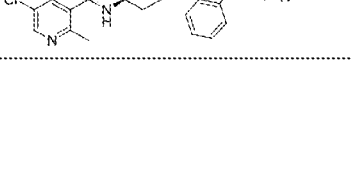
[1263]

[Table 2-11]

91		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-54, methanamine hydrochloride	J
92		5-chloro-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, ethanamine hydrochloride	J
93		5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 66, 	K
94		5-chloro-N-((1r,4r)-4-((3-(6-((3-hydroxypropyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 66, 	K
95		5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 66, 	K
96		5-chloro-N-((1r,4r)-4-((3-(6-(4-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Ex 66, 	K
97		5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
98		N-((1r,4r)-4-((3-(6-(acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
99		5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)morpholino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, 	L

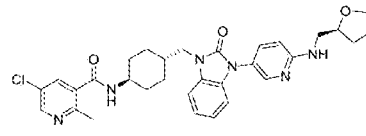
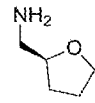
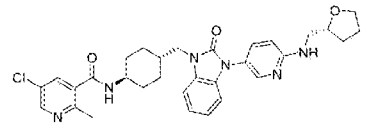
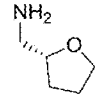
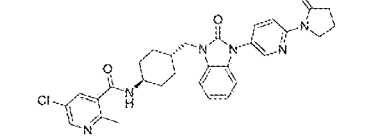
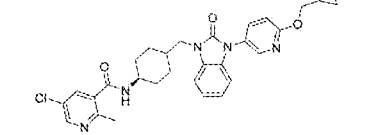
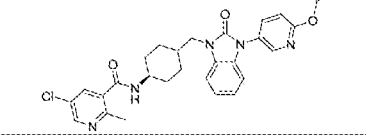
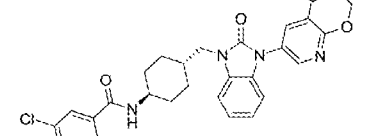
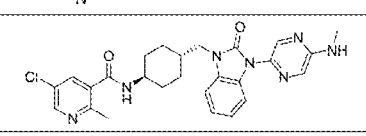
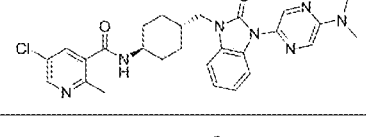
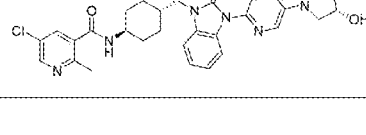
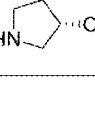
[1264]

[Table 2-12]

100		5-chloro-N-((1R,4R)-4-((3-(6-(difluoromethyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	100
101		5-chloro-N-((1R,4R)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
102		5-chloro-2-methyl-N-((1R,4R)-4-((3-(6-(((R)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
103		5-chloro-2-methyl-N-((1S,4R)-4-((3-(6-(((S)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
104		5-chloro-2-methyl-N-((1R,4R)-4-((3-(6-(methylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
105		5-chloro-N-((1R,4R)-4-((3-(6-((cyclopropylmethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, 	M
106		5-chloro-2-methyl-N-((1S,4R)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-54, 	M
107		5-chloro-2-methyl-N-((1R,4R)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-54, 	M
108		5-chloro-N-((1R,4R)-4-((3-(6-((3,3-difluorocyclobutyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, 3,3-difluorocyclobutylamine hydrochloride	M

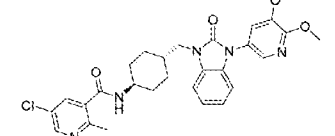
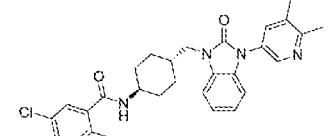
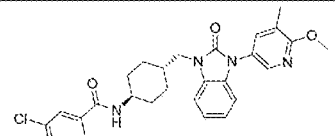
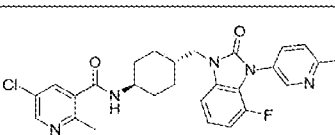
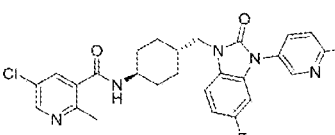
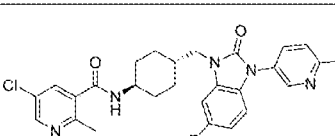
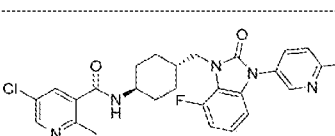
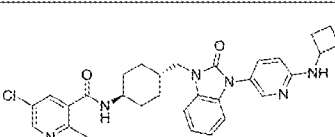
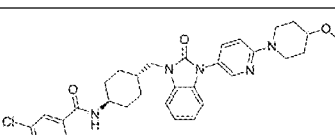
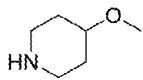
[1265]

[Table 2-13]

109		5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-54, 	M
110		5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-54, 	M
111		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
112		5-chloro-N-(4-((3-(6-(cyclopropylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, cyclopropylmethanol	N
113		5-chloro-N-(4-((3-(6-(cyclopropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, cyclopropanol	N
114		5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-56, Mesylate-1	A1
115		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-57, methanamine hydrochloride	M
116		5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-57, dimethylamine hydrochloride	M
117		5-chloro-N-((1S,4r)-4-((3-(5-((S)-3-hydroxypyrrolidin-1-yl)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-57, 	M

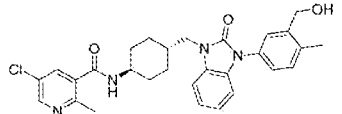
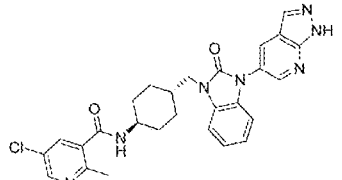
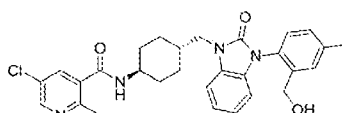
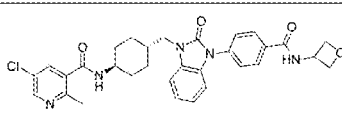
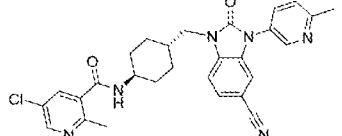
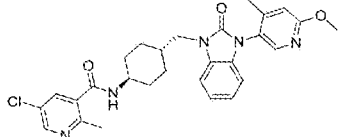
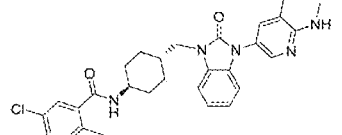
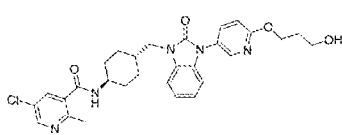
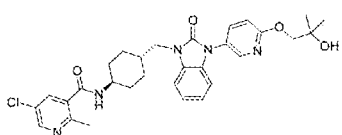
[1266]

[Table 2-14]

118		5-chloro-N-((1r,4r)-4-((3-(5,6-dimethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-58, Mesylate-1	A2
119		5-chloro-N-((1r,4r)-4-((3-(5,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-59, Mesylate-1	A2
120		5-chloro-N-((1r,4r)-4-((3-(6-methoxy-5-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-60, Mesylate-1	A2
121		5-chloro-N-((1r,4r)-4-((4-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-61, Mesylate-1	A2
122		5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-62, Mesylate-1	A2
123		5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-63, Mesylate-1	A2
124		5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-64, Mesylate-1	A2
125		5-chloro-N-((1r,4r)-4-((3-(6-(cyclobutylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, cyclobutanamine	L
126		5-chloro-N-((1r,4r)-4-((3-(6-(4-methoxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, 	L

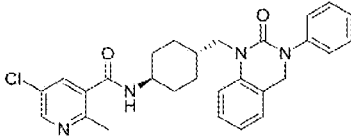
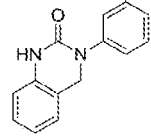
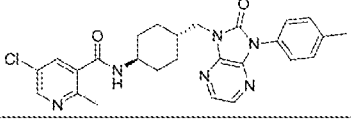
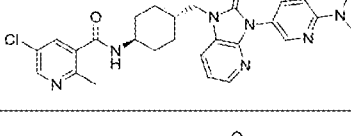
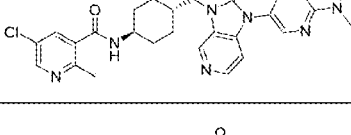
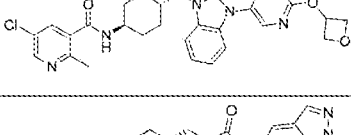
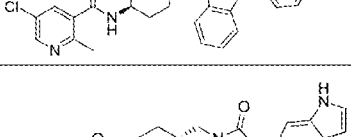
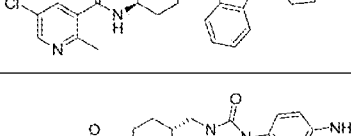
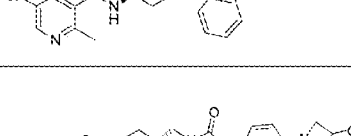
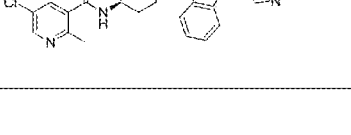
[1267]

[Table 2-15]

127		5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-65	D
128		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
129		5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-66	D
130		5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxetan-3-ylcarbamoyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
131		5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-67, Mesylate-1	A2
132		5-chloro-N-((1r,4r)-4-((3-(6-methoxy-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-68, Mesylate-1	A2
133		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-69, Mesylate-1	A2
134		5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
135		5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	

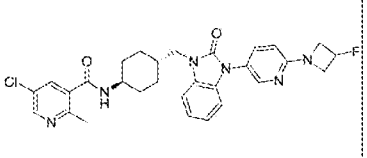
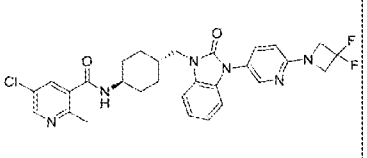
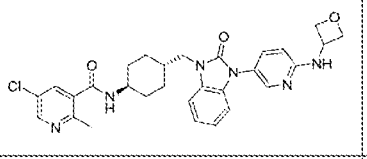
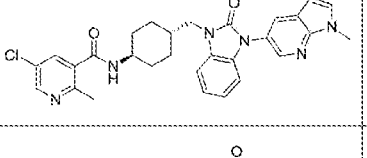
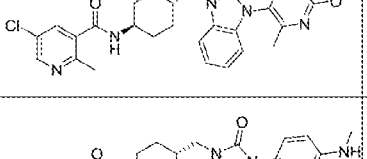
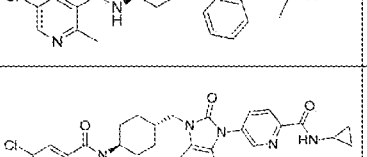
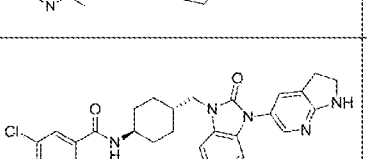
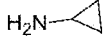
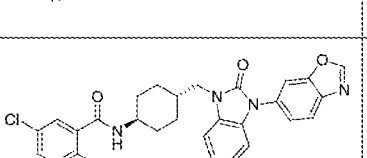
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[Table 2-16]

136		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenyl-3,4-dihydroquinazolin-1(2H)-yl)methyl)cyclohexyl)nicotinamide	Mesylate-1 	A1
137		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyrazin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-70 Mesylate-1	A1
138		5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-71 Mesylate-1	A1
139		5-chloro-N-((1r,4r)-4-((1-(6-(dimethylamino)pyridin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-72 Mesylate-1	A1
140		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
141		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-73 Mesylate-1	A2
142		N-((1r,4r)-4-((3-(1H-indol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-74 Mesylate-1	A2
143		N-((1r,4r)-4-((3-(6-aminopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
144		5-chloro-N-((1r,4r)-4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-75 Mesylate-1	A2

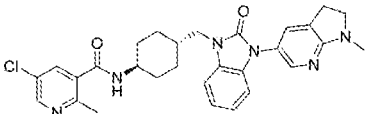
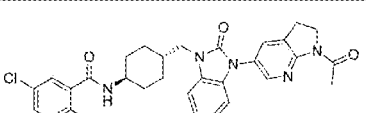
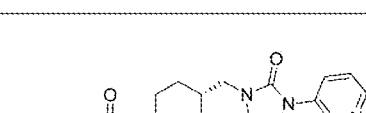
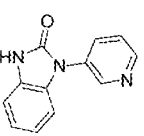
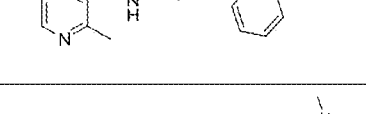
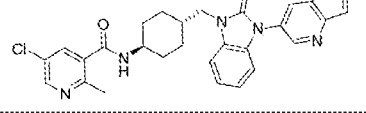
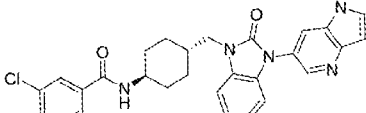
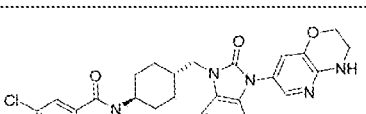
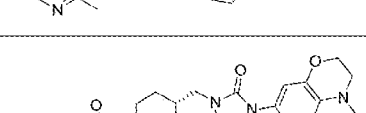
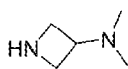
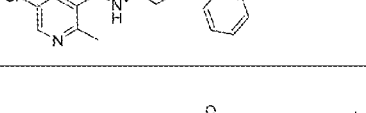
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[Table 2-17]

145		5-chloro-N-((1r,4r)-4-((3-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-76 Mesylate-1	A2
146		5-chloro-N-((1r,4r)-4-((3-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-77 Mesylate-1	A2
147		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-78 Mesylate-1	A1
148		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-79 Mesylate-1	A2
149		5-chloro-N-((1r,4r)-4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
150		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
151		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide	Intermediate-36 	Q
152		5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
153		N-((1r,4r)-4-((3-(benzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-80 Mesylate-1	A1

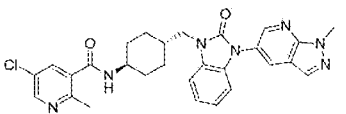
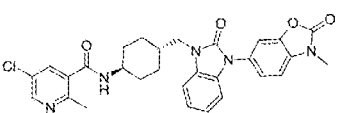
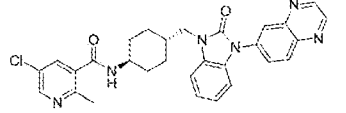
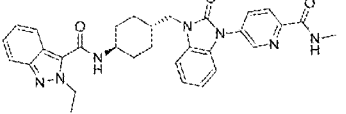
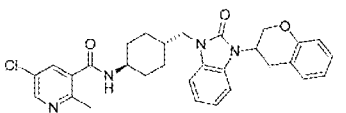
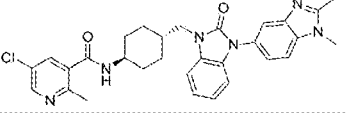
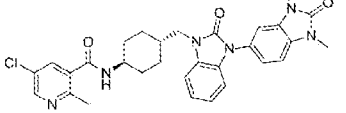
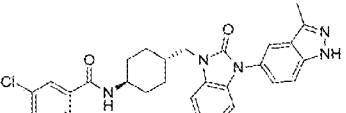
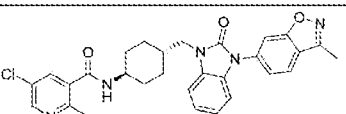
[1270]

[Table 2-18]

154		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
155		N-((1r,4r)-4-((3-(1-acetyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
156		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Mesylate-1	A1
157		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[3,2-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-81, Mesylate-1	A1
158		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-82, Mesylate-1	O
159		5-chloro-N-((1r,4r)-4-((3-(3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
160		5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex 159	H
161		5-chloro-N-((1r,4r)-4-((3-(6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, 	P
162		N-((1r,4r)-4-((3-(6-(azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-54, 	P

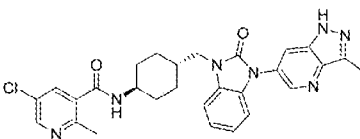
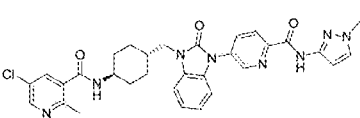
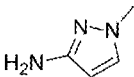
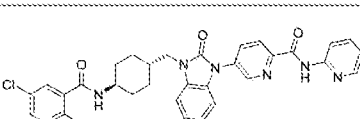
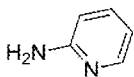
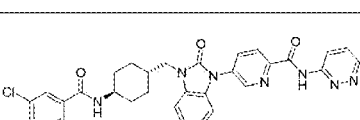
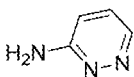
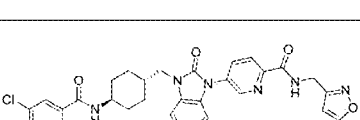
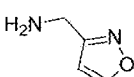
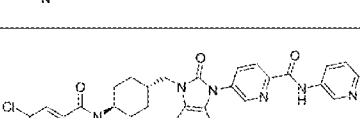
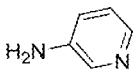
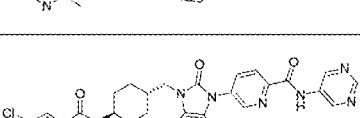
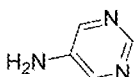
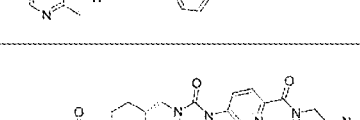
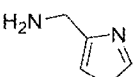
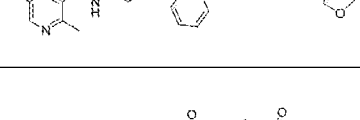
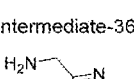
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[Table 2-19]

163		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-84, Mesylate-1	A1
164		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-85, Mesylate-1	A1
165		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-86, Mesylate-1	A1
166		2-ethyl-N-((1r,4r)-4-((3-(6-(methylcarbamoyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide	Intermediate-87, Mesylate-2	A1
167		5-chloro-N-((1r,4r)-4-((3-(chroman-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-88, Mesylate-1	A1
168		5-chloro-N-((1r,4r)-4-((1',2'-dimethyl-2-oxo-1'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-89, Mesylate-1	A1
169		5-chloro-N-((1r,4r)-4-((1',3'-dimethyl-2,2'-dioxo-2',3'-dihydro-1'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-90, Mesylate-1	A1
170		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-91, Mesylate-1	O
171		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-92, Mesylate-1	A1

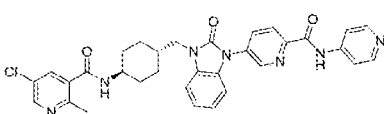
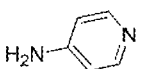
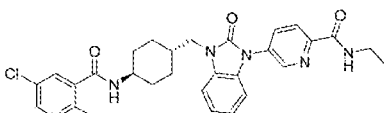
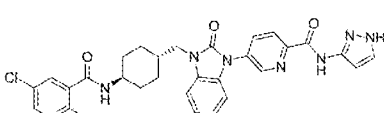
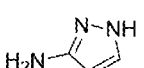
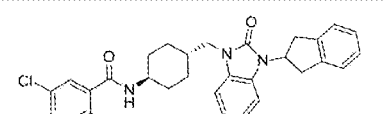
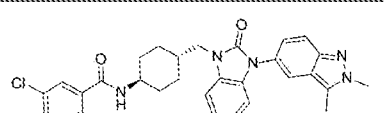
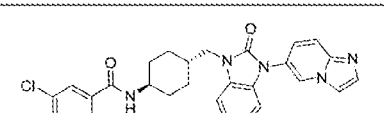
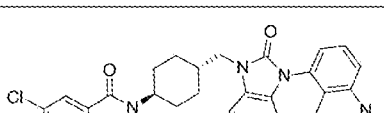
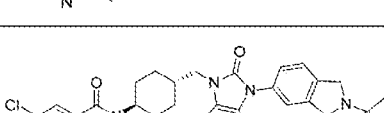
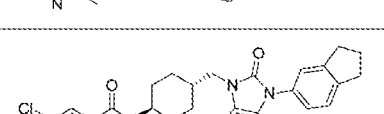
[1272]

[Table 2-20]

172		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[4,3-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
173		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(1-methyl-1H-pyrazol-3-yl)picolinamide	Intermediate-36, 	Q
174		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-2-yl)picolinamide	Intermediate-36, 	Q
175		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridazin-3-yl)picolinamide	Intermediate-36, 	Q
176		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(isoxazol-3-yl)methyl)picolinamide	Intermediate-36, 	Q
177		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-3-yl)picolinamide	Intermediate-36, 	Q
178		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyrimidin-5-yl)picolinamide	Intermediate-36, 	Q
179		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(oxazol-4-yl)methyl)picolinamide	Intermediate-36, 	Q
180		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-((4-methylthiazol-2-yl)methyl)picolinamide	Intermediate-36, 	Q

[1273]

[Table 2-21]

181		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-4-yl)picolinamide	Intermediate-36, 	Q
182		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-ethylpicolinamide	Intermediate-36, 	Q
183		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(1H-pyrazol-3-yl)picolinamide	Intermediate-36, 	Q
184		5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-inden-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-94, Mesylate-1	A1
185		5-chloro-N-((1r,4r)-4-((3-(2,3-dimethyl-2H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-95, Mesylate-1	A1
186		5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-96, Mesylate-1	A1
187		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinazolin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-97, Mesylate-1	A1
188		N-((1r,4r)-4-((3-(2-acetylisoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
189		5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-inden-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-98, Mesylate-1	A1

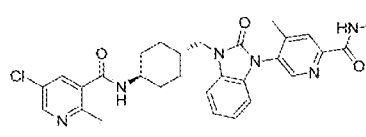
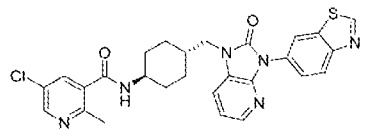
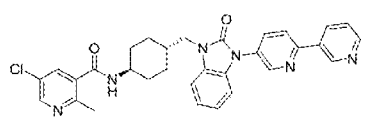
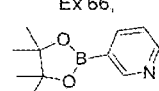
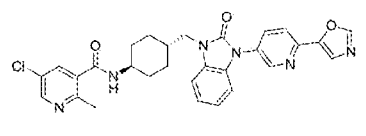
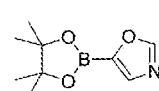
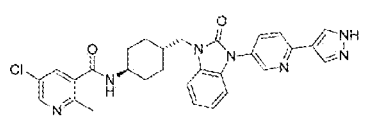
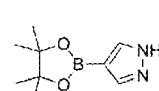
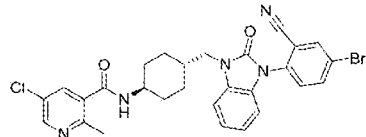
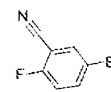
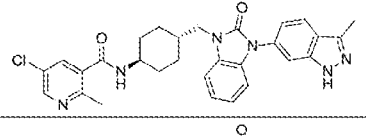
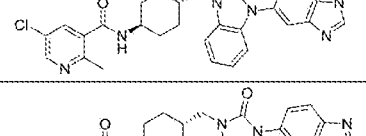
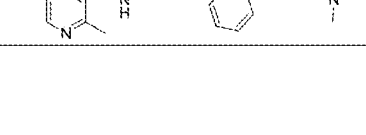
[1274]

[Table 2-22]

190		5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-99, Mesylate-1	A1
191		5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-100, Mesylate-1	A1
192		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-101, Mesylate-1	A1
193		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-102, Mesylate-1	A1
194		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-103, Mesylate-1	A1
195		5-chloro-N-((1r,4r)-4-((3-(3-(cyclopropylmethyl)-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-104, Step-2 of Ex 9	R
196		5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
197		N-((1r,4r)-4-((3-(3-amino-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
198		N-((1r,4r)-4-((3-(3-aminobenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	

[1275]

[Table 2-23]

199		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide	Intermediate-105, Mesylate-1	A1
200		N-(((1r,4r)-4-((3-(benzo[d]thiazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-106, Mesylate-1	A1
201		N-(((1r,4r)-4-((3-[2,3'-bipyridin]-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Ex 66, 	I
202		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(6-(oxazol-5-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex 66, 	I
203		N-(((1r,4r)-4-((3-(6-(1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Ex 66, 	I
204		N-(((1r,4r)-4-((3-(4-bromo-2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
205		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-107, Mesylate-1	O
206		5-chloro-2-methyl-N-(((1r,4r)-4-((1'-methyl-2-oxo-1'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-108, Mesylate-1	A1
207		5-chloro-2-methyl-N-(((1r,4r)-4-((3'-methyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-109, Mesylate-1	A1

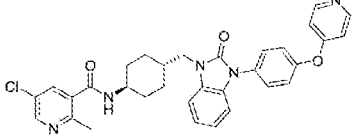
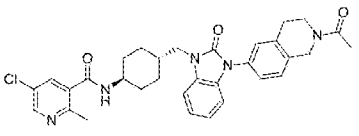
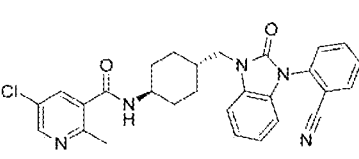
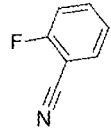
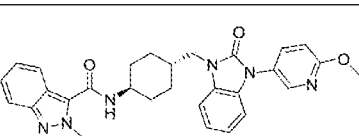
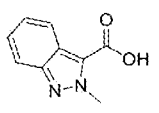
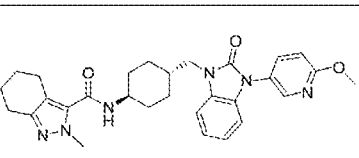
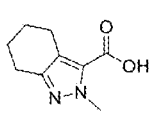
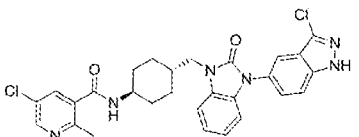
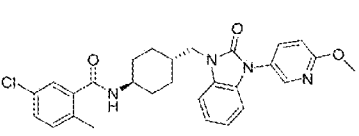
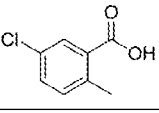
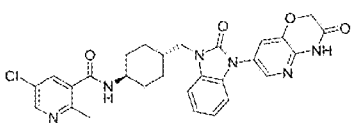
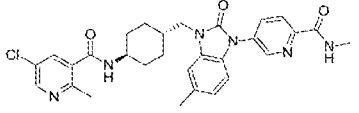
[1276]

[Table 2-24]

208		5-chloro-N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(3-chloro-1-methyl-1 <i>H</i> -indazol-6-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		R
209		5-chloro-N-((1 <i>r</i> ,4 <i>r</i>)-4-((2',3'-dimethyl-2-oxo-3' <i>H</i> -[1,5'-bibenzo[d]imidazol]-3(2 <i>H</i>)-yl)methyl)cyclohexyl)-2-methylnicotinamide		R
210		5-chloro-N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(3-chloro-1 <i>H</i> -indazol-6-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
211		N-((1 <i>r</i> ,4 <i>r</i>)-4-((1-(5-bromo-2,3-dihydro-1 <i>H</i> -inden-2-yl)-2-oxo-1 <i>H</i> -imidazo[4,5- <i>c</i>]pyridin-3(2 <i>H</i>)-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-110, Mesylate-1	A1
212		5-chloro-2-methyl-N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(3-methyl-1 <i>H</i> -indazol-5-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-111, Mesylate-1	S
213		5-chloro-N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(1,3-dimethyl-1 <i>H</i> -indazol-5-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		R
214		5-chloro-2-methyl-N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(6-(1-methyl-1 <i>H</i> -pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Ex 66,	I
215		5-chloro-2-methyl-N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(3-methyl-2-oxo-2,3-dihydrooxazolo[4,5- <i>b</i>]pyridin-6-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		T
216		N-((1 <i>r</i> ,4 <i>r</i>)-4-((3-(6'-amino-[2,3'-bipyridin]-5-yl)-2-oxo-2,3-dihydro-1 <i>H</i> -benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Ex 66,	I

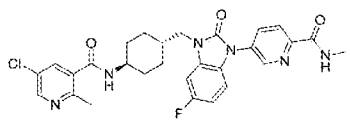
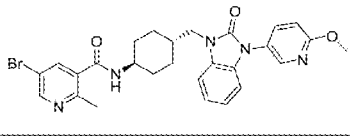
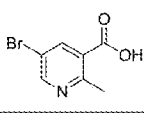
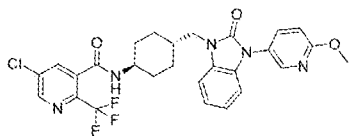
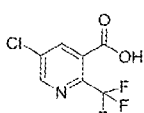
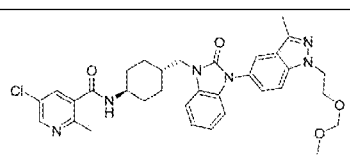
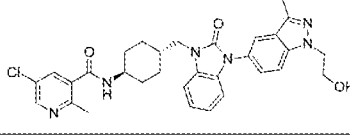
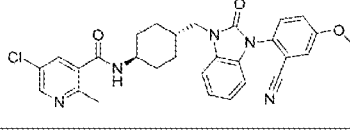
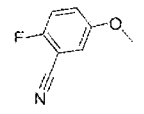
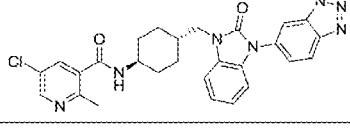
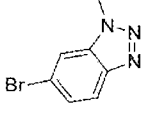
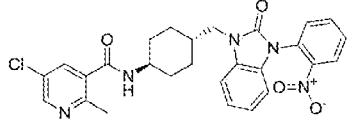
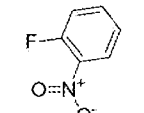
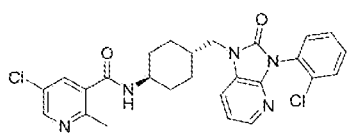
[1277]

[Table 2-25]

217		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(pyridin-4-yloxy)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-112, Mesylate-1	A1
218		N-((1r,4r)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
219		5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
220		N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl-2H-indazole-3-carboxamide	Intermediate-113, 	Q
221		N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl-4,5,6,7-tetrahydro-2H-indazole-3-carboxamide	Intermediate-113, 	Q
222		5-chloro-N-((1r,4r)-4-((3-(3-chloro-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
223		5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylbenzamide	Intermediate-113, 	Q
224		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
225		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-114, Mesylate-1	A1

[1278]

[Table 2-26]

226		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-115, Mesylate-1	A1
227		5-bromo-N-(((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-113, 	Q
228		5-chloro-N-(((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-113, 	Q
229		5-chloro-N-(((1r,4r)-4-((3-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-116, Mesylate-1	A1
230		5-chloro-N-(((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
231		5-chloro-N-(((1r,4r)-4-((3-(2-cyano-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
232		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
233		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(2-nitrophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	U
234		5-chloro-N-(((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-117, Mesylate-1	A1

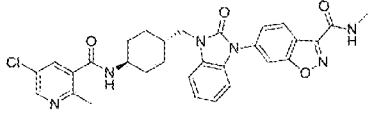
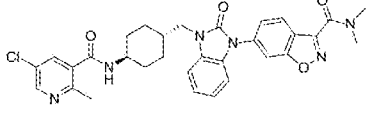
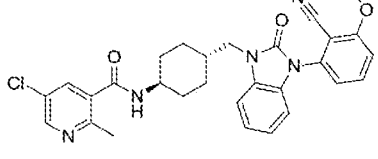
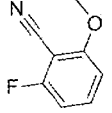
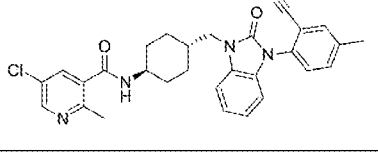
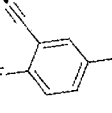
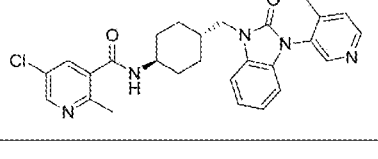
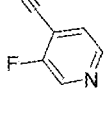
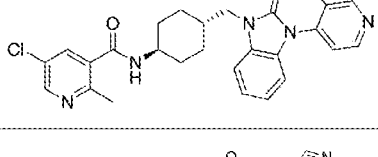
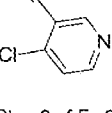
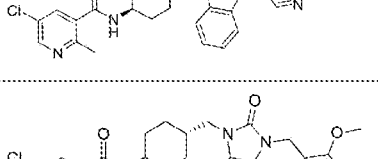
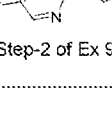
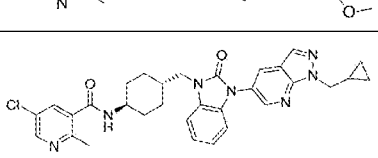
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[Table 2-27]

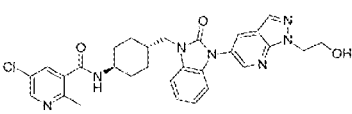
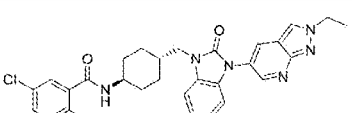
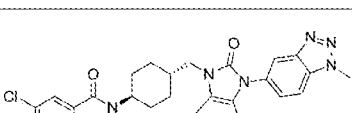
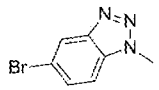
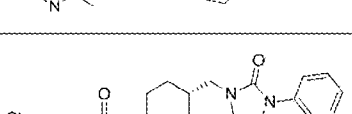
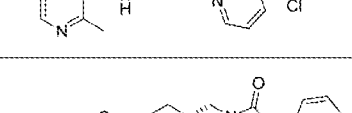
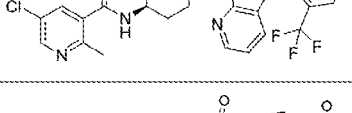
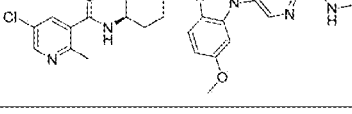
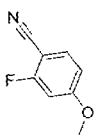
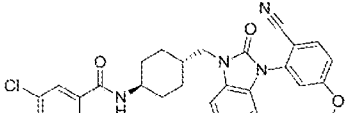
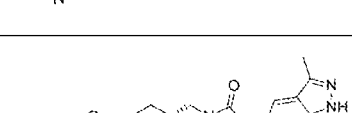
235		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-118, Mesylate-1	A1
236		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-119, Mesylate-1	A1
237		2,5-dichloro-N-(((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-113, 	Q
238		5-chloro-N-(((1r,4r)-4-((2-(2,3-dihydro-1H-inden-4-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-120, Mesylate-1	A1
239		5-chloro-N-(((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
240		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	Q
241		5-chloro-N-(((1r,4r)-4-((3-(2-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
242		5-chloro-N-(((1r,4r)-4-((3-(3-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
243		6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxamide	see Example synthesis part	

[1280]

[Table 2-28]

244		6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylbenzo[d]isoxazole-3-carboxamide	see Example synthesis part	
245		6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylbenzo[d]isoxazole-3-carboxamide	see Example synthesis part	
246		5-chloro-N-(((1r,4r)-4-((3-(2-cyano-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
247		5-chloro-N-(((1r,4r)-4-((3-(2-cyano-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
248		5-chloro-N-(((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
249		5-chloro-N-(((1r,4r)-4-((3-(3-cyanopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
250		5-chloro-N-(((1r,4r)-4-((3-(1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
251		5-chloro-N-(((1r,4r)-4-((3-(2,4-dimethoxybenzyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-122, Mesylate-1	A1
252		5-chloro-N-(((1r,4r)-4-((3-(1-(cyclopropylmethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R

[Table 2-29]

253		5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
254		5-chloro-N-((1r,4r)-4-((3-(2-ethyl-2H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-123, Step-2 of Ex 9	R
255		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
256		5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-124, Mesylate-1	A1
257		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(2-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-125, Mesylate-1	A1
258		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-126, Mesylate-1	A1
259		5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U
260		5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
261		5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	

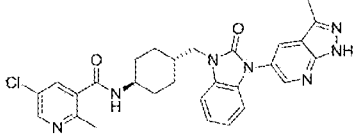
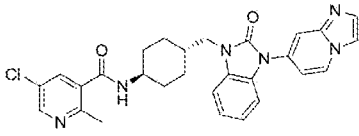
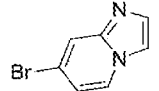
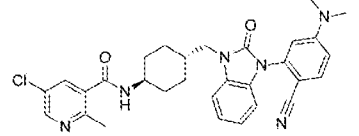
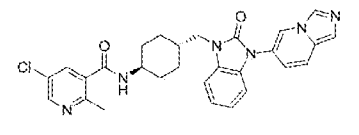
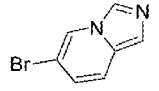
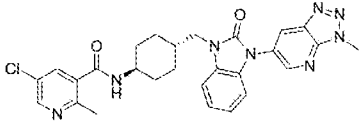
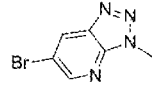
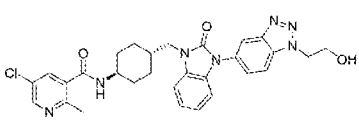
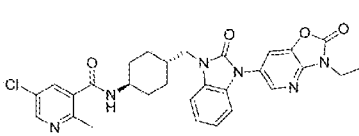
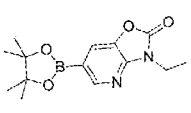
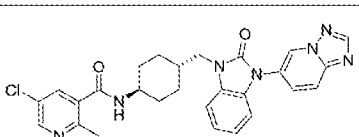
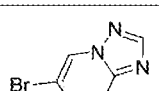
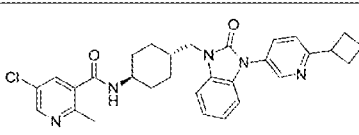
[1282]

[Table 2-30]

262		5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		R
263		N-((1r,4r)-4-((3-(2-aminobenzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
264		N-((1r,4r)-4-((3-(benzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		T
265		5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-127, 	Q
266		5-chloro-2-cyclopropyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide	Intermediate-127, 	Q
267		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide	Intermediate-127, 	Q
268		5-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide	Intermediate-127, 	Q
269		2,5-dichloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide	Intermediate-127, 	Q
270		5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide	Intermediate-127, 	Q

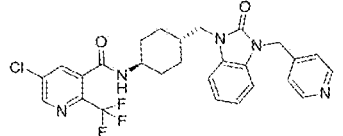
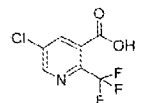
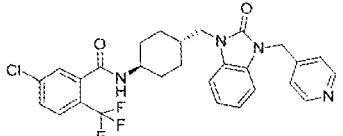
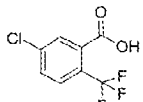
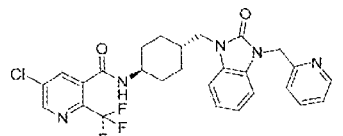
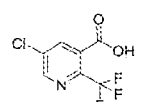
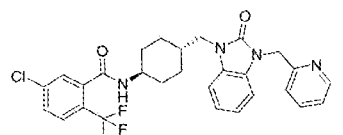
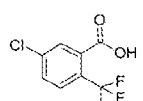
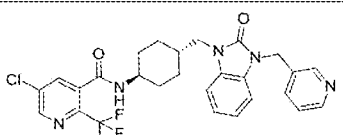
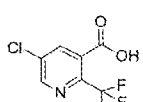
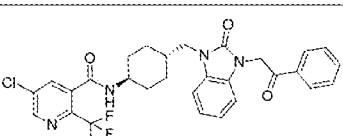
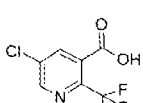
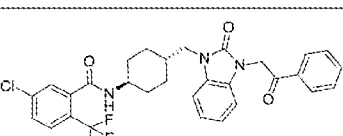
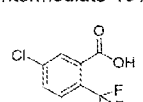
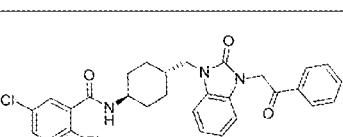
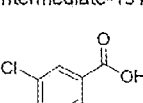
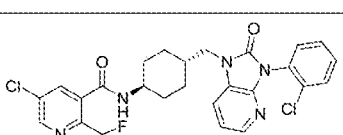
[1283]

[Table 2-31]

271		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
272		5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
273		5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
274		5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
275		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-3H-[1,2,3]triazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
276		5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
277		5-chloro-N-((1r,4r)-4-((3-(3-ethyl-2-oxo-2,3-dihydrooxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	T
278		N-((1r,4r)-4-((3-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
279		5-chloro-N-((1r,4r)-4-((3-(6-cyclobutylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	

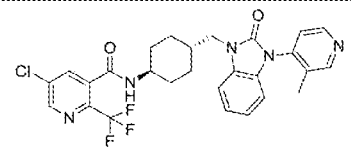
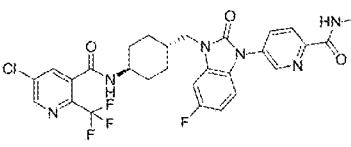
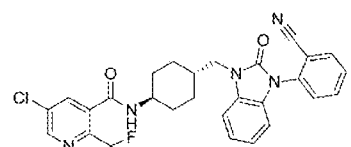
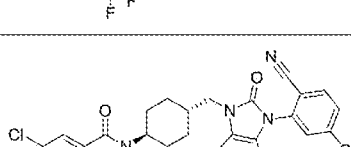
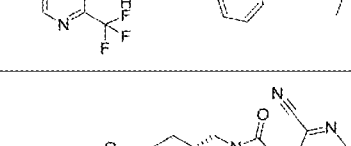
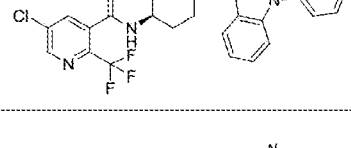
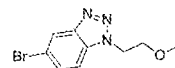
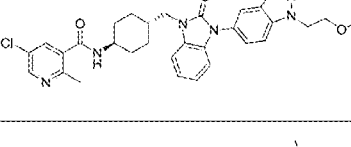
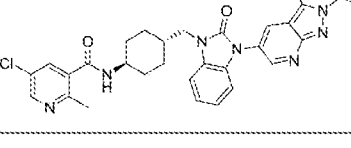
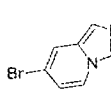
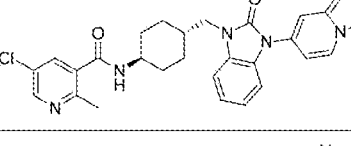
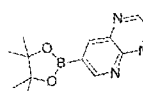
[1284]

[Table 2-32]

280		5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Q
281		5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide		Q
282		5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Q
283		5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide		Q
284		5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Q
285		5-chloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Q
286		5-chloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide		Q
287		2,5-dichloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide		Q
288		5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-117, Mesylate-3	A1

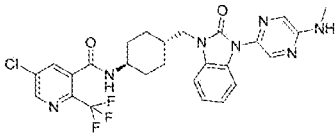
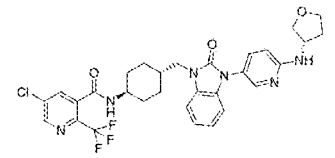
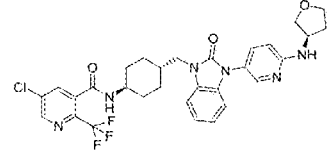
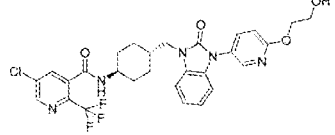
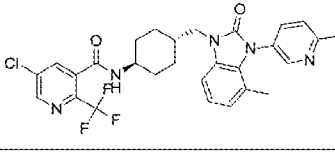
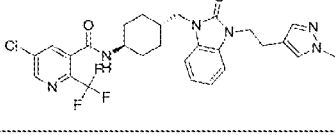
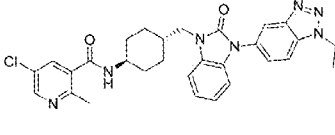
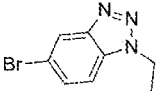
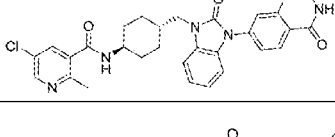
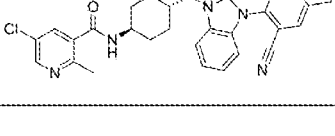
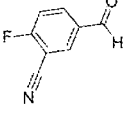
[1285]

[Table 2-33]

289		5-chloro-N-((1r,4r)-4-((3-(3-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-25, Mesylate-3	A1
290		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-115, Mesylate-3	A1
291		5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-132	U
292		5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-132	U
293		5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-132	U
294		5-chloro-N-((1r,4r)-4-((3-(1-(2-methoxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
295		5-chloro-N-((1r,4r)-4-((3-(2-ethyl-3-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-133, Step-2 of Ex 9	R
296		5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
297		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyrido[2,3-b]pyrazin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	T

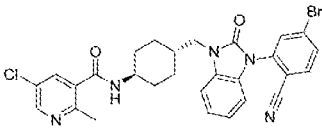
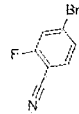
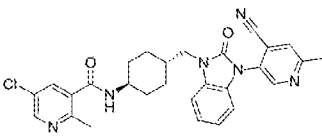
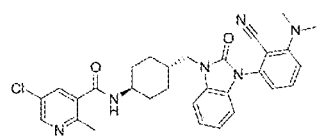
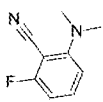
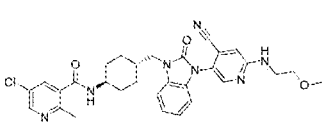
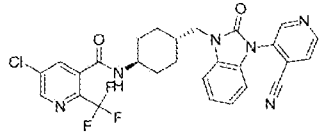
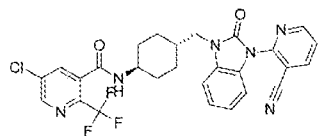
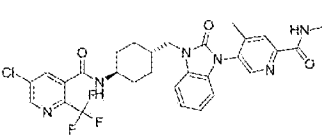
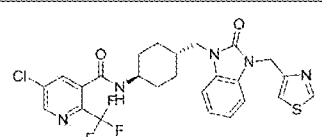
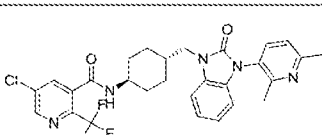
[1286]

[Table 2-34]

298		5-chloro-N-(((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-134, Mesylate-3	A1
299		5-chloro-N-(((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-135, Mesylate-3	A1
300		5-chloro-N-(((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-136, Mesylate-3	A1
301		5-chloro-N-(((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
302		5-chloro-N-(((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-31, Mesylate-3	A1
303		5-chloro-N-(((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-119, Mesylate-3	A1
304		5-chloro-N-(((1r,4r)-4-((3-(1-ethyl-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
305		5-chloro-2-methyl-N-(((1r,4r)-4-((2-oxo-3-(4-oxo-3,4-dihydroquinazolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
306		5-chloro-N-(((1r,4r)-4-((3-(2-cyano-4-formylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	U

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[Table 2-35]

307		N-((1r,4r)-4-((3-(5-bromo-2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		U
308		5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
309		5-chloro-N-((1r,4r)-4-((3-(2-cyano-3-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		U
310		5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
311		5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-137, Mesylate-3	A1
312		5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-138, Mesylate-3	A1
313		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide	Intermediate-105, Mesylate-3	A1
314		5-chloro-N-((1r,4r)-4-((2-oxo-3-(thiazol-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-139, Mesylate-3	A1
315		5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-14, Mesylate-3	A1

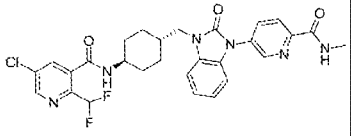
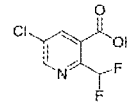
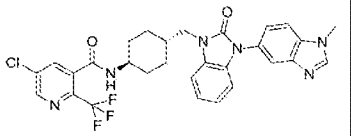
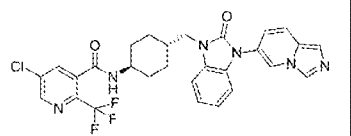
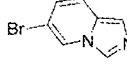
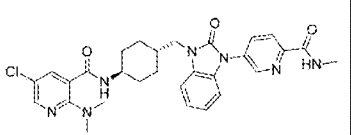
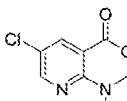
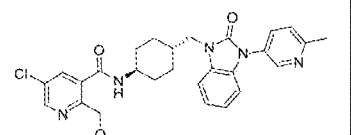
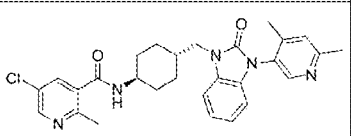
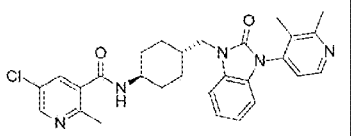
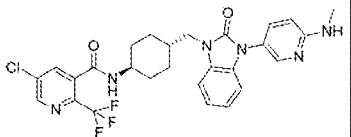
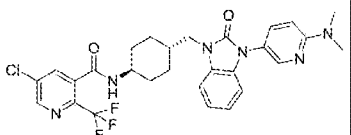
[1288]

[Table 2-36]

316		5-chloro-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-30, Mesylate-3	A1
317		5-(3-(((1r,4r)-4-(5-chloro-2-cyclopropylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121,	B
318		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-140, Mesylate-1	A1
319		N-((1r,4r)-4-((3-(4-aminopyrido[3,2-d]pyrimidin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
320		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-(trifluoromethyl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	U
321		5-(3-(((1r,4r)-4-(5-chloro-2-(2-methoxyethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, Intermediate-141	B
322		5-(3-(((1r,4r)-4-(5-chloro-2-cyclobutylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, Intermediate-142	B
323		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-113,	Q
324		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-127,	Q

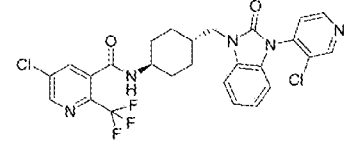
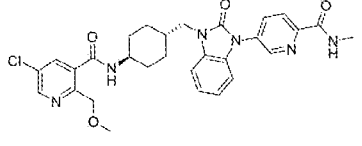
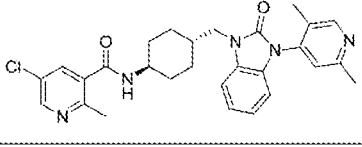
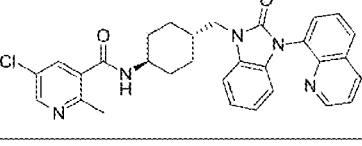
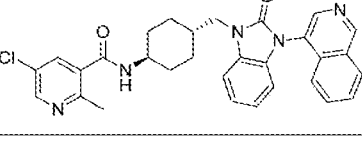
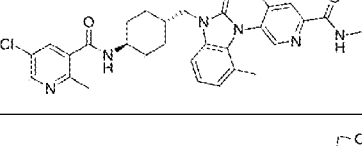
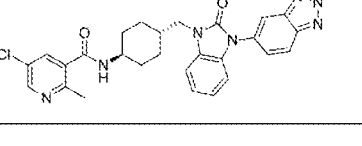
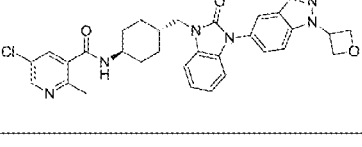
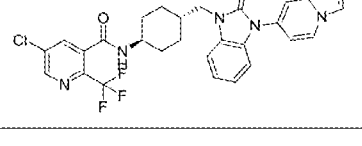
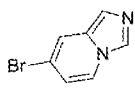
[1289]

[Table 2-37]

325		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	Q
326		5-chloro-N-(((1r,4r)-4-((1'-methyl-2-oxo-1'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-108, Mesylate-3	A1
327		5-chloro-N-(((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-132	R
328		5-(3-(((1r,4r)-4-(5-chloro-2-(dimethylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	B
329		5-chloro-2-(methoxymethyl)-N-(((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-127, Intermediate-143	Q
330		5-chloro-N-(((1r,4r)-4-((3-(4,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-144, Mesylate-1	A1
331		5-chloro-N-(((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-145, Mesylate-1	A1
332		5-chloro-N-(((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-146, Mesylate-3	A1
333		5-chloro-N-(((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-26, Mesylate-3	A1

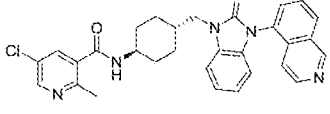
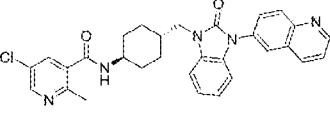
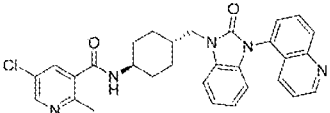
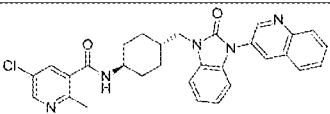
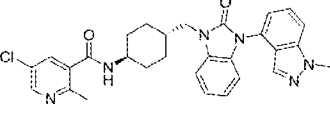
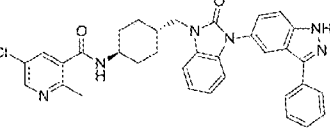
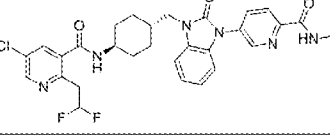
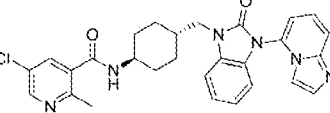
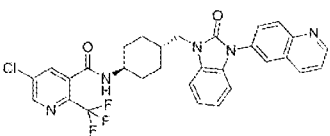
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[Table 2-38]

334		5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-147, Mesylate-3	A1
335		5-(3-(((1r,4r)-4-(5-chloro-2-(methoxymethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, Intermediate-143	Q
336		5-chloro-N-((1r,4r)-4-((3-(2,5-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-148, Mesylate-1	A1
337		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-149, Mesylate-1	A1
338		5-chloro-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-150, Mesylate-1	A1
339		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide	Intermediate-151, Mesylate-1	A1
340		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-152, Step-2 of Ex 9	T
341		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-153, Step-2 of Ex 9	T
342		5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-132	R

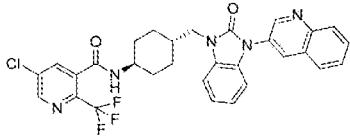
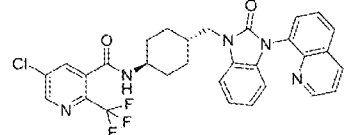
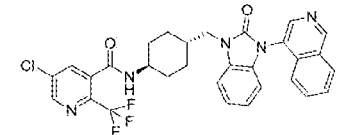
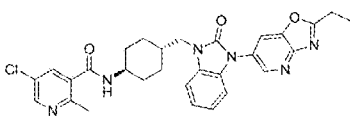
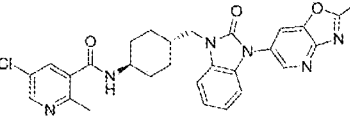
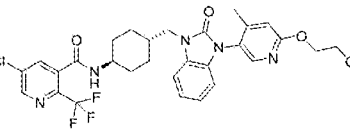
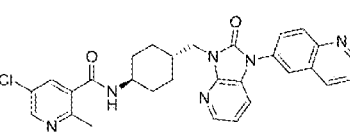
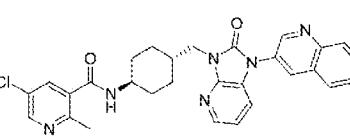
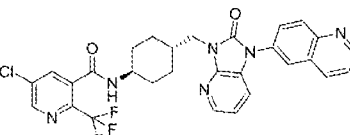
[1291]

[Table 2-39]

343		5-chloro-N-((1r,4r)-4-((3-(isoquinolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-154, Mesylate-1	A1
344		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-155, Mesylate-1	A1
345		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-156, Mesylate-1	A1
346		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-157, Mesylate-1	A1
347		5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-158, Mesylate-1	A1
348		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-phenyl-1H-indazol-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
349		5-(3-((1r,4r)-4-(5-chloro-2-(2,2-difluoroethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-159, Intermediate-121	B
350		5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-160, Mesylate-1	A1
351		5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-155, Mesylate-3	A1

[1292]

[Table 2-40]

352		5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-157, Mesylate-3	A1
353		5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-149, Mesylate-3	A1
354		5-chloro-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-150, Mesylate-3	A1
355		5-chloro-N-((1r,4r)-4-((3-(2-ethyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
356		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
357		5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
358		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-161, Mesylate-1	A1
359		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(quinolin-3-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-162, Mesylate-1	A1
360		5-chloro-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-161, Mesylate-3	A1

[1293]

[Table 2-41]

361		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-161, Mesylate-4	A1
362		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-163, Mesylate-4	A1
363		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicotinamide	Intermediate-105, Mesylate-4	A1
364		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-145, Mesylate-4	A1
365		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
366		5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-117, Mesylate-4	A1
367		5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-164, Mesylate-4	A1
368		5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	 Intermediate-165	U
369		5-chloro-N-((1r,4r)-4-((3-(3-cyanopyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	see Example synthesis part	

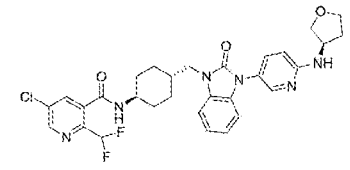
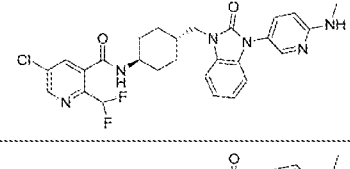
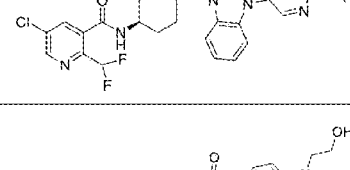
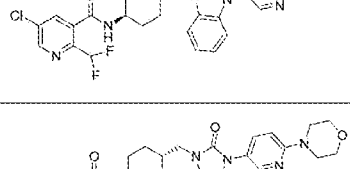
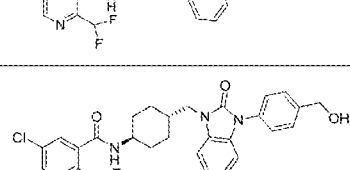
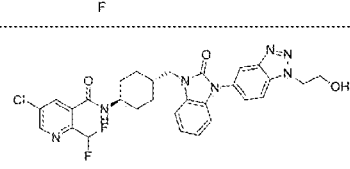
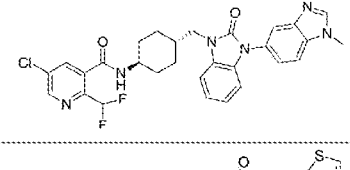
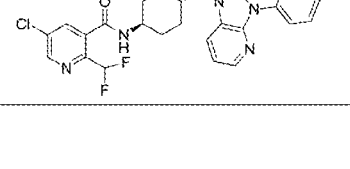
[1294]

[Table 2-42]

370		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-166, Mesylate-1	A1
371		5-chloro-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-167, Mesylate-1	A1
372		5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-135, Mesylate-4	A1
373		5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-137, Mesylate-4	A1
374		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-158, Mesylate-4	A1
375		5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-138, Mesylate-4	A1
376		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-14, Mesylate-4	A1
377		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-30, Mesylate-4	A1
378		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2,3-dihydro-1H-inden-4-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-120, Mesylate-4	A1

[1295]

[Table 2-43]

379		5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-136, Mesylate-4	A1
380		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-146, Mesylate-4	A1
381		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-26, Mesylate-4	A1
382		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-37, Mesylate-4	A1
383		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-28, Mesylate-4	A1
384		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-168, Mesylate-4	A1
385		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
386		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1'-methyl-2-oxo-1'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-108, Mesylate-4	A1
387		N-((1r,4r)-4-((3-(benzo[d]thiazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-106, Mesylate-4	A1

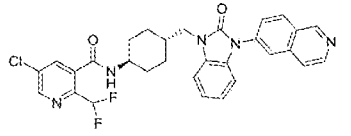
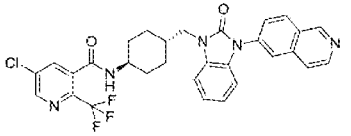
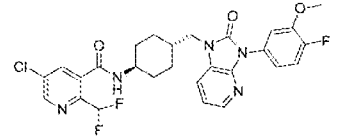
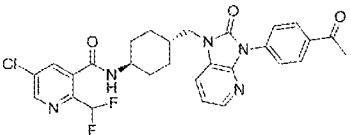
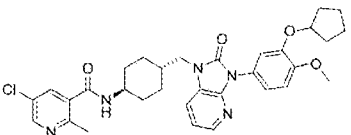
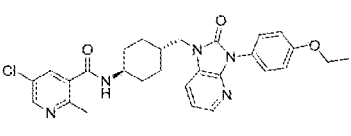
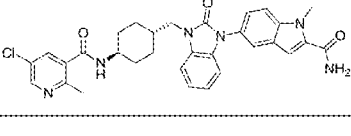
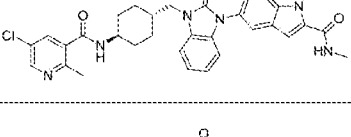
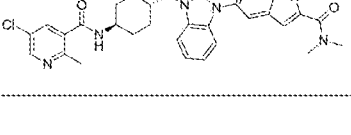
[1296]

[Table 2-44]

388		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-99, Mesylate-4	A1
389		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-169, Mesylate-4	A1
390		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-126, Mesylate-4	A1
391		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-134, Mesylate-4	A1
392		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-155, Mesylate-4	A1
393		N-((1r,4r)-4-((3-(1,8-naphthyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-170, Mesylate-4	A1
394		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinazolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-171, Mesylate-4	A1
395		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-172, Mesylate-1	A1
396		5-chloro-N-((1r,4r)-4-((3-(isoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-173, Mesylate-1	A1

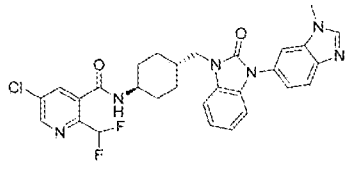
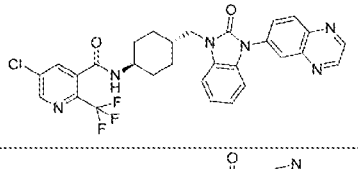
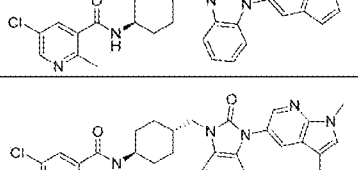
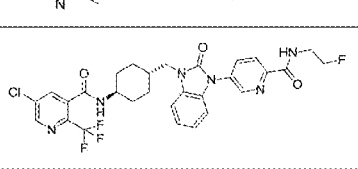
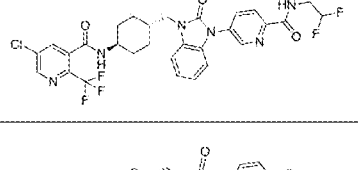
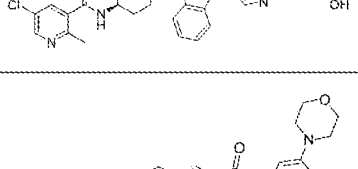
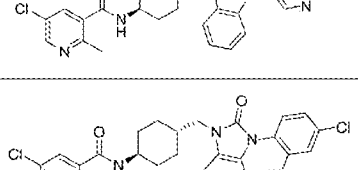
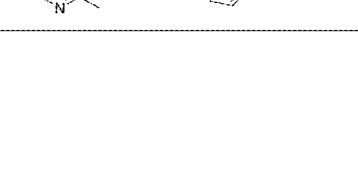
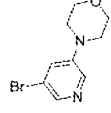
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[Table 2-45]

397		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-167, Mesylate-4	A1
398		5-chloro-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-167, Mesylate-3	A1
399		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-fluoro-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-174, Mesylate-4	A1
400		N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-175, Mesylate-4	A1
401		5-chloro-N-((1r,4r)-4-((3-(3-(cyclopentylloxy)-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-176, Mesylate-1	A1
402		5-chloro-N-((1r,4r)-4-((3-(4-ethoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-177, Mesylate-1	A1
403		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-methyl-1H-indole-2-carboxamide	Intermediate-178, NH ₃	Q
404		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,1-dimethyl-1H-indole-2-carboxamide	Intermediate-178, MeNH ₂	Q
405		5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,N,1-trimethyl-1H-indole-2-carboxamide	Intermediate-178, Me ₂ NH	Q

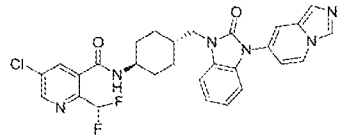
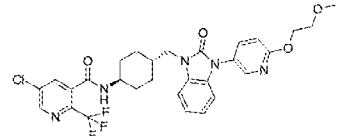
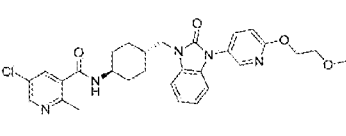
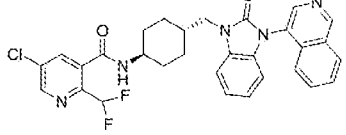
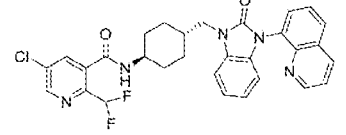
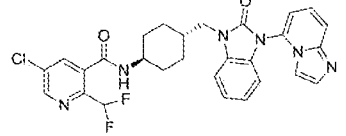
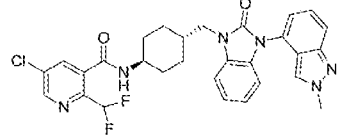
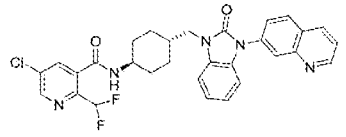
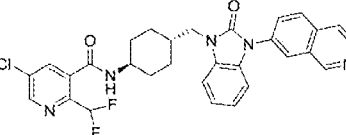
[1298]

[Table 2-46]

406		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3'-methyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-109, Mesylate-4	A1
407		5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-179, Mesylate-3	A1
408		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part Method V	
409		5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-213, Mesylate-1	A1
410		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)picolinamide	Intermediate-180, 	Q
411		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)picolinamide	Intermediate-180, 	Q
412		5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)thio)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
413		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
414		5-chloro-N-((1r,4r)-4-((3-(2,4-dichlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-181, Mesylate-1	A1

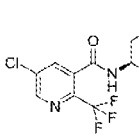
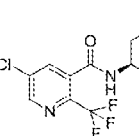
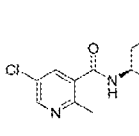
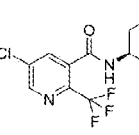
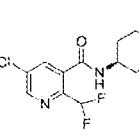
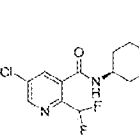
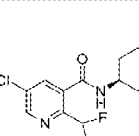
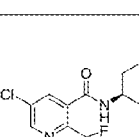
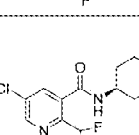
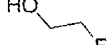
[1299]

[Table 2-47]

415		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-182, Mesylate-4	A1
416		5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-183, Mesylate-3	A1
417		5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-183, Mesylate-1	A1
418		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-150, Mesylate-4	A1
419		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-149, Mesylate-4	A1
420		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-160, Mesylate-4	A1
421		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-2H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-184, Mesylate-4	A1
422		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-172, Mesylate-4	A1
423		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-173, Mesylate-4	A1

[1300]

[Table 2-48]

424		5-chloro-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-185, Mesylate-3	V
425		5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-186, Mesylate-3	V
426		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-187, Mesylate-1	V
427		5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-187 Mesylate-3	V
428		5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-188, Mesylate-4	A1
429		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-189, Mesylate-4	A1
430		5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-190, Mesylate-4	A1
431		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methoxypicolinamide	Intermediate-180, 	Q
432		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-fluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-191, 	W

[1301]

[Table 2-49]

433		5-chloro-2-(difluoromethyl)-N-((1R,4R)-4-((3-(6-(2-morpholinoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-191, 	W
434		N-((1R,4R)-4-((3-(6-(2-amino-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-191, 	W
435		5-chloro-2-methyl-N-((1R,4R)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-192, 	J
436		5-chloro-2-methyl-N-((1R,4R)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-193, Mesylate-1	A1
437		5-chloro-N-((1R,4R)-4-((3-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-194, Mesylate-1	A1
438		5-chloro-N-((1R,4R)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
439		5-chloro-2-(difluoromethyl)-N-((1R,4R)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
440		5-chloro-2-(difluoromethyl)-N-((1S,4R)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
441		5-chloro-2-methyl-N-((1R,4R)-4-((3-(6-(((1-methyl-1H-pyrazol-4-yl)methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	

[1302]

[Table 2-50]

442		N-((1R,4R)-4-((3-(1,5-naphthyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Intermediate-195, Mesylate-1	A1
443		5-chloro-2-methyl-N-((1R,4R)-4-((2-oxo-3-(quinazolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-196, Mesylate-1	A1
444		5-chloro-2-methyl-N-((1R,4R)-4-((3-(3-morpholinophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
445		5-chloro-N-((1R,4R)-4-((3-(4-(isoxazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
446		5-chloro-2-methyl-N-((1R,4R)-4-((3-(4-(1-methyl-1H-pyrazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
447		5-chloro-2-methyl-N-((1R,4R)-4-((3-(4-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
448		N-((1R,4R)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Mesylate-1	A1
449		5-chloro-2-(difluoromethyl)-N-((1R,4R)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-197, Mesylate-4	A1
450		5-chloro-2-methyl-N-((1R,4R)-4-((3-(4-(oxazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R

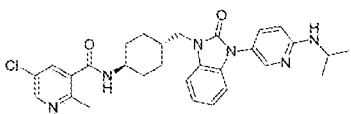
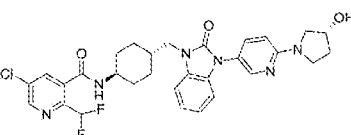
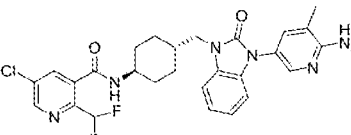
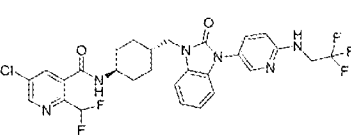
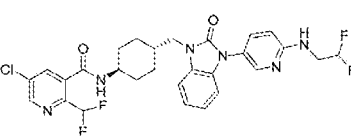
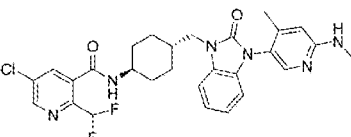
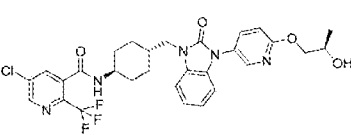
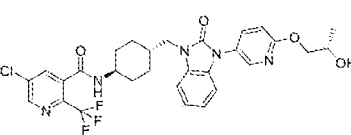
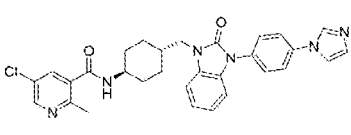
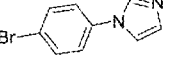
[1303]

[Table 2-51]

451		5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
452		5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-198, Mesylate-4	A1
453		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-199, Mesylate-4	A1
454		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-200, Mesylate-4	A1
455		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-185, Mesylate-4	V
456		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-186, Mesylate-4	V
457		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-201, Mesylate-4	V
458		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-phenoxyethyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-202, Mesylate-4	A1
459		5-chloro-N-((1r,4r)-4-((3-(2,4-dichlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-181, Mesylate-4	A1

[1304]

[Table 2-52]

460		5-chloro-N-((1r,4r)-4-((3-(6-(isopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-203, Mesylate-1	A1
461		5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-50, Mesylate-4	A1
462		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-69, Mesylate-4	A1
463		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-193, Mesylate-4	A1
464		5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-194, Mesylate-4	A1
465		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-204, 	J
466		5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
467		5-chloro-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
468		N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R

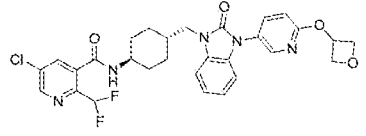
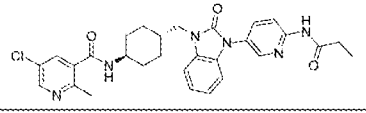
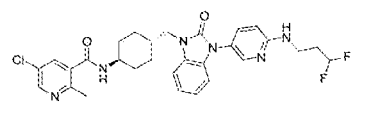
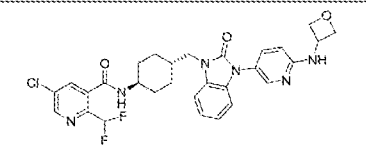
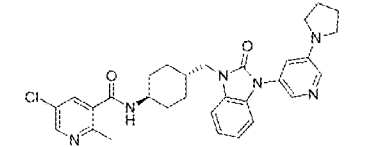
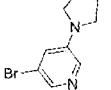
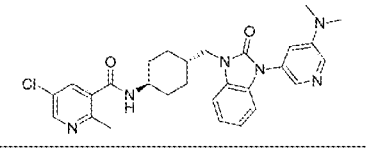
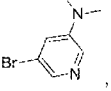
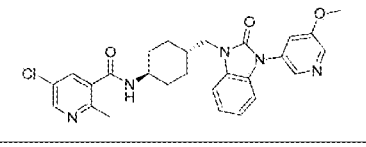
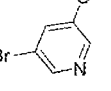
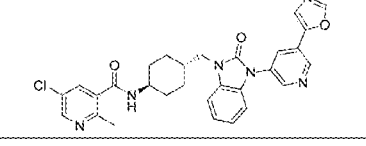
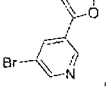
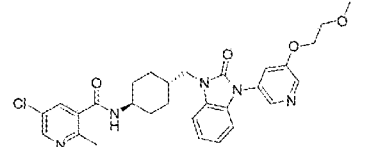
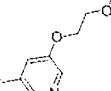
[1305]

[Table 2-53]

469		N-((1r,4r)-4-((3-(4-(1H-pyrazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		R
470		N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		R
471		N-((1r,4r)-4-((3-(4-(1H-pyrazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		R
472		N-((1r,4r)-4-((3-(6-(1H-imidazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		R
473		N-((1r,4r)-4-((3-(2-(1H-imidazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		R
474		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-187, Mesylate-4	V
475		N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide		X
476		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
477		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		N

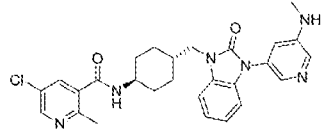
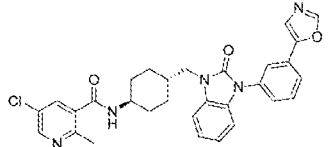
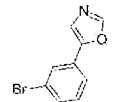
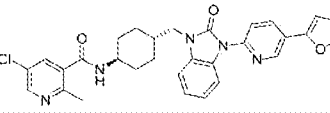
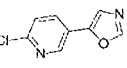
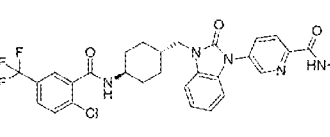
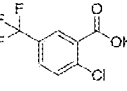
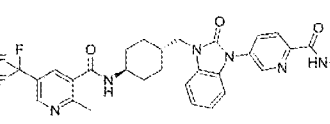
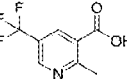
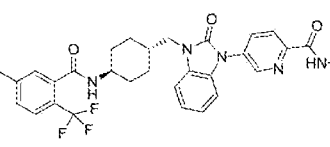
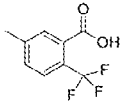
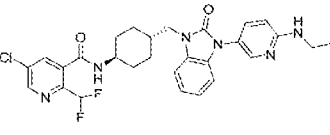
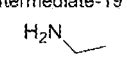
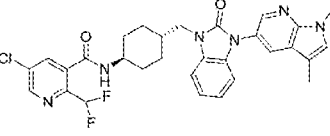
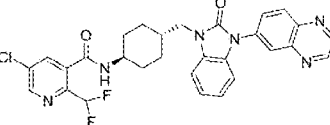
[1306]

[Table 2-54]

478		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-191	N
479		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
480		5-chloro-N-((1r,4r)-4-((3-(6-(3,3-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-205, Mesylate-1	A1
481		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-78, Mesylate-4	A1
482		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(5-(pyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
483		5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
484		5-chloro-N-((1r,4r)-4-((3-(5-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R
485		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-5-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
486		5-chloro-N-((1r,4r)-4-((3-(5-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	 Step-2 of Ex 9	R

[1307]

[Table 2-55]

487		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
488		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
489		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-5-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	X
490		5-(3-(((1r,4r)-4-(2-chloro-5-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	Q
491		N-methyl-5-(3-(((1r,4r)-4-(2-methyl-5-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide	Intermediate-121, 	Q
492		N-methyl-5-(3-(((1r,4r)-4-(5-methyl-2-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide	Intermediate-121, 	Q
493		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-191, 	J
494		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-213, Mesylate-4	A1
495		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-179, Mesylate-4	A1

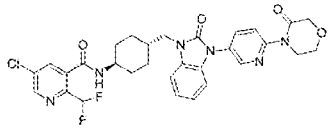
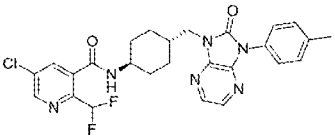
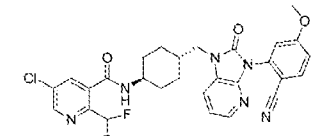
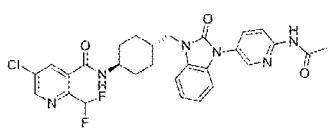
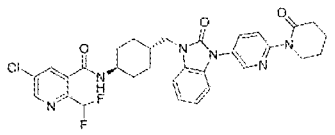
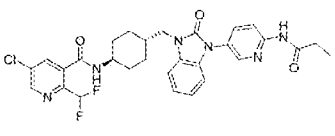
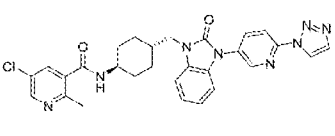
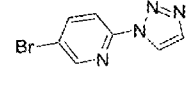
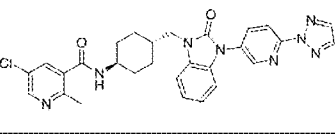
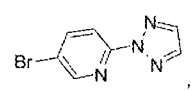
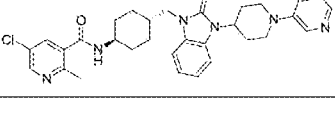
[1308]

[Table 2-56]

496		5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-206, Mesitylate-4	A1
497		5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-178	D
498		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207,	Y
499		5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	 Intermediate-165	U
500		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-(methylamino)-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
501		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoazetidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207,	Y
502		5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropanecarboxamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-207,	Y
503		N-((1S,4r)-4-((3-(6-(((S)-1-amino-1-oxopropan-2-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-191,	W
504		N-((1R,4r)-4-((3-(6-(((R)-1-amino-1-oxopropan-2-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-191,	W

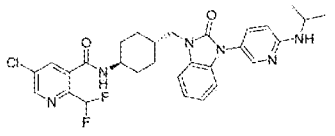
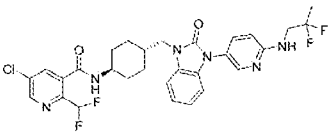
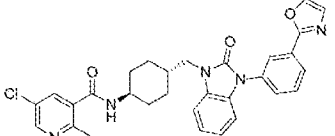
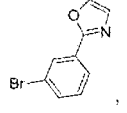
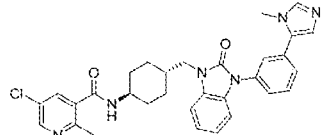
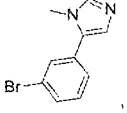
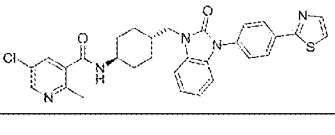
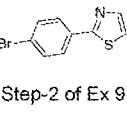
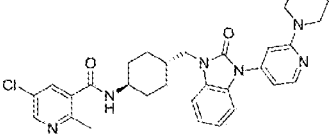
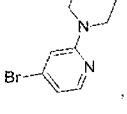
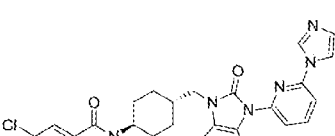
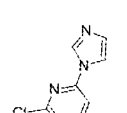
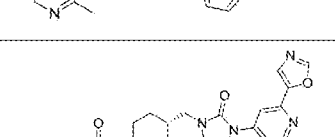
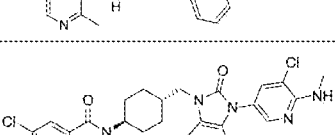
[1309]

[Table 2-57]

505		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(3-oxomorpholino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		Y
506		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyrazin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-70, Mesylate-4	A1
507		5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-208, Mesylate-4	A1
508		N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-207, 	Y
509		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207, 	Y
510		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207, 	Y
511		N-((1r,4r)-4-((3-(6-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
512		N-((1r,4r)-4-((3-(6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
513		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-(pyridin-3-yl)piperidin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-209, Mesylate-1	A1

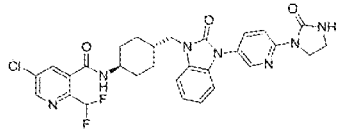
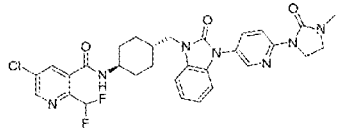
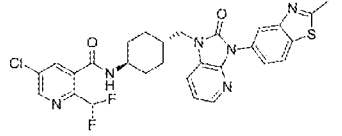
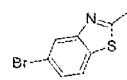
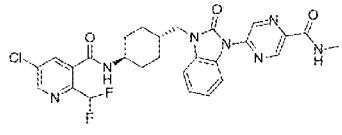
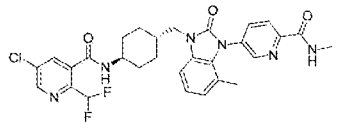
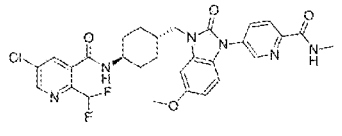
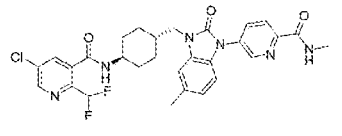
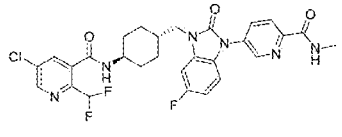
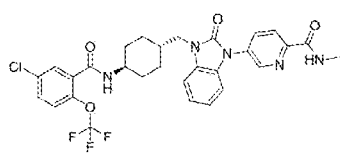
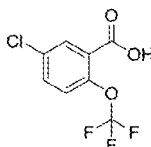
[1310]

[Table 2-58]

514		5-chloro-2-((difluoromethyl)-N-((1r,4r)-4-((3-(6-(isopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-203, Mesylate-4	A1
515		5-chloro-2-((difluoromethyl)-N-((1r,4r)-4-((3-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-210, Mesylate-4	A1
516		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
517		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
518		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(thiazol-2-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
519		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-morpholinopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
520		N-((1r,4r)-4-((3-(6-(1H-imidazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	X
521		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(oxazol-5-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-211, Step-2 of Ex 9	R
522		5-chloro-N-((1r,4r)-4-((3-(5-chloro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-212, Mesylate-1	A1

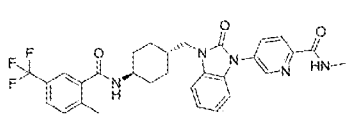
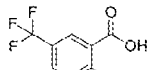
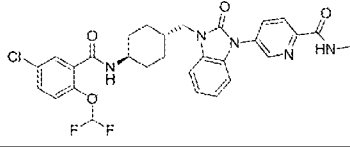
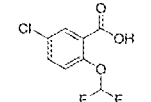
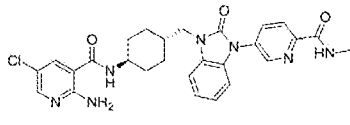
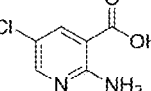
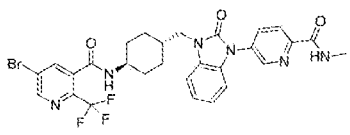
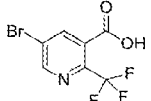
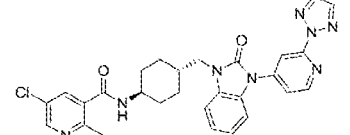
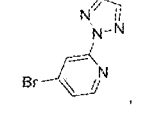
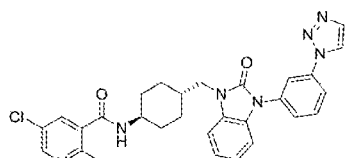
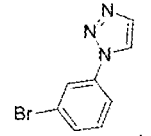
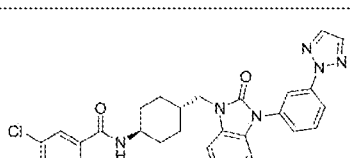
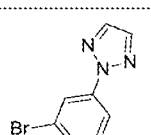
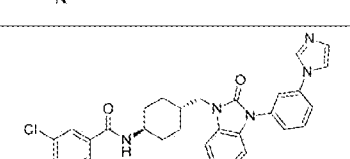
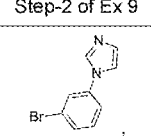
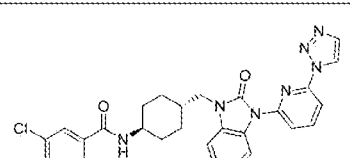
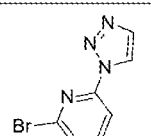
[1311]

[Table 2-59]

523		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207, 	Y
524		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207, 	Y
525		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(2-methylbenzo[d]thiazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-214	R
526		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpyrazine-2-carboxamide	Intermediate-215, Mesylate-4	A1
527		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-101, Mesylate-4	A1
528		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-103, Mesylate-4	A1
529		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-114, Mesylate-4	A1
530		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-115, Mesylate-4	A1
531		5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethoxy)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	Q

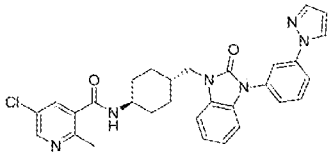
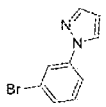
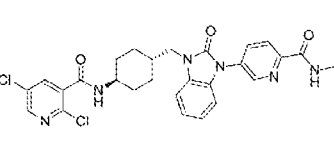
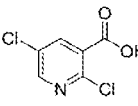
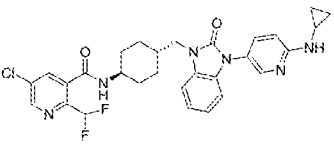
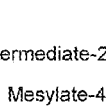
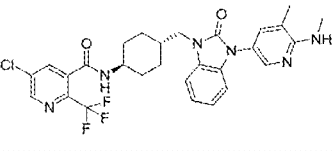
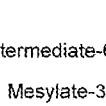
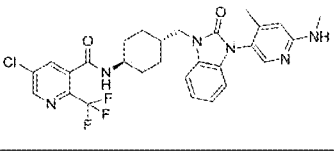
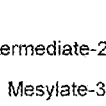
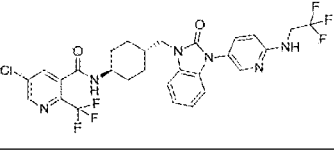
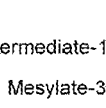
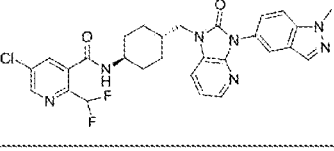
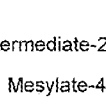
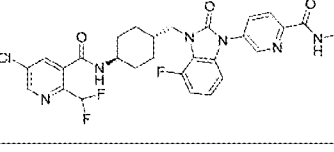
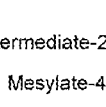
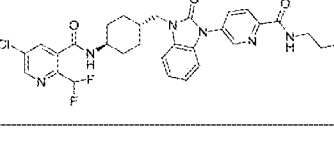
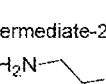
[1312]

[Table 2-60]

532		N-methyl-5-(3-(((1r,4r)-4-(2-methyl-5-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide		Q
533		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethoxy)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide		Q
534		5-(3-(((1r,4r)-4-(2-amino-5-chloronicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide		Q
535		5-(3-(((1r,4r)-4-(5-bromo-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide		Q
536		N-((1r,4r)-4-((3-(2-(2H-1,2,3-triazol-2-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
537		N-((1r,4r)-4-((3-(3-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
538		N-((1r,4r)-4-((3-(3-(2H-1,2,3-triazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
539		N-((1r,4r)-4-((3-(3-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
540		N-((1r,4r)-4-((3-(6-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R

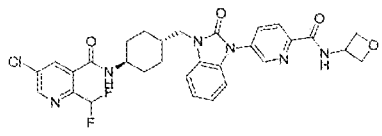
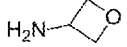
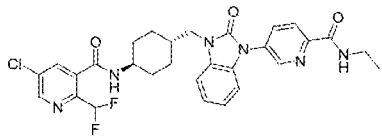
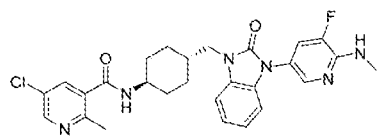
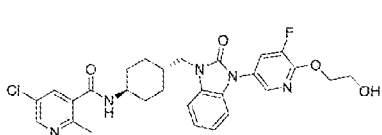
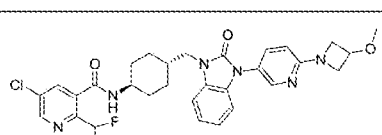
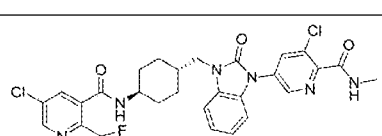
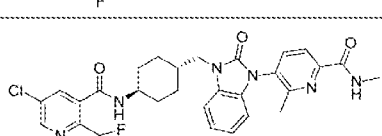
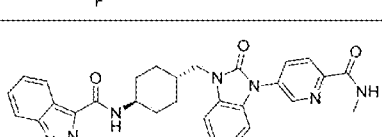
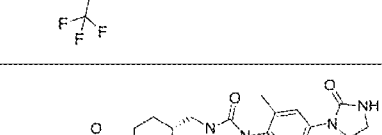
[1313]

[Table 2-61]

541		N-((1r,4r)-4-((3-(3-(1H-pyrazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
542		5-(3-(((1r,4r)-4-(2,5-dichloronicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	 Intermediate-121,	Q
543		5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	 Intermediate-216, Mesylate-4	A1
544		5-chloro-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-69, Mesylate-3	A1
545		5-chloro-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-217, Mesylate-3	A1
546		5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-193, Mesylate-3	A1
547		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-218, Mesylate-4	A1
548		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-4-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	 Intermediate-219, Mesylate-4	A1
549		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)picolinamide	 Intermediate-220, H ₂ N-CH ₂ -CH ₂ -F	Q

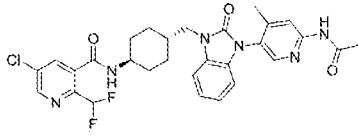
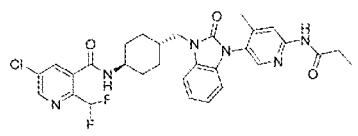
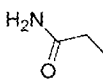
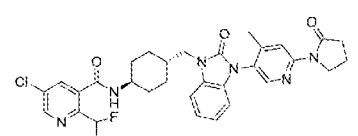
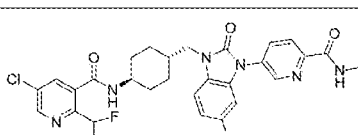
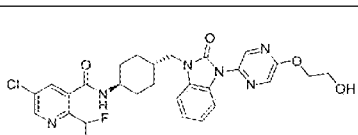
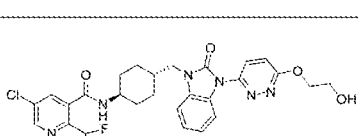
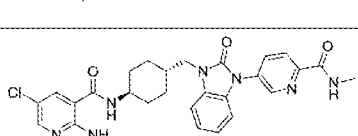
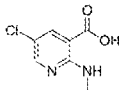
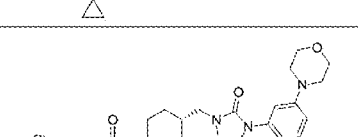
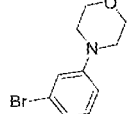
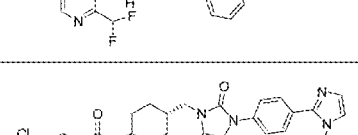
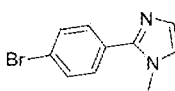
[1314]

[Table 2-62]

550		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(oxetan-3-yl)picolinamide	Intermediate-220, 	Q
551		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-ethylpicolinamide	Intermediate-220, 	Q
552		5-chloro-N-(((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
553		5-chloro-N-(((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
554		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-75, Mesylate-4	A1
555		3-chloro-5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-221, Mesylate-4	A1
556		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,6-dimethylpicolinamide	Intermediate-222, Mesylate-4	A1
557		N-(((1r,4r)-4-((3-(6-(methylcarbamoyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxamide	Intermediate-121, Intermediate-223	Q
558		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(4-methyl-6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-224, 	Y

[1315]

[Table 2-63]

559		N-(((1r,4r)-4-((3-(6-acetamido-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-224, 	Y
560		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(4-methyl-6-propionamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-224, 	Y
561		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(4-methyl-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-224, 	Y
562		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-102, Mesylate-4	A1
563		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
564		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
565		5-(3-(((1r,4r)-4-(5-chloro-2-(cyclopropylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	Q
566		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(3-morpholinophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
567		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(4-(1-methyl-1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R

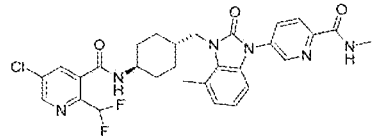
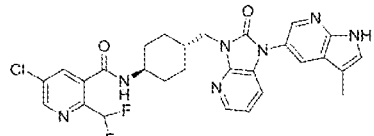
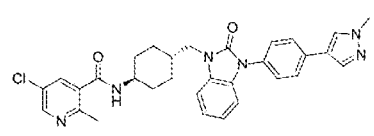
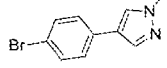
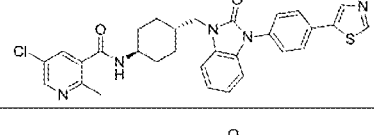
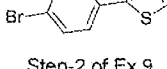
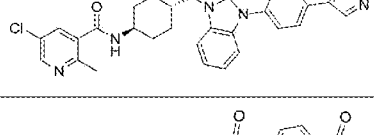
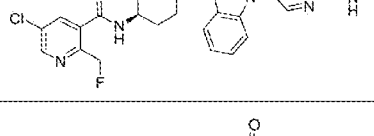
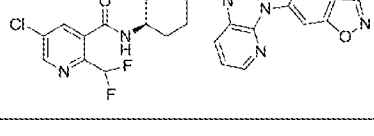
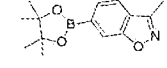
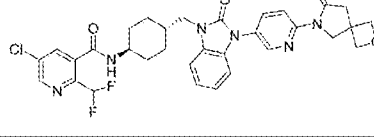
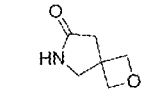
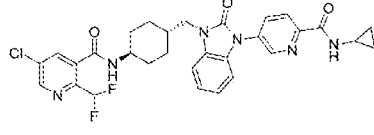
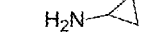
[1316]

[Table 2-64]

568		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
569		N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide		R
570		N-((1r,4r)-4-((3-(2-(1H-imidazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide		R
571		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-191, 	L
572		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-191, 	L
573		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
574		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
575		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
576		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-111, Mesylate-4	S

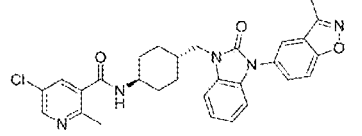
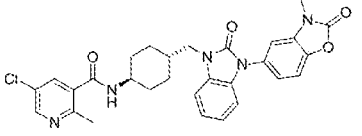
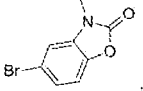
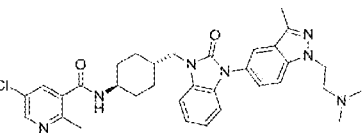
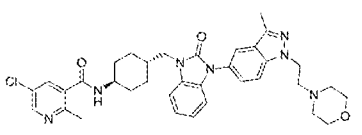
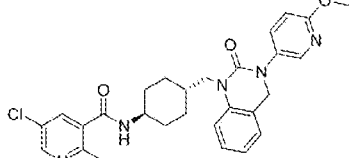
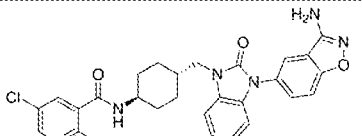
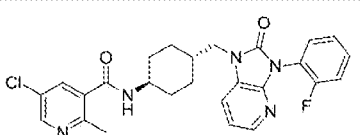
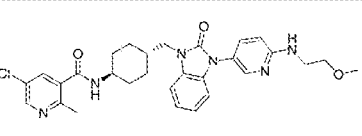
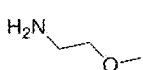
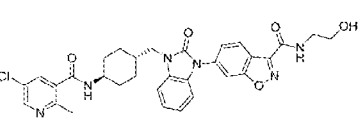
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[Table 2-65]

577		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-228, Mesylate-4	A1
578		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((1-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-229, Mesylate-4	V
579		5-chloro-2-methyl-N-(((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
580		5-chloro-2-methyl-N-(((1r,4r)-4-((2-oxo-3-(4-(thiazol-5-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
581		N-(((1r,4r)-4-((3-(4-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
582		5-(3-(((1r,4r)-4-(5-chloro-2-(fluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, Intermediate-231	Q
583		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-214, 	T
584		5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((2-oxo-3-(6-(7-oxo-2-oxa-6-azaspiro[3.4]octan-6-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207, 	Y
585		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide	Intermediate-220, 	Q

[1318]

[Table 2-66]

586		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-232, Mesylate-1	A1
587		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
588		5-chloro-N-((1r,4r)-4-((3-(1-(2-(dimethylamino)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
589		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1-(2-morpholinoethyl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
590		5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-3,4-dihydroquinazolin-1(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-233, Mesylate-1	A1
591		N-((1r,4r)-4-((3-(3-aminobenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
592		5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-197, Mesylate-1	A1
593		5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-54, 	L
594		6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-hydroxyethyl)benzo[d]isoxazole-3-carboxamide	see Example synthesis part	

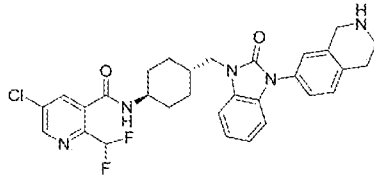
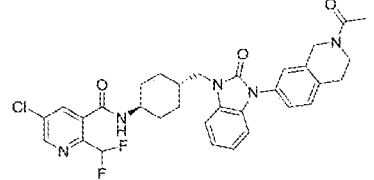
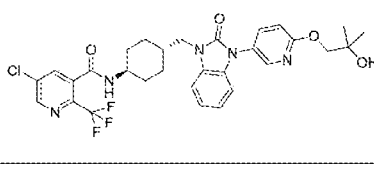
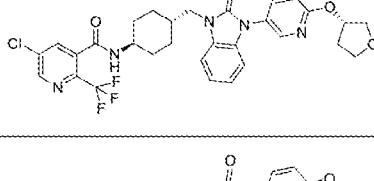
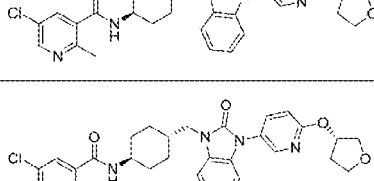
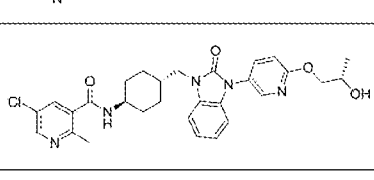
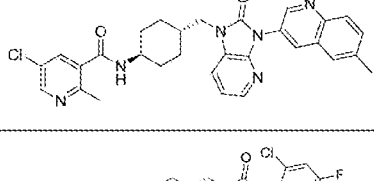
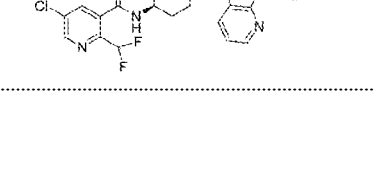
[1319]

[Table 2-67]

595		5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
596		5-(3-(((1r,4r)-4-(5-chloro-2-(methylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-121, 	Q
597		5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethyl)(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-37, Mesylate-3	A1
598		5-chloro-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-28, Mesylate-3	A1
599		5-chloro-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-29, Mesylate-3	A1
600		5-chloro-N-((1r,4r)-4-((3-(4,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-144, Mesylate-3	A1
601		5-chloro-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-145, Mesylate-3	A1
602		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-2H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-184, Mesylate-1	A1
603		5-chloro-N-((1r,4r)-4-((3-(4-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-234, Mesylate-4	A1

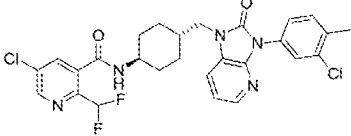
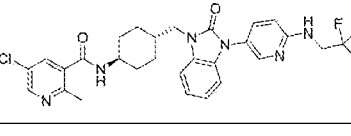
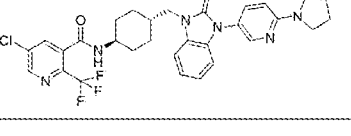
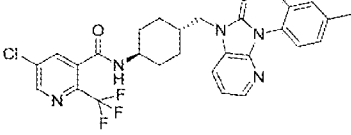
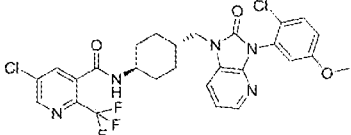
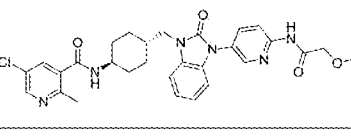
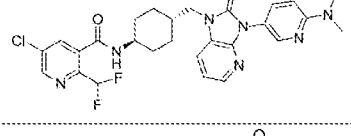
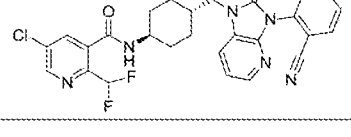
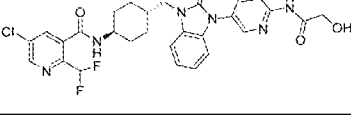
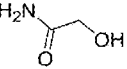
[1320]

[Table 2-68]

604		5-chloro-2-((difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
605		N-((1r,4r)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-((difluoromethyl)nicotinamide	see Example synthesis part	
606		5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-((trifluoromethyl)nicotinamide	Intermediate-189, Mesylate-3	A1
607		5-chloro-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-((trifluoromethyl)nicotinamide	Intermediate-190, Mesylate-3	A1
608		5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-188, Mesylate-1	A1
609		5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-190, Mesylate-1	A1
610		5-chloro-N-((1S,4r)-4-((3-(6-(((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
611		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylquinolin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-236, Mesylate-1	A1
612		5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-((difluoromethyl)nicotinamide	Intermediate-237, Mesylate-4	A1

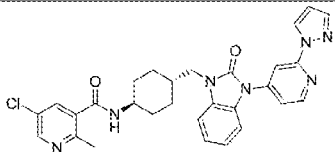
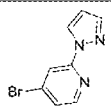
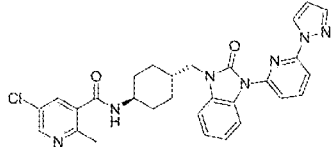
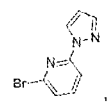
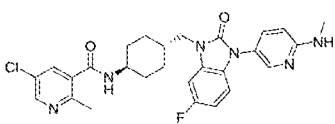
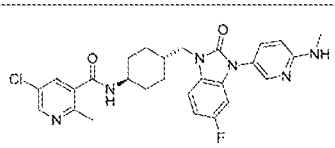
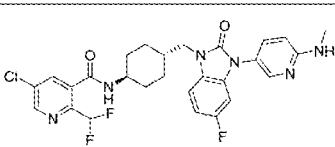
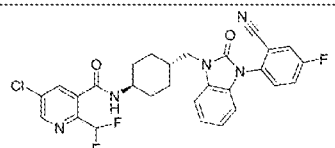
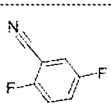
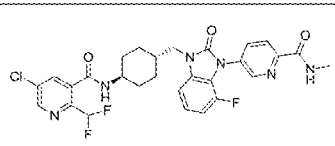
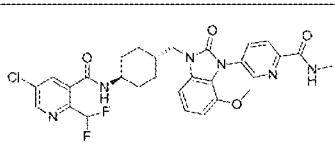
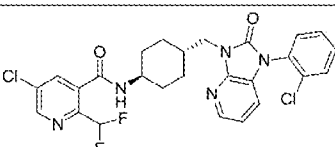
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[Table 2-69]

613		5-chloro-N-((1r,4r)-4-((3-(3-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-238, Mesylate-4	A1
614		5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-210, Mesylate-1	A1
615		5-chloro-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-50, Mesylate-3	A1
616		5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-198, Mesylate-3	A1
617		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-199, Mesylate-3	A1
618		5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	see Example synthesis part	
619		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-71, Mesylate-4	A1
620		5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-239, Mesylate-4	A1
621		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207, 	Y

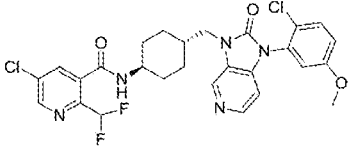
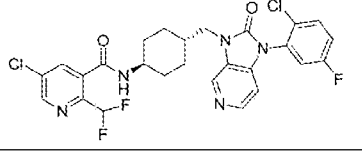
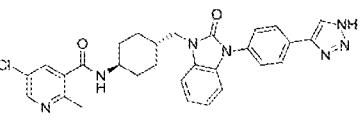
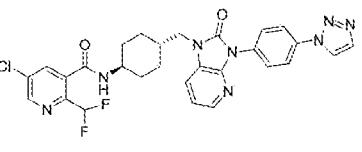
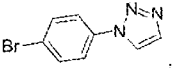
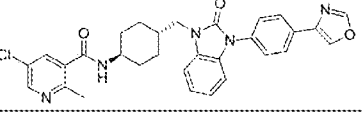
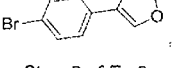
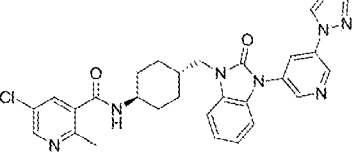
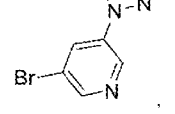
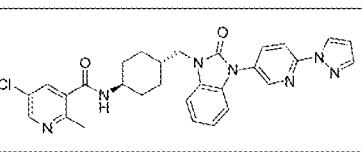
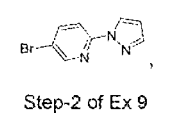
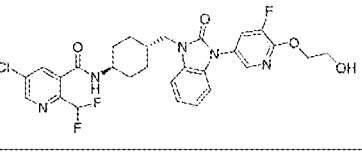
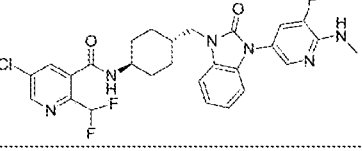
[1322]

[Table 2-70]

622		N-((1r,4r)-4-((3-(2-(1H-pyrazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
623		N-((1r,4r)-4-((3-(6-(1H-pyrazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
624		5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-(methyamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-240, Mesylate-1	A1
625		5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-(methyamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-241, Mesylate-1	A1
626		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((5-fluoro-3-(6-(methyamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-241, Mesylate-4	A1
627		5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	 Intermediate-165	U
628		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-118, Mesylate-4	A1
629		5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-242, Mesylate-4	A1
630		5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-124, Mesylate-4	A1

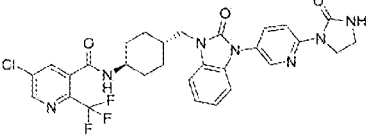
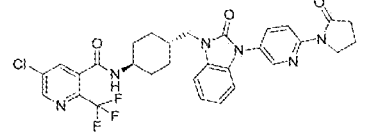
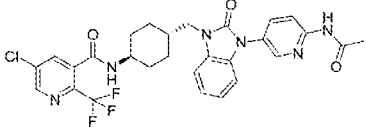
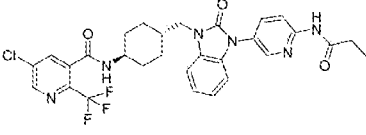
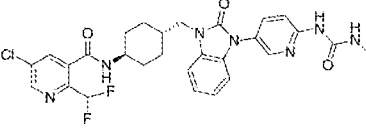
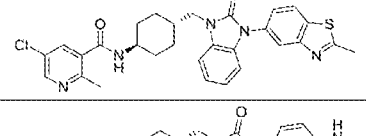
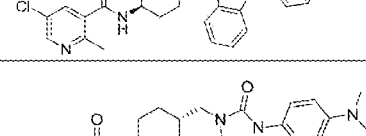
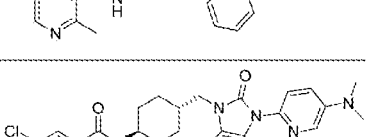
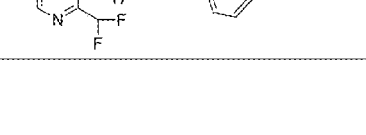
[1323]

[Table 2-71]

631		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-243, Mesylate-4	A1
632		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-244, Mesylate-4	A1
633		N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
634		N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	 Intermediate-214	R
635		5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
636		N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
637		N-((1r,4r)-4-((3-(6-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	 Step-2 of Ex 9	R
638		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
639		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	

[1324]

[Table 2-72]

640		5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Y
641		5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Y
642		N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(trifluoromethyl)nicotinamide		Y
643		5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopropionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		Y
644		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methylureido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		Y
645		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylbenzo[d]thiazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
646		5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(methylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
647		5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		R
648		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R

[1325]

[Table 2-73]

649		5-chloro-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide		R
650		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
651		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
652		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
653		N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide		R
654		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
655		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-3-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		X
656		5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
657		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-4-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R

[Table 2-74]

658		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-ureidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
659		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
660		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
661		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
662		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
663		5-chloro-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-132	R
664		5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-246, 	L
665		5-chloro-N-((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
666		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	

[1327]

[Table 2-75]

667		N-((1r,4r)-4-((3-(4-(1H-imidazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
668		5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide	Intermediate-247, Mesylate-1	A1
669		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207,	Y
670		5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207,	Y
671		5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-207,	Y
672		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((7-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-247, Mesylate-4	A1
673		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
674		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
675		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-249, Mesylate-4	A1

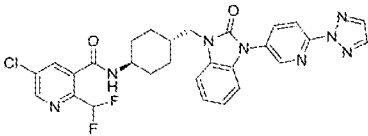
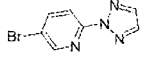
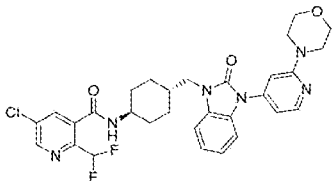
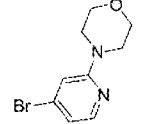
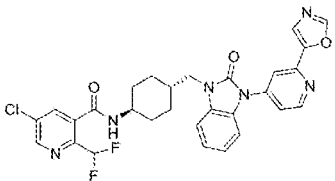
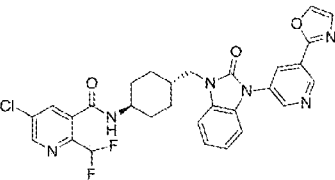
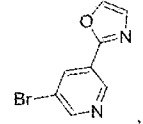
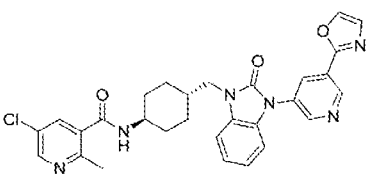
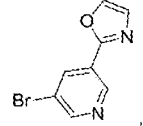
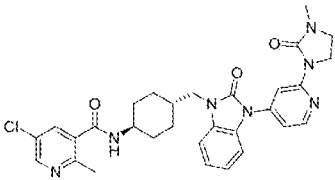
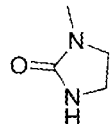
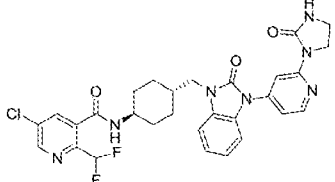
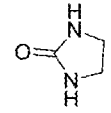
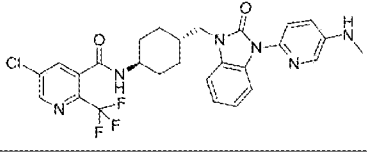
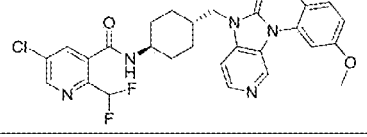
[1328]

[Table 2-76]

676		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-250, Mesylate-4	A1
677		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(4-fluoro-3-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-251, Mesylate-4	A1
678		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
679		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
680		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	X
681		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
682		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
683		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
684		N-((1r,4r)-4-((3-(4-(2H-1,2,3-triazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	 Intermediate-165	R

[1329]

[Table 2-77]

685		N-((1r,4r)-4-((3-(6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	 Intermediate-165	R
686		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-morpholinopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
687		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(oxazol-5-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-211, Intermediate-165	R
688		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(oxazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
689		5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Step-2 of Ex 9	R
690		5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-252, 	Y
691		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-(2-oxoimidazolidin-1-yl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-252, 	Y
692		5-chloro-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	see Example synthesis part	
693		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-253, Mesylate-4	A1

[Table 2-78]

694		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-254, Mesylate-4	A1
695		N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
696		N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
697		N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	see Example synthesis part	
698		N-((1r,4r)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
699		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
700		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
701		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-165	R
702		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-3-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-258, Intermediate-165	R

[Table 2-79]

703		N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide		R
704		5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-240, Mesylate-3	A1
705		5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-241, Mesylate-3	A1
706		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-(2-oxopyrrolidin-1-yl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-259, 	Y
707		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-259, 	Y
708		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
709		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
710		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-260, Mesylate-4	A1
711		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-hydroxypropyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	

[1332]

[Table 2-80]

Ex.	Structure	Name	Reactants	Method
712		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
713		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	$\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{OH}$, Intermediate-262	K
714		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(2-(2-hydroxyethoxy)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
715		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-((2-hydroxyethyl)amino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
716		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
717		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-265	R
718		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-266, Mesylate-4	A1
719		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-267, Mesylate-4	A1
720		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-268, Mesylate-4	A1

[1333]

[Table 2-81]

721		5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide	Intermediate-269, Mesylate-4	A1
722		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-270, Mesylate-4	A1
723		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-271, Mesylate-4	A1
724		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-272, Mesylate-4	A1
725		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-273, Mesylate-4	A1
726		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-274, Mesylate-4	A1
727		4-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-275, Mesylate-4	A1
728		4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-275, Mesylate-1	A1
729		4-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide	Intermediate-275, Mesylate-3	A1

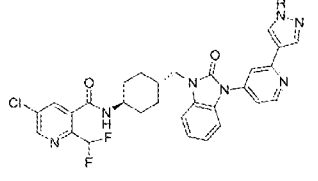
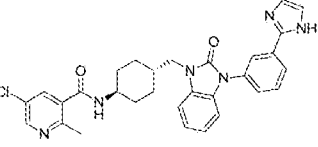
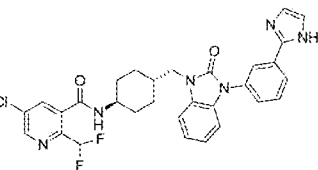
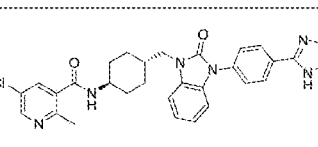
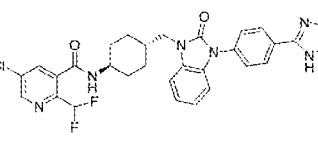
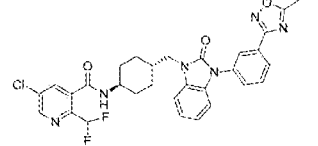
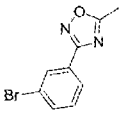
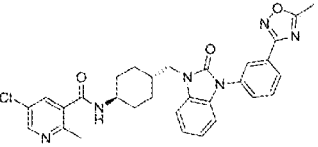
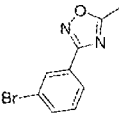
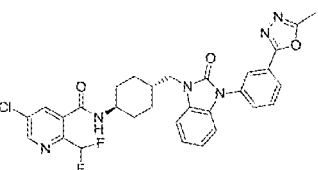
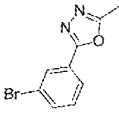
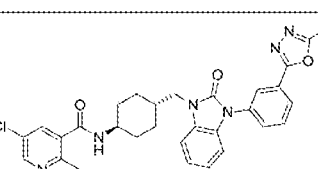
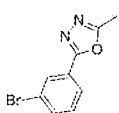
[1334]

[Table 2-82]

730		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide		Intermediate-214	T
731		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part		
732		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part		
733		N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	see Example synthesis part		
734		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part		
735		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		Intermediate-265	R
736		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-(6-fluoro-2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		Intermediate-262	U
737		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		Intermediate-165	R
738		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part		

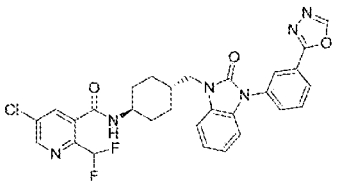
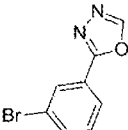
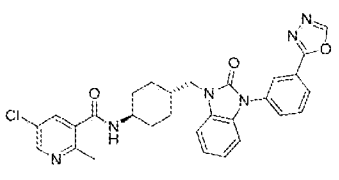
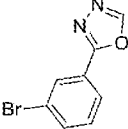
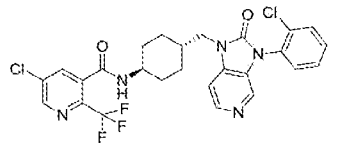
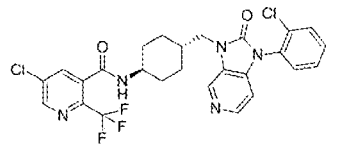
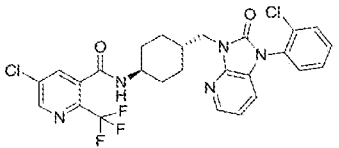
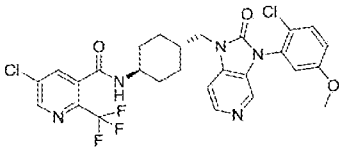
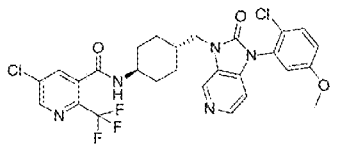
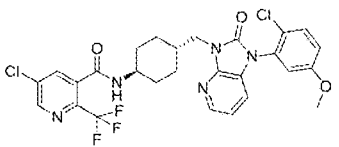
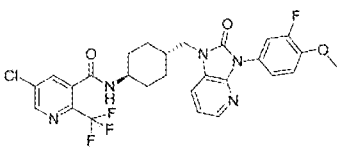
[1335]

[Table 2-83]

739		N-((1r,4r)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-257, Intermediate-165	R
740		N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
741		N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	see Example synthesis part	
742		N-((1r,4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	see Example synthesis part	
743		N-((1r,4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	see Example synthesis part	
744		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-165, 	R
745		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Step-2 of Ex 9, 	R
746		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Intermediate-165, 	R
747		5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	Step-2 of Ex 9, 	R

[1336]

[Table 2-84]

748		N-((1r,4r)-4-((3-(3-(1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	Intermediate-165, 	R
749		N-((1r,4r)-4-((3-(3-(1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide	Step-2 of Ex 9, 	R
750		5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-269, Mesylate-3	A1
751		5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-164, Mesylate-3	A1
752		5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-124, Mesylate-3	A1
753		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-253, Mesylate-3	A1
754		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-243, Mesylate-3	A1
755		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-249, Mesylate-3	A1
756		5-chloro-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-260, Mesylate-3	A1

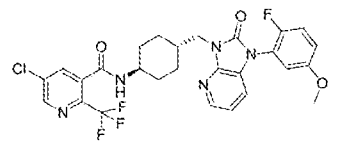
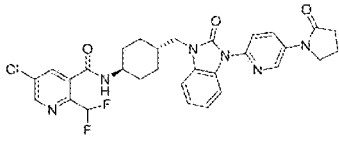
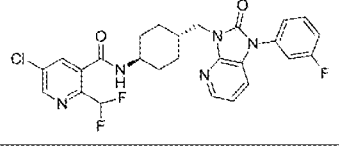
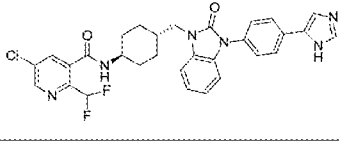
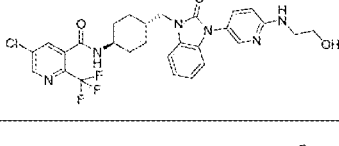
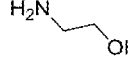
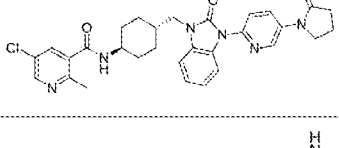
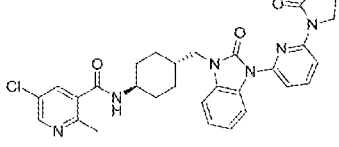
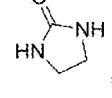
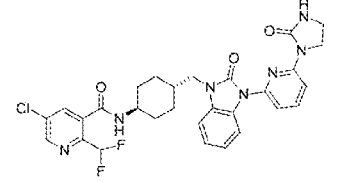
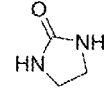
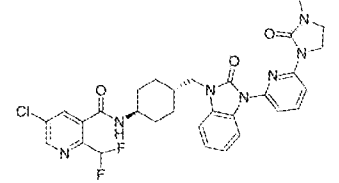
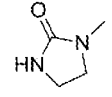
[1337]

[Table 2-85]

757		5-chloro-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-267, Mesylate-3	A1
758		5-chloro-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-272, Mesylate-3	A1
759		5-chloro-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-270, Mesylate-3	A1
760		5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-266, Mesylate-3	A1
761		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-244, Mesylate-3	A1
762		5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-250, Mesylate-3	A1
763		5-chloro-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-273, Mesylate-3	A1
764		5-chloro-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-271, Mesylate-3	A1
765		5-chloro-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-274, Mesylate-3	A1

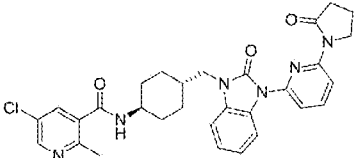
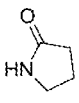
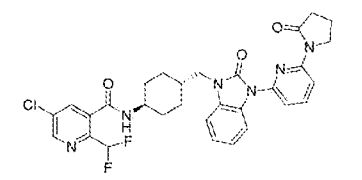
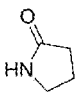
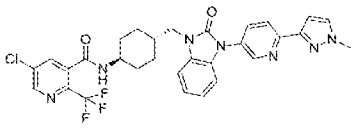
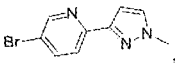
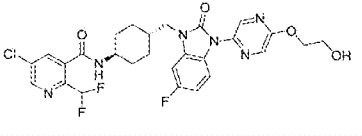
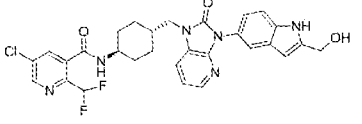
[1338]

[Table 2-86]

766		5-chloro-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	Intermediate-268, Mesylate-3	A1
767		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-265	R
768		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide	Intermediate-276, Mesylate-4	A1
769		N-((1r,4r)-4-((3-(4-(1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide	see Example synthesis part	
770		5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide	 Intermediate-246	K
771		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-277	R
772		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-278	R
773		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-279	R
774		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	 Intermediate-279	R

[1339]

[Table 2-87]

775		5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
776		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide		R
777		5-chloro-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide		R
778		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	
779		5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide	see Example synthesis part	

[1340]

[Table 3-1]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
1	475	1.90	34	505.2	1.82
2	489.1	1.88	35	556.1	1.86
3	497.1	1.66	36	520.2	1.89
4	546.1	1.55	37	524.3	2.01
5	517	1.77	38	509.3	1.81
6	490	1.62	39	525.2	1.94
7	490	1.55	40	524.2	1.90
8	490.1	1.53	41	536.2	1.94
9	547.1	1.78	42	538.2	1.81
10	547.1	1.82	43	507.2	1.63
11	519	1.64	44	535.2	1.78
12	553	1.82	45	506.2	1.81
13	542	1.72	46	511.1	1.86
14	476.1	1.59	47	507.2	1.92
15	493	1.89	48	523.2	1.87
16	493	1.91	49	490.1	1.60
17	517	1.79	50	536.1	1.53
18	517	1.80	51	490.2	1.62
19	519.1	1.66	52	519.3	1.80
20	505	1.61	53	563.3	1.81
21	505	1.59	54	561.3	1.74
22	519.1	1.60	55	574.4	1.70
23	519.1	1.58	56	490.3	1.67
24	503	1.90	57	504.3	1.68
25	489	1.98	58	520.2	1.81
26	509	2.00	59	577.3	1.60
27	505.1	1.87	60	520.2	1.86
28	543	2.03	61	588.4	1.67
29	544	1.88	62	519.3	1.49
30	506.1	1.78	63	533.3	1.57
31	490.1	1.65	64	549.3	1.58
32	504.1	1.66	65	604.4	1.52
33	493.2	1.84	66	554.2	1.83

[1341]

[Table 3-2]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
67	520.3	1.68	100	526.3	1.76
68	575.4	1.62	101	531.3	1.74
69	537.3	1.50	102	605.4	1.70
70	502.3	1.78	103	605.4	1.70
71	554.2	1.85	104	506.2	1.52
72	504.3	1.77	105	545.3	1.82
73	562.3	1.63	106	561.3	1.62
74	591.3	1.50	107	561.3	1.62
75	605.4	1.70	108	581.3	1.80
76	605.4	1.70	109	575.3	1.71
77	633.4	1.59	110	575.3	1.71
78	589.3	1.57	111	559.3	1.72
79	603.3	1.57	112	546.2	2.00
80	561.3	1.54	113	532.1	1.85
81	561.3	1.53	114	534.2	1.62
82	502.3	1.77	115	506.2	1.61
83	504.3	1.77	116	520.2	1.82
84	558.4	1.77	117	562.3	1.52
85	557.4	1.45	118	536.2	1.76
86	516.3	1.85	119	504.2	1.73
87	560.4	1.70	120	520.2	1.94
88	479.2	1.55	121	508.2	1.67
89	552.3	1.99	122	508.2	1.68
90	582.3	1.77	123	508.2	1.68
91	505.2	1.61	124	508.2	1.73
92	519.2	1.71	125	545.2	1.86
93	535.3	1.46	126	589.2	1.87
94	563.3	1.63	127	519.1	1.71
95	575.3	1.64	128	516	1.50
96	575.3	1.60	129	519.1	1.75
97	542.3	1.86	130	574.1	1.57
98	533.2	1.55	131	515	1.59
99	591.3	1.55	132	520.1	1.82

[1342]

[Table 3-3]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
133	519.1	1.69	167	531.1	1.97
134	550.1	1.58	168	543.2	1.62
135	564.1	1.67	169	559.1	1.65
136	488.2	1.90	170	529.0	1.66
137	490.2	1.81	172	530.1	1.50
138	519.2	1.58	173	599.2	1.68
139	519.2	1.48	174	596.1	1.91
140	547.2	1.73	175	597.1	1.67
141	528.2	1.75	176	600.1	1.63
142	513.2	1.83	177	596.1	1.67
143	490.2	1.48	178	597.1	1.74
144	560.2	1.70	179	600.1	1.57
145	548.2	1.73	180	630.1	1.71
146	566.2	1.82	181	596.1	1.68
148	528.2	1.78	182	547.1	1.67
149	519.2	1.86	183	585.1	1.56
150	518.2	1.68	184	515.1	2.02
151	558.2	1.69	185	543.1	1.68
152	516.2	1.58	186	515.1	1.52
153	515.2	1.72	187	527.1	1.60
154	530.2	1.74	188	558.1	1.58
155	558.2	1.68	189	516.1	1.90
156	475.2	1.58	190	506.1	1.66
157	529.0	1.63	191	543.1	1.84
158	515.0	1.52	192	547.2	1.60
159	533.1	1.60	193	551.1	1.59
160	547.0	1.78	194	563.2	1.57
161	574.1	1.62	195	586.2	1.91
162	531.1	1.76	196	561.1	1.72
163	530.0	1.67	197	530.1	1.47
164	546.1	1.71	198	531.1	1.61
165	527.1	1.71	199	547.2	1.59
166	552.1	1.73	200	533.1	1.58

[1343]

[Table 3-4]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
201	553.1	1.69	234	510.1	1.66
202	543.1	1.63	235	551.2	1.60
203	542.1	1.50	236	507.2	1.55
204	578.1	1.90	237	526.2	1.88
205	529.2	1.69	238	516.2	1.75
206	529.2	1.57	239	501.2	1.64
207	529.2	1.56	240	587.3	1.72
208	563.2	2.00	241	514.2	1.80
209	543.2	1.59	242	514.2	1.78
210	549.2	1.85	243	559.2	1.64
211	594.0	1.85	244	573.2	1.75
212	530.1	1.45	245	587.3	1.78
213	543.1	1.81	246	530.2	1.76
214	556.1	1.60	247	514.2	1.85
215	547.2	1.66	248	501.2	1.60
216	568.2	1.58	249	501.2	1.59
217	568.2	1.80	250	544.2	1.79
218	572.2	1.64	251	550.3	1.75
219	500.1	1.74	252	570.3	1.90
220	511.2	1.86	253	560.2	1.49
221	515.2	1.89	254	544.2	1.55
222	549.1	1.79	255	530.2	1.65
223	505.2	2.00	256	510.1	1.77
224	547.2	1.52	257	544.2	1.92
225	547.3	1.67	258	563.3	1.57
226	551.2	1.61	259	530.2	1.78
227	550.1	1.83	260	583.2	1.79
228	560.2	1.93	261	546.2	1.63
229	617.3	1.82	262	510.2	1.69
230	573.2	1.61	263	531.2	1.55
231	530.2	1.80	264	516.2	1.72
232	530.1	1.66	265	544.2	1.81
233	520.1	1.79	266	515.3	1.95

[1344]

[Table 3-5]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
267	489.3	1.88	300	615.3	1.76
268	523.3	1.86	301	590.3	1.68
269	509.2	1.87	302	558.3	1.84
270	543.3	1.90	303	561.3	1.71
271	530.2	1.55	304	544.3	1.74
272	515.2	1.54	305	543.2	1.48
273	543.2	1.83	306	528.2	1.70
274	515.2	1.58	307	578.1	1.90
275	531.2	1.62	308	515.3	1.68
276	560.2	1.57	309	543.3	1.85
277	561.2	1.77	310	574.3	1.69
278	516.2	1.51	311	555.2	1.75
279	530.2	1.96	312	555.2	1.82
280	544.1	1.69	313	601.3	1.75
281	543.2	1.78	314	550.2	1.76
282	544.2	1.70	315	558.2	1.83
283	543.2	1.79	316	544.2	1.81
284	544.1	1.78	317	559.2	1.78
285	571.2	1.90	318	544.2	1.74
286	570.2	1.97	319	543.2	1.46
287	536.1	1.96	320	544.2	1.72
288	564.1	1.81	321	577.3	1.68
289	544.2	1.77	322	573.3	1.85
290	605.2	1.75	323	542.2	1.88
291	554.2	1.87	324	526.2	1.75
292	584.2	1.90	325	569.3	1.67
293	555.2	1.78	326	583.3	1.72
294	574.3	1.69	327	569.3	1.73
295	558.3	1.58	328	562.3	1.76
296	515.2	1.57	329	520.3	1.69
297	528.2	1.52	330	504.2	1.68
298	560.2	1.77	331	504.3	1.67
299	615.3	1.76	332	559.3	1.76

[1345]

[Table 3-6]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
333	573.3	1.94	366	546.0	1.75
334	564.2	1.83	367	546.0	1.67
335	563.3	1.61	368	537.1	1.72
336	504.2	1.69	369	538.1	1.77
337	526.2	1.78	370	526.2	1.74
338	526.2	1.74	371	526.2	1.74
339	561.3	1.65	372	597.2	1.70
340	572.3	1.63	373	537.1	1.69
341	572.3	1.74	374	565.2	1.86
342	569.3	1.72	375	537.1	1.76
343	526.2	1.69	376	540.2	1.76
344	526.2	1.76	377	526.1	1.74
345	526.2	1.71	378	552.2	1.82
346	526.2	1.83	379	597.2	1.70
347	529.3	1.79	380	541.1	1.70
348	591.3	1.91	381	555.1	1.89
349	583.2	1.72	382	585.2	1.66
350	515.2	1.56	383	597.2	1.83
351	580.2	1.89	384	541.1	1.68
352	580.2	1.95	385	596.3	1.66
353	580.2	1.90	386	565.2	1.66
354	580.2	1.87	387	569.1	1.69
355	545.2	1.70	388	542.2	1.75
356	531.1	1.59	389	526.2	1.85
357	604.2	1.71	390	599.2	1.66
358	527.2	1.61	391	542.2	1.71
359	527.2	1.69	392	562.2	1.83
360	581.2	1.76	393	563.1	1.61
361	563.2	1.69	394	563.1	1.71
362	563.2	1.66	395	526.1	1.78
363	583.2	1.69	396	526.2	1.74
364	540.2	1.75	397	562.1	1.83
365	572.2	1.62	398	580.2	1.88

[1346]

[Table 3-7]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
399	560.1	1.79	432	574.1	1.87
400	554.1	1.73	433	641.2	1.76
401	590.2	1.90	434	585.1	1.53
402	520.1	1.77	435	519.2	1.64
403	571.2	1.63	436	573.2	1.81
404	585.2	1.72	437	555.1	1.74
405	599.2	1.75	438	550.1	1.61
406	565.1	1.66	439	586.2	1.70
407	581.2	1.86	440	586.2	1.70
408	515.2	1.63	441	585.2	1.59
409	543.2	1.89	442	527.0	1.63
410	619.2	1.78	443	527.1	1.63
411	637.1	1.83	444	560.1	1.86
412	552.2	1.62	445	542.0	1.88
413	561.2	1.61	446	555.1	1.81
414	544.1	1.82	447	555.1	1.83
415	551.2	1.66	448	490.1	1.75
416	604.3	1.90	449	530.0	1.72
417	550.3	1.77	450	542.0	1.81
418	562.2	1.81	451	542.0	1.87
419	562.2	1.85	452	560.0	1.84
420	551.2	1.65	453	576.0	1.78
421	565.2	1.77	454	564.0	1.79
422	562.2	1.86	455	551.1	1.72
423	562.2	1.83	456	565.1	1.80
424	569.2	1.76	457	552.0	1.54
425	583.2	1.85	458	556.1	1.82
426	530.2	1.53	459	580.0	1.89
427	584.2	1.68	460	533.1	1.82
428	598.3	1.86	461	597.1	1.62
429	600.3	1.76	462	555.1	1.78
430	598.2	1.86	463	609.1	1.87
431	603.1	1.68	464	591.1	1.81

[1347]

[Table 3-8]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
465	555.1	1.73	498	595.1	1.81
466	604.1	1.75	499	536.0	1.82
467	604.1	1.75	500	599.1	1.60
468	541.1	1.65	501	581.1	1.74
469	541.1	1.69	502	595.1	1.78
470	542.1	1.68	503	599.1	1.62
471	541.1	1.86	504	599.1	1.62
472	542.1	1.60	505	611.1	1.70
473	542.1	1.63	506	527.0	1.89
474	566.1	1.62	507	567.0	1.69
475	578.1	1.78	508	569.0	1.64
476	597.1	1.70	509	609.1	1.75
477	586.1	1.85	510	583.1	1.74
478	584.1	1.81	511	543.1	1.69
479	547.1	1.66	512	543.1	1.67
480	569.1	1.76	513	559.1	1.71
481	583.1	1.64	514	569.1	1.88
482	545.1	1.86	515	605.1	1.85
483	519.1	1.70	516	542.0	1.88
484	506.0	1.66	517	555.1	1.66
485	543.1	1.60	518	558.0	1.97
486	550.1	1.64	519	561.1	1.77
487	505.1	1.57	520	542.0	1.72
488	542.0	1.81	521	543.1	1.64
489	543.1	1.84	522	539.0	1.83
490	586.1	1.82	523	596.0	1.64
491	567.1	1.65	524	610.1	1.78
492	566.1	1.77	525	583.0	1.77
493	555.1	1.88	526	570.1	1.76
494	579.1	1.95	527	583.1	1.70
495	563.0	1.80	528	599.1	1.67
496	547.0	1.59	529	583.1	1.76
497	558.1	1.70	530	587.1	1.69

[1348]

[Table 3-9]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
531	602.1	1.88	564	573.0	1.59
532	566.2	1.83	565	574.0	1.92
533	584.1	1.82	566	596.0	1.92
534	534.0	1.65	567	591.1	1.74
535	631.1	1.75	568	542.0	1.85
536	543.1	1.69	569	577.1	1.73
537	542.1	1.70	570	578.0	1.72
538	542.0	1.95	571	571.1	1.54
539	541.1	1.66	572	585.1	1.73
540	543.1	1.81	573	505.0	1.64
541	541.1	1.88	574	505.0	1.69
542	553.0	1.66	575	566.0	1.60
543	567.1	1.82	576	566.0	1.55
544	573.1	1.83	577	583.0	1.74
545	573.1	1.79	578	566.0	1.67
546	627.0	1.91	579	555.1	1.78
547	566.0	1.64	580	558.0	1.87
548	587.0	1.74	581	541.0	1.65
549	601.0	1.73	582	551.1	1.61
550	611.0	1.62	583	567.0	1.80
551	583.0	1.76	584	637.1	1.69
552	523.0	1.72	585	595.0	1.77
553	554.0	1.61	586	530.2	1.85
554	597.1	1.79	587	546.2	1.72
555	603.0	1.69	588	600.2	1.68
556	583.0	1.70	589	642.3	1.76
557	606.0	1.83	590	520.2	1.81
558	610.0	1.67	591	531.2	1.62
559	583.0	1.66	592	494.2	1.63
560	597.0	1.76	593	549.0	1.65
561	609.0	1.82	594	603.3	1.58
562	587.0	1.69	595	556.2	1.74
563	573.0	1.67	596	548.3	1.85

[1349]

[Table 3-10]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
597	603.4	1.72	630	545.9	1.85
598	615.4	1.88	631	576.0	1.72
599	628.4	1.81	632	564.0	1.70
600	558.2	1.83	633	542.0	1.62
601	558.3	1.82	634	579.0	1.62
602	529.3	1.69	635	542.0	1.83
603	546.1	1.92	636	542.0	1.71
604	566.2	1.51	637	542.0	1.87
605	608.3	1.74	638	590.0	1.69
606	618.3	1.82	639	559.0	1.80
607	616.3	1.91	640	614.0	1.70
608	562.3	1.78	641	613.1	1.86
609	562.3	1.78	642	587.0	1.70
610	550.1	1.61	643	601.0	1.79
611	541.2	1.79	644	584.1	1.62
612	564.0	1.78	645	546.0	1.88
613	560.0	2.01	646	504.0	1.81
614	569.1	1.79	647	519.0	1.86
615	615.1	1.68	648	555.0	1.92
616	578.1	1.89	649	519.0	1.82
617	594.0	1.83	650	555.0	1.89
618	563.1	1.64	651	555.0	1.85
619	556.0	1.68	652	556.0	1.66
620	537.0	1.66	653	542.0	1.89
621	585.1	1.54	654	556.0	1.68
622	542.0	1.93	655	556.0	1.71
623	542.0	2.02	656	556.0	1.80
624	523.0	1.65	657	592.1	1.87
625	523.0	1.65	658	570.0	1.52
626	559.0	1.73	659	555.0	2.08
627	554.0	1.84	660	541.0	1.77
628	587.0	1.69	661	541.0	1.72
629	599.0	1.67	662	541.0	1.90

[1350]

[Table 3-11]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
663	573.0	1.94	696	541.0	1.66
664	603.0	1.78	697	577.0	1.73
665	559.0	1.78	698	542.0	1.51
666	595.0	1.67	699	592.1	1.71
667	541.0	1.56	700	591.1	1.91
668	523.0	1.70	701	592.1	1.74
669	613.0	1.70	702	592.1	1.78
670	599.0	1.62	703	578.1	1.78
671	599.0	1.62	704	577.1	1.78
672	559.0	1.77	705	577.1	1.78
673	565.0	1.78	706	595.0	1.83
674	579.0	1.93	707	610.1	1.81
675	576.0	1.87	708	580.0	1.74
676	563.9	1.86	709	581.0	1.55
677	560.0	1.82	710	560.0	1.79
678	555.0	1.79	711	570.1	1.57
679	556.0	1.57	712	590.1	1.64
680	556.0	1.62	713	589.1	1.56
681	591.1	1.85	714	590.1	1.66
682	592.1	1.66	715	571.2	1.55
683	542.0	1.74	716	590.1	1.68
684	578.0	1.98	717	596.1	1.63
685	579.0	1.75	718	564.0	1.67
686	597.1	1.84	719	560.1	1.64
687	579.0	1.73	720	560.1	1.73
688	579.0	1.76	721	546.0	1.64
689	543.0	1.69	722	560.1	1.78
690	574.0	1.73	723	560.1	1.64
691	596.0	1.66	724	560.1	1.65
692	559.0	1.83	725	560.2	1.73
693	576.0	1.69	726	560.2	1.65
694	530.0	1.67	727	569.1	1.69
695	542.0	1.56	728	533.2	1.60

[1351]

[Table 3-12]

Ex	m/z	tR (min)	Ex	m/z	tR (min)
729	587.1	1.74	762	582.1	1.91
730	566.2	1.66	763	578.1	1.79
731	609.2	1.74	764	578.1	1.70
732	595.1	1.64	765	578.1	1.71
733	578.2	1.62	766	578.1	1.80
734	595.1	1.57	767	595.1	1.78
735	610.2	1.76	768	530.1	1.85
736	614.1	1.66	769	577.1	1.62
737	592.2	1.74	770	589.2	1.59
738	566.1	1.59	771	559.2	1.69
739	578.1	1.57	772	560.2	1.65
740	541.1	1.59	773	596.2	1.73
741	577.1	1.68	774	610.2	1.88
742	541.1	1.55	775	559.2	1.84
743	577.1	1.63	776	595.2	1.91
744	593.1	1.97	777	610.2	1.80
745	557.1	1.91			
746	593.1	1.80			
747	557.1	1.72			
748	579.1	1.77			
749	543.1	1.68			
750	564.0	1.70			
751	564.1	1.71			
752	564.1	1.89			
753	594.0	1.73			
754	594.0	1.75			
755	594.1	1.93			
756	578.1	1.83			
757	578.1	1.69			
758	578.1	1.70			
759	578.1	1.84			
760	582.0	1.73			
761	582.1	1.74			

[1352]

[Table 4-1]

Ex 3	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.53 (1H, d, J = 2.3 Hz), 8.39 (1H, d, J = 8.2 Hz), 7.78 (1H, d, J = 2.7 Hz), 7.25-7.19 (2H, m), 7.10-7.01 (2H, m), 3.82 (2H, dd, J = 11.4, 2.7 Hz), 3.77-3.62 (5H, m), 3.22 (2H, t, J = 11.4 Hz), 2.46 (3H, s), 2.10-1.98 (1H, m), 1.94-1.58 (5H, m), 1.51-1.40 (2H, m), 1.35-1.12 (6H, m).
Ex 21	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.53 (1H, d, J = 2.3 Hz), 8.41 (1H, d, J = 8.2 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.55-7.45 (4H, m), 7.33 (1H, d, J = 7.8 Hz), 7.14 (1H, dt, J = 7.8, 1.4 Hz), 7.09-6.98 (2H, m), 5.32 (1H, t, J = 5.5 Hz), 4.58 (2H, d, J = 6.9 Hz), 3.78 (2H, d, J = 6.9 Hz), 3.78-3.65 (1H, m), 2.47 (3H, s), 1.98-1.69 (5H, m), 1.29-1.12 (4H, m).
Ex 31	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.64 (1H, d, J = 2.3 Hz), 8.53 (1H, d, J = 2.7 Hz), 8.39 (1H, d, J = 8.2 Hz), 7.90 (1H, dd, J = 8.2, 2.3 Hz), 7.79 (1H, d, J = 2.7 Hz), 7.47 (1H, d, J = 8.2 Hz), 7.35 (1H, d, J = 7.8 Hz), 7.16 (1H, td, J = 7.8, 1.8 Hz), 7.11-7.01 (2H, m), 3.78 (2H, d, J = 6.9 Hz), 3.78-3.63 (1H, m), 2.56 (3H, s), 2.47 (3H, s), 1.98-1.70 (5H, m), 1.31-1.14 (4H, m).
Ex 50	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.48 (1H, d, J = 2.7 Hz), 8.30 (1H, d, J = 2.7 Hz), 7.78 (1H, dd, J = 8.7, 2.7 Hz), 7.61 (1H, d, J = 2.7 Hz), 7.17 (1H, td, J = 7.7, 1.4 Hz), 7.12-7.05 (2H, m), 7.02 (1H, d, J = 7.3 Hz), 6.96 (1H, d, J = 8.7 Hz), 5.66 (1H, d, J = 8.2 Hz), 4.53-4.50 (2H, m), 4.20-3.90 (3H, m), 3.81 (2H, d, J = 6.9 Hz), 3.16 (1H, t, J = 5.5 Hz), 2.61 (3H, s), 2.15 (2H, br d, J = 9.6 Hz), 2.00-1.84 (3H, m), 1.40-1.15 (4H, m).
Ex 59	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.53 (1H, d, J = 2.3 Hz), 8.39 (1H, d, J = 7.8 Hz), 8.27 (1H, dd, J = 2.7, 0.9 Hz), 7.83 (1H, dd, J = 8.7, 2.7 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.17 (1H, d, J = 7.8 Hz), 7.02 (1H, t, J = 7.8 Hz), 6.95 (1H, d, J = 8.7 Hz), 6.81 (1H, J = 7.8 Hz), 4.49-4.31 (2H, m), 3.73 (2H, d, J = 7.3 Hz), 3.78-3.64 (1H, m), 3.73 (2H, d, J = 5.9 Hz), 2.47 (3H, s), 2.22 (6H, s), 1.83 (3H, s), 1.97-1.68 (5H, m), 1.29-1.12 (4H, m).
Ex 63	¹ H-NMR (400 MHz, CDCl ₃) delta 8.84 (1H, d, J = 2.3 Hz), 8.49 (1H, d, J = 2.3 Hz), 8.37 (1H, d, J = 8.2 Hz), 8.10 (1H, dd, J = 8.2, 2.3 Hz), 8.05-7.95 (1H, m), 7.61 (1H, d, J = 2.3 Hz), 7.25-7.05 (4H, m), 5.65-5.55 (1H, m), 4.02-3.90 (1H, m), 3.83 (2H, d, J = 6.9 Hz), 3.08 (3H, d, J = 5.0 Hz), 2.62 (3H, s), 2.20-2.13 (2H, m), 2.01-1.87 (3H, m), 1.42-1.15 (4H, m).
Ex 70	¹ H-NMR (400 MHz, CDCl ₃) delta 8.81 (1H, d, J = 2.4 Hz), 8.49 (1H, d, J = 2.4 Hz), 7.90 (1H, dd, J = 8.6, 2.4 Hz), 7.61 (1H, d, J = 2.4 Hz), 7.52 (1H, d, J = 7.9 Hz), 7.23-7.07 (4H, m), 6.89 (1H, dd, J = 17.1, 11.0 Hz), 6.26 (1H, d, J = 17.1 Hz), 5.57 (1H, br), 5.56 (1H, d, J = 11.0 Hz), 4.06-3.91 (1H, m), 3.82 (2H, d, J = 6.7 Hz), 2.61 (3H, s), 2.16 (2H, brd, J = 11.6 Hz), 2.00-1.90 (3H, m), 1.39-1.17 (4H, m).
Ex 81	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.53 (1H, d, J = 2.7 Hz), 8.41 (1H, d, J = 7.8 Hz), 8.16 (1H, d, J = 2.7 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.61 (1H, dd, J = 8.7, 2.7 Hz), 7.30 (1H, d, J = 7.8 Hz), 7.11 (1H, dd, J = 7.8, 6.9 Hz), 7.03 (1H, dd, J = 7.8, 6.9 Hz), 6.88 (1H, d, J = 6.9 Hz), 6.58 (1H, d, J = 8.7 Hz), 5.00 (1H, d, J = 3.7 Hz), 4.42 (1H, br s), 3.76 (2H, d, J = 6.9 Hz), 3.80-3.64 (1H, m), 3.60-3.47 (4H, m), 2.47 (3H, s), 2.10-1.99 (1H, m), 1.99-1.70 (6H, m), 1.29-1.15 (4H, m).
Ex 170	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.53 (1H, d, J = 2.3 Hz), 8.40 (1H, d, J = 7.8 Hz), 7.86 (1H, d, J = 1.8 Hz), 7.79 (1H, d, J = 2.3 Hz), 7.62 (1H, d, J = 8.7 Hz), 7.41 (1H, dd, J = 8.7, 1.8 Hz), 7.33 (1H, d, J = 7.8 Hz), 7.13 (1H, t, J = 7.8 Hz), 7.04 (1H, t, J = 7.8 Hz), 6.94 (1H, d, J = 7.8 Hz), 3.88-3.66 (3H, m), 2.53-2.48 (3H, m), 2.47 (3H, s), 2.00-1.70 (5H, m), 1.32-1.12 (4H, m). A signal due to NH is not observed.

[1353]

[Table 4-2]

Ex 171	¹ H-NMR (CDCl ₃) delta 8.49 (1H, d, J = 2.7 Hz), 7.80-7.75 (2H, m), 7.61 (1H, d, J = 2.7 Hz), 7.57 (1H, dd, J = 8.5, 1.6 Hz), 7.23-7.17 (2H, m), 7.15-7.07 (2H, m), 5.58 (1H, d, J = 8.2 Hz), 4.03-3.90 (1H, m), 3.84 (2H, d, J = 6.9 Hz), 2.64 (3H, s), 2.61 (3H, s), 2.23-2.09 (2H, m), 2.04-1.87 (3H, m), 1.43-1.29 (2H, m), 1.29-1.15 (2H, m).
Ex 172	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.62 (1H, d, J = 2.3 Hz), 8.53 (1H, d, J = 2.3 Hz), 8.41 (1H, d, J = 7.8 Hz), 8.16 (1H, d, J = 2.3 Hz), 7.80 (1H, d, J = 2.3 Hz), 7.38 (1H, d, J = 7.8 Hz), 7.21-7.15 (1H, m), 7.13-7.04 (2H, m), 3.81 (2H, d, J = 6.9 Hz), 3.78-3.66 (1H, m), 2.59 (3H, s), 2.47 (3H, s), 2.01-1.70 (5H, m), 1.32-1.15 (4H, m). A signal due to NH is not observed.
Ex 199	¹ H-NMR (400 MHz, CDCl ₃) delta 8.50 (1H, d, J = 2.3 Hz), 8.49 (1H, s), 8.26 (1H, s), 8.00 (1H, br d, J = 5.0 Hz), 7.61 (1H, d, J = 2.3 Hz), 7.23-7.18 (1H, m), 7.11-7.06 (2H, m), 6.72 (1H, d, J = 7.8 Hz), 5.57 (1H, br d, J = 8.2 Hz), 4.01-3.91 (1H, m), 3.84 (2H, d, J = 6.9 Hz), 3.07 (3H, d, J = 5.0 Hz), 2.61 (3H, s), 2.31 (3H, s), 2.24-2.15 (2H, m), 2.03-1.88 (3H, m), 1.41-1.18 (4H, m).
Ex 288	¹ H-NMR (400 MHz, CDCl ₃) delta 8.68 (1H, d, J = 2.3 Hz), 8.04 (1H, dd, J = 5.2, 1.4 Hz), 7.90 (1H, d, J = 2.3 Hz), 7.65-7.58 (1H, m), 7.55-7.42 (3H, m), 7.30-7.24 (1H, m), 7.08 (1H, dd, J = 7.8, 5.2 Hz), 5.60 (1H, d, J = 8.2 Hz), 4.05-3.91 (1H, m), 3.91-3.72 (2H, m), 2.28-2.09 (2H, m), 2.09-1.83 (3H, m), 1.43-1.13 (4H, m).
Ex 296	¹ H-NMR (400 MHz, CDCl ₃) delta 8.49 (1H, d, J = 2.7 Hz), 8.18 (1H, s), 8.06 (1H, dt, J = 7.5, 1.0 Hz), 7.64 (1H, t, J = 1.0 Hz), 7.61 (1H, d, J = 2.7 Hz), 7.51 (1H, s), 7.22-7.16 (2H, m), 7.16-7.10 (1H, m), 7.08 (1H, d, J = 7.8 Hz), 6.85 (1H, dd, J = 7.5, 2.1 Hz), 5.60 (1H, d, J = 7.8 Hz), 4.02-3.90 (1H, m), 3.82 (2H, d, J = 6.9 Hz), 2.61 (3H, s), 2.21-2.11 (2H, m), 2.02-1.85 (3H, m), 1.42-1.13 (4H, m).
Ex 301	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.67 (1H, d, J = 2.3 Hz), 8.31 (1H, d, J = 2.7 Hz), 7.88 (1H, d, J = 2.7 Hz), 7.79 (1H, dd, J = 8.7, 2.7 Hz), 7.20-7.14 (1H, m), 7.12-7.00 (3H, m), 6.97 (1H, d, J = 8.7 Hz), 5.70-5.63 (1H, m), 4.55-4.51 (2H, m), 4.03-3.90 (3H, m), 3.80 (2H, d, J = 6.9 Hz), 3.11 (1H, t, J = 5.9 Hz), 2.20-2.11 (2H, m), 2.00-1.87 (3H, m), 1.40-1.15 (4H, m).
Ex 325	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.90 (1H, d, J = 2.3 Hz), 8.87 (1H, br q, J = 5.0 Hz), 8.83 (1H, d, J = 2.3 Hz), 8.66 (1H, d, J = 7.8 Hz), 8.27-8.20 (2H, m), 8.15 (1H, d, J = 2.3 Hz), 7.39 (1H, d, J = 7.8 Hz), 7.21 (2H, t, J = 7.8 Hz), 7.15 (1H, t, J = 54.0 Hz), 7.11 (1H, t, J = 7.8 Hz), 3.80 (2H, d, J = 6.9 Hz), 3.78-3.65 (1H, m), 2.86 (3H, d, J = 5.0 Hz), 2.00-1.71 (5H, m), 1.32-1.15 (4H, m).
Ex 365	¹ H-NMR (400 MHz, DMSO-d ₆) delta 8.64 (1H, d, J = 2.3 Hz), 8.31 (1H, d, J = 2.7 Hz), 7.92 (1H, d, J = 2.3 Hz), 7.79 (1H, dd, J = 8.7, 2.7 Hz), 7.17 (1H, t, J = 7.8 Hz), 7.13-7.00 (3H, m), 6.97 (1H, d, J = 9.1 Hz), 6.86 (1H, t, J = 54.9 Hz), 5.92 (1H, d, J = 7.8 Hz), 4.57-4.50 (2H, m), 4.05-3.92 (3H, m), 3.81 (2H, d, J = 6.9 Hz), 3.12 (1H, t, J = 5.9 Hz), 2.20-2.10 (2H, m), 2.01-1.87 (3H, m), 1.40-1.17 (4H, m).

[1354] Pharmacological assays

The in vitro and in vivo inhibitory activities of the compounds of this invention against CRHR2 or CRHR1 are determined by the following procedures.

[1355] cAMP functional assay for human CRHR1 and CRHR2

The ability of the compounds of this invention to inhibit either CRHR2 or CRHR1 is assessed by 3',5'-cyclic adenosine monophosphate (cAMP) production in cells using the LANCE Ultra cAMP assay kit (ParkerElmer), which are designed based on the homogeneous time-resolved fluorescence resonance energy transfer (TR-FRET) immunoassay.

CHO-K1 (Chinese hamster ovary) cells stably expressing either human

CRHR2-alpha (DiscoverX, Cat. 95-0048C2) or human CRHR1-beta (DiscoverX, Cat. 95-0047C2) are grown in HAM's F12 media supplemented with 10% fetal bovine serum (FBS), 100 units/mL penicillin, 100 microg/mL hygromycin and 0.5 microg/mL geneticin at 37 °C in 5% CO₂ humidified incubator to 80% confluence. After 7 hours starvation treatment in culture media containing 0.1% FBS, the cells are washed with Hanks balanced salt solution (HBSS) and cryopreserved.

For cAMP assay, frozen cells are thawed and washed with HBSS, followed by re-suspended in assay buffer (HBSS containing 0.1% bovine serum albumin, 0.5 mM isobutylmethylxanthine and 5 mM Hepes, pH 7.4) at the appropriate concentration for the assay. The cell suspensions are plated on 384-well microplates (Greiner Bio-One) at a density of 4,000 cells per well. After preincubating the cells with various concentrations of the compounds for 30 min at 25 °C, an assay buffer containing EC₈₀ concentration of each agonist is added and the cells are incubated for 30 min at 25 °C. Human urocortin2 (Peptide Institute) and CRF (Peptide Institute) are used as agonists for CRHR2 and CRHR1, respectively. For the termination of assay, europium-labeled cAMP tracer and ULight (registered trademark) dye labeled cAMP antibodies, both prepared with Lance-Ultra cAMP detection reagent (Perkin Elmer) are added in the plate and incubate for 60 min at 25 °C. After incubation, TR-FRET signal is detected by EnVision plate reader (PerkinElmer). The IC₅₀ values for compounds are calculated from dose-response curves by fitting the percent inhibition using XLfit (ID Business Solutions).

[1356] All tested compounds show less than about 1 microM of IC₅₀ against CRHR2 in the above assays. Preferable compounds show less than about 0.3 microM of IC₅₀ against CRHR2 in the above assays.

Compounds with IC₅₀ against CRHR2 <0.3 microM are:

Example 2, 5, 9, 10, 12, 13, 15, 18, 25, 27, 30, 32, 33, 34, 35, 36, 37, 38, 39, 41, 42, 44, 45, 46, 50, 52, 53, 54, 55, 57, 58, 62, 63, 64, 66, 67, 70, 72, 82, 84, 86, 89, 90, 91, 92, 94, 95, 96, 97, 101, 105, 107, 108, 109, 110, 111, 112, 113, 115, 116, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 130, 133, 134, 140, 141, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 208, 209, 210, 211, 212, 213, 214, 215, 216, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 298, 299, 300, 301, 302, 303, 304, 305,

306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 379, 380, 381, 382, 383, 384, 385, 386, 387, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 427, 428, 429, 430, 431, 432, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 474, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 527, 528, 529, 530, 531, 532, 533, 534, 537, 539, 541, 542, 543, 544, 545, 547, 548, 549, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 566, 567, 568, 569, 570, 571, 572, 573, 574, 576, 578, 579, 580, 581, 582, 583, 584, 585, 593, 624, 625, 626, 627, 628, 630, 631, 633, 635, 636, 637, 638, 639, 640, 641, 643, 645, 646, 647, 648, 649, 650, 651, 652, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 671, 672, 673, 674, 675, 676, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 690, 691, 692, 693, 695, 696, 697, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 712, 713, 715, 717, 718, 720, 721, 722, 724, 725, 726, 730, 731, 732, 733, 735, 736, 737, 743, 748, 767, 772, 773, 774, 776, and 777.

The compounds of this invention show preferable activity, which show the above-mentioned practical use.

[1357] All tested compounds show less than about 3 microM of IC_{50} against CRHR1 in the above assays. Preferable compounds show less than about 1 microM of IC_{50} against CRHR1 in the above assays.

Compounds with IC_{50} against CRHR1 < 1 microM are:

Example 3, 15, 18, 21, 25, 27, 30, 31, 32, 34, 43, 45, 50, 59, 61, 62, 63, 64, 65, 67, 68, 69, 73, 74, 80, 81, 91, 92, and 136.

[1358] Echocardiogram analysis of mice loaded CRHR2 agonist

Male C57BL/6 mice at 8 weeks old are purchased from Charles River Japan, and housed in groups of 6 per cage under a 12-h light/dark cycle with access to food and water ad libitum. Under conscious condition, transthoracic echocardiography is performed using VivollOO imaging system (FUJIFILM VisualSonics). Left ventricular end-systolic diameter (LVDs) and left ventricular end-diastolic diameters (LVDd) are measured to calculate percent fractional shortening (%FS) in M-mode. The %FS is calculated by the following equation: $\%FS = (LVDd - LVDs) / LVDd \times 100$. After

measuring %FS, the animals are anesthetized with an anesthetic mixture (medetomidine, midazolam, butorphanol), and an Alzet (registered trademark) osmotic pump (DURECT) that release mouse urocortin 2 (Peptide Institute) at an infusion rate of 0.11 microL/h (100 ng/g/day) is implanted subcutaneously in the back. Two days after the implantation, examining urocortin 2-induced increase of the %FS, the animals are selected for evaluation and randomized to be nearly equal across all groups. The compounds of the invention or their vehicles are administered systemically. The post-value of %FS is measured at an appropriate time point after compound administration. Statistical analysis is performed by parametric methods.

[1359] Human dofetilide binding assay

Human HERG transfected HEK293S cells are prepared and grown in-house. The collected cells are suspended in 50 mM Tris-HCl (pH 7.4 at 4 °C) and homogenized using a hand held Polytron PT 1200 disruptor set at full power for 20 sec on ice. The homogenates are centrifuged at 48,000 x g at 4 °C for 20 min. The pellets are then re-suspended, homogenized, and centrifuged once more in the same manner. The final pellets are resuspended in an appropriate volume of 50 mM Tris-HCl, 10 mM KCl, 1 mM MgCl₂ (pH 7.4 at 4°C), homogenized, ali-quoted and stored at -80 °C until use. An aliquot of membrane fractions is used for protein concentration determination using BCA protein assay kit (PIERCE) and ARVOsx plate reader (Wallac). Binding assays are conducted in a total volume of 30 microL in 384-well plates. The activity is measured by PHERAstar (BMG LABTECH) using fluorescence polarization technology. Ten microL of test compounds are incubated with 10 microL of fluorescence ligand (6 nM Cy3B tagged dofetilide derivative) and 10 microL of membrane homogenate (6 microgram protein) for 120 minutes at room temperature. Nonspecific binding is determined by 10 microM E4031 at the final concentration.

All tested compounds of the invention show higher IC₅₀ values in human dofetilide binding than IC₅₀ values in CRHR1 and/or CRHR2 Assay. The high IC₅₀ values in human dofetilide binding activities lead to reducing the risk of cardiovascular adverse events.

[1360] Metabolic stability assay:

Half-life in human liver microsomes (HLM)

Test compounds (1 microM) are incubated with 3.3 mM MgCl₂ and 0.78 mg/mL HLM (HL101) or 0.74 mg/mL HLM (Gentest UltraPool 150) in 100 mM potassium phosphate buffer (pH 7.4) at 37 °C on the 96-deep well plate. The reaction mixture is split into two groups, a non-P450 and a P450 group. NADPH is only added to the reaction mixture of the P450 group. (NADPH generation system is also used instead of NADPH.) An aliquot of samples of P450 group is collected at 0, 10, 30, and 60 min time point, where 0 min time point indicated the time when NADPH is added into the

reaction mixture of P450 group. An aliquot of samples of non-P450 group is collected at -10 and 65 min time point. Collected aliquots are extracted with acetonitrile solution containing an internal standard. The precipitated protein is spun down in centrifuge (2000 rpm, 15 min). The compound concentration in supernatant is measured by LC/MS/MS system.

- [1361] The half-life value is obtained by plotting the natural logarithm of the peak area ratio of compounds/ internal standard versus time. The slope of the line of best fit through the points yield the rate of metabolism (k). This is converted to a half-life value using following equations: $\text{Half-life} = \ln 2/k$

The compounds of this invention show preferable stability, which show the above-mentioned practical use.

- [1362] Drug-drug interaction assay

This method essentially involves determining the percent inhibition of metabolites formation from probes (Tacrine (Sigma A3773-1G) 2 microM, Dextromethorphan (Sigma D-9684) 5 microM, Diclofenac (Sigma D-6899-10G) 5 microM, and Midazolam (ULTRAFINE UC-429) 2 microM) at 3 microM of the each compound.

- [1363] More specifically, the assay is carried out as follows. The compounds (60 microM, 10 microL) are pre-incubated in 170 microL of mixture including 0.1 mg protein/mL human liver microsomes, 100 mM potassium phosphate buffer (pH 7.4), 1 mM MgCl_2 and probes as substrate for 5 min. Reaction is started by adding a 20 microL of 10 mM NADPH (20 microL of NADPH generating system, which consist of 10 mM NADP^+ , 50 mM DL-Isocitric acid and 10 U/mL Isocitric Dehydrogenase, is also used). The assay plate is incubated at 37 °C. Acetonitrile is added to the incubate solution at appropriate time (e.g. 8 min).

The metabolites' concentration in the supernatant is measured by LC/MS/MS system.

The degree of drug-drug interaction is interpreted based on generation % of metabolites in the presence or absence of test compound.

The compounds of this invention show preferable results, which show the above-mentioned practical use.

- [1364] Plasma protein binding assay

Plasma protein binding of the test compound (1 microM) is measured by the method of equilibrium dialysis using 96-well plate type equipment. HTD96a (registered trademark), regenerated cellulose membranes (molecular weight cut-off 12,000-14,000, 22 mm x 120 mm) are soaked for over night in distilled water, then for 15 minutes in 30% ethanol, and finally for 20 minutes in dialysis buffer (Dulbecco's phosphate buffered saline, pH 7.4). Frozen plasma of human, Sprague-Dawley rats, and Beagle dogs are used. The dialysis equipment is assembled and added 150 microL of compound-fortified plasma to one side of each well and 150 microL of dialysis

buffer to the other side of each well. After 4 hours incubation at 37 °C for 150 r.p.m, aliquots of plasma and buffer are sampled. The compound in plasma and buffer are extracted with 300 microL of acetonitrile containing internal standard compounds for analysis. The concentration of the compound is determined with LC/MS/MS analysis. The fraction of the compound unbound is calculated by the following equation (A) or (B):

[1365] [Math.1]

$$(A) \text{ fu} = 1 - \{ ([\text{plasma}]_{\text{eq}} - [\text{buffer}]^{**}) / ([\text{plasma}]^{**}) \}$$

wherein $[\text{plasma}]_{\text{eq}}$ and $[\text{buffer}]_{\text{eq}}$ are the concentrations of the compound in plasma and buffer, respectively.

[1366] [Math.2]

$$(B) \quad \text{fu}(\%) = \frac{C_b / C_{is,b} \times 4}{C_p / C_{is,p} \times \frac{4}{3}} \times 100$$

wherein C_p is the peak area of the compound in plasma sample;

$C_{is,p}$ is the peak area of the internal standard in plasma sample;

C_b is the peak area of the compound in buffer sample;

$C_{is,b}$ is the peak area of the internal standard in buffer sample;

4 and 4/3 is the reciprocal of the dilution rate in plasma and buffer, respectively.

The compounds of this invention show preferable plasma protein binding, which show the above-mentioned practical use.

[1367] Equilibrium aqueous solubility study

The DMSO solution (2 microL, 30 mM) of each compound is dispensed into each well of a 96-well glass bottom plate. Potassium phosphate buffer solution (50 mM, 198 microL, pH 6.5) is added to each well, and the mixture is incubated at 37 °C with rotate shaking for 24 hours. After centrifugation at 2000 g for 5 minutes, the supernatant is filtered through the polycarbonate iso-pore membrane. The concentration of samples is determined by a general gradient HPLC method (J. Pharm. Sci.2006, 95, 2115-2122).

The compounds of this invention show preferable aqueous solubility, which show the above-mentioned practical use.

[1368] All publications, including but not limited to, issued patents, patent applications, and journal articles, cited in this application are each herein incorporated by reference in their entirety. Although the invention has been described above with reference to the disclosed embodiments, those skilled in the art will readily appreciate that the specific experiments detailed are only illustrative of the invention. It should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

Industrial Applicability

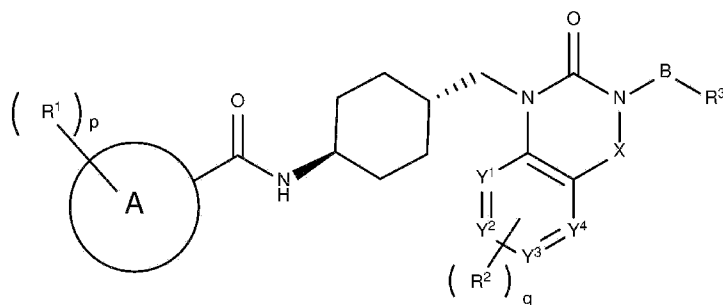
[1369] The fused cyclic urea derivatives of the present invention are useful in the treatment of a wide range of disorders in which CRHR1 and/or CRHR2 is involved.

Claims

[Claim 1]

A compound of the following formula (I):

[Chem.1]



(I)

wherein:

A is aryl or heteroaryl;

R¹ is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) C₁₋₆ alkyl, (4) C₃₋₇ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) C₁₋₆ alkoxyC₁₋₆ alkyl, (7) -NHC₁₋₆ alkyl, (8) -N(C₁₋₆ alkyl)₂, and (9) -NHC₃₋₇ cycloalkyl, wherein the C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the -O-C₁₋₆ alkyl, the C₁₋₆ alkoxyC₁₋₆ alkyl, the -NHC₁₋₆ alkyl, the -N(C₁₋₆ alkyl)₂, or the -NHC₃₋₇ cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl; or two R¹ may form a 5 to 7 membered cycloalkyl ring;

p is 1, 2, or 3;

R² is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C₁₋₆ alkyl, (5) -O-C₁₋₆ alkyl, and (6) -CN;

q is 1, 2, or 3;

Y¹, Y², Y³, and Y⁴ are independently selected from the group consisting of CH, CR², and N,

number of nitrogen atom is two at most at the same time;

X is a chemical bond or CH₂;

B is a chemical bond, -C₁₋₃ alkylene-, -C₁₋₃ alkylene-O-, or -CH₂-(C=O)-;

R³ is selected from the group consisting of:

(1) aryl, (2) 5 to 6-membered heteroaryl with 1-3 heteroatoms independently selected from O, N, and S, (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms inde-

pendently selected from O, N, and S, (4) 5 to 6-membered heterocyclyl with 1-2 heteroatoms independently selected from O, N, and S, and (5) 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl; wherein the aryl, the 5 to 6-membered heteroaryl, the 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl, the 5 to 6-membered heterocyclyl, or the 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl is unsubstituted or substituted with one or more substituents independently selected from R⁴;

R⁴ is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C₁₋₆ alkyl, (5) -O-C₁₋₆ alkyl, (6) C₂₋₆ alkenyl, (7) C₃₋₇ cycloalkyl, (8) -O-C₃₋₇ cycloalkyl, (9) C₃₋₇ cycloalkylC₁₋₆ alkoxy, (10) -(C=O)-R⁵, (11) -(C=O)-NR⁵R⁶, (12) -NR⁵(C=O)R⁶, (13) -NR⁵R⁶, (14) aryl, (15) heterocyclyl which is 4 to 7 membered partially unsaturated or saturated heterocyclic ring with 1-2 heteroatoms independently selected from O, N, and S, (16) -O-heterocyclyl, (17) heterocyclylC₁₋₆ alkyl, (18) heterocyclylC₁₋₆ alkoxy, (19) -NR⁵-S(O)₂R⁶, (20) -S(O)₂-R⁵, (21) -CN, (22) nitro, (23) heteroaryl, (24) -O-heteroaryl, (25) -S-C₁₋₆ alkyl, (26) -O-C₁₋₆ alkyl-(C=O)-NR⁵R⁶, and (26) -(C=O)-NR⁵O-C₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the -O-C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the -O-C₃₋₇ cycloalkyl, or the -S-C₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, -NR⁵R⁶, -O-C₁₋₆ alkyl, and C₃₋₇ cycloalkyl, wherein the aryl, the heterocyclyl, the -O-heterocyclyl, the heterocyclylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkoxy, the heteroaryl, or the -O-heteroaryl, is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, C₁₋₆ alkyl, hydroxylC₁₋₆ alkyl, C₁₋₆ alkoxy, and -(C=O)-R⁵;

R⁵ is independently selected from the group consisting of:

(1) hydrogen and (2) C₁₋₆ alkyl;

R⁶ is independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) C₃₋₇ cycloalkyl, (4) heterocyclyl, (5) C₃₋₇ cycloalkylC₁₋₆ alkyl, (6) heterocyclylC₁₋₆ alkyl, (7) aryl, (8) arylC₁₋₆ alkyl, (9) heteroaryl, and (10) heteroarylC₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the heterocyclyl, the C₃₋₇ cycloalkylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkyl, the aryl, the arylC₁₋₆ alkyl, the heteroaryl, or the heteroarylC₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of:

halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy C_{1-6} alkyl, hydroxy C_{1-6} alkoxy, C_{3-6} haloalkyl, and C_{3-6} haloalkoxy, $-\text{NR}^7\text{R}^8$, and $-(\text{C}=\text{O})-\text{NR}^7\text{R}^8$; or R^5 may form a 4 to 7 membered ring with R^6 which may contain a nitrogen atom, an oxygen atom, or a carbonyl; or R^5 may form a 7 to 11 membered spiro-ring with R^6 which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring or the 7 to 11 membered spiro-ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy C_{1-6} alkyl, C_{3-6} haloalkyl, and C_{3-6} haloalkoxy;

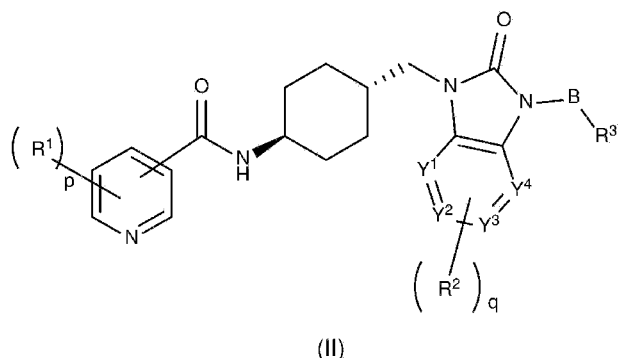
R^7 and R^8 are independently selected from the group consisting of:

(1) hydrogen and (2) C_{3-6} alkyl; or R^7 may form a 4 to 7 membered ring with R^8 which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C_{1-6} alkyl, and C_{1-6} haloalkyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[Claim 2]

The compound of the following formula (II) according to claim 1:

[Chem.2]



wherein:

R^1 is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) C_{1-6} alkyl, (4) C_{3-7} cycloalkyl, (5) $-\text{O}-\text{C}_{1-6}$ alkyl, (6) C_{1-6} alkoxy C_{1-6} alkyl, (7) $-\text{NHC}_{1-6}$ alkyl, (8) $-\text{N}(\text{C}_{1-6} \text{ alkyl})_2$, and (9) $-\text{NHC}_{3-7}$ cycloalkyl, wherein the C_{3-6} alkyl, the C_{3-7} cycloalkyl, the $-\text{O}-\text{C}_{1-6}$ alkyl, the C_{3-6} alkoxy C_{1-6} alkyl, the $-\text{NHC}_{1-6}$ alkyl, the $-\text{N}(\text{C}_{1-6} \text{ alkyl})_2$, or the $-\text{NHC}_{3-7}$ cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl; or two R^1 may form a 5 to 7 membered cycloalkyl ring;

p is 1, 2, or 3;

R² is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (4) C₁₋₆ alkyl, and (6) -CN;

q is 1, 2, or 3;

Y¹, Y², Y³, and Y⁴ are independently selected from the group consisting of: CH, CR², and N,

number of nitrogen atom is two at most at the same time;

B is a chemical bond, -CH₂-, -CH₂CH₂-, or -CH₂-(C=O)-;

R³ is selected from the group consisting of:

(1) aryl, (2) 5 to 6-membered heteroaryl with 1-3 heteroatoms independently selected from O, N, and S, (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms independently selected from O, N, and S, (4) 5 to 6-membered heterocyclyl with 1-2 heteroatoms independently selected from O, N, and S, and (5) 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl;

wherein the aryl, the 5 to 6-membered heteroaryl, the 8 to

10-membered unsaturated or partially saturated bi-cyclic heteroaryl, the 5 to 6-membered heterocyclyl, or the 8 to 10-membered unsaturated or partially saturated bi-cyclic aryl is unsubstituted or substituted with one or more substituents independently selected from R⁴;

R⁴ is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C₁₋₆ alkyl, (5) -O-C₁₋₆ alkyl, (6) C₂₋₆ alkenyl, (7) C₃₋₇ cycloalkyl, (8) -O-C₃₋₇ cycloalkyl, (9) C₃₋₇ cycloalkylC₁₋₆ alkoxy, (10) -(C=O)-R⁵, (11) -(C=O)-NR⁵R⁶, (12) -NR⁵(C=O)R⁶, (13) -NR⁵R⁶, (14) aryl, (15) heterocyclyl which is 4 to 7 membered partially unsaturated or saturated heterocyclic ring with 1-2 heteroatoms independently selected from O, N, and S, (16) -O-heterocyclyl, (17) heterocyclylC₁₋₆ alkyl, (18) heterocyclylC₁₋₆ alkoxy, (19) -NR⁵-S(O)₂R⁶, (20) -S(O)₂-R⁵, (21) -CN, (22) nitro, (23) heteroaryl, (24) -O-heteroaryl, (25) -S-C₁₋₆ alkyl, (26) -O-C₁₋₆ alkyl-(C=O)-NR⁵R⁶, and (26) -(C=O)-NR⁵OC₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the -O-C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the -O-C₃₋₇ cycloalkyl, or the -S-C₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, -NR⁵R⁶, -O-C₁₋₆ alkyl, and C₃₋₇ cycloalkyl, wherein the aryl, the heterocyclyl, the -O-heterocyclyl, the heterocyclylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkoxy, the heteroaryl, or the -O-heteroaryl, is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, C₁₋₆ alkyl, hydroxy 1C₁₋₆ alkyl, and -(C=O)-R⁵;

R⁵ is independently selected from the group consisting of:

(1) hydrogen and (2) C₁₋₆ alkyl;

R⁶ is independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) C₃₋₇ cycloalkyl, (4) heterocyclyl, (5) C₃₋₇ cycloalkylC₁₋₆ alkyl, (6) heterocyclylC₁₋₆ alkyl, (7) aryl, (8) arylC₁₋₆ alkyl, (9) heteroaryl, and (10) hctcroarylC₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the C₃₋₇ cycloalkyl, the heterocyclyl, the C₃₋₇ cycloalkylC₁₋₆ alkyl, the hctcrocyclylC₁₋₆ alkyl, the aryl, the arylC₁₋₆ alkyl, the heteroaryl, or the hctcroarylC₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxyC₁₋₆ alkyl, hydroxyC₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy, -NR⁷R⁸, and - (C=O)-NR⁷R⁸; or R⁵ may form a 4 to 7 membered ring with R⁶ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxyC₁₋₆ alkyl, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy;

R⁷ and R⁸ are independently selected from the group consisting of:

(1) hydrogen and (2) C₁₋₆ alkyl; or R⁷ may form a 4 to 7 membered ring with R⁸ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, and C₁₋₆ haloalkyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[Claim 3]

The compound according to claim 1 or 2:

wherein:

R¹ is independently selected from the group consisting of:

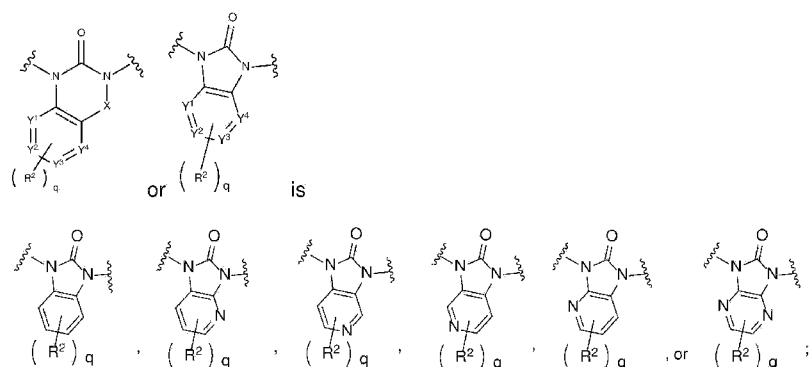
(1) hydrogen, (2) halogen, and (3) C₁₋₆ alkyl; wherein the C₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen and hydroxyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[Claim 4]

The compound according to any one of claims 1 to 3:

wherein:

[Chem.3]



[Claim 5]

or a pharmaceutically acceptable salt thereof or a prodrug thereof.

The compound according to any one of claims 1 to 4:

wherein:

B is a chemical bond or $-\text{CH}_2-$;

R^3 is selected from the group consisting of:

(1) phenyl, (2) 5 to 6-membered heteroaryl selected from pyrazole, pyridine, pyrazine, pyridazine, and pyrimidine, and (3) 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl with 1-4 heteroatoms independently selected from O, N, and S selected from indole, pyrrolo[2,3-b]pyridine, pyrrolo[2,3-c]pyridine, indazole, pyrazolo[3,4-b]pyridine, pyrazolo[4,3-b]pyridine, benzoxazole, and 2,3-dihydro-pyrrolo[2,3-b]pyridine, wherein the phenyl, the 5 to 6-membered heteroaryl or the 8 to 10-membered unsaturated or partially saturated bi-cyclic heteroaryl is unsubstituted or substituted with one or more substituents independently selected from R^4 ;

R^4 is independently selected from the group consisting of:

(1) hydrogen, (2) halogen, (3) hydroxyl, (4) C_{1-6} alkyl, (5) $-\text{O}-\text{C}_{1-6}$ alkyl, (7) C_{3-7} cycloalkyl, (8) $-\text{O}-\text{C}_{3-7}$ cycloalkyl, (10) $-(\text{C}=\text{O})-\text{R}^5$, (11) $-(\text{C}=\text{O})-\text{NR}^5\text{R}^6$, (13) $-\text{NR}^5\text{R}^6$, (14) aryl, and (23) heteroaryl wherein the C_{1-6} alkyl, the $-\text{O}-\text{C}_{1-6}$ alkyl, the C_{3-7} cycloalkyl, or the $-\text{O}-\text{C}_{3-7}$ cycloalkyl is unsubstituted or substituted with one or more substituents independently selected from halogen and hydroxyl; wherein the aryl or the heteroaryl is unsubstituted or substituted with one or more substituents independently selected from halogen, hydroxyl, C_{1-6} alkyl, hydroxyl C_{1-6} alkyl, and $-(\text{C}=\text{O})-\text{R}^5$;

R^6 is independently selected from the group consisting of:

(1) hydrogen, (2) C_{1-6} alkyl, (3) C_{3-7} cycloalkyl, (4) heterocyclyl, (5) C_{3-7} cycloalkyl C_{1-6} alkyl, (6) heterocyclyl C_{1-6} alkyl, (7) aryl, (8) aryl C_{1-6}

alkyl, (9) heteroaryl, and (10) heteroarylC₁₋₆ alkyl, wherein the C₁₋₆ alkyl, the C₃₋₇cycloalkyl, the heterocyclyl, the C₃₋₇cycloalkylC₁₋₆ alkyl, the heterocyclylC₁₋₆ alkyl, the aryl, the arylC₁₋₆ alkyl, the heteroaryl, or the heteroarylC₁₋₆ alkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxyC₁₋₆ alkyl, hydroxyC₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy, -NR⁷R⁸, and - (C=O)-NR⁷R⁸; or R⁵ may form a 4 to 7 membered ring with R⁶ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxyC₁₋₆ alkyl, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy;

R⁷ and R⁸ are independently selected from the group consisting of: (1) hydrogen and (2) C₁₋₆ alkyl; or R⁷ may form a 4 to 7 membered ring with R⁸ which may contain a nitrogen atom, an oxygen atom, or carbonyl; wherein the 4 to 7 membered ring is unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, hydroxyl, C₁₋₆ alkyl, and C₁₋₆ haloalkyl; or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[Claim 6]

A compound which is selected from the group consisting of:

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenyl-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(methylcarbamoyl)benzyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-ylmethyl)-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

ydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-(2-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 ;
 5-chloro-N-((1r,4r)-4-((3-(2-(2,4-difluorophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-(4-cyanophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(3-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 ;
 5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 ;
 5-chloro-N-((1r,4r)-4-((3-(4-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 ;
 5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 ;

5-chloro-N-((1r,4r)-4-((3-(4-(hydroxymethyl)benzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenethyl-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(4-chlorophenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(2-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(6-(2,2-difluoroethoxy)pyridin-3-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(6-ethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

2-ethyl-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide ;

2-ethyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide ;

2-ethyl-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide

ide;

2-(2-hydroxyethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-ethyl-2H-indazole-3-carboxamide;

2-ethyl-N-((1r,4r)-4-((3-(4-(1-hydroxyethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxypyrimidin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(3,4-dimethoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxypyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-difluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluoro-2-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluoro-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide ;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-

3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-(dimethylamino)ethoxy)pyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1s,4r)-4-((3-(6-((S)-3-(dimethylamino)pyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-(2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2

,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-bromopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-ethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-(2-(dimethylamino)ethoxy)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((3-(6-((R)-morpholin-2-ylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((3-(6-(((R)-4-methylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1R,4r)-4-((3-(6-(((R)-4-acetylmorpholin-2-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-((1-acetylazetidin-3-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-((1-acetylazetidin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1S,4r)-4-((3-(6-((S)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-vinylpyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-ethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-b

enzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(r,2',3',6'-tetrahydro-[2,4'-bipyridin]-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-cyclopropylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 ;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(tetrahydro-2H-pyran-4-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 e;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-phenylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)phenyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 ide;
 5-chloro-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 e;
 5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((3-hydroxypropyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 -2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(4-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

lnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)morpholino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-(4-((3-(6-(difluoromethyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((3-(6-(((R)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((3-(6-(((S)-4-methylmorpholin-3-yl)methoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((cyclopropylmethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3,3-difluorocyclobutyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4R)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-(4-((3-(6-(cyclopropylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-(4-((3-(6-cyclopropoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1S,4r)-4-((3-(5-((S)-3-hydroxypyrrolidin-1-yl)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5,6-dimethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-5-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((4-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-di

hydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclobutylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-methoxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxetan-3-ylcarbamoyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((5-cyano-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-phenyl-3,4-dihydroquinazolin-1(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyrazin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((1-(6-(dimethylamino)pyridin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r, 4r)-4-((3-(1H-indol-6-yl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-aminopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-6-(methylanilino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(benzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(1-acetyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide; and

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[Claim 7]

The compound according to claim 6, which is selected from the group consisting of:

N-((1r,4r)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(2-methoxyphenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(2,4-difluorophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(4-cyanophenyl)-2-oxoethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2,2-difluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-ethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3,4-dimethoxyphenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methoxypyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-difluorophenyl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzodimidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-bromopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-vinylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-ethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-vinylpyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3,6-dihydro-2H-pyran-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-cyclopropylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-phenylpyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-(hydroxymethyl)phenyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3-hydroxypropyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-hydroxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(difluoromethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((cyclopropylmethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3,3-difluorocyclobutyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-2-yl)methyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)ni

cotinamide;

5-chloro-N-(4-((3-(6-(cyclopropylmethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-(4-((3-(6-cyclopropoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5,6-dimethoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxy-5-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((4-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclobutylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-methoxypiperidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrazolo[3,4-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxetan-3-ylcarbamoyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-N-(4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-N-(4-((3-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-N-(4-((3-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-chloro-N-(4-((3-(6-methoxy-2-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(2-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-5-(3-((4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide ;

trans-5-chloro-N-(4-((3-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

trans-N-(4-((3-(benzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

trans-5-chloro-2-methyl-N-(4-((3-(1-methyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

trans-N-(4-((3-(1-acetyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[3,2-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[3,2-b]pyridin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(azetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-pyrazolo[3,4-b]pyridi

n-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

2-ethyl-N-((1r,4r)-4-((3-(6-(methylcarbamoyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2H-indazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(chroman-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((r,2'-dimethyl-2-oxo-rH-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((r,3'-dimethyl-2,2'-dioxo-2,3-dihydro-1H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[4,3-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(1-methyl-1H-pyrazol-3-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-2-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridazin-3-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(isoxazol-3-ylmethyl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-3-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyrimidin-5-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(oxazol-4-ylmethyl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-((4-methylthiazol-2-yl)methyl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(pyridin-4-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-ethylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(1H-pyrazol-3-yl)picolinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-inden-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dimethyl-2H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinazolin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-acetylisoindolin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dihydro-1H-inden-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(cyclopropylmethyl)-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-3-oxo-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(3-amino-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide ;

N-((1r,4r)-4-((3-(3-aminobenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide ;

N-((1r,4r)-4-((3-(benzo[d]thiazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-([2,3'-bipyridin]-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(oxazol-5-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-bromo-2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benz

o[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((r-methyl-2-oxo-rH-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3'-methyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(3-chloro-1-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((2',3'-dimethyl-2-oxo-3'H-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(3-chloro-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 N-((1r,4r)-4-((1-(5-bromo-2,3-dihydro-1H-inden-2-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrooxazol[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(6'-amino-[2,3'-bipyridin]-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(pyridin-4-yloxy)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-6-yl)-2-oxo-2,3

-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl-2H-indazole-3-carboxamide;

N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl-4,5,6,7-tetrahydro-2H-indazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloro-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylbenzamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-oxo-3,4-dihydro-2H-pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-bromo-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-(methoxymethoxy)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-nitrophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

2,5-dichloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2,3-dihydro-1H-inden-4-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzo[d]isoxazole-3-carboxamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylbenzo[d]isoxazole-3-carboxamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylbenzo[d]isoxazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-methylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-dimethoxybenzyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(cyclopropylmethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-ethyl-2H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(2-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-(hydroxymethyl)benzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

yl nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(2-aminobenzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(benzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-cyclopropyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-methyl-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

2,5-dichloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-chloro-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-3H-[1,2,3]triazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-ethyl-2-oxo-2,3-dihydrooxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-cyclobutylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-2-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(pyridin-3-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)benzamide;

2,5-dichloro-N-((1r,4r)-4-((2-oxo-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)benzamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H

-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-methoxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-ethyl-3-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(pyrido[2,3-b]pyrazin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((4-methyl-3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)

l)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-ethyl-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-oxo-3,4-dihydroquinazolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-formylphenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r,4r)-4-((3-(5-bromo-2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-3-(dimethylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyano-6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(thiazol-4-ylmethyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-cyclopropylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(2-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-aminopyrido[3,2-d]pyrimidin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-(trifluoromethyl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(2-methoxyethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-cyclobutylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide ;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((r-methyl-2-oxo-rH-[1,5'-bibenzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(dimethylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(methoxymethyl)-N-((1r,4r)-4-((3-(6-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(methoxymethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(2,5-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(oxetan-3-yl)-2H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-(oxetan-3-yl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-5-yl)-2-oxo-2,3-dihydro-1H-ben

zo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(3-phenyl-1H-indazol-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(2,2-difluoroethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-chloro-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-ethyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyloxazolo[4,5-b]pyridin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-1-(quinolin-3-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-1-(quinolin-6-yl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,4-dimethylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

mide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-cyanopyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methylpyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2,3-dihydro-1H-inden-4-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-(hydroxymethyl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-benzo[d][1,2,3]triazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1'-methyl-2-oxo-1H-[1,5'-bi

benzo[d]imidazol-3(2H)-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(benzo[d]thiazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-6-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(methylamino)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(1,8-naphthyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinazolin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(isoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(isoquinolin-6-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;
5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-fluoro-3-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(4-acetylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
5-chloro-N-((1r,4r)-4-((3-(3-(cyclopentyloxy)-4-methoxyphenyl)-2-oxo

-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-ethoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-methyl-1H-indole-2-carboxamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,1-dimethyl-1H-indole-2-carboxamide;

5-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,N,1-trimethyl-1H-indole-2-carboxamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3'-methyl-2-oxo-3'H-[1,5-b]benzo[d]imidazol]-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)picolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)thio)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-dichlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(imidazo[1,5-a]pyridin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)ni

cotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-8-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(imidazo[1,2-a]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-2H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(isoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)met

hyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methoxypicolinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-fluoroethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-morpholinoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(6-(2-amino-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-(((1-methyl-1H-pyrazol-4-yl)methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(1,5-naphthyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]

]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(quinazolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-morpholinophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(4-(isoxazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-benzyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1H-pyrrolo[2,3-b]

pyridin-5-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-phenoxyethyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,4-dichlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(isopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoroethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-(1H-pyrazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-(1H-pyrazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(1H-imidazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(2-(1H-imidazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(oxetan-3-yloxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((3,3-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(oxetan-3-ylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(5-(pyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

mide;

5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-5-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(2-methoxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-5-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(2-chloro-5-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

N-methyl-5-(3-(((1r,4r)-4-(2-methyl-5-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

N-methyl-5-(3-(((1r,4r)-4-(5-methyl-2-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(ethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(quinoxalin-6-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloropyridin-4-yl)-2-oxo-2,3-dihydro-1H

-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-(methylamino)-2-oxoethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoazetidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropanecarboxamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

N-((1S,4r)-4-((3-(6-(((S)-1-amino-1-oxopropan-2-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1R,4r)-4-((3-(6-(((R)-1-amino-1-oxopropan-2-yl)oxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(3-oxomorpholin-2-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(p-tolyl)-2,3-dihydro-1H-imidazo[4,5-b]pyrazin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

hexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(1-(pyridin-3-yl)piperidin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(isopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(oxazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(thiazol-2-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-morpholinopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-imidazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(oxazol-5-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-chloro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazoli

din-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methylbenzo[d]thiazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpyrazine-2-carboxamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-5-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethoxy)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

N-methyl-5-(3-(((1r,4r)-4-(2-methyl-5-(trifluoromethyl)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)picolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethoxy)benzamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(2-amino-5-chloronicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-bromo-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

N-((1r,4r)-4-((3-(2-(2H-1,2,3-triazol-2-yl)pyridin-4-yl)-2-oxo-2,3-dihy

dro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(2H-1,2,3-triazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-pyrazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(2,5-dichloronicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(cyclopropylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-methyl-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-((2,2,2-trifluoroethyl)amino)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-4-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)

methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(oxetan-3-yl)picolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-ethylpicolinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-N-((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methoxyazetidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 3-chloro-5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;
 5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N,6-dimethylpicolinamide;
 N-((1r,4r)-4-((3-(6-(methylcarbamoyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(2,2,2-trifluoroethyl)-2H-indazole-3-carboxamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 N-((1r,4r)-4-((3-(6-acetamido-4-methylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-propionamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(4-methyl-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-6-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(5-(2-hydroxyethoxy)pyrazin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-(2-hydroxyethoxy)pyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(cyclopropylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(3-morpholinophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(4-(1-methyl-1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((3-(3-(oxazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-(((1r,4r)-4-((3-(4-(1H-imidazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-(((1r,4r)-4-((3-(2-(1H-imidazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-(((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-(((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-4-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(4-(thiazol-5-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;
N-((1r,4r)-4-((3-(4-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(fluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-6-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(7-oxo-2-oxa-6-azaspiro[3.4]octan-6-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-cyclopropylpicolinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methylbenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(1-(2-(dimethylamino)ethyl)-3-methyl-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-methyl-1-(2-morpholinoethyl)-1H-indazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-methoxypyridin-3-yl)-2-oxo-3,4-dihydroquinazolin-1(2H)-yl)methyl)cyclohexyl)-2-methylnicotinamide;

N-((1r, 4r)-4-((3-(3-aminobenzo[d]isoxazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

6-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-(2-hydroxyethyl)benzo[d]isoxazole-3-carboxamide;

5-chloro-N-((1r,4r)-4-((3-(4-cyanopyridazin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(methylamino)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)(methyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-morpholinopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4,6-dimethylpyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2,3-dimethylpyridin-4-yl)-2-oxo-2,3-dihydro

-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methyl-2H-indazol-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(4-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(1,2,3,4-tetrahydroisoquinolin-7-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-acetyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1R,4r)-4-((2-oxo-3-(6-(((R)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1S,4r)-4-((2-oxo-3-(6-(((S)-tetrahydrofuran-3-yl)oxy)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1S,4r)-4-((3-(6-(((S)-2-hydroxypropoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(6-methylquinolin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2,2-difluoropropyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1R,4r)-4-((3-(6-((R)-3-hydroxypyrrolidin-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-4-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(2-methoxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(dimethylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyanophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxyacetamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-(1H-pyrazol-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(1H-pyrazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

clohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-cyano-4-fluorophenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-7-methoxy-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(4-(1H-1,2,3-triazol-1-yl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(oxazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(6-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-fluoro-6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(6-acetamidopyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((2-oxo-3-(6-propionamidopyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methylureido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-methylbenzo[d]thiazol-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(4-(methylamino)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1*r*,4*r*)-4-((3-(5-(1*H*-pyrazol-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(6-(1-methyl-1*H*-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(2-(1-methyl-1*H*-pyrazol-3-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1*r*,4*r*)-4-((3-(6-(1-methyl-1*H*-pyrazol-4-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(6-(1-methyl-1*H*-pyrazol-4-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((2-oxo-3-(6-ureidopyridin-3-yl)-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(6-(dimethylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1*r*,4*r*)-4-((3-(6-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1*r*,4*r*)-4-((3-(2-(dimethylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1*r*,4*r*)-4-((3-(6-((2-methoxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1*r*,4*r*)-4-((3-(2-(methylamino)pyridin-4-yl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl

)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r, 4r)-4-((3-(4-(1H-imidazol-4-yl)phenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((7-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(2-hydroxy-2-methylpropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1R,4r)-4-((3-(6-((R)-2-hydroxypropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1S,4r)-4-((3-(6-((S)-2-hydroxypropanamido)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((7-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(4-fluoro-3-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-4-yl)phen

yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-methoxypyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(2H-1,2,3-triazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-morpholinopyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(oxazol-5-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(oxazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(5-(oxazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(2-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-(2-oxoimidazolidin-1-yl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(5-(methylamino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-pyrazol-4-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(1-methyl-1H-pyrazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(1-methyl-1H-pyrazol-3-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(5-(1H-pyrazol-1-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)

yl)nicotinamide;

5-chloro-N-((1r,4r)-4-((6-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((5-fluoro-3-(6-(methylamino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(2-(2-oxopyrrolidin-1-yl)pyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1,2-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-hydroxypropyl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-(2-hydroxyethoxy)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(2-(2-hydroxyethoxy)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-((2-hydroxyethyl)amino)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide; 5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethoxy)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benz

o[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide;

4-(3-(((1r,4r)-4-(5-chloro-2-(difluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

4-(3-(((1r,4r)-4-(5-chloro-2-methylnicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicolinamide;

4-(3-(((1r,4r)-4-(5-chloro-2-(trifluoromethyl)nicotinamido)cyclohexyl)methyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-N-methylpicoli

namide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(1-(2-hydroxyethyl)-3-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(6-(1H-imidazol-2-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1-methyl-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(5-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-3-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(2-(1H-pyrazol-4-yl)pyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r,4r)-4-((3-(3-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-b

enzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

N-((1r, 4r)-4-((3-(4-(1H-imidazol-2-yl)phenyl)-2-oxo-2, 3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((3-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

N-((1r,4r)-4-((3-(3-(1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

N-((1r,4r)-4-((3-(3-(1,3,4-oxadiazol-2-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-methylnicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chlorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

namide;

5-chloro-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(3-fluoro-4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(3-fluoro-4-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-chloro-5-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-chloro-5-fluorophenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(2-fluoro-5-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((1-(2-fluoro-5-methoxyphenyl)-2-oxo-1H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((1-(3-fluorophenyl)-2-oxo-1

H-imidazo[4,5-b]pyridin-3(2H)-yl)methyl)cyclohexyl)nicotinamide; N-((1r,4r)-4-((3-(4-(1H-imidazol-5-yl)phenyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-5-chloro-2-(difluoromethyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-((2-hydroxyethyl)amino)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide ;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxoimidazolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-methyl-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((2-oxo-3-(6-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide;

5-chloro-N-((1r,4r)-4-((3-(6-(1-methyl-1H-pyrazol-3-yl)pyridin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)-2-(trifluoromethyl)nicotinamide ;

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((6-fluoro-3-(5-(2-hydroxyethyl)pyridin-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)cyclohexyl)nicotinamide; and

5-chloro-2-(difluoromethyl)-N-((1r,4r)-4-((3-(2-(hydroxymethyl)-1H-indol-5-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)cyclohexyl)nicotinamide ;

or a pharmaceutically acceptable salt thereof or a prodrug thereof.

[Claim 8]

A use of a compound described in any one of claims 1 to 7 or a pharmaceutically acceptable salt, prodrug, solvate or composition thereof for the manufacture of a medicament for the treatment of a condition or

disorder in which CRHR1 and/or CRHR2 are involved.

- [Claim 9] The use as described in claim 8, wherein said condition or disorder is selected from the group consisting of: gastrointestinal disorders, major depressive disorders, schizophrenic disorders, neurodegenerative diseases, pain, dysfunction of appetite and food intake, sleep disorders, cognitive disorders, tolerance to and dependence on a number of substances, inflammation, fertility problems, sexual dysfunctions and pre-term birth and non-inflammatory urogenital disorders, allergic disorders, mast cell activation disorders, Cushing's syndrome, emesis, gastrointestinal disorders, neurotoxic injury, loss of hair, heart disease, and combinations thereof.
- [Claim 10] The use as described in claim 9, wherein the heart disease is selected from the group consisting of: acute and chronic heart failure, cardiovascular disease, hyper tension, myocardial infarction, coronary artery disease, and abdominal aortic aneurysm.
- [Claim 11] A method for the treatment of a condition or disorder in which CRHR1 and/or CRHR2 are involved, in an animal, including a human, which comprises administering to the animal in need of such treatment a therapeutically effective amount of a compound or a prodrug thereof or a pharmaceutically acceptable salt thereof, as described in any one of claims 1 to 7.
- [Claim 12] The method as described in claim 11, wherein said condition or disorder is selected from the group consisting of: gastrointestinal disorders, major depressive disorders, schizophrenic disorders, neurodegenerative diseases, pain, dysfunction of appetite and food intake, sleep disorders, cognitive disorders, tolerance to and dependence on a number of substances, inflammation, fertility problems, sexual dysfunctions and pre-term birth and non-inflammatory urogenital disorders, allergic disorders, mast cell activation disorders, Cushing's syndrome, emesis, gastrointestinal disorders, neurotoxic injury, loss of hair, heart disease, and combinations thereof.
- [Claim 13] The method as described in claim 12, wherein the heart disease is selected from the group consisting of: acute and chronic heart failure, cardiovascular disease, hyper tension, myocardial infarction, coronary artery disease, and abdominal aortic aneurysm.
- [Claim 14] A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt thereof or a prodrug thereof, as described in any one of claims 1 to 7, and a pharmaceutically acceptable carrier.

- [Claim 15] The pharmaceutical composition as described in claim 14, further comprising another pharmacologically active agent.
- [Claim 16] A compound described in any one of claims 1 to 7 or a prodrug thereof or a pharmaceutically acceptable salt for use in the treatment of a condition or disorder in which CRHR1 and/or CRHR2 are involved.
- [Claim 17] A process for preparing a pharmaceutical composition, wherein the process comprises mixing a compound described in any one of claims 1 to 7 or a pharmaceutically acceptable salt thereof or a prodrug thereof and a pharmaceutically acceptable carrier or excipient.
- [Claim 18] An assay process for identifying a compound which has CRHR1 and/or CRHR2 antagonistic activity, comprising administering of a compound described in any one of claims 1 to 7 to mice loaded exogenous CRHR2 agonist within 1 week and investigating cardiovascular functions.
- [Claim 19] An assay process for identifying a compound which has CRHR1 and/or CRHR2 antagonistic activity, comprising administering of a compound described in any one of claims 1 to 7 to mice infused urocortin 2 within 2 days and measuring cardiac function by echocardiography.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2019/015392

A. CLASSIFICATION OF SUBJECT MATTER Int.Cl. See extra sheet 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) Int.Cl. See extra sheet Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Published examined utility model applications of Japan 1922-1996 Published unexamined utility model applications of Japan 1971-2019 Registered utility model specifications of Japan 1996-2019 Published registered utility model applications of Japan 1994-2019 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAplus/REGISTRY (STN)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2011/092293 A2 (NOVARTIS AG) 2011.08.04, THE WHOLE DOCUMENT & US 2011/0201629 A1 & AR 80056 A & UY 33209 A & TW 201130815 A	1-19
A	BECK, J. P. et al., PURIN-8-ONES AS CORTICOTROPIN-RELEASING HORMONE (CRH-R1) RECEPTOR ANTAGONISTS, Bioorganic & Medicinal Chemistry Letters, 1999, 9(7), pp.967-972	1-19
A	JP 2007-161585 A (TAISHO PHARMACEUTICAL CO., LTD) 2007.06.28, THE WHOLE DOCUMENT & JP 2008-503442 A & JP 4924037 B2 & US 2008/0280928 A1 & US 2011/0124862 A1 & WO 2006/001511 A1 & EP 1758903 A1 & EP 1953160 A1 & CA 2568804 A & NO 20070466 L & KR 10-2007-0026637 A & CN 1972940 A & BR	1-19
☒ 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 "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 07.06.2019		Date of mailing of the international search report 25.06.2019
Name and mailing address of the ISA/JP Japan Patent Office 3-4-3, Kasumigasaki, Chiyoda-ku, Tokyo 100-8915, Japan		Authorized officer Koji ITO Telephone No. +81-3-3581-1101 Ext. 3492

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2019/015392

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PI0512418 A & ZA 200610039 A & NZ 551427 A JP 2004-533465 A (GLAXO GROUP LIMITED) 2004.11.04, THE WHOLE DOCUMENT & JP 2004-528349 A & US 2005/0054661 A1 & US 2004/0176400 A1 & GB 114343 D & GB 114349 D & GB 117399 D & GB 114343 D0 & GB 110569 D & GB 110567 D & GB 110570 D & GB 117420 D & GB 117401 D & GB 203201 D & GB 206834 D & WO 2002/100863 A1 & WO 2002/088095 A1	1-19
A	JP 2008-517060 A (SB Pharmco Puerto Rico Inc) 2008.05.22, THE WHOLE DOCUMENT & US 2008/0064719 A1 & WO 2006/044821 A1 & EP 1802621 A1 & DE 602005014375 D & AT 430746 T & ES 2326827 T	1-19

INTERNATIONAL SEARCH REPORT

International application No.

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CLASSIFICATION OF SUBJECT MATTER

C07D235/26 (2006. 01) i, A61K31/4184 (2006. 01) i, A61K31/437 (2006. 01) i,
A61K31/4375 (2006. 01) i, A61K31/4439 (2006. 01) i, A61K31/4709 (2006. 01) i,
A61K31/4725 (2006. 01) i, A61K31/497 (2006. 01) i, A61K31/4985 (2006. 01) i,
A61K31/501 (2006. 01) i, A61K31/506 (2006. 01) i, A61K31/517 (2006. 01) i,
A61K31/519 (2006. 01) i, A61K31/5377 (2006. 01) i, A61K31/5383 (2006. 01) i,
A61P1/00 (2006. 01) i, A61P9/00 (2006. 01) i, A61P25/00 (2006. 01) i,
A61P29/00 (2006. 01) i, A61P43/00 (2006. 01) i, C07D401/12 (2006. 01) i,
C07D401/14 (2006. 01) i, C07D403/12 (2006. 01) i, C07D405/14 (2006. 01) i,
C07D413/14 (2006. 01) i, C07D417/14 (2006. 01) i, C07D471/04 (2006. 01) i,
C07D487/04 (2006. 01) i, C07D491/107 (2006. 01) i, C07D498/04 (2006. 01) i

INTERNATIONAL SEARCH REPORT

International application No.

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Minimum documentation searched

C07D235/26, A61K31/4184, A61K31/437, A61K31/4375, A61K31/4439, A61K31/4709,
A61K31/4725, A61K31/497, A61K31/4985, A61K31/501, A61K31/506, A61K31/517,
A61K31/519, A61K31/5377, A61K31/5383, A61P1/00, A61P9/00, A61P25/00, A61P29/00,
A61P43/00, C07D401/12, C07D401/14, C07D403/12, C07D405/14, C07D413/14,
C07D417/14, C07D471/04, C07D487/04, C07D491/107, C07D498/04

摘要：

本发明涉及一种耦合环状脲衍生物，其对 CRHR1 和/或 CRHR2 具有拮抗活性，并且可用于治疗或预防 CRHR1 和/或 CRHR2 相关病症及疾病。本发明还涉及一种包含这些化合物的药物组合物和这些化合物及组合物在预防或治疗 CRHR1 和/或 CRHR2 相关疾病中的用途。

