(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
6 February 2025 (06.02.2025)

WIPO | PCT

(10) International Publication Number
WO 2025/026270 A1

(51) International Patent Classification:
C07D 471/04 (2006.01) ***A61P 1/16*** (2006.01)
C07D 498/22 (2006.01) ***A61P 3/04*** (2006.01)
A61K 31/437(2006.01) ***A61P3/10*** (2006.01)
A61K 31/4709 (2006.01)

(21) International Application Number: PCT/CN 2024/108192
(22) International Filing Date: 29 July 2024 (29.07.2024)
(25) Filing Language: Chinese
(26) Publication Language: Chinese
(30) Priority Data:

202310946477.8	28 July 2023 (28.07.2023)	CN
202311087184.5	25 August 2023 (25.08.2023)	CN
202311110642.2	30 August 2023 (30.08.2023)	CN
202311269491.5	27 September 2023 (27.09.2023)	CN
202311372605.9	20 October 2023 (20.10.2023)	CN
202311546779.2	17 November 2023 (17.11.2023)	CN
202311690443.3	8 December 2023 (08.12.2023)	CN
202311866263.6	29 December 2023 (29.12.2023)	CN
202410140555.X	31 January 2024 (31.01.2024)	CN
202410241733.8	1 March 2024 (01.03.2024)	CN
202410385768.9	29 March 2024 (29.03.2024)	CN
202410587643.4	11 May 2024 (11.05.2024)	CN
202410882329.9	2 July 2024 (02.07.2024)	CN

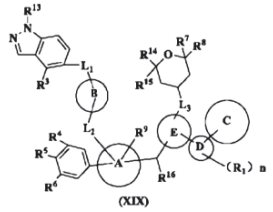
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI,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

(54) Title: BENZO NITROGEN-CONTAINING HETEROCYCLIC DERIVATIVE REGULATOR, PREPARATION METHOD THEREFOR AND USE THEREOF



(XIX)

(57) Abstract: A benzo nitrogen-containing heterocyclic derivative regulator, a preparation method therefor and a use thereof. Particularly, the present invention relates to a compound represented by general formula (XIX), a preparation method therefor, a pharmaceutical composition containing the compound, and a use of the compound as a regulator in the preparation of drugs for treating metabolic diseases and related diseases, wherein each substituent in the general formula (XIX) is the same as the definition in the description.

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

Published:
- with international search report (Art. 21(3)).

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BENZO NITROGEN-CONTAINING HETEROCYCLIC DERIVATIVE REGULATOR, PREPARATION METHOD THEREFOR AND USE THEREOF

Technical Field

The present disclosure belongs to the field of medicine and biology, and in particular relates to a benzo nitrogen-containing heterocyclic derivative regulator, and a preparation method therefor and the use thereof.

Background Art

Diabetes mellitus is a prevalent endocrine and metabolic disease with metabolic disorders resulting from multiple factors, leading to multiorgan and multisystem damage. Diabetes mellitus exhibits a high incidence rate, with approximately 425 million diabetic patients worldwide. The incidence rate of diabetes mellitus in China is about 10%, among which type II diabetes accounts for 90% of all diabetes cases, with an increasing prevalence trend and a notable shift towards younger ages.

Currently, there are many types of drugs on the market for the treatment of type II diabetes, including insulin, biguanides, glucagon-like peptide-1 (GLP-1) receptor agonists, dipeptidyl peptidase (DPP-IV) inhibitors, sodium-glucose co-transporter 2 (SGLT-2) inhibitors, α-glucosidase inhibitors, etc., among which GLP-1 receptor agonists are of greatest concern.

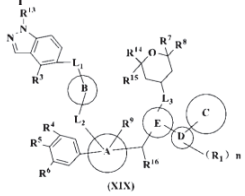
GLP-1 is a peptide hormone secreted by human intestinal L cells, and its receptors are distributed in pancreas islet cells, various gastrointestinal cells, and neurons of the central nervous system and peripheral nervous system. After activation, GLP-1 receptors have physiological effects such as promoting insulin secretion, inhibiting glucagon secretion, suppressing appetite and delaying gastric emptying. Clinical evidence shows that compared with other hypoglycemic drugs, GLP-1 receptor agonists have better glucose-lowering effect and are less likely to cause side effects such as hypoglycemia. In addition, it has additional cardiovascular benefits and may be conductive to weight control by reducing food intake and delaying gastric emptying.

Currently, the GLP-1 receptor agonists available on the market are all polypeptide drugs, most of which require subcutaneous administration, leading to suboptimal patient compliance. Furthermore, oral polypeptides exhibit an extremely low bioavailability. Therefore, there is a substantial clinical need for the development of small molecule GLP-1 receptor agonists for oral administration.

There are currently no approved small molecule GLP-1 receptor agonists, and therefore there is a substantial clinical need. Oral small molecule GLP-1 receptor agonists with lower cost and better compliance have the potential to treat a variety of metabolic diseases and have broad market prospects.

Summary of the Invention

An object of the present disclosure is to provide a compound of general formula (XIX), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XIX)

wherein

R^{13} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

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L_1, L_2 or L_3 each is independently selected from a bond, C_{2-4}alkenylene, C_{2-4}alkynylene or -$(CH_2)_{n1}$-;

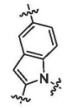
ring A is selected from C_{3-14}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl;

ring B is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy or C_{1-6}deuterated haloalkoxy;

ring C is selected from C_{3-14}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy or C_{1-6}deuterated haloalkoxy;

ring D is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl, or 5- to 14-membered heteroaryl;

ring E is selected from C_{3-14}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or ring E is , optionally substituted by one or more substituents of methyl, ethyl, methoxy or ethoxy;

R^1, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$(CH_2)_{m1}OR_{c1}$ or (=C)$R_{c3}R_{c4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$(CH_2)_{m1}OR_{c1}$ or (=C)$R_{c3}R_{c4}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{c1}, R_{c3} or R_{c4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$(CH_2)_{m2}OR_{c2}$, -$(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or -$(CH_2)_{m4}C(O)OR_{a2}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$(CH_2)_{m2}OR_{c2}$, -$(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or -$(CH_2)_{m4}C(O)OR_{a2}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio,

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C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{a2}, R_{b1} or R_{c2} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^9or R^{16}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

or when n is not 1,

R^1 and R^1, R^2 and R^1, R^4 and R^5, R^5 and R^6, and R^7 and R^8, respectively, are linked with the atoms to which they are connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

n, n1, m1, m2, m3 or m4 each is independently selected from 0, 1, 2, 3, 4 or 5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

R^{13} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

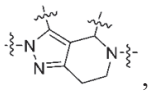
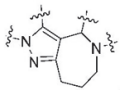
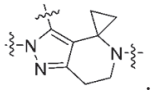
preferably, R^{13} is selected from -CD_3, hydrogen, deuterium, fluoro, chloro, bromo, methyl or cyclopropyl, wherein the methyl or cyclopropyl is optionally further substituted by one or more substituents of deuterium, halogen or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

ring A is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-12}aryl or 5- to 12-membered heteroaryl containing 1-3 atoms selected from N, O or S;

preferably, ring A is selected from C_{6-12}cycloalkyl, 6- to 12-membered heterocyclyl containing 1-3 N, O or S atoms or 6- to 12-membered heteroaryl containing 1-3 N, O or S atoms; and

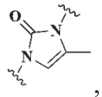
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more preferably, ring A is selected from ,  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

ring B is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 atoms selected from N, O or S; optionally further substituted by one or more substituents of deuterium, halogen, amino, oxo, mercapto, thio or C_{1-3}alkyl;

preferably, ring B is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of deuterium, halogen, amino, oxo, thio or C_{1-3}alkyl;

more preferably, ring B is selected from ,  or , optionally further substituted by one or more substituents of deuterium, halogen, amino, oxo, thio or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy or C_{1-3}deuterated haloalkoxy;

preferably, ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 selected from N, O or S or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of deuterium, hydroxyl, thio, oxo or C_{1-3}haloalkoxy; and

more preferably, ring C is selected from , , , , ,  or ; optionally further substituted by one or more substituents of deuterium, hydroxyl, thio or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

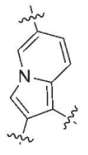
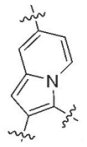
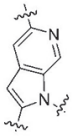
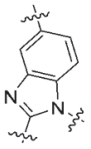
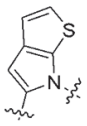
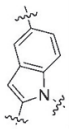
ring D is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 atoms selected from N, O or S;

preferably, ring D is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; and

more preferably, ring D is selected from , ,  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

ring E is selected from C_{3-8}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 atoms selected from N, O or S, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, ring E is selected from , , , ,  or , optionally substituted by one or more substituents of methyl, ethyl, methoxy or ethoxy.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

R^1, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{14}, R^{15}or R^{16} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-(CH_2)_{m1}OR_{c1}$ or $(=C)R_{c3}R_{c4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-(CH_2)_{m1}OR_{c1}$ or $(=C)R_{c3}R_{c4}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^1, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-(CH_2)_{m1}OR_{c1}$ or $(=C)R_{c3}R_{c4}$, wherein the amino, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-(CH_2)_{m1}OR_{c1}$ or $(=C)R_{c3}R_{c4}$ is optionally further substituted by one or more substituents of deuterium, amino, halogen, deuterated methyl, hydroxyl, methyl, cyclopropyl, oxo, thio, C_{1-3}alkyl or C_{1-3}alkoxy; and

more preferably, R^1, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, oxo, thio, cyano, methyl, fluoro, chloro, cyclopropyl, ethynyl, $-(CH_2)_{m1}OR_{c1}$ or $(=C)R_{c3}R_{c4}$, wherein the cyclopropyl, ethynyl, $-(CH_2)_{m1}OR_{c1}$ or $(=C)R_{c3}R_{c4}$ is optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, hydroxyl, $-CD_3$, methyl, ethyl, cyclopropyl, oxo, thio or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

R_{c1}, R_{c3} or R_{c4} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{c1}, R_{c3} or R_{c4} is selected from fluoro, methyl, cyano, $-CH_2F$, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl, oxetane, phenyl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$, wherein the amino, methyl, $-CH_2F$, difluoromethyl, trifluoromethyl, ethynyl, methylthio, cyclopropyl, oxetane, phenyl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$ is optionally further substituted by one or more substituents of deuterium, halogen, methoxy, deuterated methyl or hydroxyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

R_{a1}, R_{a2}, R_{b1} or R_{c2} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a1}, R_{a2}, R_{b1} or R_{c2} each is independently selected from fluoro, methyl, ethyl, $-CH_2F$, cyano, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl, oxetane or phenyl, wherein the amino, methyl, ethyl, $-CH_2F$, difluoromethyl, trifluoromethyl, ethynyl, methylthio, cyclopropyl, oxetane or phenyl is optionally further substituted by one or more substituents of deuterium, halogen, methoxy, deuterated methyl or hydroxyl.

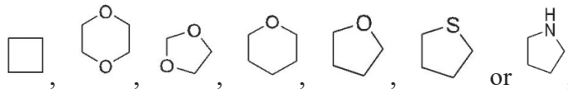
In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

R^9 or R^{16}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

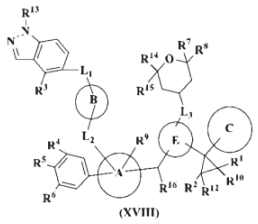
preferably, R^9 or R^{16}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XIX):

R^1 and R^1, R^2 and R^1, R^4 and R^5, R^5 and R^6, and R^7 and R^8, respectively, are linked with the atoms to which they are connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^1 and R^1, R^2 and R^1, R^4 and R^5, R^5 and R^6, and R^7 and R^8, respectively, are linked with the atoms to which they are connected to form cyclopropyl, , optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, amino, nitro, hydroxyl, cyano, oxo, thio, methyl or ethyl.

An object of the present disclosure is to provide a compound of general formula (XVIII), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XVIII)

wherein

R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{a2}, R_{b1} or R_{c2} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^9or R^{16}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

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or

R^1 and R^{10}, R^2 and R^{12}, R^4 and R^5, R^5 and R^6, R^7 and R^8, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^{13}, L_1, L_2, L_3, ring A, ring B, ring C, and ring E are defined as in formula (XIX); and

n1, m1, m2, m3 or m4 each is independently selected from 0, 1, 2, 3, 4 or 5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or $-(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, amino, halogen, deuterated methyl, hydroxyl, methyl, cyclopropyl, oxo, thio, C_{1-3}alkyl or C_{1-3}alkoxy; and

further preferably, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{14}, R^{15} or R^{16} each is independently selected from hydrogen, oxo, thio, cyano, methyl, fluoro, chloro, cyclopropyl, ethynyl or $-(CH_2)_{m1}OR_{c1}$, wherein the cyclopropyl, ethynyl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, hydroxyl, $-CD_3$, methyl, ethyl, cyclopropyl, oxo, thio or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-(CH_2)_{m2}OR_{c2}$, $-(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or $-(CH_2)_{m4}C(O)OR_{a2}$

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is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{c1} is selected from fluoro, methyl, cyano, -CH_2F, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl, oxetane, phenyl, -$(CH_2)_{m2}OR_{c2}$, -$(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or -$(CH_2)_{m4}C(O)OR_{a2}$, wherein the amino, methyl, -CH_2F, difluoromethyl, trifluoromethyl, ethynyl, methylthio, cyclopropyl, oxetane, phenyl, -$(CH_2)_{m2}OR_{c2}$, -$(CH_2)_{m3}C(O)NR_{a1}R_{b1}$ or -$(CH_2)_{m4}C(O)OR_{a2}$ is optionally further substituted by one or more substituents of deuterium, halogen, methoxy, deuterated methyl or hydroxyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

R_{a1}, R_{a2}, R_{b1} or R_{c2} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a1}, R_{a2}, R_{b1} or R_{c2} each is independently selected from fluoro, methyl, ethyl, -CH_2F, cyano, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl, oxetane or phenyl, wherein the methyl, ethyl, -CH_2F, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl, oxetane or phenyl, optionally further substituted by one or more substituents of deuterium, halogen, methoxy, deuterated methyl or hydroxyl.

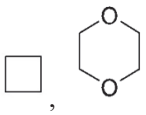
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

R^9 or R^{16}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

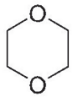
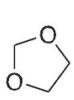
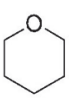
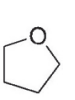
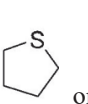
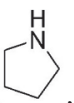
preferably, R^9 or R^{16}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

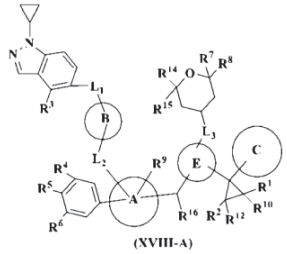
R^1 and R^{10}, R^2 and R^{12}, R^4 and R^5, R^5 and R^6, R^7 and R^8, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^1 and R^{10}, R^2 and R^{12}, R^4 and R^5, R^5 and R^6, R^7 and R^8, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form cyclopropyl, , optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, amino, nitro, hydroxyl, cyano, oxo, thio, methyl or ethyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

R^1 and R^{10}, R^2 and R^{12}, R^4 and R^5, R^5 and R^6, R^7 and R^8, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form cyclopropyl, , , , , , , , optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, amino, nitro, hydroxyl, cyano, oxo, thio, methyl or ethyl.

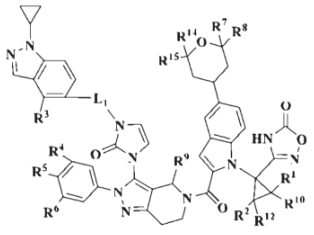
In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-A):



(XVIII-A)

wherein, ring A, ring B, ring C, ring E, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, L_1, L_2 and L_3 are defined as in general formula (XVIII).

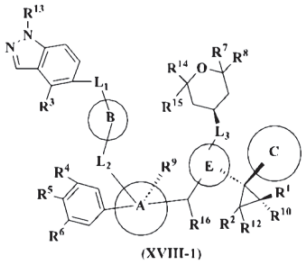
In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-B):



(XVIII-B)

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}, R^{15} and L_1 are defined as in general formula (XVIII).

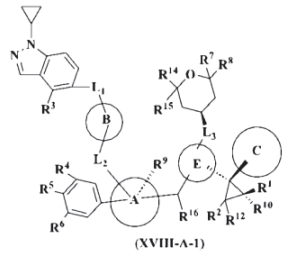
In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-1):



(XVIII-1)

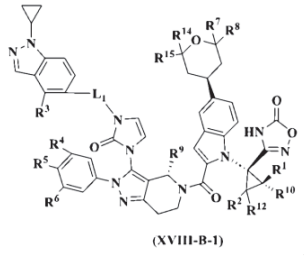
.

In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-A-1):



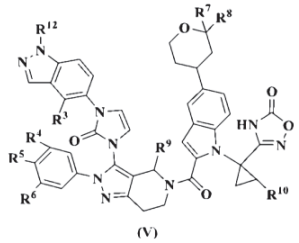
(XVIII-A-1)

In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-B-1):



(XVIII-B-1)

An object of the present disclosure is to provide a compound of general formula (V), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(V)

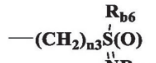
wherein

R^4, R^5or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^5 and R^6 are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$,

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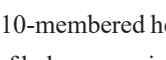
-$NR_{a5}S(O)NR_{a4}R_{b4}$, -$(CH_2)_{n2}R_{a5}R_{b5}$ or , wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -$NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6} or R_{b6} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a5} and R_{b5}, and R_{a6} and R_{b6}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$(CH_2)_{n2}R_{a5}R_{b5}$ or , optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

n1-n3 are an integer of 0-5; and

m1 is an integer of 0-5;

wherein when R^7 and R^8 are hydrogen, R^9, R^{10}, and R^{12} are methyl, and when R^3 and R^5 are fluoro, R^4 and R^6 are not both methyl;

when R^7 and R^8 are hydrogen, R^9, R^{10}, and R^{12} are methyl, when $R^3$is hydrogen and $R^5$is halogen, R^4 and $R^6$are not both methyl;

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when R^7, R^8, R^9, R^{10}, and R^{12} are methyl, $R^5$is fluoro, and R^4 is halogen, trifluoromethyl or cyclopropyl, R^6 is not hydrogen;

when R^7, R^8, R^9, and R^{10} are methyl, R^{12} is deuterated methyl, R^3 is fluoro, R^5 is halogen, and R^4 is deuterated methyl, R^6 is not deuterated methyl;

when R^4, R^6, R^7, R^8, R^9, and R^{10} are methyl, and R^3 and R^5 are fluoro, R^{12} is not deuterated methyl;

when R^7, R^8, R^9, R^{10}, and R^{12} are methyl, R^3 is fluoro, R^5 is halogen, and R^4 is methyl, R^6 is not methyl;

when R^7, R^8, R^9, and R^{10} are methyl, R^{12} is deuterated methyl, R^3 is fluoro, R^5 is halogen, and R^4 is deuterated methyl, R^6 is not deuterated methyl; and

when R^4, R^6, R^7, R^8, R^9, and R^{10} are methyl, and R^3 and R^5 are fluoro, R^{12} is not deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

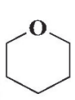
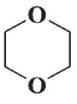
R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, cyano, C_{1-3}alkyl, C_{1-3}sulfanyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, and 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}alkoxy; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, methyl, cyano, ethynyl, methylthio, amino, cyclopropyl, and oxetane; optionally further substituted by halogen, methoxy, or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^5 and R^6 are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, C_{1-3}alkyl, and oxo;

preferably, R^5 and R^6 are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of halogen, amino, C_{1-3}alkyl, and oxo; and

further preferably, R^5 and R^6 are linked with adjacent atoms to form , , or ; optionally further substituted by one or more substituents of halogen, amino, C_{1-3}alkyl, and oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^7 and R^8 each are independently selected from deuterium or C_{1-6}deuterated alkyl; and

preferably, R^7 and R^8 each are independently selected from deuterium or C_{1-3}deuterated alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^9 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^9 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-8}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

further preferably, R^9 is selected from cyano and cyclopropyl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl.

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In another preferred embodiment of the present disclosure, in the compound of general formula (V):

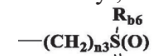
R^9 is linked with the carbon atoms to which it is connected to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^9 is linked with the carbon atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

further preferably, R^9 is linked with the carbon atoms to which it is connected to further preferably form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n2}R_{a5}R_{b5}$ or , wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n2}R_{a5}R_{b5}$ or , wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$ or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

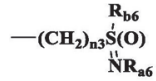
R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

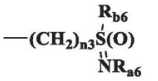
preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

further preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$ or C_{1-3}alkyl.

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In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^{12} is selected from C_{1-3}alkyl, C_{3-6}cycloalkyl, $-(CH_2)_{n2}R_{a5}R_{b5}$ or , optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^{12} is selected from methyl, cyclopropyl, $-(CH_2)_{n2}R_{a5}R_{b5}$ or , optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^{12} is selected from C_{1-3}alkyl; and

further preferably, R^{12} is selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6} or R_{b6} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6} or R_{b6} each is independently selected from hydrogen, deuterium, halogen or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a5} and R_{b5}, and R_{a6} and R_{b6}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a2} and R_{b2}, and R_{a3} and R_{b3}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

further preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl,

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C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

further preferably, R_{a2} and R_{b2}, and R_{a3} and R_{b3}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^7, R^8, R^9or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^7, R^8, R^9or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

further preferably, R^7, R^8, R^9or R^{10} each is independently selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^7, R^8, R^9 or R^{10}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, cyano, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

further preferably, R^7, R^8, R^9 or R^{10} each is independently selected from methyl, fluoro, cyclopropyl or ethynyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

preferably, R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

further preferably, R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl,

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C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

further preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, cyano, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or -$(CH_2)_{m1}OR_{c1}$; and

more preferably, R^7, R^8, R^9 or R^{10} each is independently selected from methyl, fluoro, cyclopropyl, ethynyl or -$(CH_2)_{m1}OR_{c1}$.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

further preferably, R_{c1} is selected from fluoro, methyl, cyano, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl or oxetane; optionally further substituted by halogen, methoxy or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

R^{10} is linked with the atoms to which it is connected and adjacent atoms to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

preferably, R^{10} is linked with the atoms to which it is connected and adjacent atoms to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

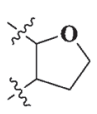
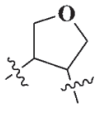
further preferably, R^{10} is linked with the atoms to which it is connected and adjacent atoms to form .

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

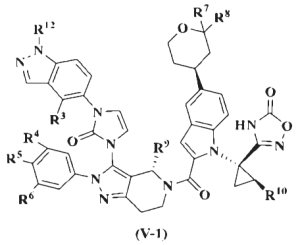
R^{10} is linked with the atoms to which it is connected and adjacent atoms to form  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (V):

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R^{10} is linked with the atoms to which it is connected and adjacent atoms to form ,  or .

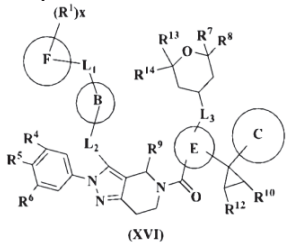
In a further preferred embodiment of the present disclosure, the compound of general formula (V) is further shown as general formula (V-1):



(V-1)

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An object of the present disclosure is to provide a compound of general formula (XVI), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XVI)

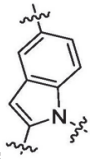
wherein

ring F is selected from C_{3-18}cycloalkyl, 3- to 18-membered heterocyclyl, C_{6-18}aryl or 5- to 18-membered heteroaryl;

ring B is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy or C_{1-6}deuterated haloalkoxy;

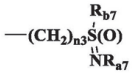
ring C is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy or C_{1-6}deuterated haloalkoxy;

ring E is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

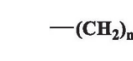
or ring E is , optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl;

L_1, L_2 or L_3 each is independently selected from a bond, C_{2-4}alkenylene, C_{2-4}alkynylene, $-(CH_2)_{n1}-$ or $-(CH_2)_{n5}NR_{b5}$, wherein the C_{2-4}alkenylene, C_{2-4}alkynylene, $-(CH_2)_{n1}-$ or $-(CH_2)_{n5}NR_{b5}$ is optionally further substituted by one or more substituents of halogen, amino, nitro,

hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^1 each is independently selected from , hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$ is optionally further substituted by one or more substituents of , halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or

R^1 each is linked with the atoms to which it is connected to form C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, optionally further substituted by one or more substituents of , deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl,

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C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -NS(O)$R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl,

C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

or

R^{10} and R^{12} are linked with the atoms to which they are connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl; and

n1-n5, m1 or x each is independently selected from 0, 1, 2, 3, 4 or 5.

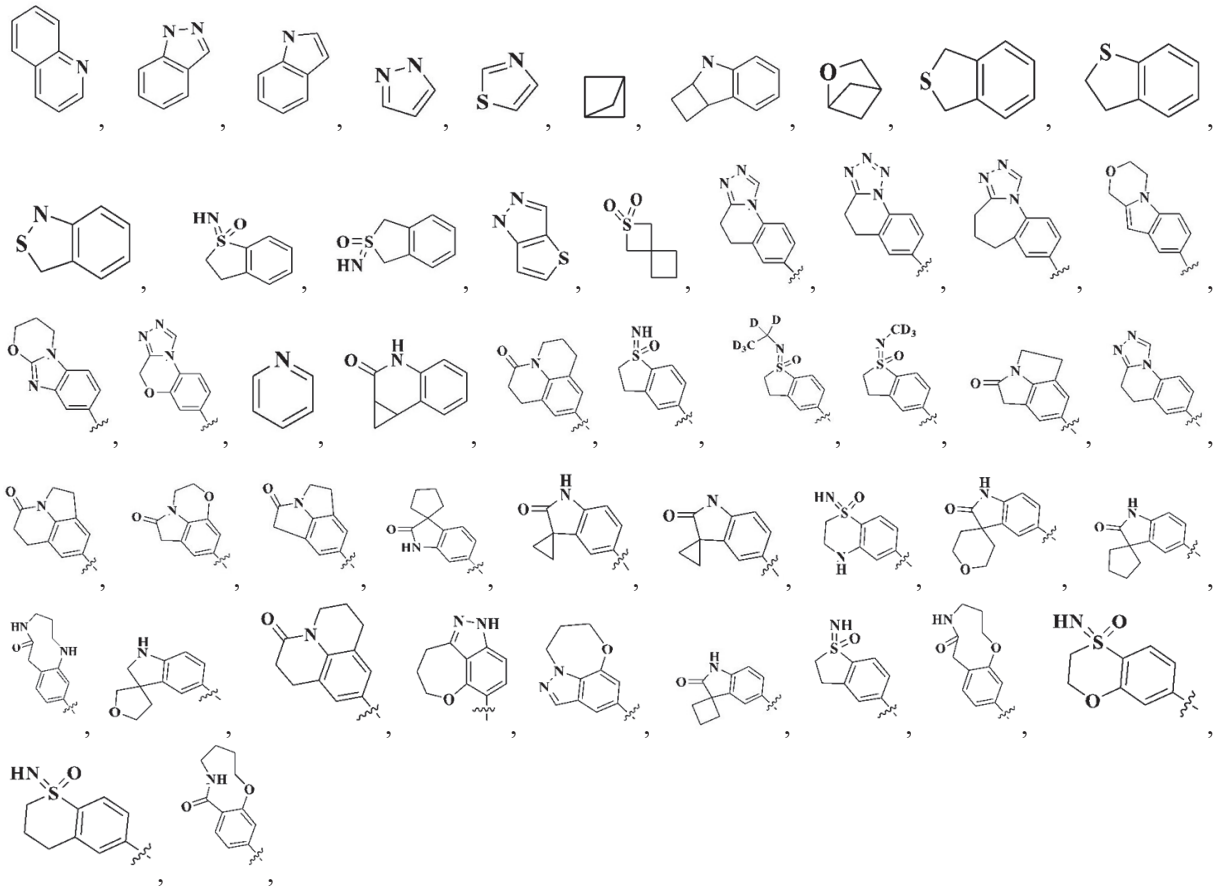
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

ring F is selected from C_{3-12}cycloalkyl, 3- to 14-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-14}aryl or 5- to 14-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S;

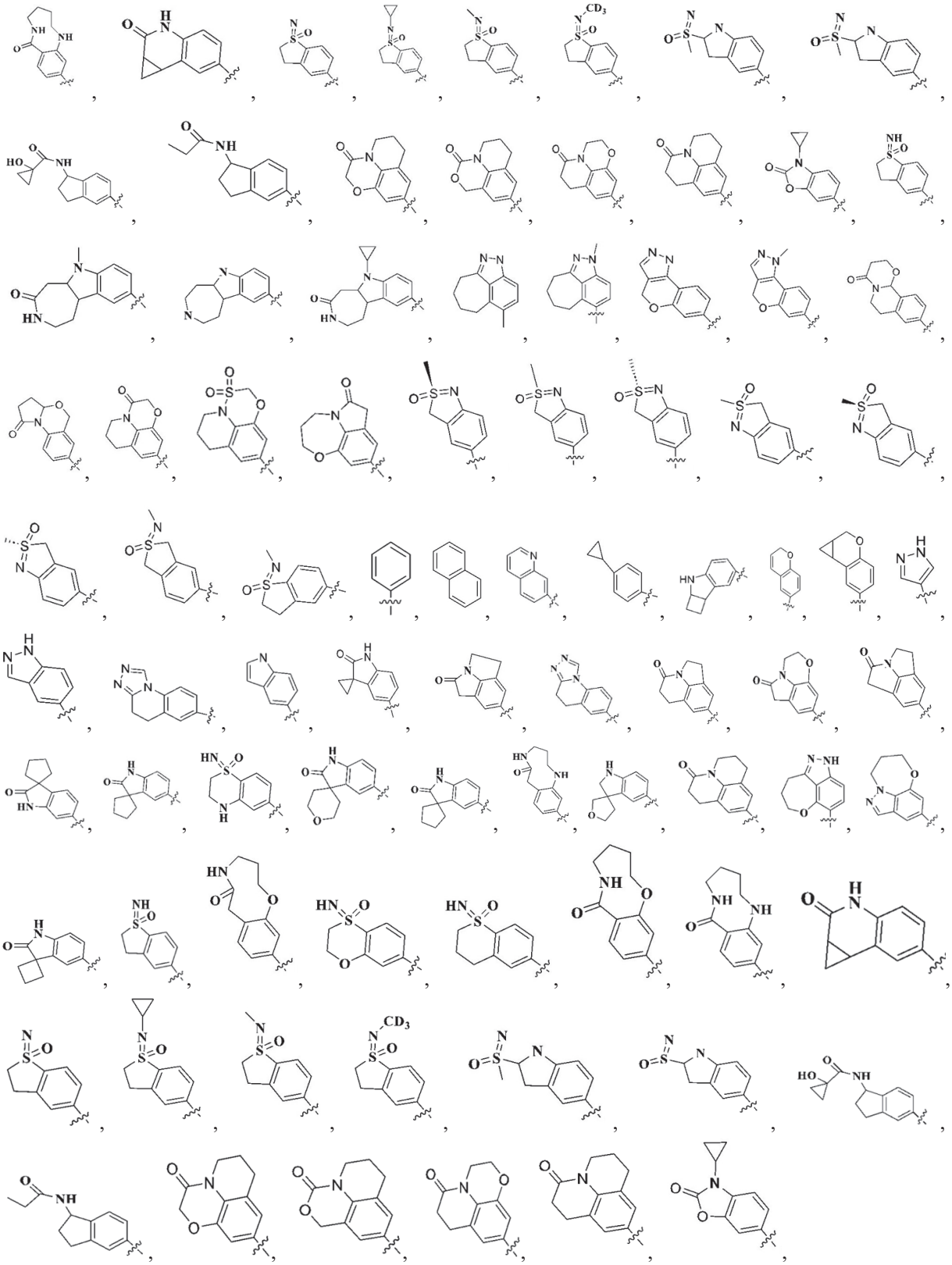
preferably, ring F is selected from C_{3-10}cycloalkyl, 5- to 14-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S;

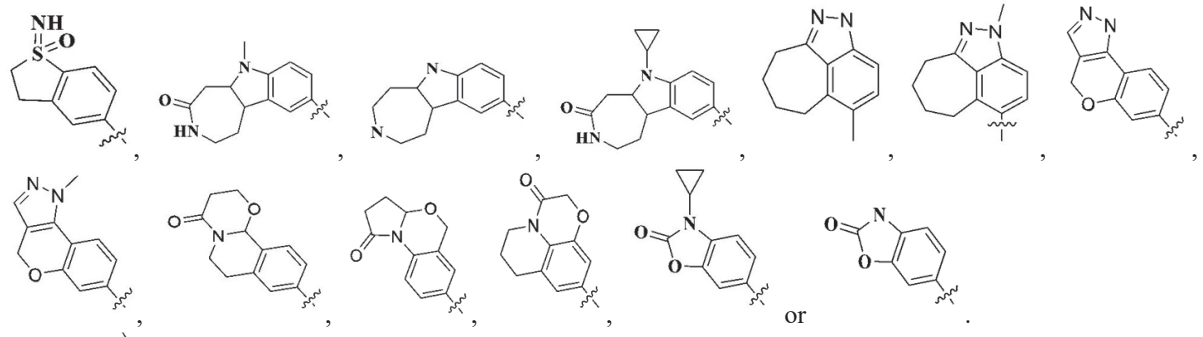
further preferably, ring F is selected from C_{3-6}bridged cycloalkyl, 8- to 14-membered tricyclic fused heterocyclyl containing 1-5 heteroatoms, 3- to 8-membered bridged heterocyclyl containing 1-3 heteroatoms, fused heterocyclyl containing 1-3 heteroatoms, bridged heterocyclyl containing 1-3 heteroatoms, C_{6-10}aryl or 5- to 10-membered fused heteroaryl containing 1-3 heteroatoms; and

more preferably, ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl,



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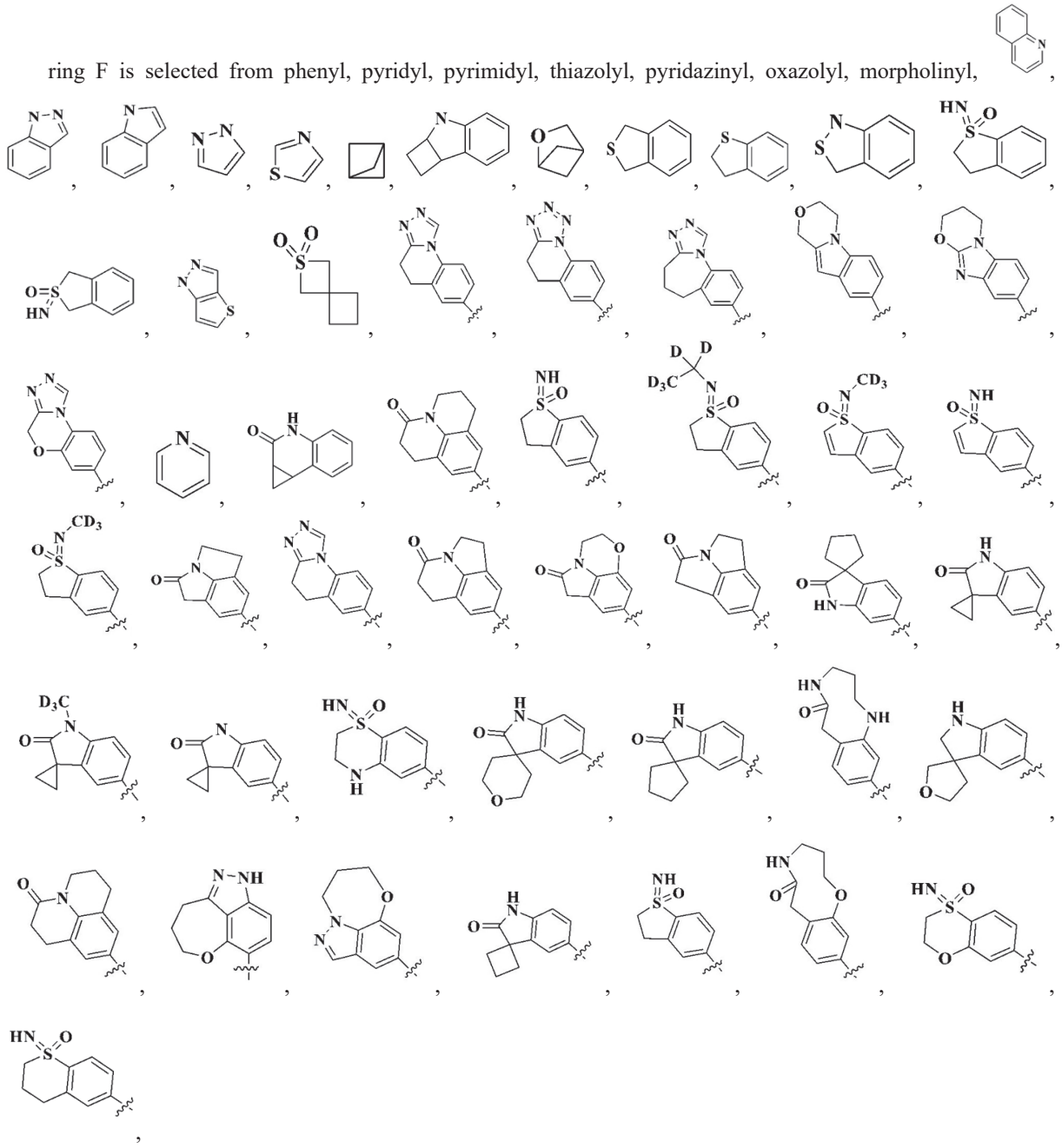


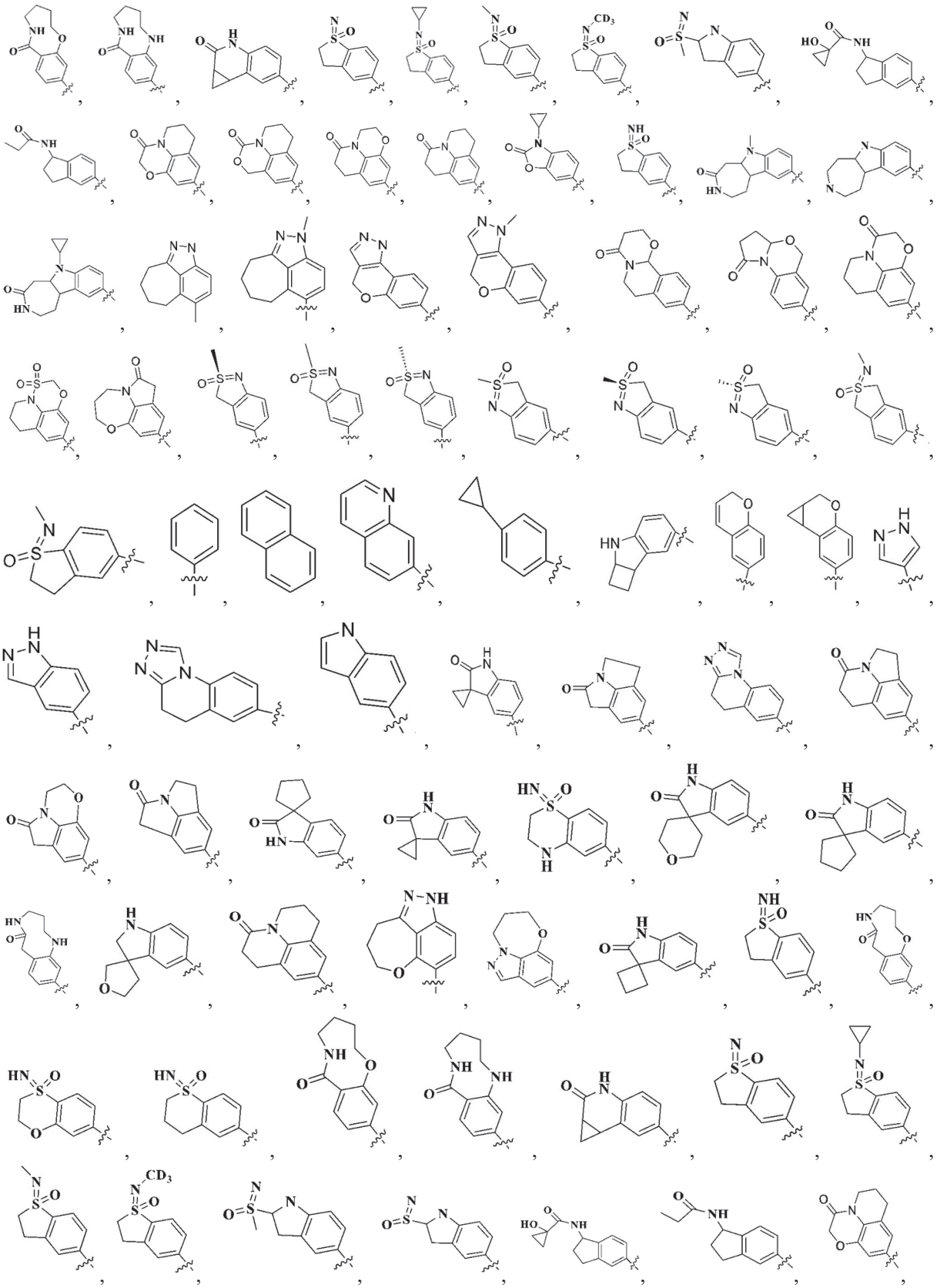


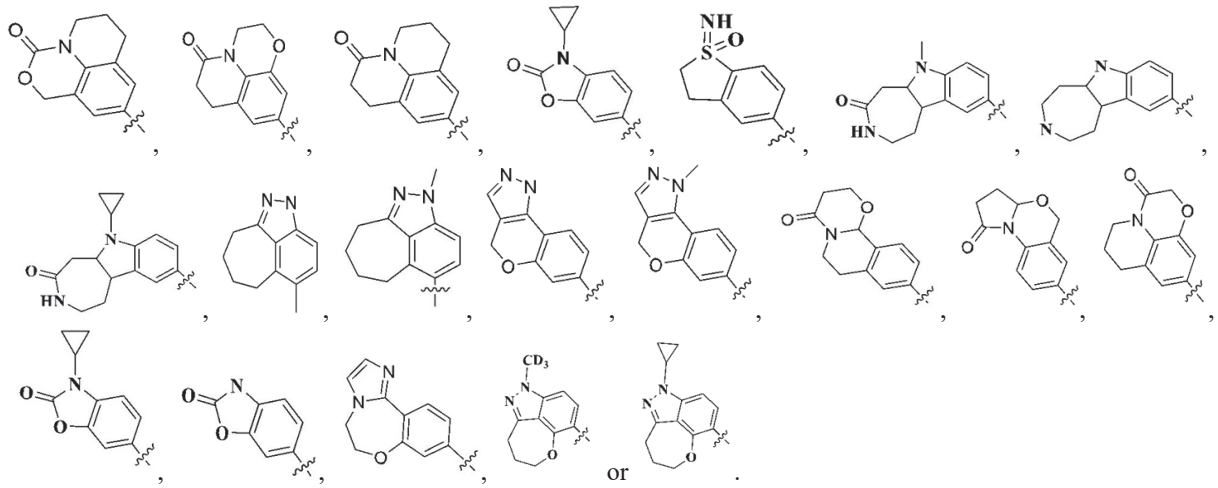
Note: “ ” represents connection with L_1.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl,





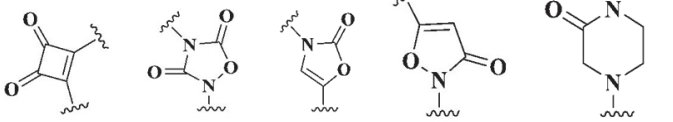


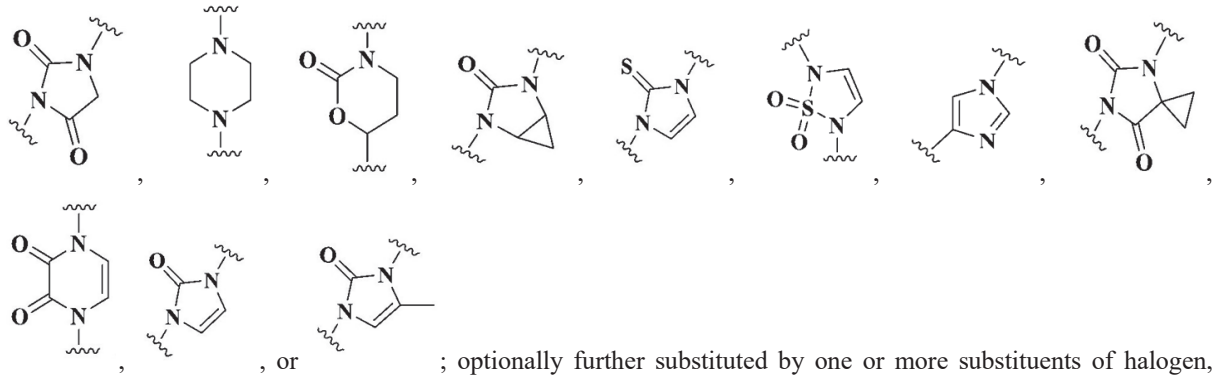
Note: “ ” represents connection with L_1.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

ring B is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy or C_{1-3}deuterated haloalkoxy;

preferably, ring B is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

further preferably, ring B is selected from 

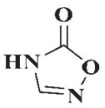
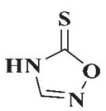
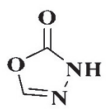
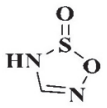


; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy or C_{1-3}deuterated haloalkoxy;

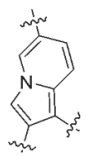
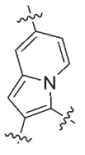
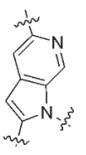
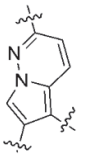
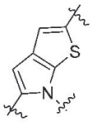
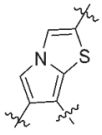
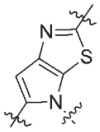
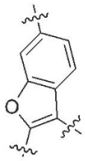
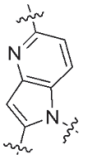
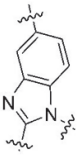
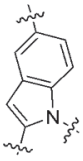
preferably, ring C is selected from C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 selected from N, O or S or 5- to 6-membered heteroaryl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of hydroxyl, thio, oxo or C_{1-6}haloalkoxy; and

further preferably, ring C is selected from , , , or ; optionally further substituted by one or more substituents of hydroxyl, thio or oxo.

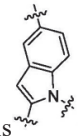
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

ring E is selected from C_{3-10}cycloalkyl, 3- to 12-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-12}aryl or 5- to 12-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

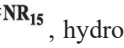
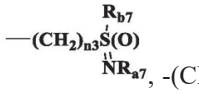
preferably, ring E is selected from C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl; and

further preferably, ring E is selected from , , , , , , , , , , or , optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

ring E is , optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^1 each is independently selected from , hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n1}S(O)_2R_{b5}$, wherein the amino,

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C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n1}S(O)_2R_{b5}$ is optionally further substituted by one or more substituents of $=NR_{15}$, halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^1 each is independently selected from $=NR_{15}$, hydrogen, deuterium, amino, oxo, fluoro, chloro, bromo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}bridged cycloalkyl, C_{3-8}spirocycloalkyl, 3- to 8-membered spiro heterocyclyl containing 1-3 heteroatoms, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}bridged cycloalkyl, C_{3-8}spirocycloalkyl, 3- to 8-membered spiro heterocyclyl containing 1-3 heteroatoms, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$ is optionally further substituted by one or more substituents of $=NR_{15}$, halogen, cyano or C_{1-3}alkyl.

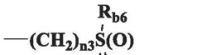
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

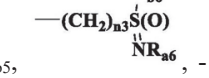
more further preferably, R^1 each is independently selected from $=NR_{15}$、hydrogen, deuterium, amino, oxo, cyano, fluoro, chloro, bromo, methyl, ethyl, cyclopropyl, $-CD_3$, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, methyl, ethyl, cyclopropyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$ is optionally further substituted by one or more substituents of $=NR_{15}$, halogen, cyano or C_{1-3}alkyl.

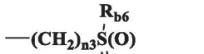
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^1 each is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 selected from N, O or S,

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C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S, optionally further substituted by one or more substituents of $\{=NR_{15}$, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

preferably, R^1 each is linked with the atoms to which it is connected to form C_{3-4}cycloalkyl or 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by one or more substituents of $\{=NR_{15}$、deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino, oxo, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$; and

further preferably, R^1 each is linked with the atoms to which it is connected to form cyclopropyl, optionally further substituted by one or more substituents of $\{=NR_{15}$, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino, oxo, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{3-6}bridged cycloalkyl, C_{3-6}spirocycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 6-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{3-6}bridged cycloalkyl, C_{3-6}spirocycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 6-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S is optionally further substituted by one or more substituents of halogen or C_{1-3}alkyl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, methyl, ethyl, cyano, deuterated methyl, cyclopropyl, cyclopentyl, phenyl, , , ,  or , wherein the methyl, ethyl, deuterated methyl, cyclopropyl,

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cyclopentyl, phenyl, , , ,  or  is optionally further substituted by one or more fluoro.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, cyano, cyclopropyl or methyl, wherein the cyclopropyl or methyl is optionally further substituted by one or more substituents of deuterium, deuterated methyl, methyl, cyclopropyl or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or -$(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15} each is independently selected from hydrogen, deuterium, halogen, cyano, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or -$(CH_2)_{m1}OR_{c1}$, wherein the C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or -$(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, deuterated methyl, methyl, cyclopropyl or oxo; and

further preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15} each is independently selected from cyano, methyl, fluoro,

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cyclopropyl, ethynyl or -$(CH_2)_{m1}OR_{c1}$, wherein the methyl, cyclopropyl, ethynyl or -$(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, deuterated methyl, methyl, cyclopropyl or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}or R^{15} each is independently selected from cyano, methyl, fluoro, cyclopropyl, ethynyl or -$(CH_2)_{m1}OR_{c1}$, wherein the methyl, cyclopropyl, ethynyl or -$(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, hydroxyl, deuterated methyl, methyl, cyclopropyl or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{c1} is selected from fluoro, methyl, cyano, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl or oxetane, wherein the methyl, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl or oxetane is optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms;

preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}or R^{15}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; and

further preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} or R^{15}, respectively, is linked with the atoms to which it is connected to form cyclopropyl or .

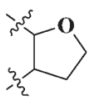
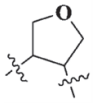
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^{10} and R^{12} are lined with the atoms to which they are connected to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms;

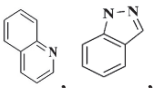
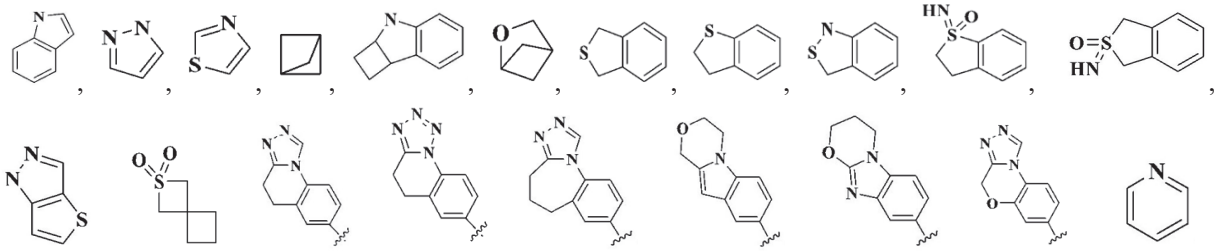
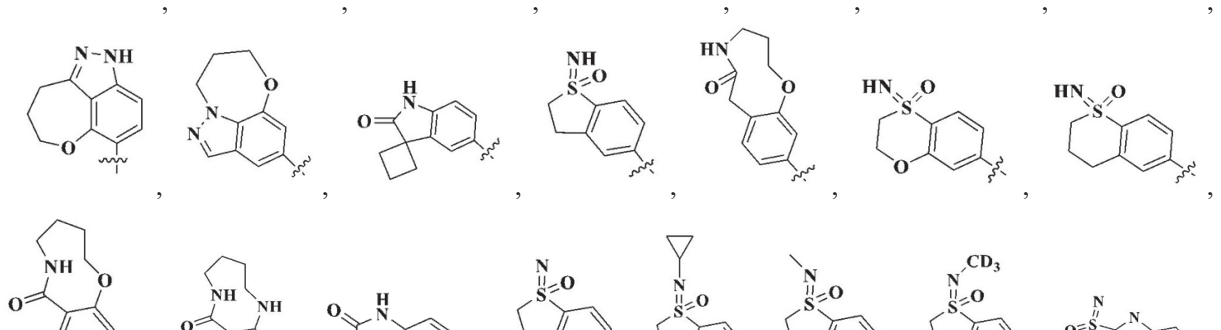
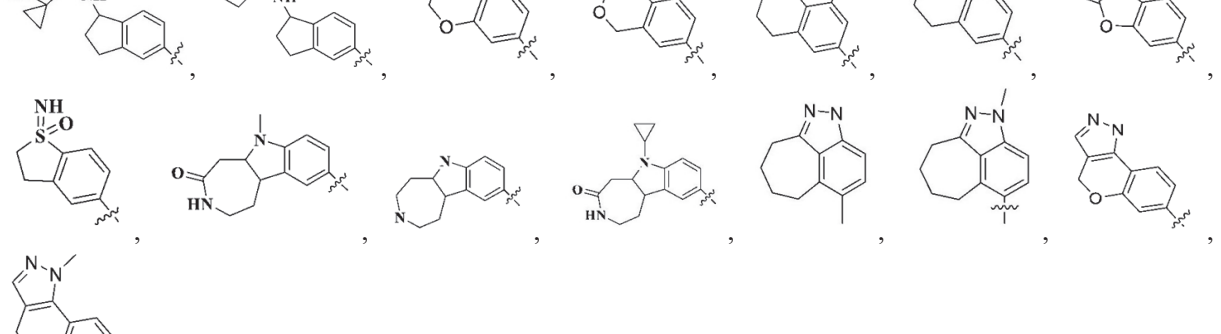
preferably, R^{10} and R^{12} are lined with the atoms to which they are connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; and

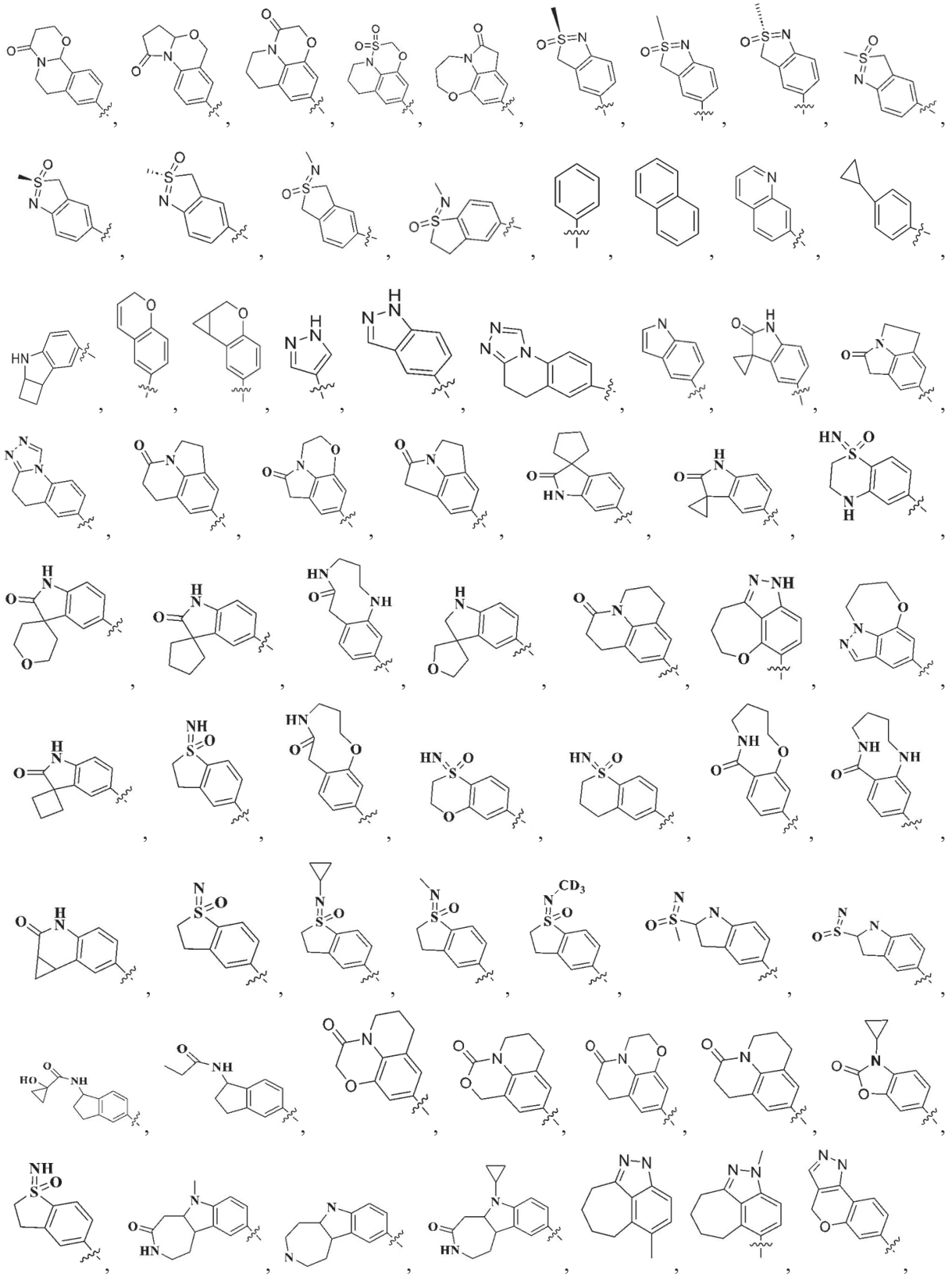
further preferably, R^{10} and R^{12} are lined with the atoms to which they are connected to form .

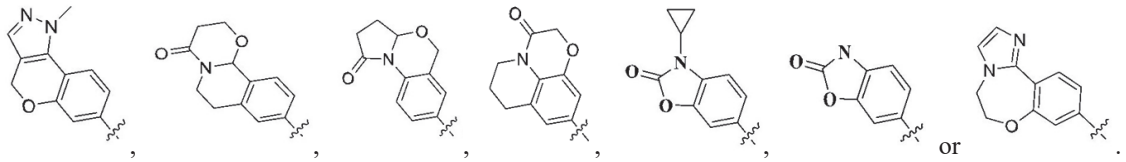
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

R^{10} is linked with the atoms to which it is connected and adjacent atoms to form  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

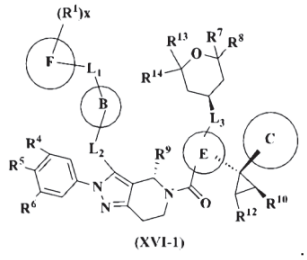
ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl, , , , , , , , , , , .





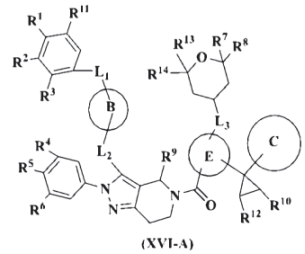
Note: "" represents connection with L_1.

In a further preferred embodiment of the present disclosure, the compound of general formula (XVI) is further shown as general formula (XVI-1):



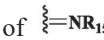
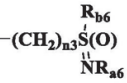
(XVI-1)

In a further preferred embodiment of the present disclosure, the compound of general formula (XVI) is further shown as general formula (XVI-A):

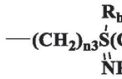


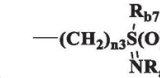
(XVI-A)

wherein

R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, optionally further substituted by one or more substituents of , hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

or

R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl,

C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$ is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

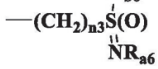
R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

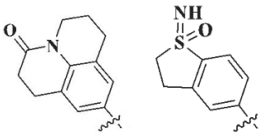
ring B, ring C, ring E, L_1, L_2, L_3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}, R^{15}, n1, n2, n3, n4, n5, m1, and x are defined as in general formula (XVI).

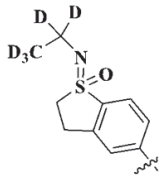
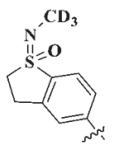
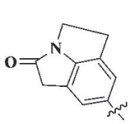
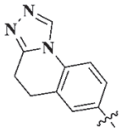
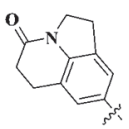
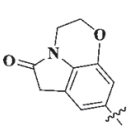
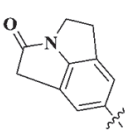
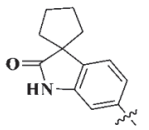
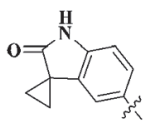
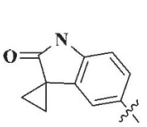
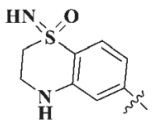
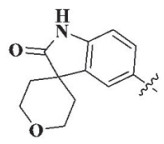
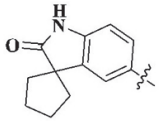
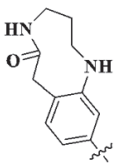
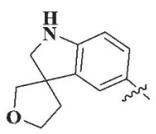
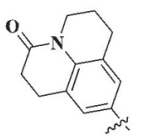
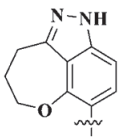
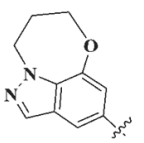
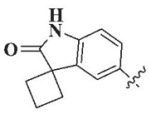
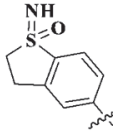
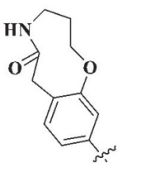
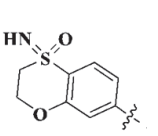
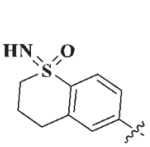
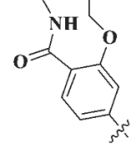
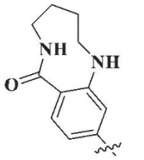
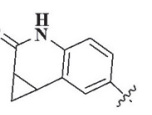
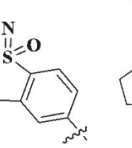
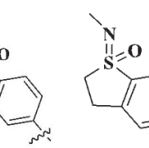
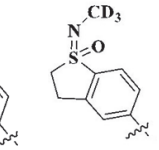
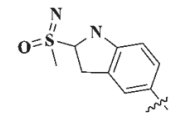
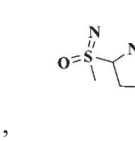
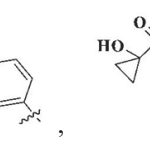
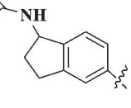
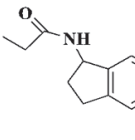
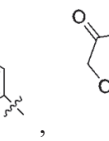
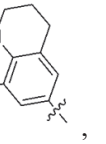
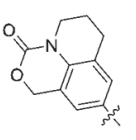
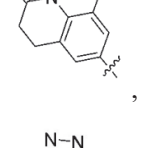
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

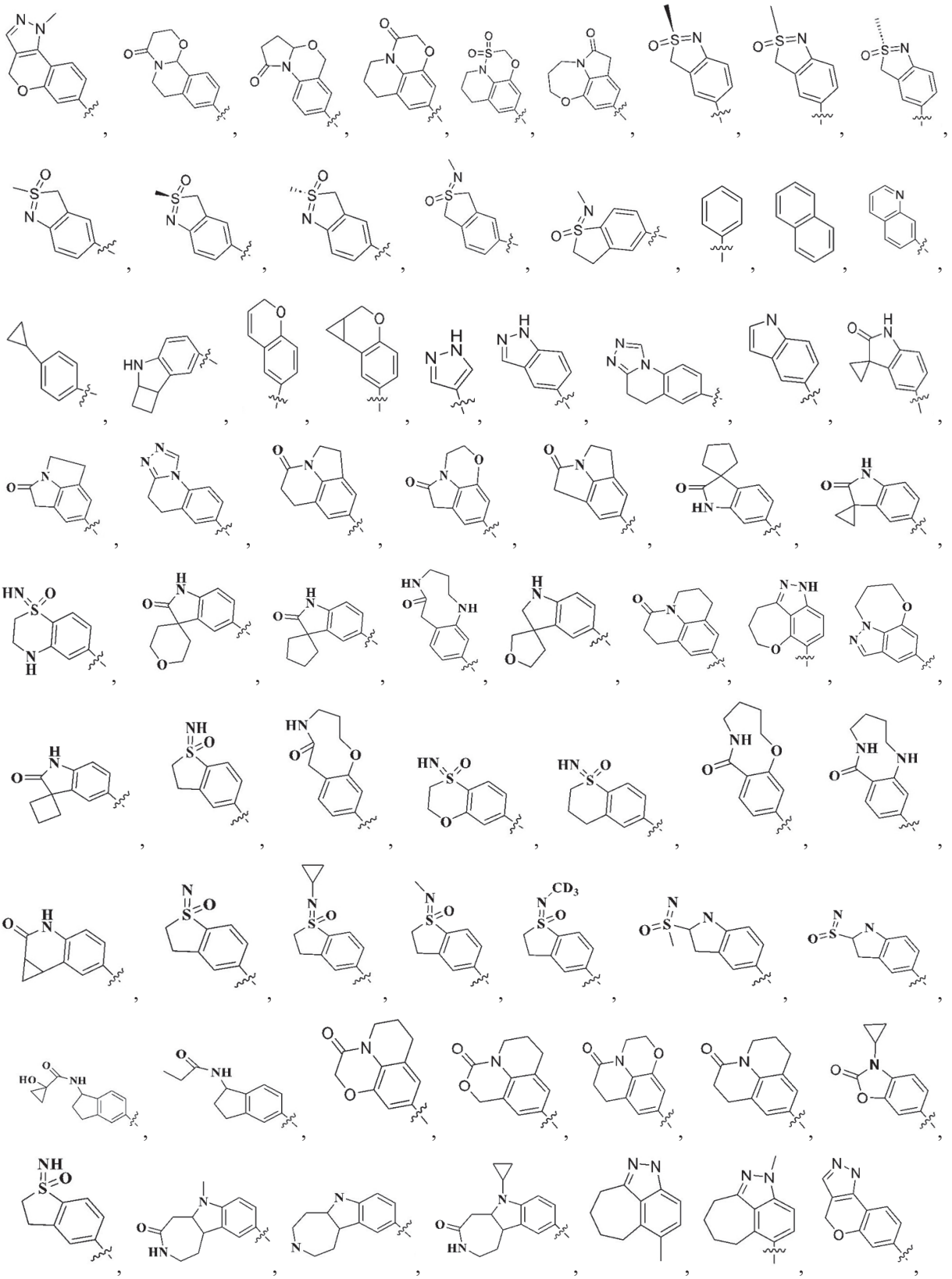
R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S, optionally further substituted by one or more substituents of , deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

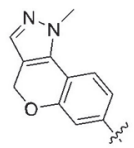
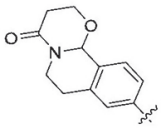
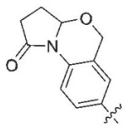
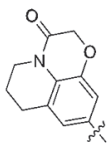
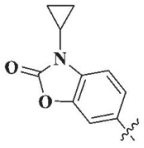
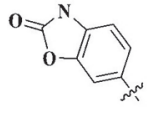
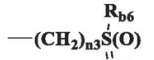
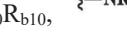
preferably, R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by one or more substituents of $=NR_{15}$, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino, oxo, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n3}S(O)(R_{b6})=NR_{a6}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$; and

further preferably, R^1 and R^2, and R^1 and R^{11} are linked with adjacent phenyl to form



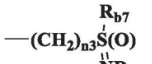
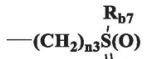







































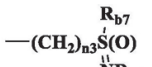


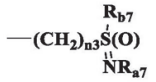
, , , ,  or ; optionally further substituted by one or more substituents of -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, -$(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, -$(CH_2)_{n1}$S(O)$_2R_{b5}$, -$(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, , deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino or oxo.

Note: "" represents connection with L_1.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

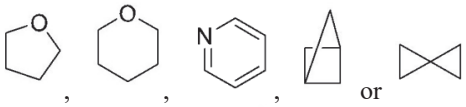
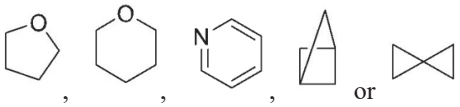
R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}$P(O)$R_{a3}R_{b3}$, , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, -$(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, -$(CH_2)_{n1}$S(O)$_2R_{b5}$ or -$(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}$P(O)$R_{a3}R_{b3}$, , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, -$(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, -$(CH_2)_{n1}$S(O)$_2R_{b5}$ or -$(CH_2)_{n5}C(O)NR_{a10}R_{b10}$ is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -NS(O)$R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, amino, oxo, fluoro, chloro, bromo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}bridged cycloalkyl, C_{3-8}spirocycloalkyl, 3- to 8-membered spiro heterocyclyl containing 1-3 heteroatoms, 5- to 8-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}$P(O)$R_{a3}R_{b3}$, , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, -$(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, -$(CH_2)_{n1}$S(O)$_2R_{b5}$ or -$(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}bridged cycloalkyl, C_{3-8}spirocycloalkyl, 3- to 8-membered spiro heterocyclyl containing 1-3 heteroatoms, 5- to 8-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$,


$-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$ is optionally further substituted by one or more substituents of halogen, cyano or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{3-6}bridged cycloalkyl, C_{3-6}spirocycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 6-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{3-6}bridged cycloalkyl, C_{3-6}spirocycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 6-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S is optionally further substituted by one or more substituents of halogen or C_{1-3}alkyl; and

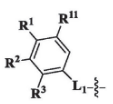
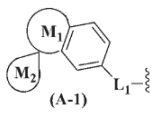
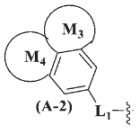
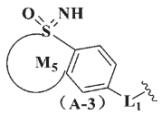
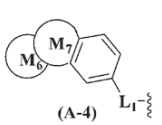
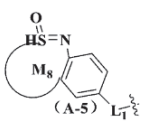
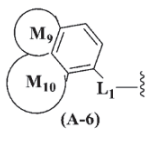
preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, methyl, ethyl, cyano, deuterated methyl, cyclopropyl, cyclopentyl, phenyl,  or , wherein the methyl, ethyl, deuterated methyl, cyclopropyl, cyclopentyl, phenyl,  or is optionally further substituted by one or more fluoro.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

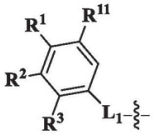
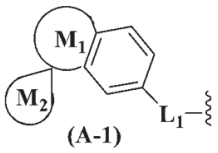
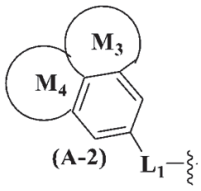
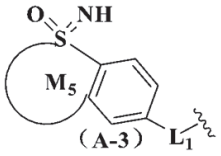
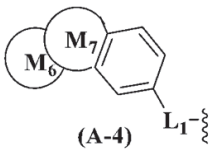
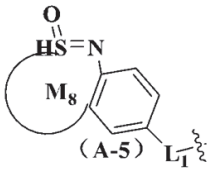
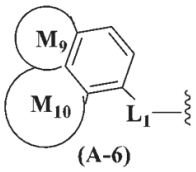
in general formula (XVI-A),  is further shown as , , , ,  or , optionally further substituted by one or more substituents of halogen,

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methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl; and

ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7, ring M_8, M_9 or M_{10} each is independently selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

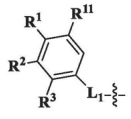
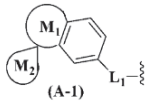
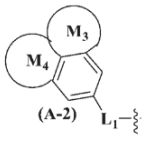
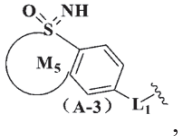
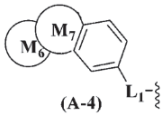
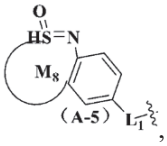
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

in general formula (XVI-A),  is further shown as , , , ,  or , optionally further substituted by one or more substituents of halogen, methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl;

ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7, ring M_8, M_9 or M_{10} each is independently selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7, ring M_8, M_9 or M_{10} each is independently selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of halogen, methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl.

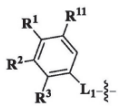
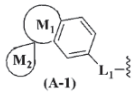
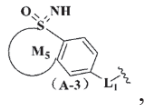
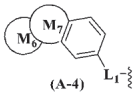
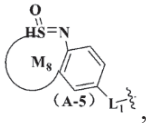
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

in general formula (XVI-A),  is further shown as , , , , , optionally further substituted by one or more substituents of halogen, methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl; and

ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7 or ring M_8 each is independently selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl,

cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

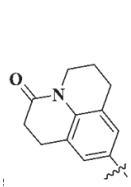
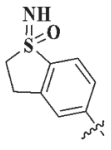
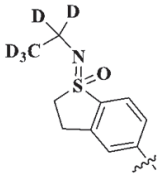
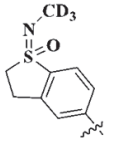
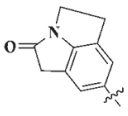
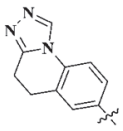
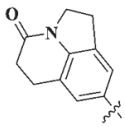
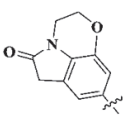
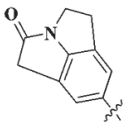
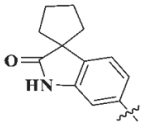
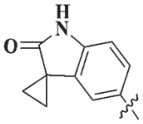
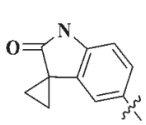
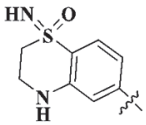
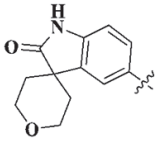
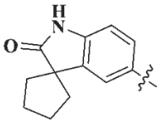
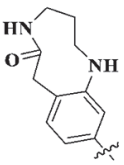
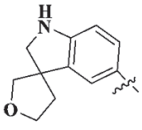
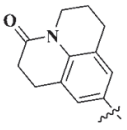
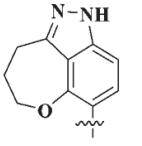
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

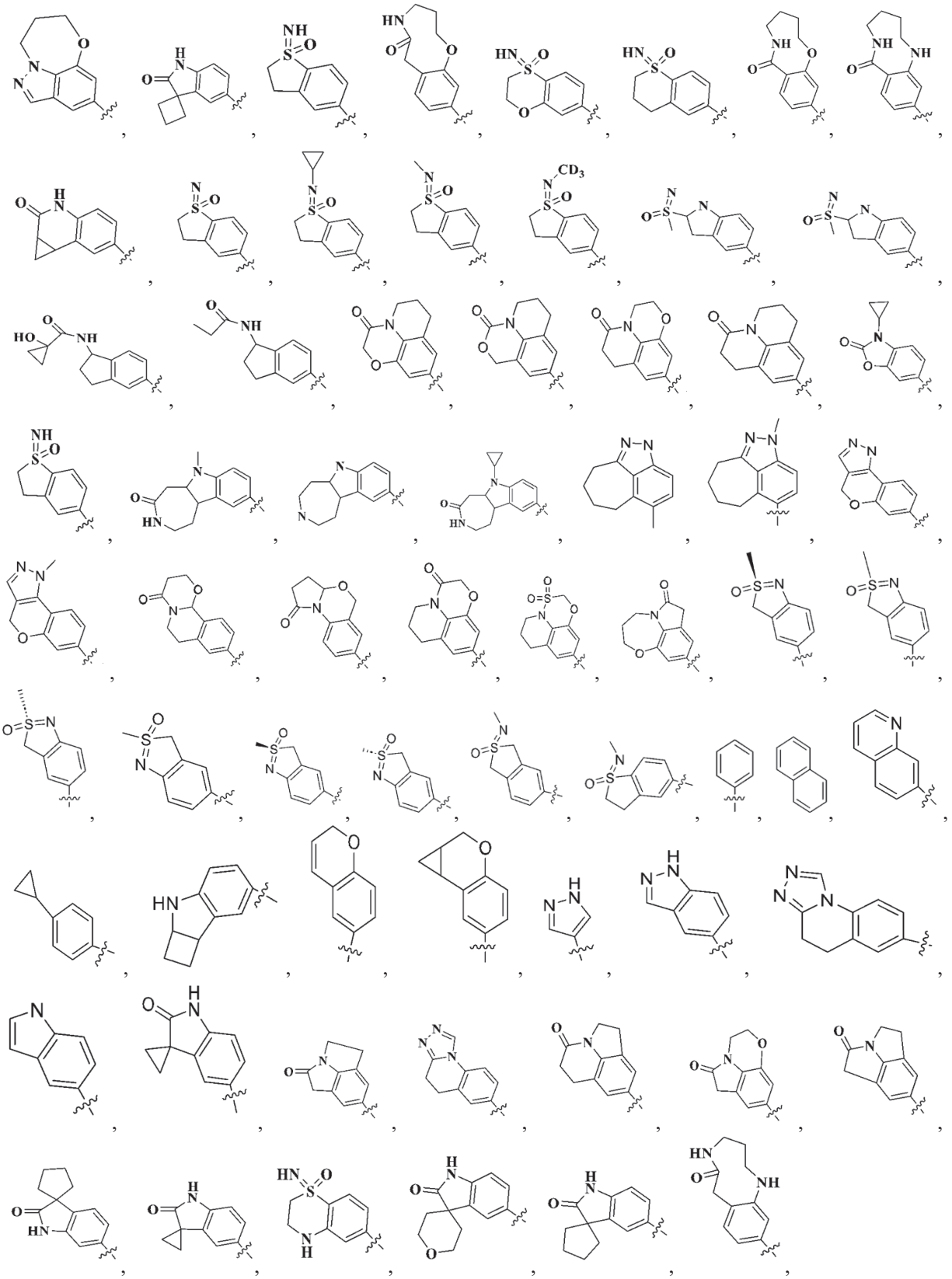
in general formula (XVI-A),  is further shown as , , ,  or , optionally further substituted by one or more substituents of halogen, methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl;

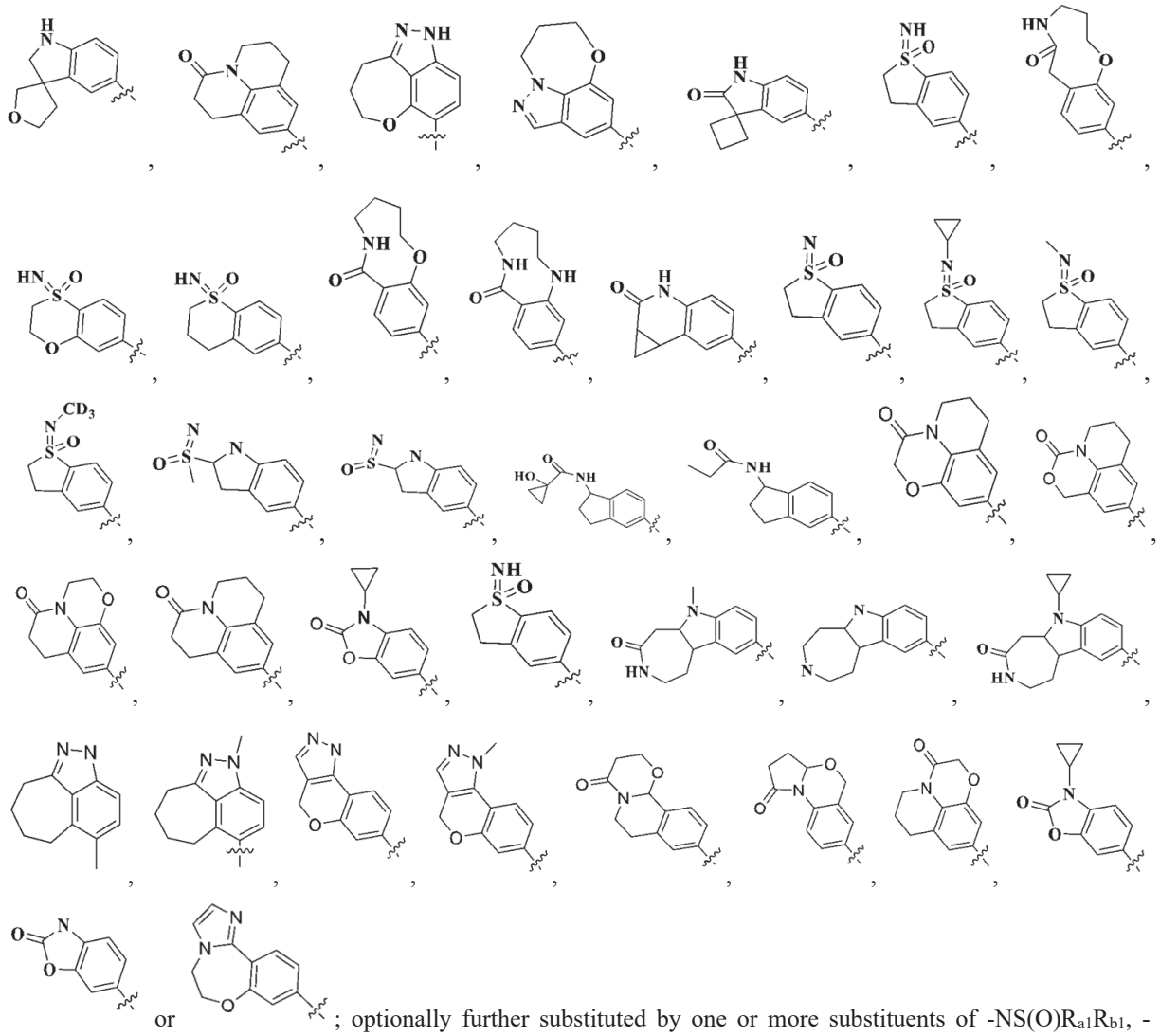
ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7 or ring M_8 each is independently selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

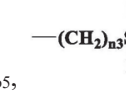
preferably, ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7 or ring M_8 each is independently selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of halogen, methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

R^1 and R^2, and R^1 and $R^{11}$are lined with adjacent phenyl to form , , , , , , , , , , , , , , , , , , , .

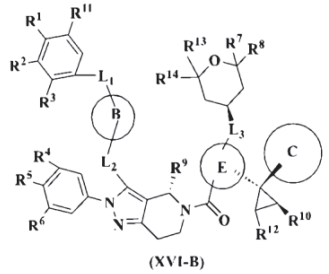




or ; optionally further substituted by one or more substituents of -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}$O$(CH_2)_{n2}R_{b5}$, , -$(CH_2)_{n1}NR_{a8}$C(O)R_{b8}, -$(CR_{a8}R_{b8})_{n4}$C(O)$NR_{a9}R_{b9}$, -$(CH_2)_{n1}$S(O)$_2R_{b5}$, -$(CH_2)_{n5}$C(O)$NR_{a10}R_{b10}$, , deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino or oxo.

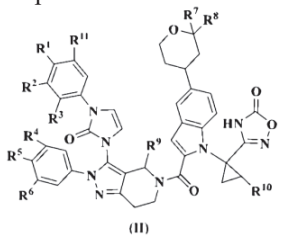
Note: "" represents connection with L_1.

In a further preferred embodiment of the present disclosure, the compound of general formula (XVI-A) is further shown as general formula (XVI-B):



(XVI-B)

An object of the present disclosure is to provide a compound of general formula (II), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(II)

wherein

R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, wherein the C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^1, R^2, R^3 or R^{11} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl,

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C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

n1 is an integer of 0-5; and

m1 is an integer of 0-5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

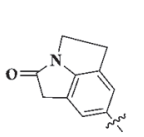
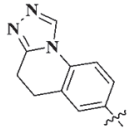
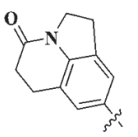
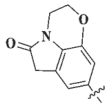
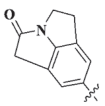
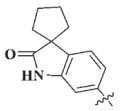
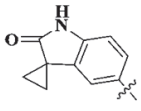
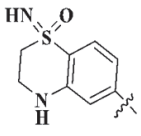
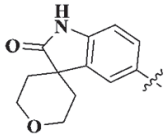
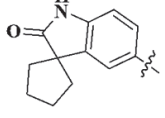
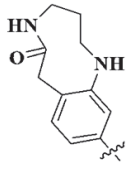
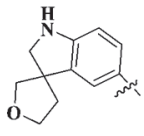
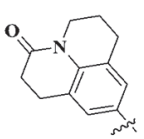
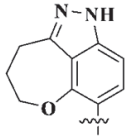
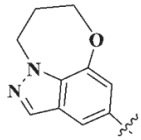
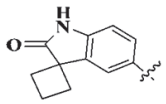
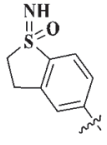
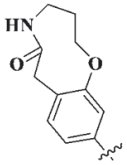
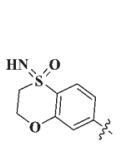
R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

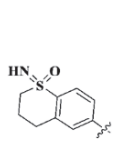
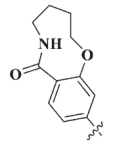
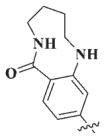
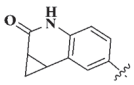
R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, amino or oxo; and

preferably, R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^1 and R^2, and R^1 and $R^{11}$are lined with adjacent phenyl to form , , , , , , , , , , , , , , , , , , .

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, ,  or , optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, and oxo;

preferably, R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

further preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$ or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^1, R^2, R^3 or R^{11}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

preferably, R^1, R^2, R^3or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl,

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C_{1-3}haloalkyl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$ or -NR_{a5}S(O)$NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, -NS(O)$R_{a1}R_{b1}$ or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R_{a2} and R_{b2}, and R_{a3} and R_{b3}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5or R^6 each is independently selected from fluoro or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

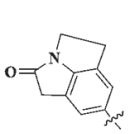
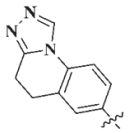
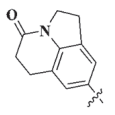
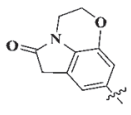
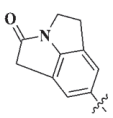
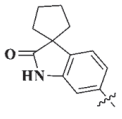
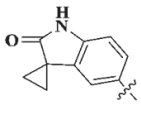
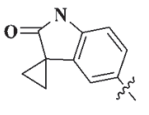
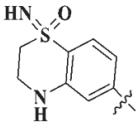
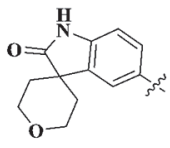
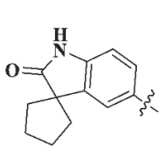
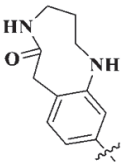
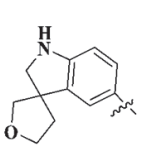
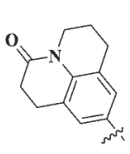
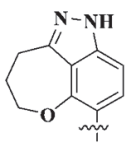
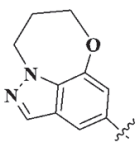
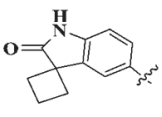
R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

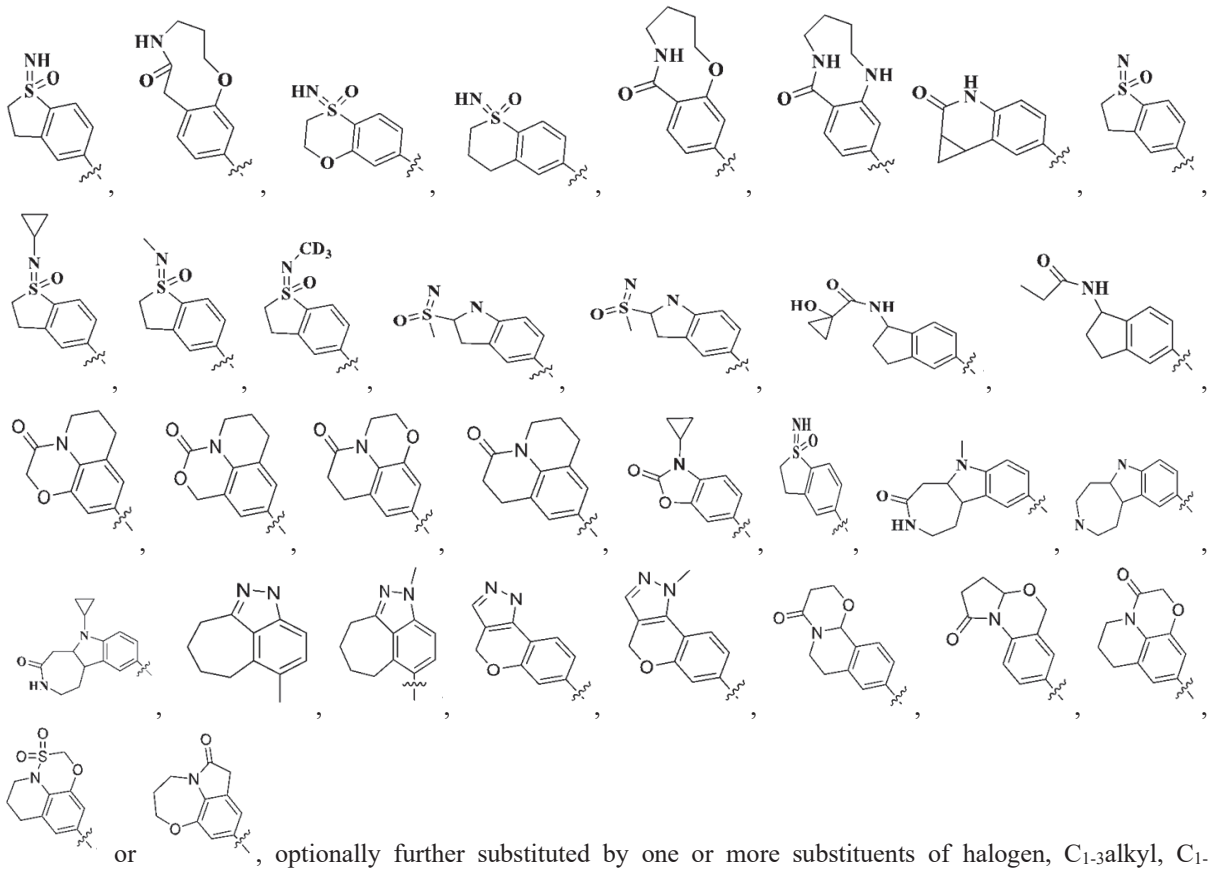
preferably, R^7, R^8, R^9or R^{10} each is independently selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{3-6}cycloalkyl, amino or oxo;

preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by C_{3-6}cycloalkyl, or oxo; and

further preferably, R^1 and R^2, and R^1 and $R^{11}$are linked with adjacent phenyl to form , , , , , , , , , , , , , , , , ,



or , optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, cyano, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, cyano, cyclopropyl or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^7, R^8, R^9 or R^{10} each is independently selected from methyl or cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

preferably, R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

further preferably, R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

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In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^{10} is linked with the atoms to which it is connected and adjacent atoms to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

preferably, R^{10} is linked with the atoms to which it is connected and adjacent atoms to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

further preferably, R^{10} is linked with the atoms to which it is connected and adjacent atoms to form .

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^{10} is linked with the atoms to which it is connected and adjacent atoms to form  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{c1} is selected from fluoro, methyl, cyano, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl or oxetane; optionally further substituted by halogen, methoxy or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

R^7, R^8, R^9or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

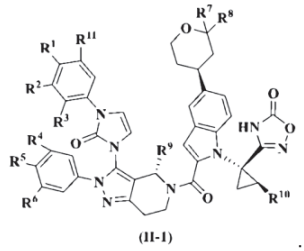
preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

further preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, cyano, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or $-(CH_2)_{m1}OR_{c1}$; and

more preferably, R^7, R^8, R^9 or R^{10} each is independently selected from methyl, fluoro, cyclopropyl, ethynyl or $-(CH_2)_{m1}OR_{c1}$.

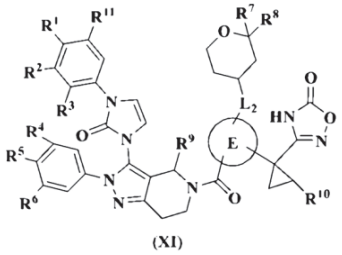
In a further preferred embodiment of the present disclosure, the compound of general formula (II) is further shown as general formula (II-1):

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(II-1)

An object of the present disclosure is to provide a compound of general formula (XI), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XI)

wherein

ring E is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl;

L_2 is selected from a bond, $-(CH_2)_{n4}-$, C_{2-4}alkenylene, or C_{2-4}alkynylene;

R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n3}\overset{R_{b6}}{\underset{\|}{S}}(O)\overset{}{\underset{NR_{a6}}{}}$, $-(CH_2)_nP(O)R_{a7}R_{b7}$ or $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9 or R^{10}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

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or R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a7} and R_{b7}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9 or R^{10}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

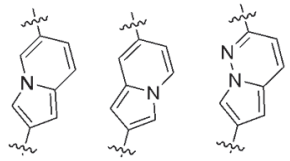
R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a7} and R_{b7}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

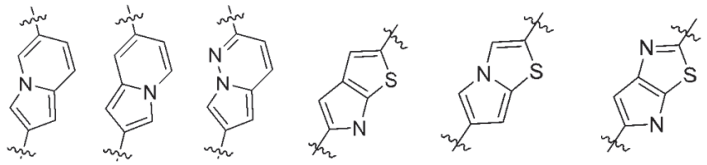
n1-n4 are an integer of 0-5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

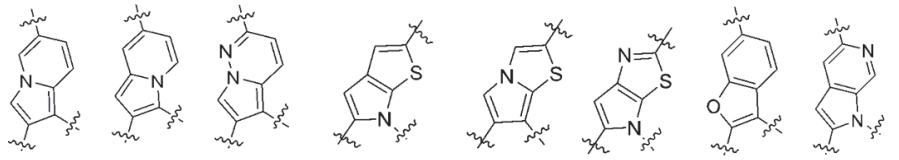
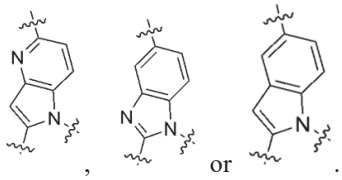
ring E is selected from C_{3-8}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms; and

preferably, ring E is selected from  or .

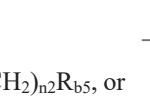
In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

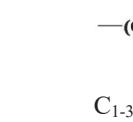
ring E is selected from  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

ring E is selected from , , , or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^1, R^2, R^3or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, or , wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl. In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

preferably, R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_nP(O)R_{a7}R_{b7}$ or $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl,

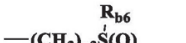
cyano, oxo, -NS(O)$R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, , -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}$O$(CH_2)_{n2}R_{b5}$, or , wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -NS(O)$R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}$O$(CH_2)_{n2}R_{b5}$, or . In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

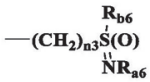
preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}$O$(CH_2)_{n2}R_{b5}$ or ; and

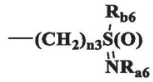
further preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form phenyl, or 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by oxo, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}$O$(CH_2)_{n2}R_{b5}$, or .

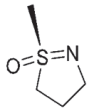
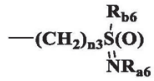
In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$,

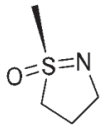
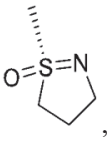
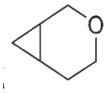
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, -(CH$_2$)$_n$P(O)R$_{a7}$R$_{b7}$ or -(CR$_{a8}$R$_{b8}$)$_{n4}$C(O)NR$_{a9}$R$_{b9}$;

preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form phenyl or 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by one or more substituents of methyl, halogen, oxo, -NS(O)R$_{a1}$R$_{b1}$, -(CH$_2$)$_{n1}$S(O)NR$_{a2}$R$_{b2}$, -P(O)R$_{a3}$R$_{b3}$, -NR$_{a5}$S(O)NR$_{a4}$R$_{b4}$, -(CH$_2$)$_{n1}$S(O)$_2$R$_{a5}$, -(CH$_2$)$_{n1}$O(CH$_2$)$_{n2}$R$_{b5}$, , -(CH$_2$)$_n$P(O)R$_{a7}$R$_{b7}$ or -(CR$_{a8}$R$_{b8}$)$_{n4}$C(O)NR$_{a9}$R$_{b9}$; and

further preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form , , , , , , , , , ,  or , optionally further substituted by one or more substituents of methyl, halogen, oxo, -NS(O)R$_{a1}$R$_{b1}$, -(CH$_2$)$_{n1}$S(O)NR$_{a2}$R$_{b2}$, -P(O)R$_{a3}$R$_{b3}$, -NR$_{a5}$S(O)NR$_{a4}$R$_{b4}$, -(CH$_2$)$_{n1}$S(O)$_2$R$_{a5}$, -(CH$_2$)$_{n1}$O(CH$_2$)$_{n2}$R$_{b5}$, , -(CH$_2$)$_n$P(O)R$_{a7}$R$_{b7}$ or -(CR$_{a8}$R$_{b8}$)$_{n4}$C(O)NR$_{a9}$R$_{b9}$.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form , , , , , ,  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, C$_{1-3}$alkyl, C$_{1-3}$deuterated alkyl, C$_{3-6}$cycloalkyl, C$_{1-3}$haloalkyl; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, methyl, or cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C$_{1-3}$alkyl, C$_{1-3}$deuterated alkyl, or C$_{1-3}$haloalkyl; and

preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R$_{a1}$, R$_{b1}$, R$_{a2}$, R$_{b2}$, R$_{a3}$, R$_{b3}$, R$_{a4}$, R$_{b4}$, R$_{a5}$, R$_{b5}$, R$_{a6}$ or R$_{b6}$ each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C$_{1-6}$alkyl, C$_{1-6}$deuterated alkyl, C$_{1-6}$haloalkyl, C$_{1-6}$hydroxyalkyl, C$_{1-6}$alkoxy, C$_{1-6}$haloalkoxy, C$_{2-6}$alkenyl, C$_{2-6}$alkynyl, C$_{3-8}$cycloalkyl, 3- to 8-membered heterocyclyl, C$_{6-10}$aryl, or 5- to 10-membered heteroaryl; or R$_{a1}$ and R$_{b1}$, or R$_{a2}$ and R$_{b2}$, or R$_{a3}$ and R$_{b3}$, or R$_{a4}$ and R$_{b4}$, respectively, are linked with adjacent atoms to form C$_{3-8}$cycloalkyl,

3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, amino, cyano, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

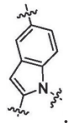
preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, cyano, cyclopropyl, cyclopentyl, methyl, ethyl, phenyl or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6} or R_{b6} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, or C_{1-3}haloalkyl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6} or R_{b6} each is independently selected from hydrogen, deuterium, halogen, or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

ring E is .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, cyano, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, methyl, cyano or cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

preferably, R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

further preferably, R^7, R^8, R^9 or R^{10}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, cyano, cyclopropyl, cyclopentyl, methyl, ethyl, deuterated methyl, phenyl or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

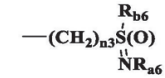
R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a7} and R_{b7}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy,

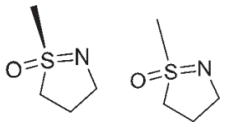
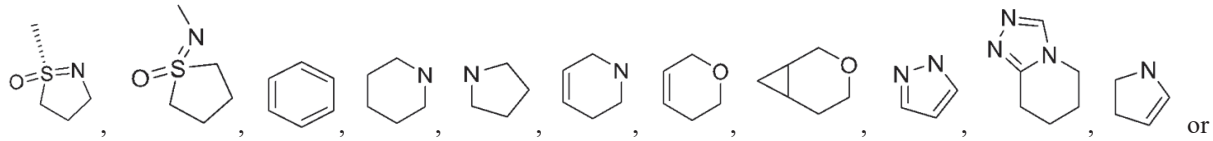
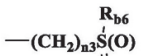
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C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

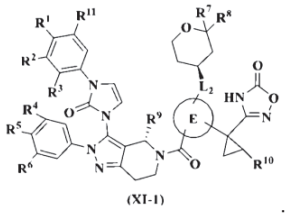
preferably, R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a7} and R_{b7}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, respectively, are linked with adjacent atoms to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form phenyl or 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by one or more substituents of methyl, halogen, oxo, cyclopropyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}P(O)R_{a7}R_{b7}$ or $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$; and

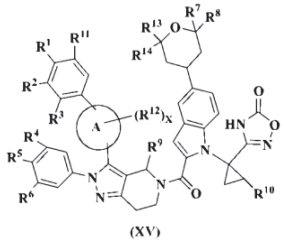
preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form , , or , optionally further substituted by one or more substituents of methyl, halogen, oxo, cyclopropyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, , $-(CH_2)_{n1}P(O)R_{a7}R_{b7}$ or $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$.

In a further preferred embodiment of the present disclosure, the compound of general formula (XI) is further shown as general formula (XI-1):



(XI-1)

An object of the present disclosure is to provide a compound of general formula (XV), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:

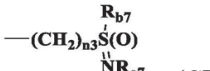


(XV)

wherein

R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl,

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C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or

R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, wherein the C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a6} and R_{b6}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, or R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

ring A is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy or C_{1-6}haloalkoxy;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

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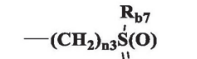
R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

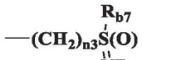
or R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

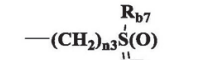
n1-n5 are an integer of 0-5; and

x is an integer of 0-5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or C_{2-4}alkynyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl or C_{3-6}cycloalkyl; and

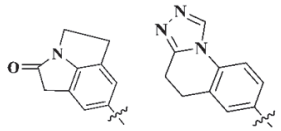
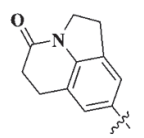
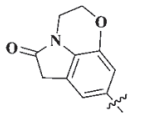
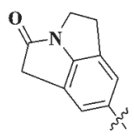
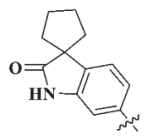
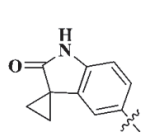
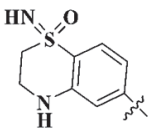
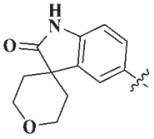
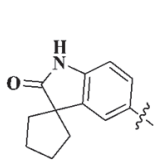
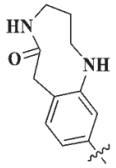
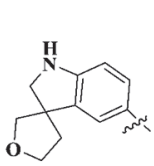
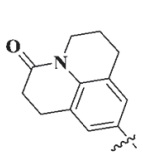
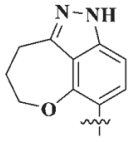
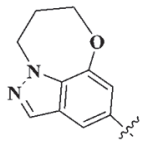
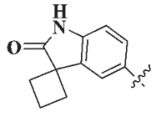
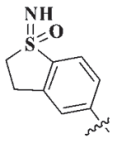
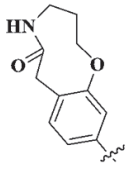
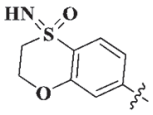
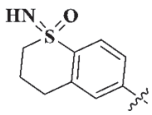
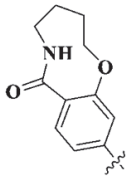
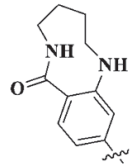
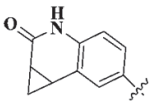
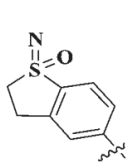
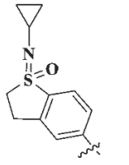
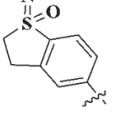
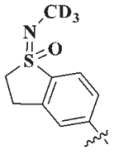
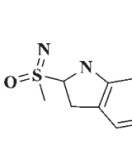
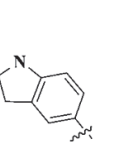
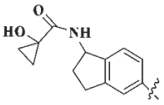
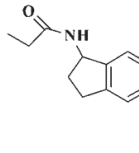
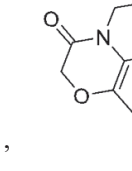
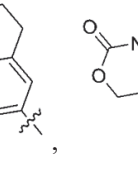
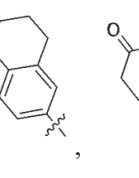
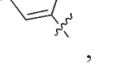
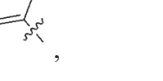
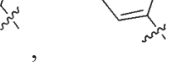
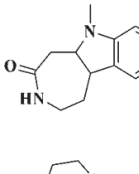
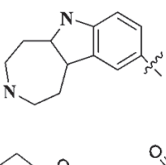
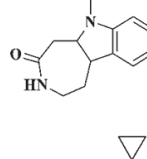
further preferably, R^1, R^2, R^3 or R^{11}each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}bridged cycloalkyl, C_{3-8}spirocycloalkyl, 3- to 8-membered spiro heterocyclyl containing 1-3 heteroatoms, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or C_{2-4}alkynyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl or C_{3-6}cycloalkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{3-6}cycloalkyl, amino or oxo;

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preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by C_{3-6}cycloalkyl, or oxo; and

further preferably, R^1 and R^2, or R^1 and $R^{11}$are lined with adjacent phenyl to form , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , or , optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl,

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C_{3-6}bridged cycloalkyl, C_{3-6}spirocycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 6-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{3-6}bridged cycloalkyl, C_{3-6}spirocycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 6-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S is optionally further substituted by one or more substituents of halogen or C_{1-3}alkyl;

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, methyl, deuterated methyl, cyclopropyl, , ,  or , optionally, further substituted by fluoro.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

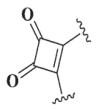
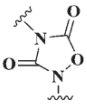
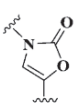
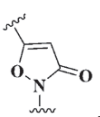
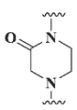
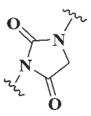
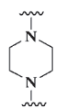
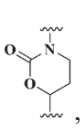
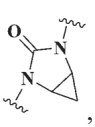
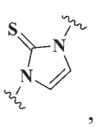
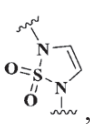
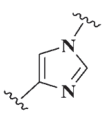
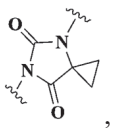
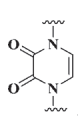
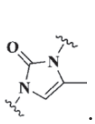
R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a6} and R_{b6}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, or R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a6} and R_{b6}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, or R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

ring A is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, oxo, mercapto, thio or C_{1-6}alkyl;

preferably, ring A is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

further preferably, ring A is selected from , , , , , , , , , , , , ,  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, cyano, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, cyano, cyclopropyl or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14} each is independently selected from hydrogen, deuterium, halogen, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

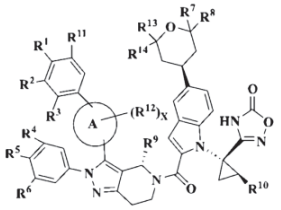
preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14} each is independently selected from methyl or cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14}respectively, is linked with the atoms to which they are connected to form cyclopropyl.

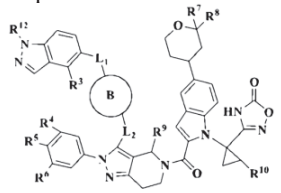
In a further preferred embodiment of the present disclosure, the compound of general formula (XV) is further shown as general formula (XV-1):



(XV-1)

.

An object of the present disclosure is to provide a compound of general formula (IV), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(IV)

wherein

L_1 and L_2 each are independently selected from a bond, C2-4alkenylene, C2-4alkynylene, -$(CH_2)_{n2}$-, or -$(CH_2)_{n3}NR_{b5}$;

ring B is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy or C_{1-6}haloalkoxy;

R_{b5} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl;

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$NS(O)R_{a1}R_{b1}$, -$(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, -$P(O)R_{a3}R_{b3}$ or -$NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -$NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl,

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C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

n1 is an integer of 0-5;

n2 is an integer of 0-5; and

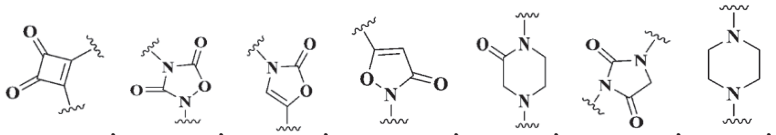
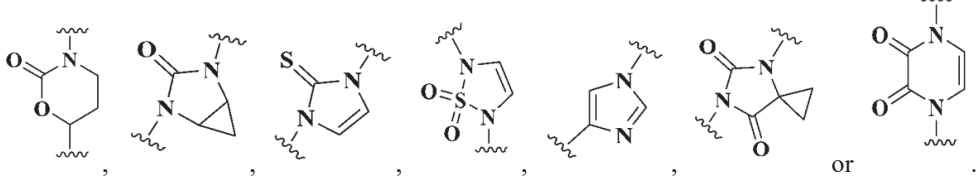
n3 is an integer of 0-5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

L_1 and L_2 each are independently selected from a bond, or $-(CH_2)_{n3}NR_{b5}$.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

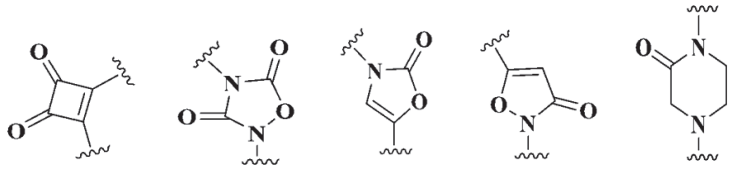
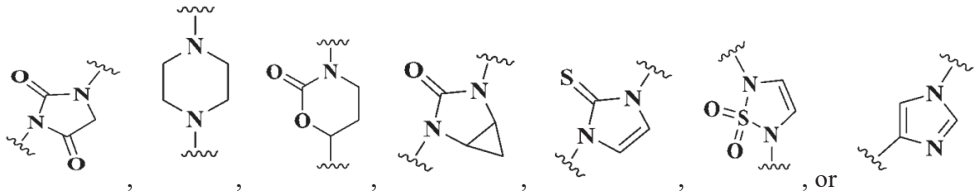
ring B is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

preferably, ring B is selected from , , or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

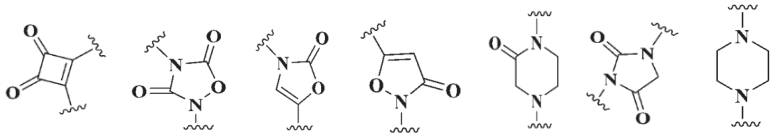
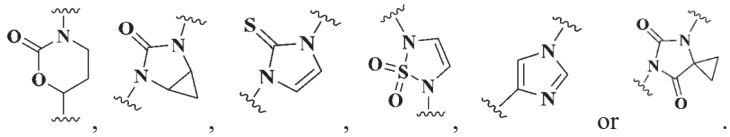
ring B is selected from C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

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preferably, ring B is selected from , , or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

ring B is selected from C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

preferably, ring B is selected from , , or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$ or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R_{a2} and R_{b2}, and R_{a3} and R_{b3}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5or R^6 each is independently selected from fluoro or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

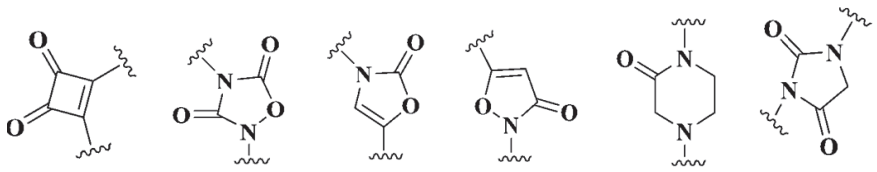
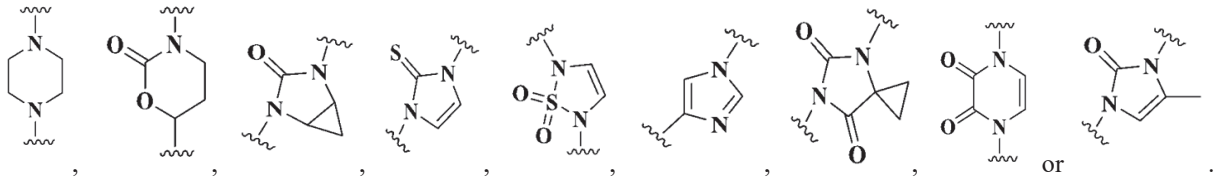
preferably, R^7, R^8, R^9or R^{10} each is independently selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R^{12} is selected from C_{1-3}alkyl; and

preferably, R^{12} is selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

ring B is selected from , , , , or .

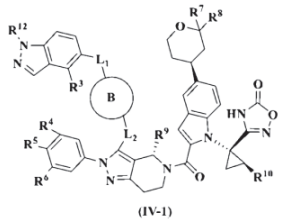
In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

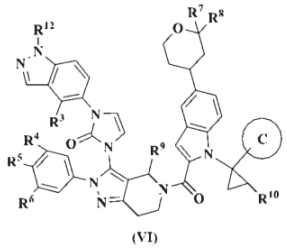
preferably, R^{12} is selected from C_{1-3}alkyl or C_{3-6}cycloalkyl; and

further preferably, R^{12} is selected from methyl or cyclopropyl.

In a further preferred embodiment of the present disclosure, the compound of general formula (IV) is further shown as general formula (IV-1):


(IV-1)

An object of the present disclosure is to provide a compound of general formula (VI), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(VI)

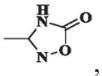
wherein

ring C is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, or -$NR_{a6}S(O)_2R_{b6}$;

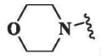
R^{10} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^{10} is linked with the C atoms to which it is connected to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a6} or R_{b6} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl;

wherein when R^3 is fluoro, R^4 and R^6 are methyl, R^5 is fluoro, R^7 and R^8 are hydrogen or methyl, $R^{12}$is methyl, ring C is , and R^{10} is not methyl;

when R^3 is fluoro, R^4 and R^6 are methyl, R^5 is fluoro, R^7 and R^8 are hydrogen, R^{12} is methyl, ring C is , and R^{10} is not hydroxymethyl; and

when R^3 is fluoro, R^4 and R^6 are methyl, R^5 is fluoro, R^7 and R^8 are hydrogen, R^{12} is methyl, ring C is , and R^{10} is not ;

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$NS(O)R_{a1}R_{b1}$, -$(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, -$P(O)R_{a3}R_{b3}$ or -$NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl

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is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -NS(O)$R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8 or R^9 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

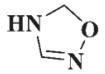
R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

n1 is an integer of 0-5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, or -$NR_{a6}S(O)_2R_{b6}$;

preferably, ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 selected from N, O or S, or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of hydroxyl, oxo, or -$NR_{a6}S(O)_2R_{b6}$; and

further preferably, ring C is selected from , , , ,  or ; optionally further substituted by one or more substituents of hydroxyl, oxo, or -$NR_{a6}S(O)_2R_{b6}$.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R^{10} is selected from hydrogen, deuterium, halogen, or C_{1-3}alkyl; and

preferably, R^{10} is selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R^{10} is linked with the C atoms to which it is connected to form C_{3-6}cycloalkyl; and

preferably, R^{10} is linked with the C atoms to which it is preferably connected to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R_{a6}, and R_{b6} each are independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-8}cycloalkyl, 5- to 7-membered heterocyclyl, C6-10aryl, and 5- to 8-membered heteroaryl; and

preferably, R_{a6} and R_{b6} each are independently selected from hydrogen and methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$ or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4} are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{a2} and R_{b2}, and R_{a3} and R_{b3}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5or R^6 each is independently selected from fluoro or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

R^7, R^8, or R^9 each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^7, R^8, or R^9 each is independently selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (VI):

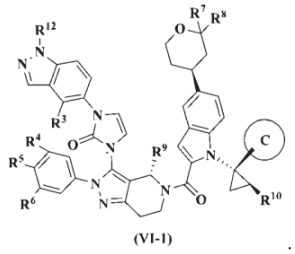
R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy,

C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^{12} is selected from C_{1-3}alkyl; and

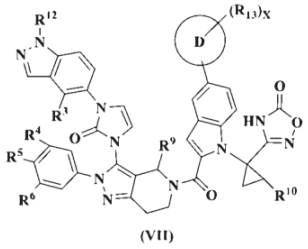
further preferably, R^{12} is selected from methyl.

In a further preferred embodiment of the present disclosure, the compound of general formula (VI) is further shown as general formula (VI-1):



(VI-1)

An object of the present disclosure is to provide a compound of general formula (VII), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(VII)

wherein

ring D is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl;

R^{13} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$ or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl,

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C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

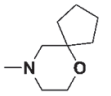
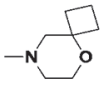
R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^9 or R^{10}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

n1 is an integer of 0-5; and

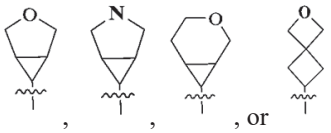
x is an integer of 0-5.

When R^3 is hydrogen, R^4 and R^6 are methyl, R^5 is fluoro, R^9, R^{10}, and R^{12} are methyl, and R^{10} is not ,  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (VII):

ring D is selected from 5- to 12-membered bicyclic fused heterocyclyl, 5- to 12-membered bispiroheterocyclyl, or 5- to 12-membered bicyclic bridged heterocyclyl;

ring D is preferably 5- to 8-membered bicyclic fused heterocyclyl, 5- to 8-membered bispiroheterocyclyl, or 5- to 8-membered bicyclic bridged heterocyclyl; and

ring D is more preferably .

In a further preferred embodiment of the present disclosure, in the compound of general formula (VII):

R^{13} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and R^{13} is further preferably methyl.

In another embodiment of the present disclosure, in the compound of general formula (VII):

ring D is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl;

R^{13} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl and 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, and R_{a4} and R_{b4}, respectively, are preferably linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^9 or R^{10}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

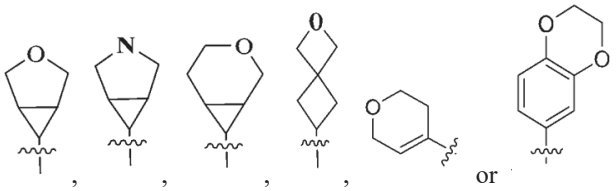
n1 is an integer of 0-5; and

x is an integer of 0-5.

In another embodiment of the present disclosure, in the compound of general formula (VII):

ring D is selected from 3- to 8-membered monocyclic heterocyclyl, 5- to 12-membered bicyclic fused heterocyclyl, 5- to 12-membered bispiroheterocyclyl, or 5- to 12-membered bicyclic bridged heterocyclyl;

preferably, ring D is selected from 5- to 6-membered monoheterocyclyl, 5- to 10-membered bicyclic fused heterocyclyl, 5- to 10-membered bispiroheterocyclyl, or 5- to 8-membered bicyclic bridged heterocyclyl; and

more preferably, ring D is selected from .

In another embodiment of the present disclosure, in the compound of general formula (VII):

R^{13} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

preferably, R^{13} is selected from methyl.

In another embodiment of the present disclosure, in the compound of general formula (VII):

R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl, 5- to 8-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl or 5- to 8-membered heteroaryl; and

preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, or $-NR_{a5}S(O)NR_{a4}R_{b4}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, or C_{1-3}haloalkyl is optionally further substituted by one or more substituents of halogen, $-NS(O)R_{a1}R_{b1}$, or C_{1-3}alkyl.

In another embodiment of the present disclosure, in the compound of general formula (VII):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4} or R_{b4} each is independently selected from hydrogen, deuterium, halogen or methyl.

In another embodiment of the present disclosure, in the compound of general formula (VII):

R_{a2} and R_{b2}, and R_{a3} and R_{b3}, respectively, each are independently linked with adjacent atoms to form C_{3-8}cycloalkyl or 3- to 6-membered heterocyclyl containing 1-3 heteroatoms.

In another embodiment of the present disclosure, in the compound of general formula (VII):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5or R^6 each is independently selected from fluoro or methyl.

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In another embodiment of the present disclosure, in the compound of general formula (VII):

R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

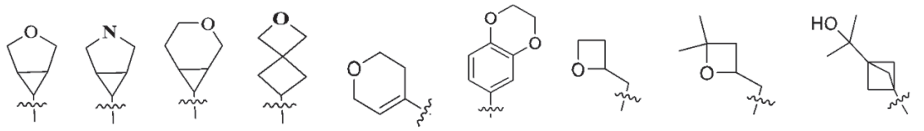
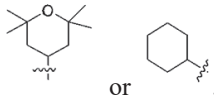
preferably, R^9 or R^{10} each is independently selected from methyl.

In another embodiment of the present disclosure, in the compound of general formula (VII):

R^{12} is selected from C_{1-3}alkyl; and

preferably, R^{12} is selected from methyl.

In another embodiment of the present disclosure, in the compound of general formula (VII):

ring D is selected from ,  or .

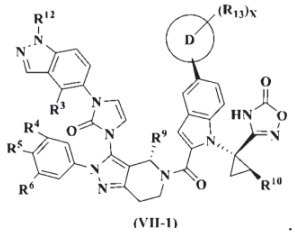
In another embodiment of the present disclosure, in the compound of general formula (VII):

R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^{12} is selected from C_{1-3}alkyl or C_{3-6}cycloalkyl; and

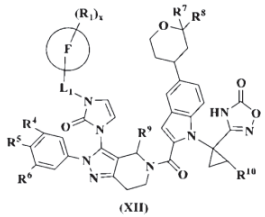
further preferably, R^{12} is selected from methyl or cyclopropyl.

In a further preferred embodiment of the present disclosure, the compound of general formula (VII) is further shown as general formula (VII-1):



(VII-1)

An object of the present disclosure is to provide a compound of general formula (XII), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XII)

L_1 is selected from a bond, C_{2-4}alkenylene, C_{2-4}alkynylene, $-(CH_2)_{n4}-$, or $-(CH_2)_{n5}NR_{b5}$, wherein the C2-4alkenylene, C_{2-4}alkynylene, $-(CH_2)_{n4}-$ or $-(CH_2)_{n5}NR_{b5}$ is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

ring F is selected from C_{3-12}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl;

R^1 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$,, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, or $-(CH_2)_{n4}NR_{a8}C(O)R_{b8}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or

R^1 is linked with the C atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9 or R^{10}each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8} or R_{b8} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl, wherein the amino C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

n1-n5 are an integer of 0-5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

ring F is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl. In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

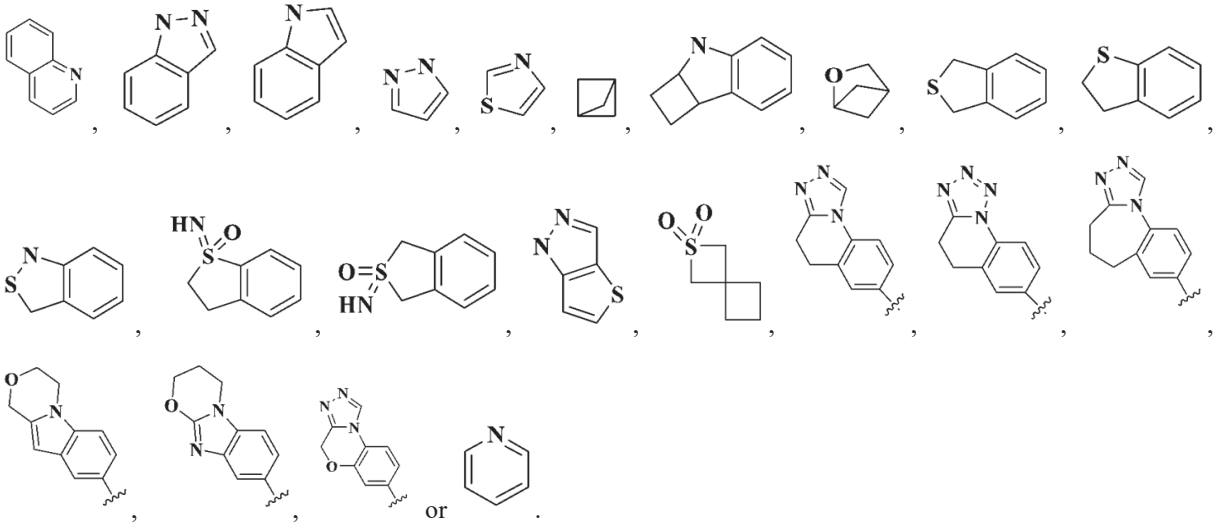
preferably, ring F is selected from C_{3-10}cycloalkyl, 5- to 14-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

further preferably, ring F is selected from C_{3-6}bridged cycloalkyl, 8- to 14-membered tricyclic fused heterocyclyl containing 1-5 heteroatoms,

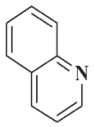
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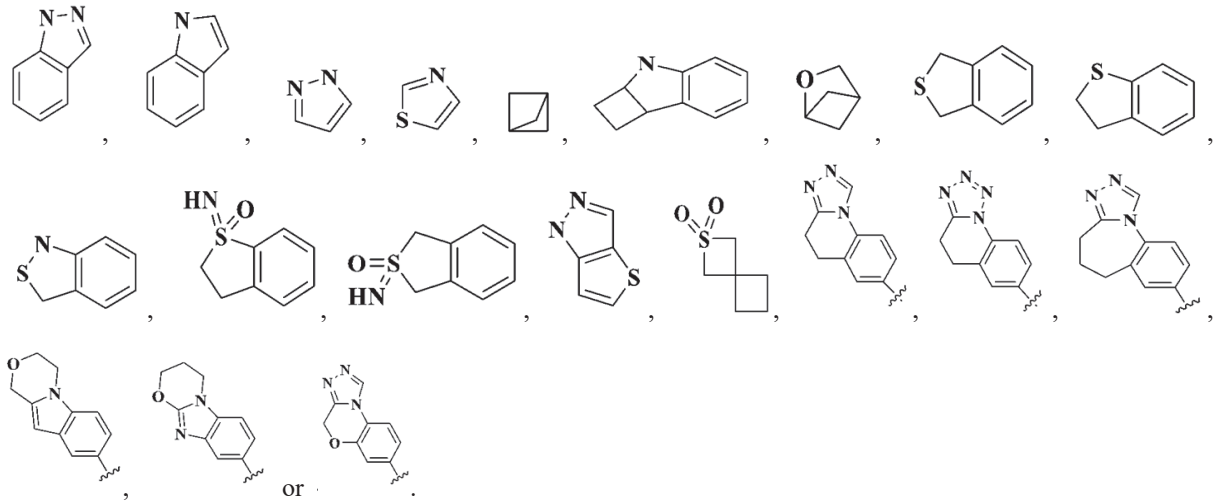
3- to 8-membered bridged heterocyclyl containing 1-3 heteroatoms, fused heterocyclyl containing 1-3 heteroatoms, bridged heterocyclyl containing 1-3 heteroatoms, C_{6-10}aryl or 5- to 10-membered fused heteroaryl containing 1-3 heteroatoms; and

more preferably, ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl,



In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl, ,

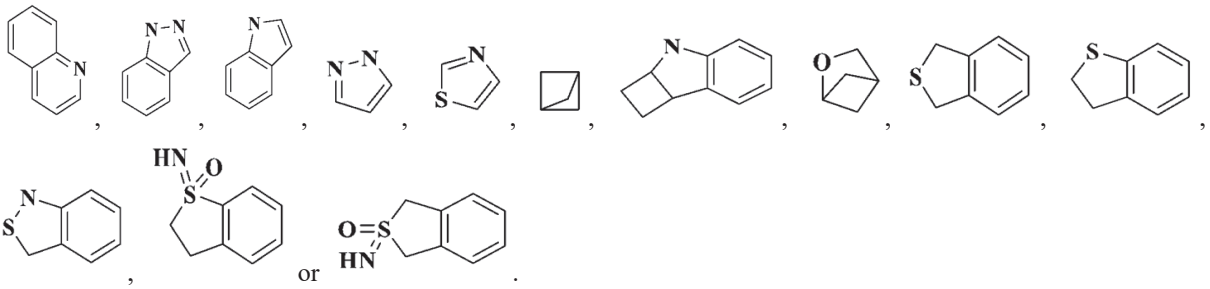


In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

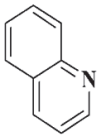
ring F is selected from C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

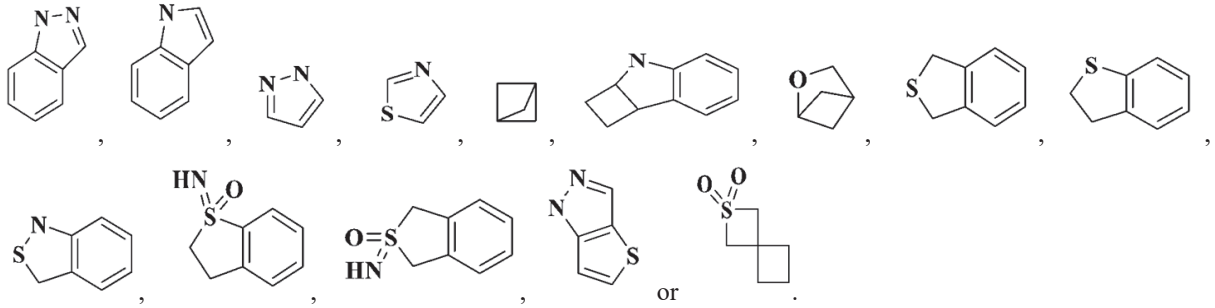
preferably, ring F is selected from C_{3-6}bridged cycloalkyl, 3- to 8-membered bridged heterocyclyl containing 1-3 heteroatoms, fused heterocyclyl containing 1-3 heteroatoms, bridged heterocyclyl containing 1-3 heteroatoms, C_{6-10}aryl or 5- to 10-membered fused heteroaryl containing 1-3 heteroatoms; and

further preferably, ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl,

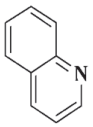


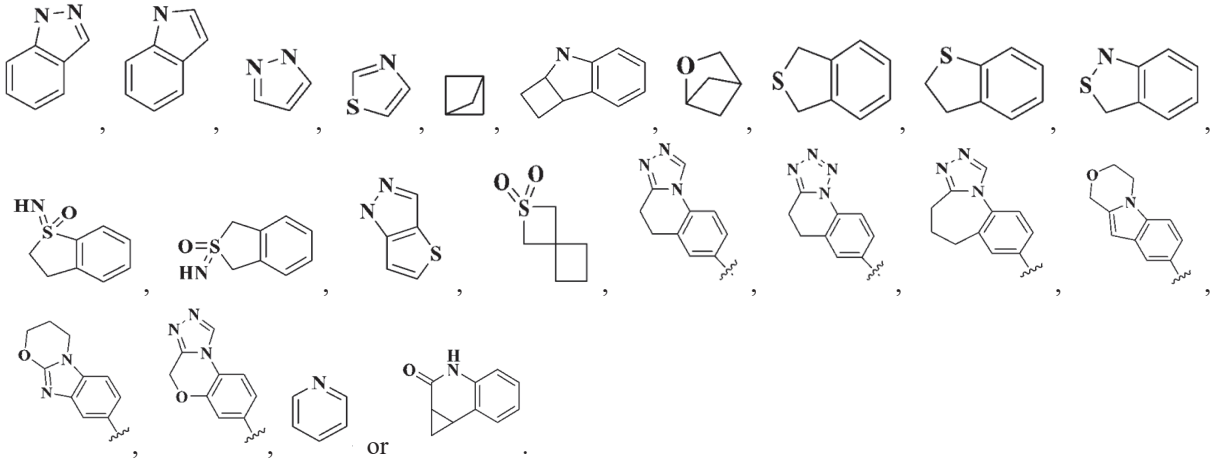
In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl, ,



In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

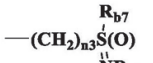
ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl, ,

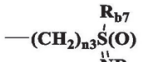


In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R^1 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$,, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$,

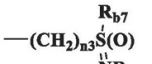
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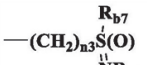
, -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$ or -$(CH_2)_{n1}S(O)_2R_{b5}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -$NS(O)R_{a1}R_{b1}$, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^1 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$NS(O)R_{a1}R_{b1}$, -$(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, -$P(O)R_{a3}R_{b3}$, -$NR_{a5}S(O)NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$ or -$(CH_2)_{n1}S(O)_2R_{b5}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -$NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

further preferably, R^1 each is independently selected from amino, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, -$NS(O)R_{a1}R_{b1}$, -$(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, -$P(O)R_{a3}R_{b3}$, -$NR_{a5}S(O)NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$ or -$(CH_2)_{n1}S(O)_2R_{b5}$, wherein the amino, or C_{1-3}alkyl is optionally further substituted by cyano, or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R^1 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, -$NS(O)R_{a1}R_{b1}$, -$(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, -$P(O)R_{a3}R_{b3}$, -$NR_{a5}S(O)NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}P(O)R_{a3}R_{b3}$,  , or -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, -$NS(O)R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

preferably, R^1 each is independently selected from amino, oxo, C_{1-3}alkyl, -$NS(O)R_{a1}R_{b1}$, -$(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, -$P(O)R_{a3}R_{b3}$, -$NR_{a5}S(O)NR_{a4}R_{b4}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, -$(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, -$(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , or -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, wherein the amino, or C_{1-3}alkyl is optionally further substituted by cyano, or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R^1 is linked with the C atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl; and

preferably, R^1 is further linked with the C atoms to which it is connected to form C_{3-4}cycloalkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

preferably, R^4, R^5or R^6 each is independently selected from fluoro or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, or C_{1-3}haloalkyl; and

preferably, R^7, R^8, R^9or R^{10} each is independently selected from methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl,3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

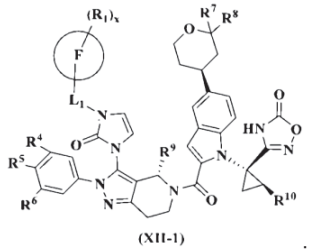
further preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, phenyl or methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl; and

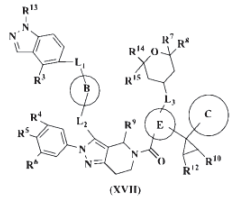
preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, or methyl.

In a further preferred embodiment of the present disclosure, the compound of general formula (XII) is further shown as general formula (XII-1):



(XII-1)

An object of the present disclosure is to provide a compound of general formula (XVII), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XVII)

wherein

R^3 or R^{13} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

L_1, L_2 or L_3 each is independently selected from a bond, C_{2-4}alkenylene, C_{2-4}alkynylene or $-(CH_2)_{n1}-$;

ring B is selected from C_{3-12} cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy or C_{1-6}deuterated haloalkoxy;

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

R^7, R^8, R^9, R^{10}, R^{12}, R^{14} or R^{15} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl,

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C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

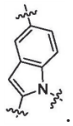
R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

or R^7, R^8, R^9, R^{10}, R^{12}, R^{14}or R^{15}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

or

R^7 and R^8, R^{14} and R^{15}, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy, C_{1-6}deuterated haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

ring E is selected from C_{3-14}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl;

or ring E is ;

ring C is selected from C_{3-14}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated alkoxy, C_{1-6}haloalkoxy or C_{1-6}deuterated haloalkoxy; and

n1, n2 or m1 each is independently selected from 0, 1, 2, 3, 4 or 5.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R^3 or R^{13} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl,

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C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^3 or R^{13} each is independently selected from hydrogen, deuterium, fluoro, chloro, bromo, methyl or cyclopropyl, wherein the methyl or cyclopropyl is optionally further substituted by one or more substituents of halogen or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

ring B is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 atoms selected from N, O or S; optionally further substituted by one or more substituents of halogen, amino, oxo, mercapto, thio or C_{1-3}alkyl;

preferably, ring B is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

further preferably, ring B is selected from ,  or , optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R^4, R^5 or R^6 each is independently selected from fluoro, cyano, cyclopropyl or methyl, wherein the cyclopropyl or methyl is optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R^7, R^8, R^9, R^{10}, R^{12}, R^{14} or R^{15} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl, 5- to 8-membered heteroaryl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{14} or R^{15} each is independently selected from hydrogen, deuterium, halogen, cyano, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or $-(CH_2)_{m1}OR_{c1}$, wherein the C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, deuterated methyl, methyl, cyclopropyl or oxo; and

further preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{14} or R^{15} each is independently selected from cyano, methyl, fluoro, cyclopropyl, ethynyl or $-(CH_2)_{m1}OR_{c1}$, wherein the methyl, cyclopropyl, ethynyl or $-(CH_2)_{m1}OR_{c1}$ is optionally further substituted by one or more substituents of deuterium, deuterated methyl, methyl, cyclopropyl or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

preferably, R_{c1} is selected from fluoro, methyl, cyano, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl or oxetane, wherein the methyl, difluoromethyl, trifluoromethyl, ethynyl, methylthio, amino, cyclopropyl or oxetane is optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R^7, R^8, R^9, R^{10}, R^{12}, R^{14}or R^{15}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{14} or R^{15}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

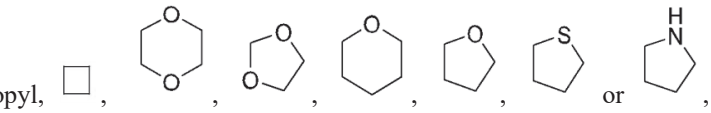
R^{10} and R^{12} are linked with the atoms to which they are connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

R^{10} and R^{12} are lined with the atoms to which they are connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

preferably, R^{10} and R^{12} are lined with the atoms to which they are connected to form .

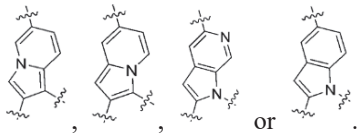
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R^7 and R^8, R^{14} and R^{15}, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S, optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, C_{1-3}deuterated haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

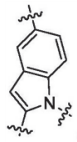
preferably, R^7 and R^8, R^{14} and R^{15}, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form cyclopropyl, , optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, amino, nitro, hydroxyl, cyano, oxo, thio, methyl or ethyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

ring E is selected from C_{3-8}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

preferably, ring E is selected from .

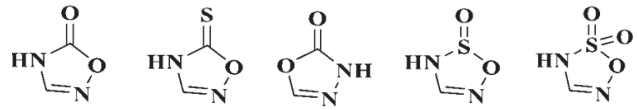
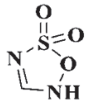
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

ring E is .

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated sulfanyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy or C_{1-3}deuterated haloalkoxy;

preferably, ring C is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 selected from N, O or S or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of hydroxyl, thio, oxo or C_{1-3}haloalkoxy; and

further preferably, ring C is selected from , ; optionally further substituted by one or more substituents of hydroxyl, thio or oxo.

In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

R^{13} is selected from C_{1-6}deuterated alkyl, C_{1-6}deuterated haloalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}deuterated alkoxy, C_{1-6}deuterated haloalkoxy, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{1-6}deuterated alkyl, C_{1-6}deuterated haloalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}deuterated alkoxy, C_{1-6}deuterated haloalkoxy, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

preferably, R^{13} is selected from C_{1-3}deuterated alkyl, C_{1-3}deuterated haloalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}deuterated sulfanyl, C_{1-3}deuterated alkoxy, C_{1-3}deuterated haloalkoxy, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein the C_{1-3}deuterated alkyl, C_{1-3}deuterated haloalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}deuterated sulfanyl, C_{1-3}deuterated alkoxy,

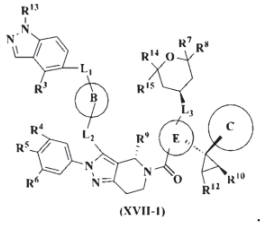
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C_{1-3}deuterated haloalkoxy, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

further preferably, R^{13} is selected from $-CD_3$ or cyclopropyl, wherein the $-CD_3$ or cyclopropyl is optionally further substituted by one or more substituents of deuterium, halogen or C_{1-3}alkyl; and

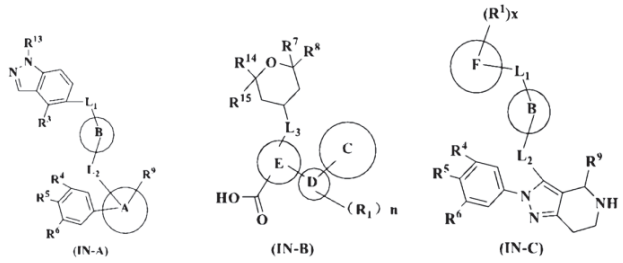
more preferably, R^{13} is selected from cyclopropyl, optionally further substituted by one or more substituents of deuterium, halogen or C_{1-3}alkyl.

In a further preferred embodiment of the present disclosure, the compound of general formula (XVII) is further shown as general formula (XVII-1):



(XVII-1)

The present disclosure further provides a compound of general formula (IN-A), (IN-B) or (IN-C), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(IN-A) (IN-B) (IN-C)

wherein in general formula (IN-A), R^{13}, ring A, ring B, L_1, L_2, R^4, R^5, R^6, and R^9 are defined as in general formula (XIX);

in general formula (IN-B), ring C, ring D, ring E, L_3, R^1, R^7, R^8, R^{14}, R^{15}, and n are defined as in general formula (XIX); and

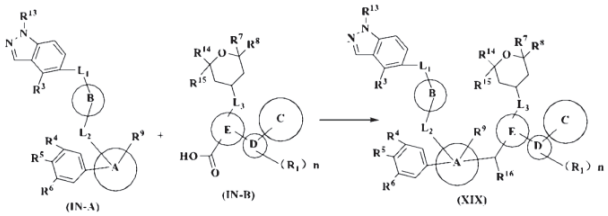
in general formula (IN-C), ring F, ring B, L_1, L_2, R^1, R^4, R^5, R^6, R^9, and x are defined as in general formula (XVI).

In a further preferred embodiment of the present disclosure, in the compound of general formula (IN-A): R^{13} is selected from C_{3-8}cycloalkyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, C_{6-10}aryl, or 5- to 10-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, or C_{1-6}alkyl.

In a further preferred embodiment of the present disclosure, in the compound of general formula (IN-B): ring D is selected from C_{3-8}bicyclic cycloalkyl, 3- to 8-membered bicyclic heterocyclyl or 5- to 10-membered bicyclic heteroaryl containing 1-3 atoms selected from N, O or S; preferably, ring D is selected from C_{3-6}bicyclic cycloalkyl, 3- to 8-membered bicyclic heterocyclyl containing 1-3 atoms selected from N, O or S or 5- to 8-membered bicyclic heteroaryl containing 1-3 N, O or S atoms; and preferably, ring D is selected from  or .

In a further preferred embodiment of the present disclosure, in the compound of general formula (IN-C): ring F is selected from 8- to 14-membered tricyclic fused heterocyclyl containing 1-5 heteroatoms.

The present disclosure further provides a method for the compound of the general formula described above, including the following steps:



wherein ring A, ring B, ring C, ring D, ring E, L_1, L_2, L_3, R^1, R^4, R^5, R^6, R^7, R^8, R^9, R^{13}, R^{14}, R^{15}, and R^{16} are defined as in general formula (XIX);

reacting general formula (IN-A) with general formula (IN-B) under the action of a condensation agent and a base to obtain general formula (XIX);

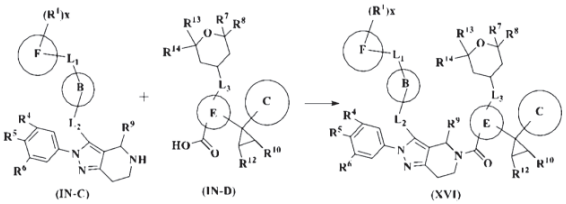
wherein the condensation agent is selected from EDC, DIC, DCC, TBTU, HATU, HBTU, HCTU, DEPBT, PyBOP or PyAOP; and

the base is selected from DIPEA, DIEA, Et_3N, NMP, DBU or DABCO.

In a further preferred embodiment of the present disclosure, in the preparation method, the condensation agent is selected from HATU; and the base is selected from DIPEA.

In a further preferred embodiment of the present disclosure, the preparation method is carried out under the condition of a solvent, wherein the reaction solvent is selected from N,N-dimethylformamide, N,N-dimethylacetamide, tetrahydrofuran, acetonitrile or dichloromethane; preferably N,N-dimethylformamide.

The present disclosure further provides a method for the compound of the general formula described above, including the following steps:



wherein ring F, ring B, ring C, ring E, L_1, L_2, L_3, R^1, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}, and x are defined as in general formula (XVI);

reacting general formula (IN-C) with general formula (IN-D) under the action of a condensation agent and a base to obtain general formula (XVI);

wherein the condensation agent is selected from EDC, DIC, DCC, TBTU, HATU, HBTU, HCTU, DEPBT, PyBOP or PyAOP; preferably HATU; and

the base is selected from DIPEA, DIEA, Et_3N, NMP, DBU or DABCO.

In a further preferred embodiment of the present disclosure, in the preparation method, the condensation agent is selected from HATU; and the base is selected from DIEA.

In a further preferred embodiment of the present disclosure, the preparation method is carried out under the condition of a solvent, wherein the reaction solvent is selected from N,N-dimethylformamide, N,N-dimethylacetamide, tetrahydrofuran, acetonitrile or dichloromethane; preferably N,N-dimethylformamide.

The present disclosure further relates to a pharmaceutical composition, comprising a therapeutically effective dose of any compound of the general formula, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers, diluents or excipients.

In certain embodiments of the present disclosure, the weight percentage of the compound or the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof in the pharmaceutical composition is 0.1-95%, preferably 5-70%, e.g., 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% on a free base basis.

In certain embodiments of the present disclosure, the pharmaceutical composition is selected from a tablet, a capsule, a liquid preparation or an injection, preferably further comprises a filler, optionally further comprises a disintegrant, or further comprises one or more of a glidant or lubricant.

In certain embodiments of the present disclosure, the pharmaceutical composition is an immediate release preparation or a sustained release preparation.

In certain embodiments of the present disclosure, the unit dose of the compound, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof in the pharmaceutical composition is 1-1000 mg, preferably 1-500 mg, or preferably 1 mg, 2 mg, 3 mg, 5 mg, 10 mg, 20 mg, 40 mg, 50 mg, 60 mg, 80 mg, 100 mg, 200 mg, 300 mg, 400 mg, or 500 mg on a free base basis.

In certain embodiments of the present disclosure, the compound, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof can be administered by any convenient method, for example, by oral, parenteral, buccal, sublingual, nasal, rectal, intrathecal or transdermal administration, and the pharmaceutical composition can be adjusted accordingly.

In certain embodiments of the present disclosure, the compound, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof can be formulated into a liquid or solid preparation, such as a syrup, a suspension, an emulsion, tablets, capsules, powder, granules, or a lozenge.

The present disclosure further relates to the use of any compound of the general formula, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition in the preparation of a GLP-1 receptor agonist drug.

The present disclosure further relates to the use of the compound of the general formula, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition thereof in the preparation of a drug for treating a metabolic disease, wherein the disease is selected from diabetes, obesity or non-alcoholic steatohepatitis-related disease or other related diseases caused by diabetes, obesity or non-alcoholic steatohepatitis.

The present disclosure further relates to the use of the compound of the general formula, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition thereof in the preparation of a drug for the treatment of a metabolic disease and the related diseases.

The present disclosure further relates to a method for preventing and/or treating metabolic diseases, which comprises administering to a patient a therapeutically effective dose of the compound of the general formula, the prodrug thereof, the stereoisomer thereof or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition thereof.

The present disclosure further provides a method for treating a disease condition with the compound or pharmaceutical composition of the present disclosure. The disease condition includes, but is not limited to, conditions related to a GLP-1 receptor regulator.

The present disclosure further relates to a method for treating a metabolic disease in a mammal, and the method comprises administering to the mammal a therapeutically effective amount of the compound of the present disclosure, or a pharmaceutically acceptable salt, ester, prodrug, solvate, hydrate or derivative thereof.

Detailed Description of the Invention

Unless stated to the contrary, the terms used in the description and claims have the following meanings.

The term “alkyl” refers to a saturated aliphatic hydrocarbon group, which is a linear or branched group containing 1 to 20 carbon atoms, preferably alkyl containing 1 to 8 carbon atoms, more preferably alkyl containing 1 to 6 carbon atoms, and most preferably alkyl containing 1 to 3 carbon atoms. Non-limiting examples include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, n-pentyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, 1-ethylpropyl, 2-methylbutyl, 3-methylbutyl, n-hexyl, 1-ethyl-2-methylpropyl, 1,1,2-trimethylpropyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 2,2-dimethylbutyl, 1,3-dimethylbutyl, 2-ethylbutyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2,3-dimethylbutyl, n-heptyl, 2-methylhexyl, 3-methylhexyl, 4-methylhexyl, 5-methylhexyl, 2,3-dimethylpentyl, 2,4-dimethylpentyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 2-ethylpentyl, 3-ethylpentyl, n-octyl, 2,3-dimethylhexyl, 2,4-dimethylhexyl, 2,5-dimethylhexyl, 2,2-dimethylhexyl, 3,3-dimethylhexyl, 4,4-dimethylhexyl, 2-ethylhexyl, 3-ethylhexyl, 4-ethylhexyl, 2-methyl-2-ethylpentyl, 2-methyl-3-ethylpentyl, n-nonyl, 2-methyl-2-ethylhexyl, 2-methyl-3-ethylhexyl, 2,2-diethylpentyl, n-decyl, 3,3-diethylhexyl, 2,2-diethylhexyl, and various branched isomers thereof, etc. More preferably, the alkyl is a lower alkyl group containing 1 to 6 carbon atoms, and non-limiting examples include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, n-pentyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, 1-ethylpropyl, 2-methylbutyl, 3-methylbutyl, n-hexyl, 1-ethyl-2-methylpropyl, 1,1,2-trimethylpropyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 2,2-dimethylbutyl,

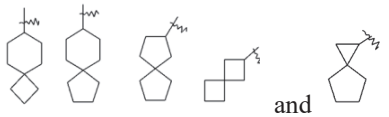
1,3-dimethylbutyl, 2-ethylbutyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2,3-dimethylbutyl, etc. Alkyl can be substituted or unsubstituted, and when substituted, the substituent can be substituted at any available connection point, and the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, oxo, carboxyl or a carboxylate group. In the present disclosure, alkyl is preferably methyl, ethyl, isopropyl, tert-butyl, haloalkyl, deuteroalkyl, alkoxy-substituted alkyl and hydroxyl-substituted alkyl.

The term “alkylene” refers to one hydrogen atom of alkyl being further substituted, for example: "methylene" refers to $-CH_2-$, "ethylene" refers to $-(CH_2)_2-$, "propylene" refers to $-(CH_2)_3-$, and "butylene" refers to $-(CH_2)_4-$, etc.

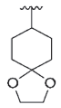
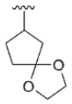
The term "alkenyl" refers to an alkyl group as defined above consisting of at least two carbon atoms and at least one carbon-carbon double bond, such as ethenyl, 1-propenyl, 2-propenyl, 1-, 2- or 3 -butenyl, etc. Alkenyl can be substituted or unsubstituted. When the alkenyl is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, or heterocycloalkylthio.

The term “alkenylene” refers to one hydrogen atom of alkenyl being further substituted, such as “ethenylene” refers to $-CH_2=CH_2-$, “propenylene” refers to $-CH_2-=CH_2-CH_2-$, etc. Alkenylene can be substituted or unsubstituted. When the alkenylene is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, or heterocycloalkylthio. The term “cycloalkyl” refers to a saturated or partially unsaturated monocyclic or polycyclic cyclic hydrocarbon substituent, and the cycloalkyl comprises 3 to 20 carbon atoms, preferably 3 to 12 carbon atoms, more preferably 3 to 8 carbon atoms, and further preferably 3 to 6 carbon atoms. Non-limiting examples of monocyclic cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cyclohexadienyl, cycloheptyl, cycloheptatrienyl, cyclooctyl, etc.; and polycyclic cycloalkyl includes spiro, fused and bridged cycloalkyl, preferably cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

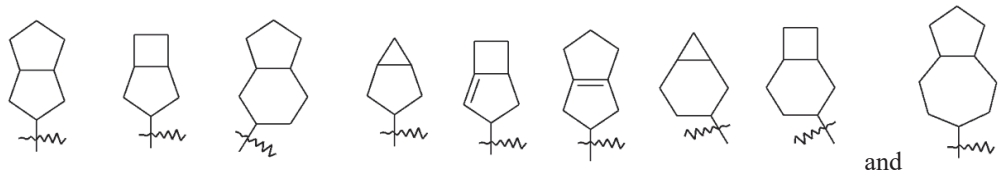
The term "spirocycloalkyl" refers to a polycyclic group with 5- to 20-membered monocyclic rings sharing one carbon atom (called a spiro atom). It may contain one or more double bonds, but no ring has a completely conjugated π electron system. Preferably, the bridged heterocyclyl is 6- to 14-membered, and more preferably 7- to 10-membered. According to the number of shared spiro atoms between the rings, the spirocycloalkyl is divided into monospirocycloalkyl, bispirocycloalkyl or polyspirocycloalkyl, preferably monospirocycloalkyl and bispirocycloalkyl. More preferably, the group is a 4-membered/4-membered, 4-membered/5-membered, 4-membered/6-membered, 5-membered/5-membered or 5-membered/6-membered monospirocycloalkyl. Non-limiting examples of spirocycloalkyl include:

 and ;

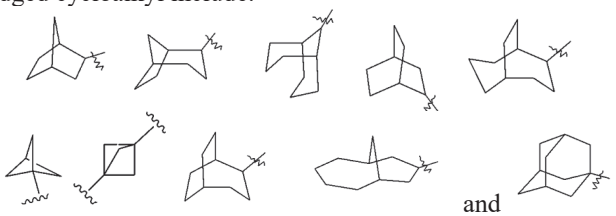
Also included are spirocycloalkyl groups in which monospirocycloalkyl and heterocycloalkyl share a spiro atom. Non-limiting examples include:

 and .

The term "fused cycloalkyl" refers to a 5- to 20-membered all-carbon polycyclic group in which each ring in the system shares an adjacent pair of carbon atoms with other rings in the system, one or more ring of which may contain one or more double bonds, but no ring has a fully conjugated π electron system. Preferably, the bridged heterocyclyl is 6- to 14-membered, and more preferably 7- to 10-membered. According to the number of constituent rings, it can be divided into bicyclic, tricyclic, tetracyclic or polycyclic fused cycloalkyl, preferably bicyclic or tricyclic, and more preferably 5-membered/5-membered or 5-membered/6-membered bicyclic cycloalkyl. Non-limiting examples of fused cycloalkyl include:


and .

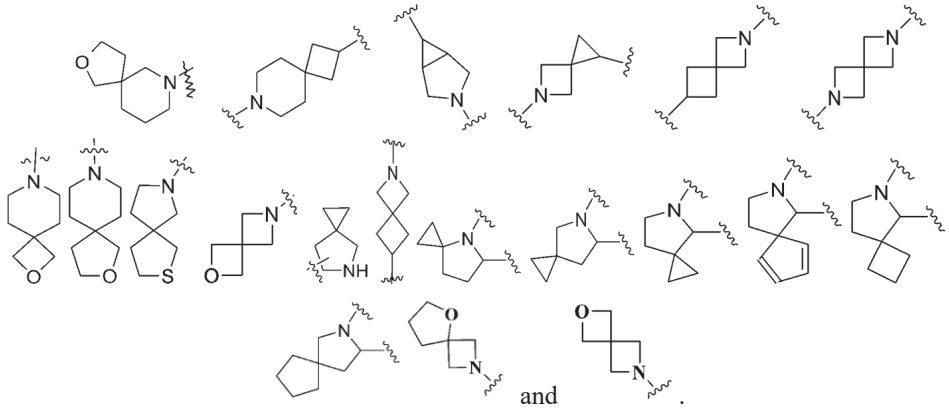
The term “bridged cycloalkyl” refers to a 5- to 20-membered all-carbon polycyclic group with any two rings sharing two carbon atoms that are not directly connected. It may contain one or more double bonds, but no ring has a fully conjugated π electron system. Preferably, the bridged heterocyclyl is 6- to 14-membered, and more preferably 7- to 10-membered. According to the number of constituent rings, it can be divided into bicyclic, tricyclic, tetracyclic or polycyclic bridged cycloalkyl, preferably bicyclic, tricyclic or tetracyclic, and more preferably bicyclic or tricyclic. Non-limiting examples of bridged cycloalkyl include:


and .

The cycloalkyl ring can be fused to an aryl, heteroaryl or heterocycloalkyl ring, wherein the ring connected to the parent structure is cycloalkyl, and non-limiting examples include indanyl, tetrahydronaphthyl, benzocycloheptanyl, etc. Cycloalkyl can be optionally substituted or unsubstituted. When the cycloalkyl is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, oxo, carboxyl or a carboxylate group.

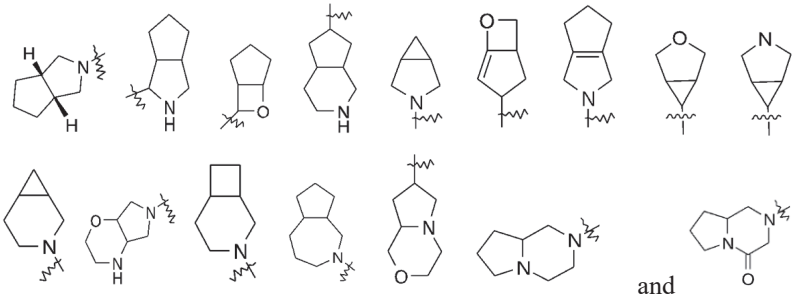
The term "heterocyclyl" refers to a saturated or partially unsaturated monocyclic or polycyclic cyclic hydrocarbon substituent, which comprises 3 to 20 ring atoms, wherein one or more ring atoms are heteroatoms selected from nitrogen, oxygen or $S(O)_m$ (wherein m is an integer of 0 to 2), but excluding ring moieties of -O-O-, -O-S- or -S-S-, and the remaining ring atoms are carbon. Preferably, the heterocyclyl comprises 3 to 12 ring atoms, among which 1-4 are heteroatoms; more preferably, the heterocyclyl comprises 3 to 10 ring atoms; and further preferably, the heterocyclyl comprises 3 to 8 ring atoms. Non-limiting examples of monocyclic heterocyclyl include pyrrolidyl, azetidinyl, oxetanyl, oxanyl, imidazolidinyl, tetrahydrofuryl, tetrahydrothiophenyl, dihydroimidazolyl, dihydrofuryl, dihydropyrazolyl, dihydropyrrolyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl, homopiperazinyl, pyranyl, etc.; preferably pyrrolidinyl, azetidinyl, oxetanyl, tetrahydrofuryl, pyrazolidinyl, morpholinyl, , piperazinyl and pyranyl; more preferably pyrrolidinyl, azetidinyl, oxetanyl, oxanyl, piperidyl, , piperazinyl and pyranyl. Polycyclic heterocyclyl includes spiro, fused and bridged heterocyclyl, wherein the spiro, fused and bridged heterocyclyl groups are optionally connected to other groups through a single bond, or further fused to other cycloalkyl, heterocyclyl, aryl and heteroaryl through any two or more atoms on the ring.

The term “spiroheterocyclyl” refers to a 5- to 20-membered polycyclic heterocyclyl with monocyclic rings sharing one atom (called a spiro atom), wherein one or more ring atoms are heteroatoms selected from nitrogen, oxygen, or $S(O)_m$ (wherein m is an integer of 0 to 2), and the remaining ring atoms are carbon. The spiroheterocyclyl may contain one or more double bonds, but no ring has a fully conjugated π electron system. Preferably, the bridged heterocyclyl is 6- to 14-membered, and more preferably 7- to 10-membered. According to the number of shared spiro atoms between the rings, the spiro heterocyclyl is divided into monospiroheterocyclyl, bispiroheterocyclyl or polyspiroheterocyclyl, preferably monospiroheterocyclyl and bispiroheterocyclyl. More preferably, it is a 4-membered/4-membered, 4-membered/5-membered, 4-membered/6-membered, 5-membered/5-membered, or 5-membered/6-membered monospiroheterocyclyl. Non-limiting examples of spiro heterocyclyl include:



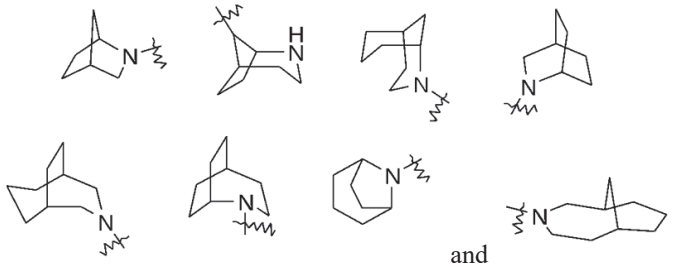
and .

The term "fused heterocyclyl" refers to a 5- to 20-membered polycyclic heterocyclyl with each ring in the system sharing a pair of atoms neighboring other rings in the system, and one or more rings may contain one or more double bonds, but no ring has a fully conjugated π electron system, wherein one or more ring atoms are heteroatoms selected from nitrogen, oxygen, or $S(O)_m$ (wherein m is an integer of 0 to 2), and the remaining ring atoms are carbon. Preferably, the bridged heterocyclyl is 6- to 14-membered, and more preferably 7- to 10-membered. According to the number of constituent rings, it can be divided into bicyclic, tricyclic, tetracyclic or polycyclic fused heterocyclyl, preferably bicyclic or tricyclic, more preferably 5-membered/5-membered or 5-membered/6-membered bicyclic fused heterocyclyl. Non-limiting examples of fused heterocyclyl include:



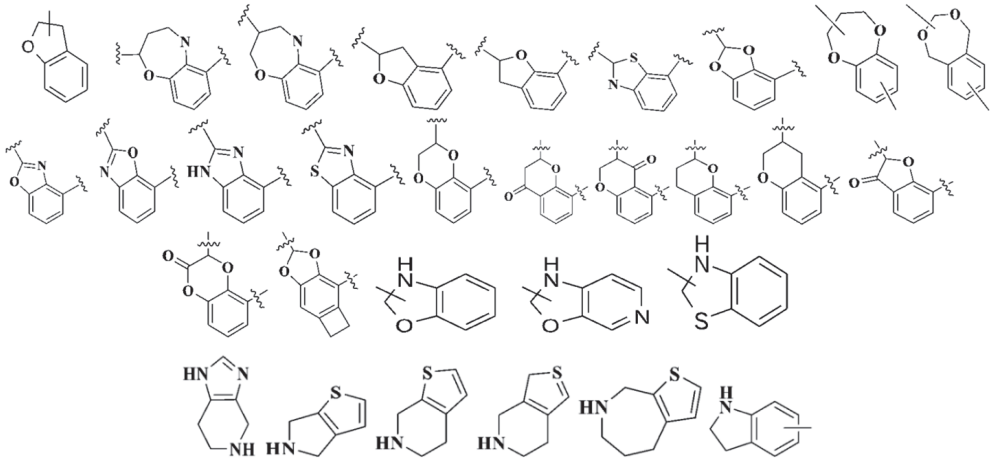
and .

The term "bridged heterocyclyl" refers to a 5- to 14-membered polycyclic heterocyclyl with any two rings sharing two atoms that are not directly connected. It may contain one or more double bonds, but no ring has a fully conjugated π electron system, wherein one or more ring atoms are heteroatoms selected from nitrogen, oxygen, or $S(O)_m$ (wherein m is an integer of 0 to 2), and the remaining ring atoms are carbon. Preferably, the bridged heterocyclyl is 6- to 14-membered, and more preferably 7- to 10-membered. According to the number of constituent rings, it can be divided into bicyclic, tricyclic, tetracyclic or polycyclic bridged heterocyclyl, preferably bicyclic, tricyclic or tetracyclic, and more preferably bicyclic or tricyclic. Non-limiting examples of bridged heterocyclyl include:



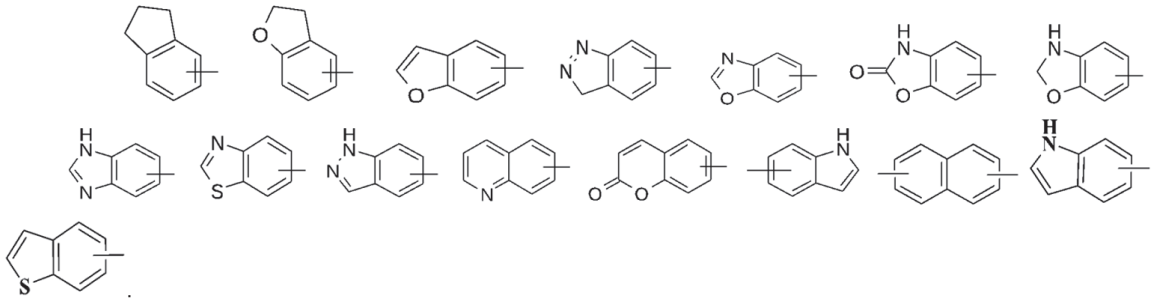
and .

The heterocyclyl ring can be fused to an aryl, heteroaryl or cycloalkyl ring, wherein the ring connected to the parent structure is heterocyclyl, and the non-limiting examples thereof include:



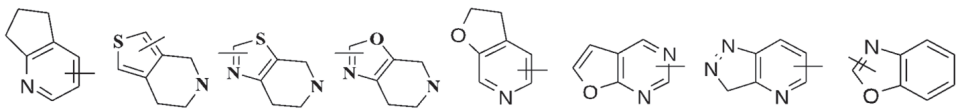
Heterocyclyl can be optionally substituted or unsubstituted. When the heterocyclyl is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, oxo, carboxyl or a carboxylate group.

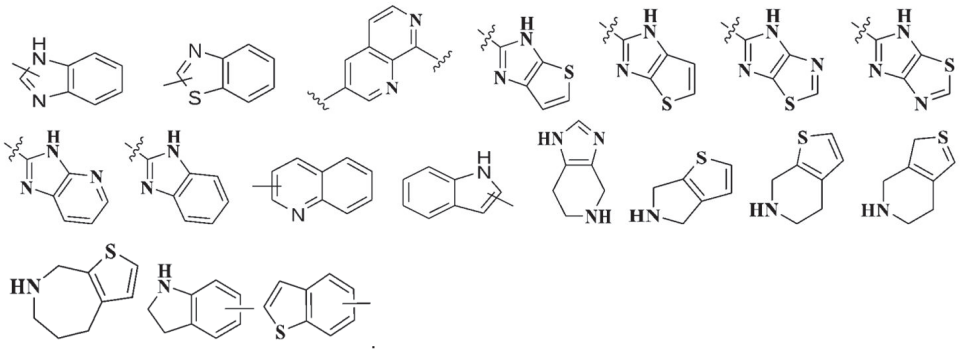
The term "aryl" refers to a 6- to 14-membered all-carbon monocyclic or fused polycyclic (i.e., rings sharing an adjacent pair of carbon atoms) group having a conjugated π electron system, preferably 6- to 10-membered, more preferably 6- to 8-membered aryl, such as phenyl and naphthyl, and more preferably phenyl. The aryl ring can be fused to a heteroaryl, heterocyclyl or cycloalkyl ring, wherein the ring connected to the parent structure is an aryl ring, and the non-limiting examples thereof include:



Aryl can be substituted or unsubstituted. When the aryl is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, carboxyl or a carboxylate group.

The term "heteroaryl" refers to a heteroaromatic system containing 1 to 4 heteroatoms and 5 to 14 ring atoms, wherein the heteroatoms are selected from oxygen, sulfur and nitrogen. The heteroaryl is preferably 5- to 10-membered, more preferably 5- to 8-membered, most preferably 5- or 6-membered, such as imidazolyl, furyl, thienyl, thiazolyl, pyrazolyl, oxazolyl, pyrrolyl, triazolyl, tetrazolyl, pyridyl, pyrimidinyl, thiadiazole, pyrazinyl, etc., preferably triazolyl, thienyl, imidazolyl, pyrazolyl, or pyrimidinyl or thiazolyl; more preferably triazolyl, pyrrolyl, thienyl, thiazolyl and pyrimidyl. The heteroaryl ring can be fused to an aryl, heterocyclyl or cycloalkyl ring, wherein the ring connected to the parent structure is heteroaryl ring, and the non-limiting examples thereof include:





Heteroaryl can be optionally substituted or unsubstituted. When the heteroaryl is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, carboxyl or a carboxylate group.

The term "alkoxy" refers to -O- (alkyl) and -O- (unsubstituted cycloalkyl), where alkyl is as defined above, preferably alkyl containing 1 to 8 carbon atoms, more preferably alkyl containing 1 to 6 carbon atoms, and most preferably alkyl containing 1 to 3 carbon atoms. Non-limiting examples of alkoxy include: methoxy, ethoxy, propoxy, butoxy, cyclopropoxy, cyclobutoxy, cyclopentoxy, and cyclohexoxy. Alkoxy can be optionally substituted or unsubstituted. When the alkoxy is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, carboxyl or a carboxylate group.

“Haloalkyl” refers to alkyl substituted with one or more halogen, wherein alkyl is defined as above.

“Haloalkoxy” refers to alkoxy substituted with one or more halogen, wherein alkoxy is defined as above.

“Hydroxyalkyl” refers to alkyl substituted with hydroxyl, wherein alkyl is defined as above.

"Alkenyl" refers to a chain alkenyl group, also known as an alkene group, preferably alkyl containing 2 to 8 carbon atoms, more preferably alkyl containing 2 to 6 carbon atoms, and most preferably alkyl containing 2 to 3 carbon atoms. Moreover, the alkenyl can be further substituted with other related groups, such as: alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, carboxyl or a carboxylate group.

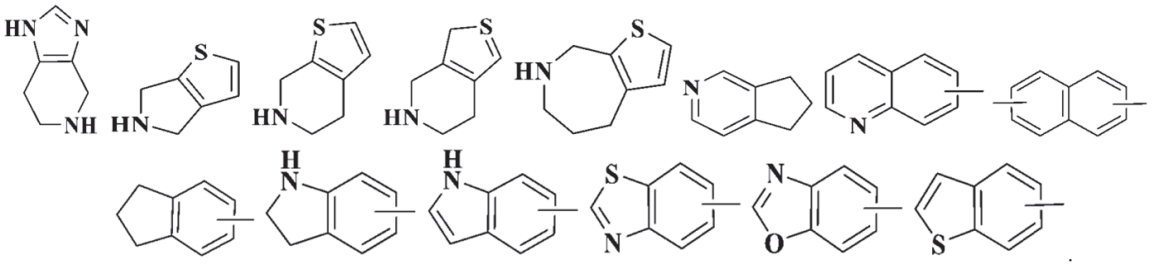
“Alkynyl” refers to (CH≡C-), preferably alkyl containing 2 to 8 carbon atoms, more preferably alkyl containing 2 to 6 carbon atoms, and most preferably alkyl containing 2 to 3 carbon atoms. Moreover, the alkynyl can be further substituted with other related groups, such as: alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, carboxyl or a carboxylate group.

The term “alkynylene” refers to one hydrogen atom of alkynyl being further substituted, such as “ethynylene” refers to -C≡C-, “propenylene” refers to -C≡C-CH_2-, etc. Alkynylene (containing three or more carbon atoms) can be substituted or unsubstituted. When the alkenylene is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, or heterocycloalkylthio.

“Fused cyclyl” refers to a polycyclyl formed from two or more carbocyclic or heterocyclic rings by sharing a common ring edge, and the fused cyclyl includes fused cycloalkyl, fused cyclic heteroaryl, fused cycloaryl and fused cycloheteroaryl, wherein the fused cycloalkyl refers to a polycyclyl formed from cycloalkyl and heterocyclyl, aryl, and

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heteroaryl by sharing a common ring edge; the fused cyclic heterocyclyl refers to a polycyclyl formed from heterocyclyl and cycloalkyl, aryl, and heteroaryl by sharing a common ring edge; the fused cyclic aryl refers to a polycyclyl formed from aryl and cycloalkyl, heterocyclyl, and heteroaryl by sharing a common ring edge; and the fused cyclic heteroaryl refers to a polycyclyl formed from heteroaryl and cycloalkyl, heterocyclyl, and heteroaryl by sharing a common ring edge; for example:



"Haloalkyl" refers to alkyl substituted with one or more halogen, wherein alkyl is defined as above.

"Haloalkoxy" refers to alkoxy substituted with one or more halogen, wherein alkoxy is defined as above.

"Hydroxyalkyl" refers to alkyl substituted with hydroxyl, wherein alkyl is defined as above.

"Hydroxyl" refers to an -OH group.

"Halogen" refers to fluorine, chlorine, bromine or iodine.

"Amino" refers to $-NH_2$.

"Cyano" refers to –CN.

"Nitro" refers to $-NO_2$.

"Carboxyl" refers to -C(O)OH.

"THF" refers to tetrahydrofuran.

"EtOAc" refers to ethyl acetate.

"MeOH" refers to methanol.

"DMF" refers to N, N-dimethylformamide.

"DIPEA" refers to diisopropylethylamine.

"TFA" refers to trifluoroacetic acid.

"MeCN" refers to acetonitrile.

"DMA" refers to N,N-dimethylacetamide.

"Et_2O" refers to diethyl ether.

"DCE" refers to 1,2-dichloroethane.

"DIPEA" refers to N,N-diisopropylethylamine.

"NBS" refers to N-bromosuccinimide.

"NIS" refers to N-iodosuccinimide.

"Cbz-Cl" refers to benzyl chloroformate.

"$Pd_2(dba)_3$" refers to tris(dibenzylideneacetone)dipalladium.

"Dppf" refers to 1,1'-bisdiphenylphosphine ferrocene.

"HATU" refers to 2-(7-azabenzotriazolyl)-N,N,N',N'-tetramethyluronium hexafluorophosphate.

"KHMDS" refers to potassium hexamethyldisilamide.

"LiHMDS" lithium bistrimethylsilylamide.

"MeLi" refers to lithium methyl.

"n-BuLi" refers to n-butyl lithium.

"$NaBH(OAc)_3$" refers to sodium triacetoxyborohydride.

Different terms such as "X is selected from A, B, or C", "X is selected from A, B and C", "X is A, B or C", and "X is A, B and C" all express the same meaning, i.e., X can be any one or more of A, B, and C.

The hydrogen atoms of the present disclosure can be replaced with its isotope deuterium, and any hydrogen atom in the example compounds involved in the present disclosure can also be replaced with a deuterium atom.

"Optional" or "optionally" means that the event or circumstance subsequently described may but need not occur, and the description includes the occasion where the event or circumstance occurs or does not occur. For example, "heterocyclic group optionally substituted with alkyl" means the alkyl may but need not be present, and the description includes the case where the heterocyclic group is substituted with alkyl and the case where the heterocyclic group is not substituted with alkyl.

“Substituted” means that one or more hydrogen atoms, preferably at most 5, more preferably 1-3 hydrogen atoms in the group are each independently substituted with a corresponding number of substituents. It goes without saying, the substituents may be only in their possible chemical positions, a person skilled in the art can determine the possible or impossible substitutions (by experiment or theory) without paying too much effort. For example, the amino group having a free hydrogen or a hydroxyl group may be unstable when combined the carbon atoms having an unsaturated (e.g., olefinic) bond.

“Pharmaceutical composition” denotes a mixture containing one or more compounds described herein or physiologically/pharmaceutically acceptable salts or prodrug thereof and other chemical components, as well as other components, such as physiologically/pharmaceutically acceptable carriers and excipients. The purpose of pharmaceutical compositions is to facilitate administration to living organisms and facilitate the absorption of active ingredients to exert biological activity.

"Pharmaceutically acceptable salts" refer to salts of the compounds of the present disclosure, which are safe and effective when used in mammals, and have appropriate biological activity.

Detailed Description of Embodiments

The present disclosure will be further described below in conjunction with examples, but these examples are not meant to limit the scope of the present disclosure.

Examples

The structure of the compound of the present disclosure was determined by nuclear magnetic resonance (NMR) and/or liquid chromatography-mass spectrometry (LC-MS). NMR chemical shift (δ) was given in parts per million (ppm). NMR was determined using a Bruker AVANCE-400 nuclear magnetic instrument. The solvents for determination are deuterated dimethyl sulfoxide (DMSO-d_6), deuterated methanol (CD_3OD) and deuterated chloroform ($CDCl_3$), and the internal standard is tetramethylsilane (TMS).

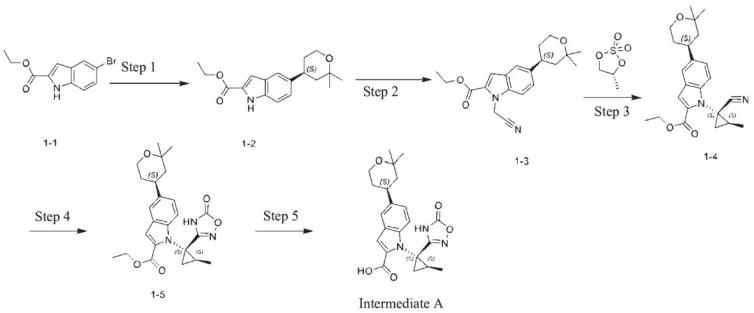
Agilent 1200 Infinity Series mass spectrometer was used for measurement by liquid chromatography-mass chromatography (LC-MS). HPLC determination used Agilent 1200DAD high-pressure liquid chromatograph instrument (Sunfire C18 150 × 4.6 mm chromatographic column) and Waters 2695-2996 high-pressure liquid chromatograph instrument (Gimini C18 150 × 4.6 mm chromatographic column).

Yantai Huanghai HSGF254 or Qingdao GF254 silica gel plate was used as a thin layer chromatography silica gel plate, with the specification for TLC being 0.15 mm - 0.20 mm and the specification for product separation and purification by thin layer chromatography being 0.4 mm - 0.5 mm. For the column chromatography, Yantai Huanghai silica gel of 200-300 mesh silica gel was generally used as a carrier.

The starting materials in the examples of the present disclosure were known and could be purchased on the market, or could be synthesized using or according to methods known in the art.

Unless otherwise specified, all reactions in the present disclosure were carried out under continuous magnetic stirring in a dry nitrogen or argon atmosphere, the solvent was a dry solvent, and the reaction temperature unit was degrees Celsius.

Intermediate A



Step 1: a zinc powder (4.88 g, 74.6 mmol) was suspended in DMF (20 mL), and the suspension was protected by nitrogen replacement. Chlorotrimethylsilane (1.01 g, 9.32 mmol) and 1,2-dibromoethane (1.75 g, 9.32 mmol) were added, and the resulting mixture was stirred at room temperature for 5 minutes. To the mixture was added dropwise a solution of 4-iodo-2,2-dimethyltetrahydropyran (13.43 g, 55.95 mmol) in DMF (25 mL), and the mixture was stirred at room temperature for 20 minutes. To the above solution were added palladium acetate (209 mg, 0.93 mmol), 4-(N,N-dimethylamino)phenyl]di-tert-butylphosphine (494 mg, 1.86 mmol), and ethyl 5-bromoindole-2-carboxylate (5.0 g, 18.65 mmol), and nitrogen gas was introduced into the container. The mixture was stirred with an external temperature of 50°C for 1 hour, and then the external temperature was reduced to 0°C and 5 N hydrochloric acid (6 mL) was added for neutralization. A 30% aqueous sodium chloride solution (50 mL) and ethyl acetate (300 mL) were added, and the insoluble matter was removed with diatomaceous earth. The filtrate was extracted with ethyl acetate, and the organic layer was washed with a 30% aqueous sodium chloride solution. Then, the resulting solution was dried over magnesium sulfate and passed through a filter, and the solvent was removed by evaporation under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 1) to obtain a product, which was subjected to chiral separation to obtain the product compound (1.96 g, yield 35%).

MS m/z (ESI): 302.2 [M+1].

Step 2: at room temperature, ethyl (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (1.96 g, 6.5 mmol) was dissolved in acetonitrile (30 mL), and potassium carbonate (2.70 g, 19.51 mmol) was added to the solution. With an external temperature of 10°C, to the resulting solution was added 2-chloroacetonitrile (736 mg, 9.75 mmol), and the solution was stirred for 12 hours. To the reaction solution were added saturated brine (50 mL) and ethyl acetate (100 mL) for extraction, and the aqueous layer was extracted a second time using ethyl acetate (20 mL). The combined organic layer was washed with saturated brine (50 mL), followed by concentration under reduced pressure with an external temperature of 40°C to obtain the target product, which was used in the subsequent step without purification.

MS m/z (ESI): 341.2 [M+1].

Step 3: ethyl (S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (2 g, 5.88 mmol) and (4R)-4-methyl-1,3,2-dioxathiolane 2,2-dioxide (2.43 g, 17.6 mmol) were dissolved in tetrahydrofuran (15 mL), and the mixture was cooled to 0°C. Under a nitrogen atmosphere, a solution of potassium bis(trimethylsilyl)amide in THF (23.5 mL, 23.5 mmol, 1M) was slowly added dropwise. The reaction mixture was stirred at 0°C for 2.5 hours, and then formic acid (3 mL) was added, and the mixture was extracted with ethyl acetate (40 mL). The organic layer was washed three times with water, twice with a saturated aqueous solution of sodium bicarbonate, and once with brine, and then dried over sodium sulfate. After filtration, the filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 4) to obtain the target product (1.20 g, yield 54%).

MS m/z (ESI): 381.2 [M+1].

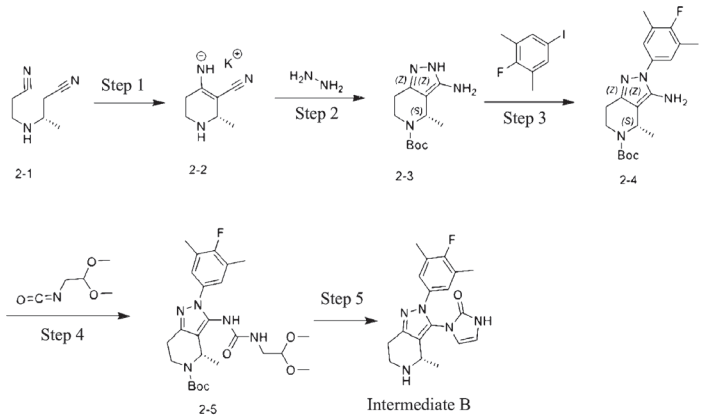
Step 4: to a solution of ethyl 1-((1S, 2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (1.20 g, 3.15 mmol) in dimethyl sulfoxide (DMSO) (10 mL) was added a 50% aqueous hydroxylamine solution (2.08 g, 31.5 mmol), and the mixture was stirred at room temperature for 17 hours. Ethyl acetate (50 mL) was added, and the mixture was washed with water (50 mL) and brine (50 mL), and then dried over magnesium sulfate. The mixture was filtered, then the filtrate was concentrated under reduced pressure, and the resulting residue was dissolved in DMSO (10 mL). Then, carbonyldiimidazole (1.02 g, 6.31 mmol) and 1,8-diazabicycloundec-7-ene (1.20, 7.88 mmol) were added, and the resulting mixture was stirred at room temperature for 0.5 hours. To the mixture was added formic acid, followed by purification by reverse phase chromatography (acetonitrile/water, 0.1% formic acid), to obtain the target product (0.96 g, yield 69%).

MS m/z (ESI): 440.2 [M+1].

Step 5: to a solution of ethyl 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylate (0.96 g, 2.18 mmol) in DMSO (8 mL) was added a 2M aqueous sodium hydroxide solution (3.28 mL, 6.55 mmol), and the mixture was stirred at room temperature for 1.5 hours. To the mixture was added formic acid, followed by purification by reverse phase chromatography (acetonitrile/water, 0.1% formic acid), to obtain the target product (0.65 g, yield 72%).

MS m/z (ESI): 412.2 [M+1].

Intermediate B



Step 1: to a solution of raw material 2-1 (2.4 g, 17.9 mmol) in tetrahydrofuran (THF) (20 mL) was added a solution of 1M potassium tert-butoxide in THF (17.9 mL), and the mixture was stirred at room temperature for 1 hour. The reaction mixture was filtered and washed with THF (50 mL), and then the filtrate was dried under reduced pressure to obtain intermediate 2-2 (2.7 g, yield 88%).

MS m/z (ESI): 138.1 [M+1].

Step 2: to a solution of hydrazine hydrochloride (1.06 g, 15.4 mmol) and intermediate 2-2 (2.7 g, 15.4 mmol) in ethanol (30 mL) was added 2 N hydrochloric acid (11.5 mL, 23.1 mmol), and the mixture was stirred at 50°C for 1 hour. The reaction mixture was cooled to 0°C, then a 5M aqueous sodium hydroxide solution (4.62 mL, 23.1 mmol) and di-tert-butyl dicarbonate (3.36g, 15.4mmol) were added, and the mixture was stirred at 0°C for 1 hour. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and then the organic layer was washed with brine and dried over anhydrous magnesium sulfate. After filtration, the filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (dichloromethane : methanol = 20 : 1) to obtain intermediate 2-3 (2.5 g, yield 65%).

MS m/z (ESI): 253.1 [M+1].

Step 3: intermediate 2-3 (2.5 g, 9.91 mmol), 2-fluoro-5-iodo-1,3-dimethylbenzene (2.48 g, 9.91 mmol), and L-proline (342.23 mg, 2.97 mmol) were dissolved in dimethyl sulfoxide (30 mL), and under nitrogen protection, cuprous iodide (754.82 mg, 3.96 mmol) and potassium carbonate (1.10 g, 7.93 mmol) were added. The mixture was stirred for reaction at 120°C for 19 hours. Saturated brine (150 mL) was added to the mixture to quench the reaction, followed by extraction with ethyl acetate (50 mL × 3). The organic phases were combined, washed with saturated brine (50 mL × 5), dried over anhydrous sodium sulfate, and concentrated under reduced pressure, successively. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 50 : 50), to obtain intermediate 2-4 (2.9 g, yield 78%).

MS m/z (ESI): 375.2 [M+1].

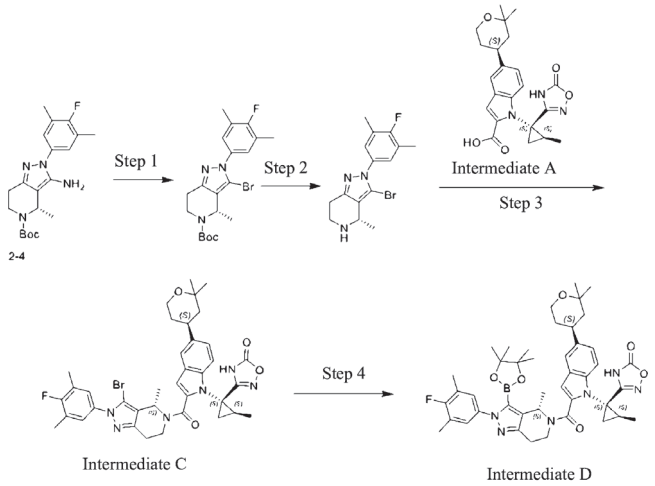
Step 4: to a solution of intermediate 2-4 (2.9 g, 7.4 mmol) in pyridine (10 mL) was added 2-isocyanato-1,1-dimethoxyethane (2.03 g, 15.49 mmol), and the mixture was stirred at room temperature. After 3 hours, diethylamine (1.13 g, 15.49 mmol) was added, and the mixture was stirred at room temperature for 5 minutes, and then water (50 mL) was added and the resulting mixture was stirred at room temperature for 20 minutes. The reaction mixture that had become a suspension was filtered, and the resulting solid was washed with water (20 mL) and then dried under reduced pressure to obtain intermediate 2-5 (3.6 g, yield 92%).

MS m/z (ESI): 506.3 [M+1].

Step 5: formic acid (40 mL) was added to intermediate 2-5 (3.6 g, 7.12 mmol), and the mixture was stirred at room temperature for 21 hours. The reaction mixture was concentrated under reduced pressure, and toluene was added, and the solvent was removed by evaporation under reduced pressure. The residue was dissolved with dichloromethane (10 mL), and then at room temperature, hydrogen chloride (a 4 M dioxane solution, 10 mL) was added and stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure. Toluene was added, and the solvent was removed by evaporation under reduced pressure to obtain a crude product (3.6 g).

MS m/z (ESI): 342.2 [M+1].

Intermediate C and intermediate D



Step 1: tert-butyl (S)-3-amino-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (2.5 g, 6.68 mmol) was dissolved in bromoform (8 mL), and under nitrogen protection, isoamyl nitrite (2.07 g, 20.03 mmol) was added. The mixture was stirred for reaction at 60°C for 2 hours. The mixture was concentrated under reduced pressure, and saturated brine (30 mL) was added to quench the reaction; and the mixture was extracted with ethyl acetate (50 mL), washed with saturated brine (50 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure, successively. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 50 : 50) to obtain the target product tert-butyl (S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (2.1 g, yield 72%).

MS m/z (ESI): 438.1, 440.1 [M+1].

Step 2: tert-butyl (S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (2.1 g, 4.79 mmol) was added to hydrogen chloride (a 4M dioxane solution, 20 mL) at room temperature and stirred at room temperature for 2 hours. The resulting crude product (S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine (1.7 g) was concentrated under reduced pressure, and the crude product was used directly in the next step.

MS m/z (ESI): 338.0, 340.0 [M+1].

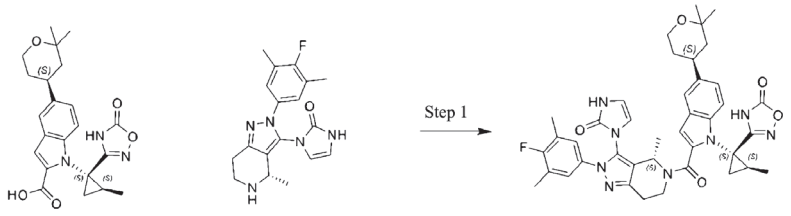
Step 3: (S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine hydrochloride (1.7 g, 4.54 mmol), intermediate A (526.84 mg, 4.54 mmol), and diisopropylethylamine (1.76 g, 13.61 mmol, 2.37 mL) were dissolved in N,N'-dimethylformamide (15 mL), and under nitrogen protection, 2-(7-azobenzotriazole)-N,N,N',N'-tetramethyluronium hexafluorophosphate (2.59 g, 6.81 mmol) was added. The mixture was stirred for reaction at 25°C for 12 hours. The crude reaction solution was separated by preparative high-performance liquid chromatography to give the product 3-((1S, 2S)-1-(2-((S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)-2-methylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one (2 g, yield 60%).

MS m/z (ESI): 731.2, 733.2 [M+1].

Step 4: 3-((1S, 2S)-1-(2-((S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)-2-methylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one (1 g, 1.37 mmol), bis(pinacolato)diboron (0.52 g, 2.05 mmol), and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium dichloromethane complex (100 mg, 137 μmol) were dissolved in 1'4-dioxane (30 mL), and under nitrogen protection, potassium acetate (335 mg, 3.42 mmol) was added. The mixture was stirred for reaction at 90°C for 12 hours. The mixture was concentrated under reduced pressure. The crude product was added into saturated brine (50 mL) to quench the reaction, and extracted with ethyl acetate (50 mL × 2), and the organic phases were combined, washed with saturated brine (50 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure, successively. The crude reaction solution was separated by preparative high-performance liquid chromatography to give the product (0.6 g, yield 56%).

MS m/z (ESI): 779.4 [M+1].

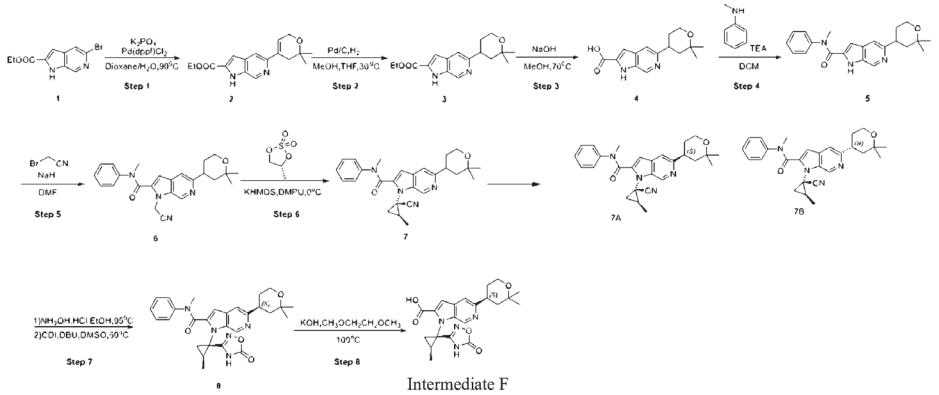
Intermediate E



Intermediate A Intermediate B Intermediate E

Step 1: The product was obtained by following step 3 for intermediate C and intermediate D.
MS m/z (ESI): 735.3 [M+1].

Intermediate F



Intermediate F

Step 1: ethyl 5-bromo-1H-pyrrolo[2,3-c]pyridine-2-carboxylate (5.0 g, 18.58 mmol, 1.0 eq.), 2-(6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8.6 g, 22.30 mmol, 1.2 eq.), K_3PO_4 (11.8 g, 55.75 mmol, 3.0 eq.), and $Pd(dppf)Cl_2$ (1.52 g, 1.86 mmol, 0.1 eq.) were successively added to a 500 ml three-necked flask, then dioxane (100 mL) and H_2O (20 mL) were added, nitrogen replacement was performed three times, and the mixture was reacted under reflux for 12 h. After raw materials were completely reacted as detected by LCMS, the reaction solution was cooled to room temperature, and 100 mL H_2O was added to the system for extraction and layering; and the aqueous phase was extracted with ethyl acetate (100 mL × 3), and the organic phases were combined, washed with saturated brine (100 mL × 2), dried over anhydrous sodium sulfate, filtered and concentrated. The resulting crude product was purified by silica gel column chromatography to obtain a product 2 (4.18 g, 74.90% yield) as a yellow oily compound.

MS m/z (ESI): 301.1 [M+1].

Step 2: the product 2 (4.0 g, 13.32 mmol, 1.0 eq.) was dissolved in a mixed solution of anhydrous methanol (20 mL) and THF (20 mL), Pd/C (0.4 g, 10% w/w) was added to the system, and the system was subjected to nitrogen replacement 3 times and then hydrogen replacement 3 times, followed by catalytic hydrogenation using a hydrogen balloon at 30°C for 10 hours. After raw materials were completely reacted as monitored by LCMS, Pd/C was filtered off using diatomaceous earth, and the filtrate was concentrated to dryness at 45°C to obtain a product 3 (4 g, 99.32% yield) as a pale yellow oil.

MS m/z (ESI): 303.1 [M+1].

Step 3: the product 3 (4.0 g, 13.23 mmol, 1.0 eq.) and sodium hydroxide solution (14.6 ml, 29.11 mmol, 2N, 2.2 eq.) were dissolved in methanol (40 mL), and the system was allowed to react at 70°C for 3 hours. The reaction solution was cooled to room temperature, and the aqueous phase was washed with ethyl acetate (50 mL x 3), then adjusted to pH 5 with hydrochloric acid (3 N), then extracted with ethyl acetate (50 mL x 3), washed with saturated brine (20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. Thus, a product 4 (2.72 g, 74.98% yield) as an off-white solid was obtained.

MS m/z (ESI): 275.1 [M+1].

Step 4: the product 4 (2.0 g, 7.29 mmol) was added to a 100 mL single-necked bottle, then 20 mL of toluene was added, and under nitrogen protection, oxalyl chloride (1.85 g, 14.58 mmol, 2.0 eq.) and 2 drops of anhydrous DMF were added slowly at room temperature. After the addition was completed, the system was allowed to react at 100°C for 2 hours. The reaction solution was concentrated to dryness, then anhydrous dichloromethane (100 ml) was added, and N-methylaniline (1.56 g, 14.58 mmol, 2.0 eq.) was slowly added to the reaction system; after the addition was completed, triethylamine (1.48 g, 14.58 mmol, 2.0 eq.) was slowly added dropwise; and after the addition was completed, the system was allowed to react at 300°C for 8 hours. After the reaction was completed as monitored by LCMS, H2O (50 ml) was added to the reaction system, followed by extraction with dichloromethane (100 mL x 3); and the organic phases were combined, washed with saturated brine (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The resulting residue was purified by silica gel column chromatography to obtain the target product (1.58 g, 59.63% yield) as a yellow oil.

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MS m/z (ESI): 364.2 [M+1].

Step 5: the product 5 (1.5 g, 4.13 mmol, 1.0 eq.) was dissolved in 15 ml anhydrous DMF, and under nitrogen protection, the system was cooled in an ice bath to 0°C, and then NaH (495 mg, 12.38 mmol, 3.0 eq.) was added slowly; after the addition was completed, the system was stirred for reaction at 0°C for 0.5 hours, and bromoacetonitrile (2.48 g, 20.65 mmol, 5.0 eq.) was added slowly; and after the addition was completed, the system was allowed to react at 30°C for 8 hours. To the reaction system were added ethyl acetate and water, followed by extraction with ethyl acetate (50 mL x 3); and the organic phases were combined, washed with saturated brine (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The resulting residue was purified by silica gel column chromatography to obtain the target product (997 mg, 60% yield) as a yellow foamy solid.

MS m/z (ESI): 403.2 [M+1].

Step 6: the product 6 (900 mg, 2.24 mmol, 1.0 eq.) and (R)-4-methyl-1,3,2-dioxathiane 2,2-dioxide (1.08 g, 7.84 mmol, 3.5 eq.) were dissolved in DMPU (20 mL), the system was cooled in an ice bath to 0°C, and then KHMDS (22.4 mmol, 10.0 eq., 1M in THF) was slowly added dropwise; and after the dropwise addition was completed, the system was held at the temperature for reaction for 5 hours. To the reaction system were added ethyl acetate and water, followed by extraction with ethyl acetate (50 mL x 3); and the organic phases were combined, washed with saturated brine (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The resulting residue was purified by silica gel column chromatography to obtain the target product (496 mg, 50% yield) as a yellow foamy solid.

MS m/z (ESI): 443.2 [M+1].

7 was chirally resolved to obtain 7A and 7B

MS m/z (ESI): 443.2 [M+1].

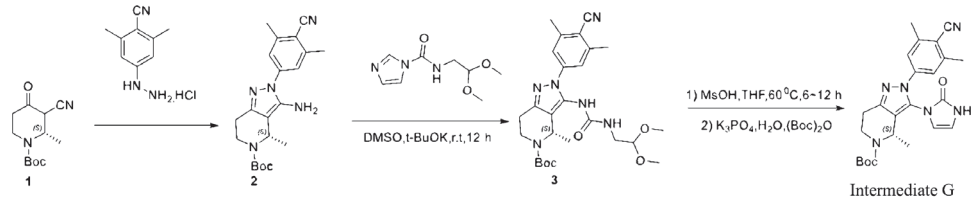
Step 7: the product 7A (450 mg, 1.02 mmol, 1.0 eq.), hydroxylamine hydrochloride (354 mg, 5.10 mmol, 5.0 eq.), K_2CO_3 (775 mg, 5.61 mmol, 5.5 eq.) and anhydrous ethanol (25 mL) were successively added to a 100 mL single-necked bottle, and the system was allowed to react at 95°C for 5 hours. The reaction solution was concentrated to dryness, then anhydrous THF (30 ml) was added, the mixture was stirred until the solution was clear, and the insoluble matter was filtered off; and N,N'-carbonyldiimidazole (364 mg, 2.24 mmol, 2.2 eq.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (466 mg, 3.06 mmol, 3.0 eq.) were added to the filtrate. The reaction mixture was stirred at 50°C for three hours. The reaction solution was concentrated to dryness, and then the resulting residue was purified by silica gel column chromatography to obtain a product 8 (417 mg, 81.6% yield) as a pale yellow solid.

MS m/z (ESI): 502.2 [M+1].

Step 8: the product 8 (400 mg, 0.80 mmol, 1.0 eq.) was dissolved in ethylene glycol dimethyl ether (20 mL), KOH (404 mg, 7.2 mmol, 9.0 eq.) was added, and the system was allowed to react at 100°C for 5 hours. The reaction solution was concentrated to dryness. The resulting residue was purified by silica gel column chromatography to obtain the target product (200 mg, 60.60% yield) as a yellow solid.

MS m/z (ESI): 413.2 [M+1].

Intermediate G



Intermediate G

Step 1: To a bottle were added tert-butyl (2S)-3-cyano-2-methyl-4-carbonylpiperidine-1-carboxylate (2 g, 8.4 mmol), toluene (20 mL, 10 v), 4-hydrazino-2,6-dimethylbenzonitrile hydrochloride (1.65 g, 8.4 mmol), and pyridine hydrochloride (485 mg, 4.2 mmol); and after the addition was completed, the system was heated to 96°C under nitrogen protection and stirred overnight. After the reaction was completed, water was added, and the mixture was extracted with ethyl acetate (50 mL * 3); and the organic phase was dried with Na_2SO4, and the residue was purified by silica gel column chromatography (PE : EA = 1 : 1) to obtain a product (1.32 g, yield 41.3%).

MS m/z (ESI): 382.2 [M+1].

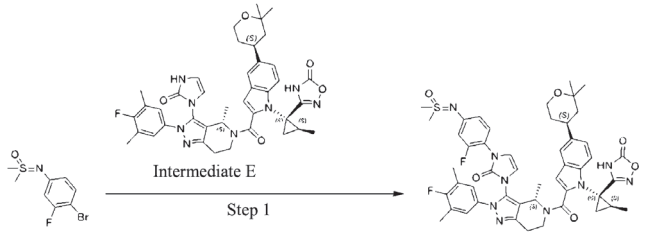
Step 2: To a bottle were added compound 2 (1.22 g, 3.2 mmol), dimethyl sulfoxide (30 ml, 15 v), N-(2,2-dimethoxyethyl)-1H-imidazole-1-carboxamide (766 mg, 3.8 mmol), and potassium tert-butoxide (1.29 g, 11.6 mmol), and the system was subjected to nitrogen replacement and then stirred at room temperature overnight. After the reaction was completed as detected by LC-MS, water was added to the reaction solution, and the mixture was extracted with ethyl acetate (80 mL * 3); and the organic phase was dried with Na_2SO_4, and the residue was purified by silica gel column chromatography (PE : EA = 3 : 1) to obtain a product (1.08 g, yield 65.8%).

MS m/z (ESI): 513.2 [M+1].

Step 3: To a bottle were added compound 3 (500 mg, 0.98 mmol), tetrahydrofuran (15 ml, 30 v), and MsOH (470.4 mg, 4.90 mmol); and after the addition was completed, the system was subjected to nitrogen replacement, and heated to 60°C for reaction for 6 hours, with LC-MS detecting no compound 3. The system was cooled to room temperature, and potassium phosphate (1.67 g, 7.84 mmol) was added to the reaction solution; and after the reaction system was detected to be alkaline, Boc anhydride (320 mg, 1.47 mmol) was added. The system was stirred at room temperature for 2 hours, water was added to the reaction solution, and the mixture was extracted with ethyl acetate (80 mL * 3); and the organic phase was dried with Na_2SO_4, and the residue was purified by silica gel column chromatography (PE : EA = 3 : 1) to obtain a product (380 mg, yield 86.5%).

MS m/z (ESI): 449.2 [M+1].

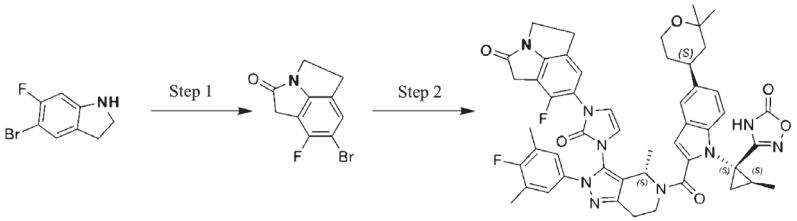
Example 1



Step 1: At room temperature, to a suspension of intermediate E (20 mg, 0.027 mmol), ((4-bromo-3-fluorophenyl)imino)dimethyl-6-thione (14.5 mg, 0.054 mmol), (1S, 2S)-1-N, 2-N-dimethylcyclohexane-1,2-diamine (1.9 mg, 0.013 mmol), and potassium carbonate (11.3 mg, 0.082 mmol) in N-methylpyrrolidone (0.5 mL) was added cuprous(I) iodide (1.0 mg, 0.0054 mmol), and the mixture was stirred at 130°C for 3 hours under a nitrogen atmosphere. The reaction mixture was purified by reverse phase silica gel chromatography (acetonitrile/water, 0.1% formic acid) to obtain the target compound (10 mg, yield 40%).

MS m/z (ESI): 920.3 [M+1].

Example 2



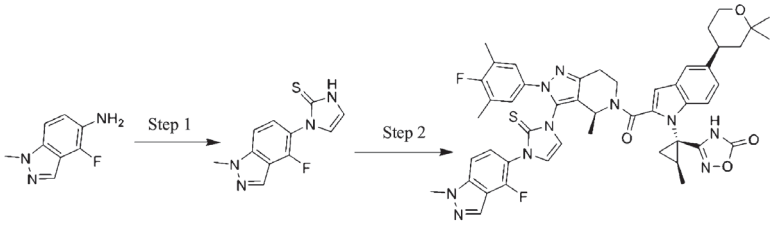
Step 1: 5-bromo-6-fluoroindoline was used as a raw material, and the target product was obtained according to Journal of Organic Chemistry, 1992, vol. 57, #8, p. 2508-2511.

MS m/z (ESI): 256.0, 258.0 [M+1].

Step 2: Following Example 1, the target product was obtained.

MS m/z (ESI): 910.4 [M+1].

Example 3



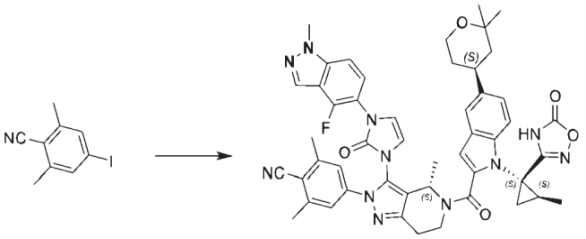
Step 1: 4-fluoro-1-methyl-1H-indazol-5-amine was used as a raw material, and the target product was obtained according to New Journal of Chemistry, 2014, vol. 38, #9, p. 4071-4082.

MS m/z (ESI): 249.1 [M+1].

Step 2: intermediate C was used as a raw material, and the target product was obtained following Example 1.

MS m/z (ESI): 899.4 [M+1].

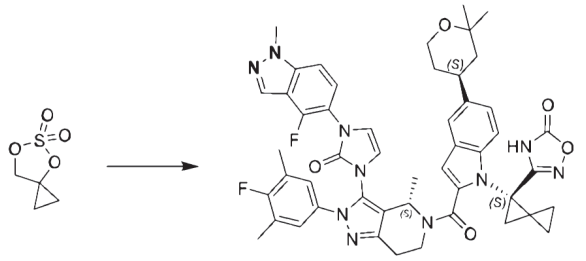
Example 4



Step 1: following step 3 of intermediate B, 4-iodo-2,6-dimethylbenzonitrile was used instead of 2-fluoro-5-iodo-1,3-dimethylbenzene to synthesize an intermediate, and then following intermediate E and Example 1 (5-bromo-4-fluoro-1-methyl-1H-indazole was used instead of ((4-bromo-3-fluorophenyl)imino)dimethyl-6-thione), the target product was synthesized.

MS m/z (ESI): 890.4 [M+1].

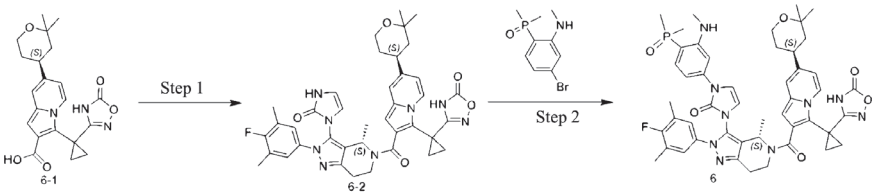
Example 5



Step 1: following step 3 of intermediate A, 4,6-dioxa-5-thiaspiro[2.4]heptane 5,5-dioxide was used instead of (4R)-4-methyl-1,3,2-dioxathiolane 2,2-dioxide to synthesize an intermediate, and then following intermediate E and Example 1 (5-bromo-4-fluoro-1-methyl-1H-indazole was used instead of ((4-bromo-3-fluorophenyl)imino)dimethyl-6-thione), the target product was synthesized.

MS m/z (ESI): 895.4 [M+1].

Example 6



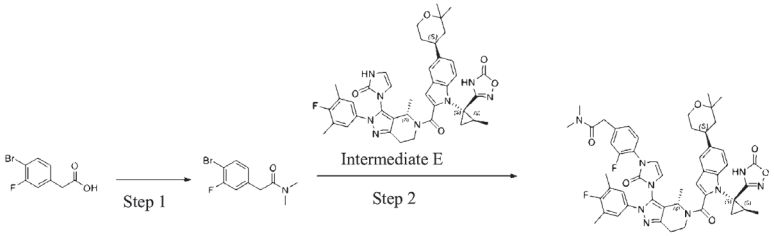
Step 1: 6-1 was used as a raw material, and 6-2 was obtained by following step 3 of intermediate C and intermediate D.

MS m/z (ESI): 721.3 [M+1].

Step 2: (4-bromo-2-(methylamino)phenyl)dimethylphosphine oxide was used, following Example 1, to obtain the target product 6.

MS m/z (ESI): 902.4 [M+1].

Example 7



Step 1: 2-(4-bromo-3-fluorophenyl)-N,N-dimethylacetamide

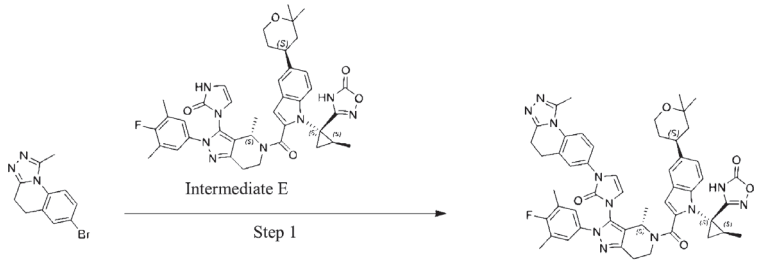
At room temperature, 2-(4-bromo-3-fluorophenyl)acetic acid (2.33 g, 10 mmol) was dissolved in N,N-dimethylformamide (30 mL), and then dimethylamine hydrochloride (0.98 g, 12 mmol) and triethylamine (4.05 g, 40 mmol), were added, followed by 2-(7-azobenzotriazole)-N,N,N',N'-tetramethyluronium hexafluorophosphate (5.7 g, 15 mmol); the mixture was stirred at room temperature overnight, with LCMS indicating the completion of the reaction; the reaction solution was diluted with ethyl acetate (60 mL), and then washed with saturated brine (15 mL×4); and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography (PE : EA = 1 : 1), to obtain the target product as a white solid (1.30 g, yield 50%).

MS m/z (ESI): 260.0, 262.0 [M+H]+.

Step 2: 2-(4-bromo-3-fluorophenyl)-N,N-dimethylacetamide and intermediate E were used as raw materials, and the target product was obtained following Example 1.

MS m/z (ESI): 914.4 [M+H]+.

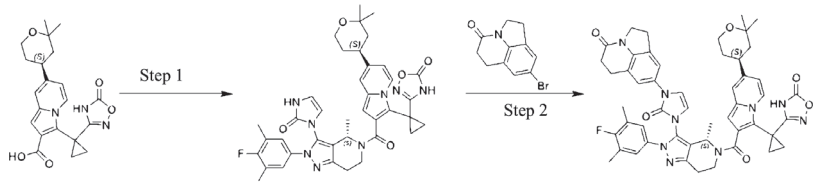
Example 8



Step 1: 7-bromo-1-methyl-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline and intermediate E are used as raw materials, and the target product was obtained following Example 1.

MS m/z (ESI): 918.4 [M+H]+.

Example 9



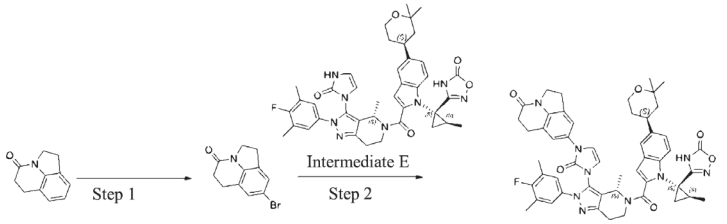
Step 1: The product was obtained by following step 3 for intermediate C and intermediate D.

MS m/z (ESI): 721.3 [M+1].

Step 2: 8-bromo-5,6-dihydro-1H-pyrrolo[3,2,1-ij]quinoline-4(2H)-one was used as a raw material, and the target product was obtained following Example 1.

MS m/z (ESI): 892.4 [M+1].

Example 10



Step 1: at 0°C, 1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinoline-4-one (1.73 g, 10 mmol) was dissolved in N,N-dimethylformamide (12 mL), and then N-bromosuccinimide (1.96 g, 11 mmol) in N,N-dimethylformamide (20 mL) was added dropwise, followed by stirring at room temperature for 2 hours; the reaction solution was quenched with water (60 mL), and then extracted with ethyl acetate (25 mL × 3); and

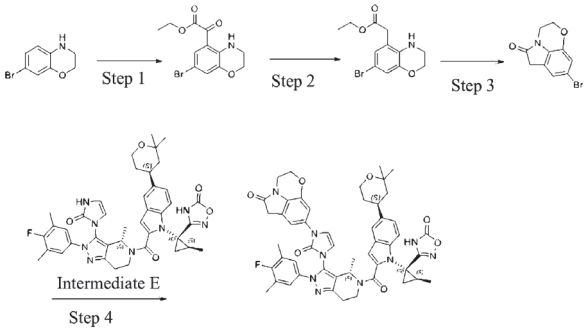
the organic phases were combined, washed with saturated brine (25 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried, and the crude product was crystallized with acetone/water, to obtain the target product as a yellow solid (1.89 g, yield 75%).

MS m/z (ESI): 252.1, 254.1 [M+H]+.

Step 2: 8-bromo-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinoline-4-one and intermediate E were used as raw materials, and the target product was obtained following Example 1.

MS m/z (ESI): 906.4 [M+H]+.

Example 11



Step 1: Under an ice bath, ethyl oxalyl monochloride (1.64 g, 12 mmol) was dissolved in dichloromethane (20 mL), and then aluminum trichloride (8.0 g, 60 mmol) was added; the mixture was stirred under the ice bath for 30 minutes, then 7-bromo-3,4-dihydro-2H-benzo[b][1,4]oxazine (2.14 g, 10 mmol) was added, and the mixture was stirred at room temperature for 2 hours, with LCMS indicating the generation of the target product; the reaction solution was quenched with a 10% aqueous sodium hydroxide solution, and filtered; the filter residue was washed with dichloromethane, and the organic phase was washed with a saturated sodium bicarbonate solution (25 mL × 2) and saturated brine (25 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography to obtain the target product (0.31 g, yield 10%).

MS m/z (ESI): 314.1, 316.1 [M+H]+.

Step 2: at room temperature, ethyl 2-(7-bromo-3,4-dihydro-2H-benzo[b][1,4]oxazin-5-yl)-2-carbonyl acetate (0.31 g, 1 mmol) was dissolved in trifluoroacetic acid (5 mL), then triethylsilane (0.23 g, 2 mmol) was added, and the system was heated to 60°C for reaction for 2 hours, with LCMS indicating the completion of the reaction; the system was cooled to room temperature and spin-dried, and the residue was diluted with ethyl acetate (20 mL), and then washed with a saturated sodium bicarbonate solution (25 mL × 2) and saturated brine (25 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was used directly in the next step.

MS m/z (ESI): 300.1, 302.1 [M+H]+.

Step 3: at room temperature, ethyl 2-(7-bromo-3,4-dihydro-2H-benzo[b][1,4]oxazin-5-yl)acetate (0.30 g, 1 mmol) was dissolved in ethanol (5 mL), then acetic acid (0.2 mL) was added, and the system was heated to 80°C for reaction for 2 hours and cooled to room temperature, with LCMS indicating the generation of the target product; the system was spin-dried, and the residue was dissolved with ethyl acetate (20 mL), and then washed with a saturated sodium bicarbonate solution (25 mL × 2) and saturated brine (25 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography to obtain the target product 11-3 (0.05 g, yield 20%).

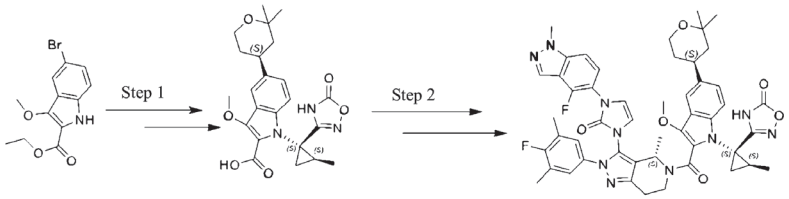
MS m/z (ESI): 254.1, 256.1 [M+H]+.

Step 4: 8-bromo-2,3-dihydro-[1,4]oxaazino[2,3,4-hi]indole-5(6H)-one and intermediate E were used as raw materials, and the target product 11 was obtained following Example 1.

MS m/z (ESI): 908.4 [M+H]+.

Example 12

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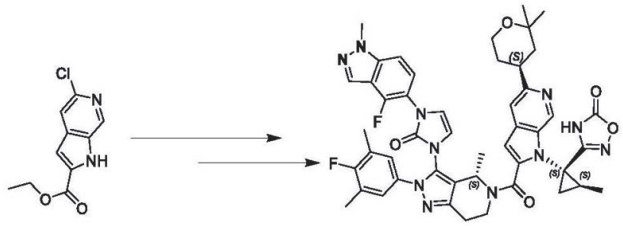
Step 1: ethyl 5-bromo-3-methoxyindole-2-carboxylate was used as a raw material, and the target product was obtained following intermediate A

MS m/z (ESI): 442.2 [M+1].

Step 2: following step 3 for intermediate C and intermediate D, a product was obtained, and then 5-bromo-4-fluoro-1-methyl-1H-indazole was used as a raw material to obtain the target product by following Example 1.

MS m/z (ESI): 913.4 [M+1].

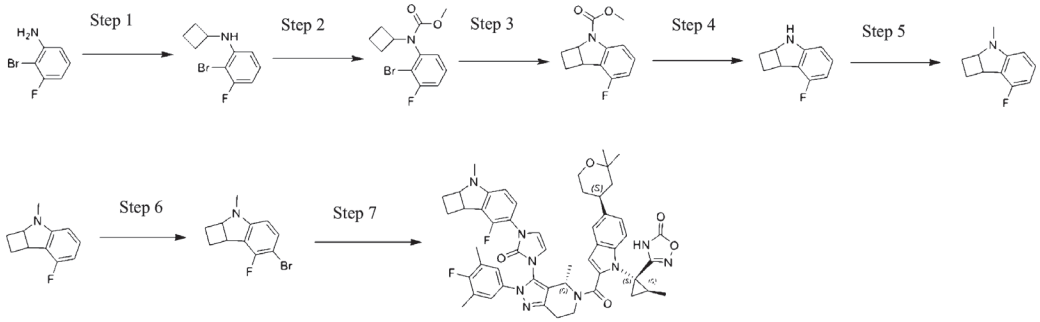
Example 13



Ethyl 5-chloro-1H-pyrrolo[2,3-c]pyridine-2-carboxylate was used as a raw material to obtain the target product by following Example 12.

MS m/z (ESI): 884.4 [M+1].

Example 14



Step 1: 2-bromo-3-fluoroaniline was used as a raw material to obtain the target product according to MERCK & CO INC-WO 2020/96871, 2020, A1.

MS m/z (ESI): 244.0 [M+1].

Step 2: 2-bromo-N-cyclobutyl-3-fluoroaniline was used as a raw material to obtain the target product according to MERCK & CO INC-WO 2020/96871, 2020, A1.

MS m/z (ESI): 302.0 [M+1].

Step 3: methyl (2-bromo-3-fluorophenyl)(cyclobutyl)carbamate was used as a raw material to obtain the target product according to Bioorganic and Medicinal Chemistry Letters, 2021, vol. 47.

MS m/z (ESI): 222.0 [M+1].

Step 4: methyl 7-fluoro-1,2,2a,7b-tetrahydro-3H-cyclobutadieno[b]indole-3-carboxylate was used as a raw material to obtain the target product according to Tetrahedron, 2015, vol. 71, #37, art.no. 26568, p. 6499-6505.

MS m/z (ESI): 164.0 [M+1].

Step 5: 7-fluoro -2,2a,3,7b-tetrahydro-1H-cyclobutadieno[b]indole was used as a raw material to obtain the target product according to European Journal of Medicinal Chemistry, 2020, vol. 190.

MS m/z (ESI): 178.1 [M+1].

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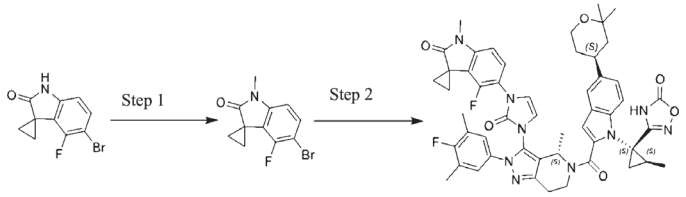
Step 6: 7-fluoro -3-methyl -2,2a,3,7b-tetrahydro-1H-cyclobutadieno[b]indole was used as a raw material to obtain the target product according to Chemistry - A European Journal, 2022, vol. 28, #2, art.no. E202103135.

MS m/z (ESI): 256.0 [M+1].

Step 7: 6-bromo-7-fluoro-3-methyl-2,2a,3,7b-tetrahydro-1H-cyclobutadieno[b]indole and intermediate E were used as raw materials to obtain the target product, following Example 1.

MS m/z (ESI): 910.4 [M+1].

Example 15



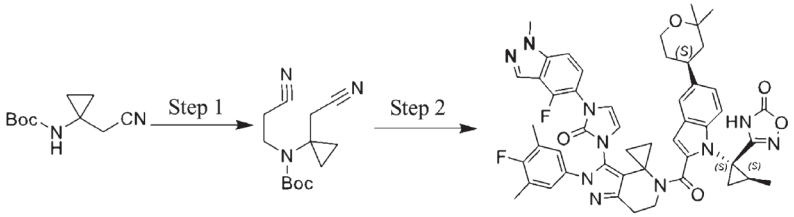
Step 1: 5'-bromo-4'-fluorospiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material to obtain the target product according to European Journal of Medicinal Chemistry, 2020, vol. 190.

MS m/z (ESI): 269.9 [M+1].

Step 2: Intermediate E was used as a raw material to obtain the target product, following Example 1.

MS m/z (ESI): 924.3 [M+1].

Example 16



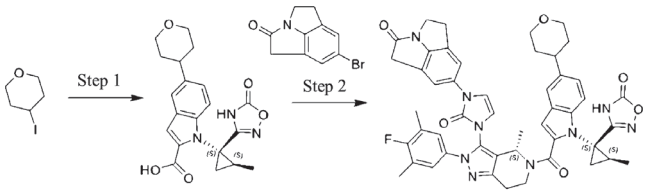
Step 1: tert-butyl (1-(cyanomethyl)cyclopropyl)carbamate (5 g, 25.48 mmol) and 3-bromopropanenitrile (3.41 g, 25.48 mmol) were dissolved in acetonitrile (100 mL), and potassium carbonate (10.56 g, 76.43 mmol) was added under nitrogen protection. The mixture was stirred for reaction at 25°C for 12 hours. The reaction solution was evaporated to dryness, and to the crude product was added saturated brine (130 mL), followed by extraction with ethyl acetate (80 mL × 2); and the organic phases were combined, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain tert-butyl (2-cyanoethyl)(1-(cyanomethyl)cyclopropyl)carbamate (6 g, yield: 94.46%).

MS m/z (ESI): 250.2 [M+1].

Step 2: tert-butyl (1-(cyanomethyl)cyclopropyl)carbamate was used as a raw material to obtain the target product, following intermediate B, intermediate E, and Example 1.

MS m/z (ESI): 895.4 [M+1].

Example 17



Step 1: 4-iodotetrahydro-2H-pyran was used as a raw material, following intermediate A, to synthesize 1-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-(tetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid.

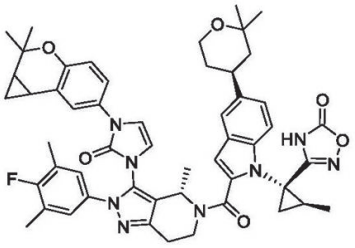
MS m/z (ESI): 384.2 [M+1].

Step 2: 7-bromo-4,5-dihydropyrrolo[3,2,1-hi]indole-2(1H)-one was used as a raw material to synthesize the target compound, following Example 1.

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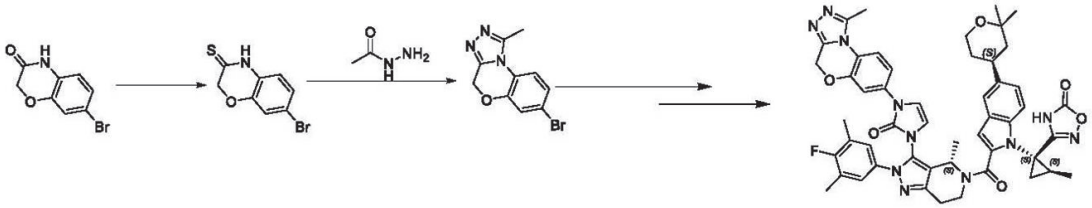
MS m/z (ESI): 864.4 [M+1].

Example 18



6-bromo-2,2-dimethyl-1,1a,2,7b-tetrahydrocyclopropeno[c]chromene was used as a raw material, and the target product was obtained following Example 1. MS m/z (ESI): 907.4 [M+1].

Example 19



Step 1: a mixture of 7-bromo-2H-benzo[b][1,4]oxazine-3(4H)-one (3 g, 13.16 mmol), a Lawesson reagent (3.19 g, 7.89 mmol), and toluene (100 mL) was stirred at 110°C for 1 hour, cooled, directly concentrated with silica gel, and separated by column chromatography (PE/EtOAc = 10 : 1), to obtain a pale yellow solid (600 mg, yield: 18%)

MS m/z (ESI): 244.0 246.0 [M+1].

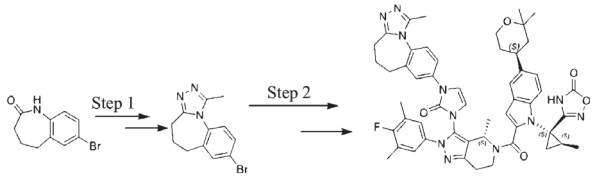
Step 2: A mixture of 7-bromo-2H-benzo[b][1,4]oxazine-3(4H)-thione (300 mg, 1.23 mmol), acetylhydrazine (109 mg, 1.47 mmol), and n-butanol (10mL) was stirred at 120°C for 24 hours, cooled, directly concentrated with silica gel, and separated by column chromatography (DCM/MeOH = 10 : 1), to obtain the target product (190 mg, yield: 58%)

MS m/z (ESI): 266.0 268.0 [M+1].

Step 3: 7-bromo-1-methyl-4H-benzo[b][1,2,4]triazolo[4,3-d][1,4]oxazine was used as a raw material to obtain the target product, following Example 1.

MS m/z (ESI): 920.4 [M+1].

Example 20



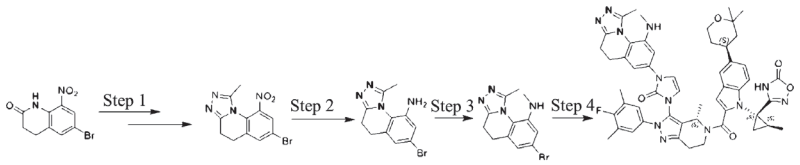
Step 1: 7-bromo-1,3,4,5-tetrahydro-2H-1-benzoazepine-2-one was used as a raw material, following steps 1 and 2 in Example 19, to obtain 8-bromo-1-methyl-5,6-dihydro-4H-benzo[f][1,2,4]triazolo[4,3-a]azepine

MS m/z (ESI): 278.0 280.0 [M+1].

Step 2: 8-bromo-1-methyl-5,6-dihydro-4H-benzo[f][1,2,4]triazolo[4,3-a]azepine was used as a raw material to obtain the target product, following Example 1

MS m/z (ESI): 932.4 [M+1].

Example 21



Step 1: 6-bromo-8-nitro-3,4-dihydroquinoline-2(1H)-one was used as a raw material, following Example 1, to obtain the target product.

MS m/z (ESI): 309.0 311.0 [M+1].

Step 2: To a solution of 7-bromo-1-methyl-9-nitro-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline (2 g, 6.49 mmol) in ethanol (20 mL) and water (15 mL) was added sodium dithionite (9.03 g, 51.92 mmol), and the mixture was stirred at room temperature for 12 hours, and filtered; the filter cake was washed with EtOH, and water was added to filtrate, followed by extraction with EtOAc; and the organic phases were combined, washed with saturated brine, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated under reduced pressure to dryness, to obtain 21-3 (1.5 g, yield: 83.1%)

MS m/z (ESI): 279.0 281.0 [M+1].

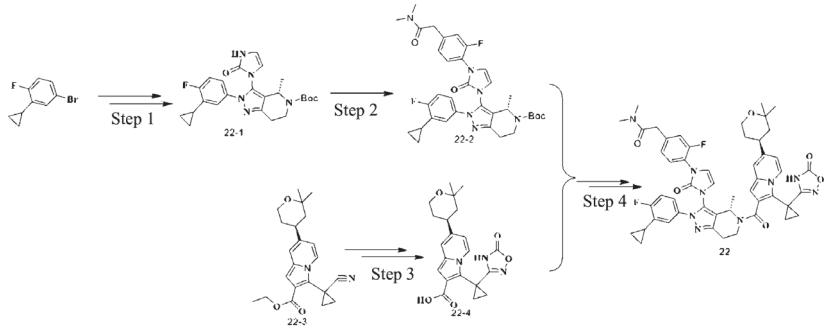
Step 3: To a solution of 7-bromo-1-methyl-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline-9-amine (600 mg, 2.16 mmol) in DMF (10 mL) was added NaH (130 mg, 3.24 mmol, 60% purity), and the mixture was stirred at room temperature for 30 minutes, and then iodomethane (457 mg, 3.24 mmol) was added dropwise and stirred at room temperature for 1 hour; water was added, followed by extraction with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; the filtrate was concentrated to dryness under reduced pressure and separated by column chromatography, to obtain a pale yellow oil 21-4 (300 mg, yield: 47.6%)

MS m/z (ESI): 293.0 295.0 [M+1].

Step 4: 7-bromo-N, 1-dimethyl-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline-9-amine was used as a raw material to obtain the target product, with reference to Example 1.

MS m/z (ESI): 947.4 [M+1].

Example 22



Step 1: 4-bromo-2-cyclopropyl-1-fluorobenzene was used as a raw material, and a product 22-1 was obtained by following the synthesis in steps 3 to 5 for intermediate B.

MS m/z (ESI): 454.2 [M+1].

Step 2: 22-1 and 2-(4-bromo-3-fluorophenyl)-N,N-dimethylacetamide were used as raw materials, and a product 22-2 was obtained by following the synthesis steps in Example 1.

MS m/z (ESI): 633.3 [M+1].

Step 3: 22-3 was used as a raw material, and a product 22-4 was obtained by following the synthesis steps 4 and 5 for intermediate A.

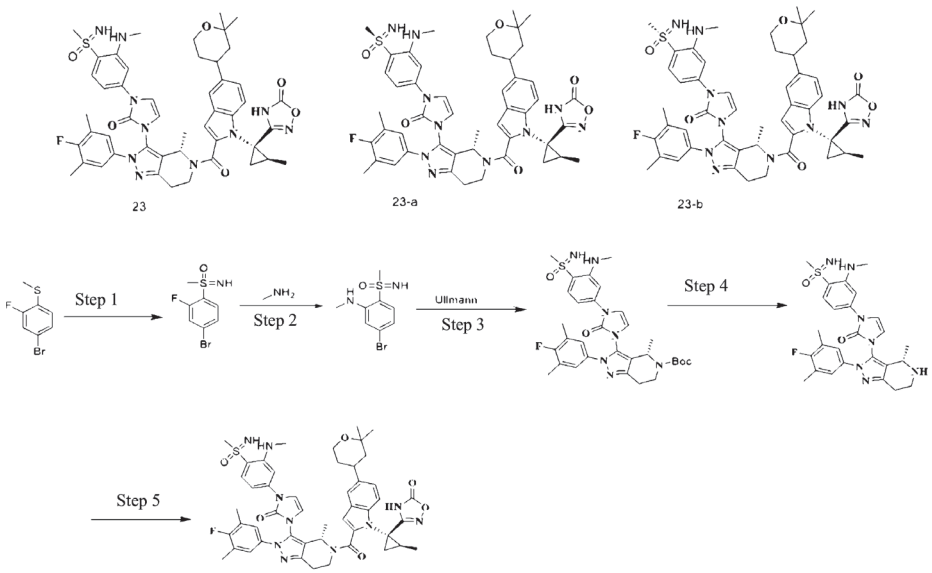
MS m/z (ESI): 398.2 [M+1].

Step 4:

22-2 and 22-4 were used as raw materials, and a product 22 was obtained by following the synthesis in steps 2 and 3 for intermediate C.

MS m/z (ESI): 912.4 [M+1].

Example 23



Step 1: To a solution of 4-bromo-2-fluoro-1-methylsulfanyl-benzene (2 g, 9.05 mmol) in methanol (100 mL) were added successively ammonium carbamate (2.82 g, 36.18 mmol) and [di(acetoxy)iodo]benzene (8.74 g, 27.14 mmol), and the mixture was then stirred at room temperature for half an hour, and water was added, followed by extraction with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure, and separated by column chromatography (DCM/MeOH = 10 : 1) to obtain a pale yellow oil (2 g, yield: 87.7%)

MS m/z (ESI): 252.0, 254.0M+H]+.

Step 2: A mixture of (4-bromo-2-difluorophenyl)(imino)(methyl)-l6-sulfanone (400 mg, 1.59 mmol), methylamine hydrochloride (214 mg, 3.17 mmol), potassium carbonate (657 mg, 4.76 mmol) and DMF (10 mL) was stirred at 120°C for 3 hours, and water was added, followed by extraction with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure and separated by column chromatography (DCM/MeOH = 10 : 1) to obtain a pale yellow oil (200 mg, yield: 47.9%)

MS m/z (ESI): 263.0 265.0 [M+H]+

Step 3: (4-bromo-2-(methylamino)phenyl)(imino)(methyl)-l6-sulfanone was used as a raw material to obtain a product, following Example 1.

MS m/z (ESI): 624.3 [M+H]+

Step 4: To a solution of tert-butyl (4S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(3-(methylamino)-4-(S-methylsulfonimidoyl)phenyl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4, 3-c]pyridine-5-carboxylate (60 mg, 96.19 μmol) in DCM (3 mL), TFA (1 mL) was added dropwise, and the mixture was stirred at room temperature for 0.5 hours and spin-dried; saturated NaHCO3 was added to adjust pH = 10, followed by extraction with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure to obtain a pale yellow oil (50 mg, crude)

MS m/z (ESI): 524.2 [M+H]+

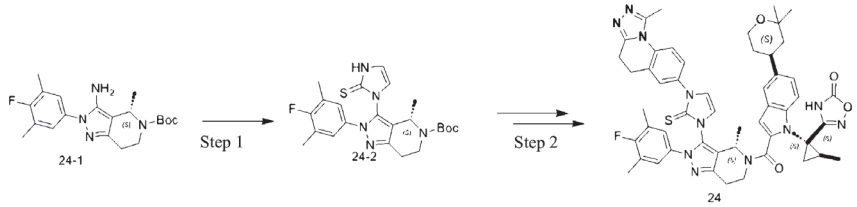
Step 5: To a solution of 1-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-3-(3-(methylamino)-4-(S-methylsulfonimidoyl)phenyl)-1,3-dihydro-2H-imidazole-2-one (23.57 mg, 57.29 μmol) and intermediate A (30 mg, 57.29 μmol) in DMF (3 mL), HATU (43.23 mg, 114.59 μmol) and DIEA (22 mg, 171.88 μmol) were added, the mixture was stirred at room temperature for 16 hours, and water was added, followed by extraction with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure to obtain a pale yellow oil, which was separated by preparative chromatography (acid) to obtain the target product **23** (9 mg, yield: 16.7%)

MS m/z (ESI): 917.4 [M+H]+

The product 23 was chirally resolved to obtain target products 23-a and 23-b

MS m/z (ESI): 917.4 [M+H]+.

Example 24



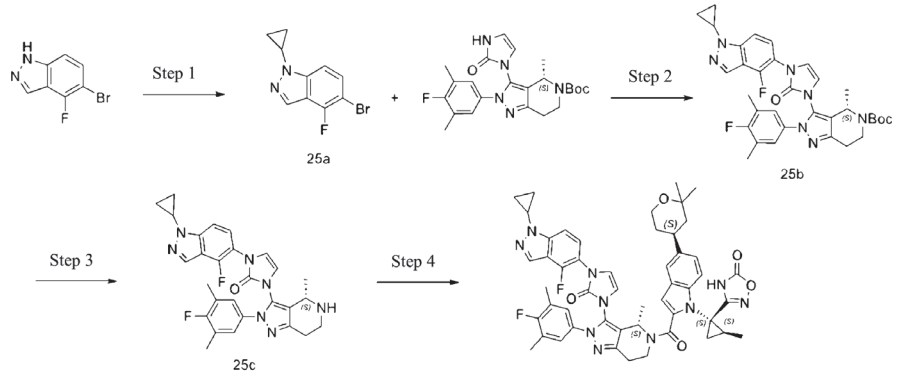
Step 1: 24-1 was used as a raw material, and a product 24-2 was obtained by following the synthesis step 1 in Example 3.

MS m/z (ESI): 458.2 [M+1].

Step 2: 24-2 was used as a raw material, and the title product 24 was obtained following the synthesis steps in intermediate E and Example 1 (with ((4-bromo-3-fluorophenyl)imino)dimethyl-6-thione in Example 1 being replaced with 7-bromo-1-methyl-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline).

MS m/z (ESI): 934.4 [M+1].

Example 25



Step 1: 5-bromo-4-fluoro-1H-indazole (200 mg, 0.93 mmol), cyclopropylboronic acid (160 mg, 1.86 mmol), copper acetate (169 mg, 0.93 mmol), 2,2'-bipyridine (146 mg, 0.93 mmol), and sodium carbonate (197 mg, 1.86 mmol) were dispersed in acetonitrile (6 mL), and the reaction solution was heated to 70°C for reaction under stirring for 4 hours. The reaction solution was cooled to room temperature and concentrated under reduced pressure reaction, and the residue was purified by silica gel column chromatography, to obtain the target product 25a (204 mg, yield 86%).

MS m/z (ESI): 255.0, 257.0 [M+1].

Step 2: 25a (52 mg, 0.20 mmol), tert-butyl 4(*S*)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-oxo-1H-imidazol-3-yl)-6,7-dihydro-4H-pyrazolo[4,3-c]pyridine-5-carboxylate (60 mg, 0.14 mmol), (1*S,* 2*S*)-1-*N*, 2-*N*-dimethylcyclohexane-1,2-diamine (19 mg, 0.14 mmol), potassium carbonate (19 mg, 0.14 mmol), and cuprous iodide (26 mg, 0.14 mmol) were dispersed in *N*-methylpyrrolidone (2 mL), and the reaction solution was heated to 130°C for reaction under stirring for 4 hours. The reaction solution was cooled to room temperature, and the reaction was quenched by adding saturated brine (5 mL), followed by extraction with ethyl acetate (5 mL × 3); and the organic phases were combined, washed with saturated brine (20 mL × 5), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to obtain the target product 25b (55 mg, yield: 62%).

MS m/z (ESI): 616.3 [M+1].

Step 3: 25b (55 mg, 89.33 μmol) and trifluoroacetic acid (0.5 mL) were dissolved in dichloromethane (2 mL), and the resulting mixture was stirred for reaction at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure to obtain the target product 25c (42 mg, yield: 91%)

MS m/z (ESI): 516.2 [M+1].

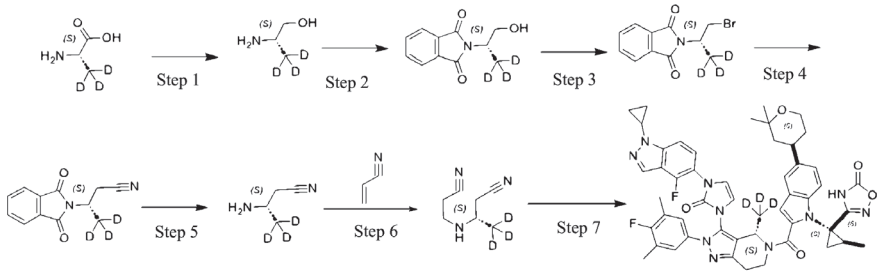
Step 4: 25c (42 mg, 81.5 μmol), intermediate A (51 mg, 0.122 mmol), HATU (46 mg, 0.122 mmol), and DIEA (53 mg, 0.407 mmol) were dissolved in DMF (3 mL), and the resulting mixture was stirred for reaction at room temperature for 3 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (5 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (10 mL), dried over anhydrous sodium sulfate, and filtered; the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain the target product (62 mg, yield: 84%).

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MS m/z (ESI): 909.4 [M+1]。

^{1}H NMR (400MHz, DMSO) δ 11.74 (s, 1H), 8.27 (s, 1H), 7.67 (d, 1H), 7.56-7.47 (m, 2H), 7.40 (d, 1H), 7.26 (d, 1H), 7.18 (d, 2H), 7.07 (d, 1H), 6.95 (s, 2H), 5.58 (d, 1H), 4.38 (d, 1H), 3.85 (s, 1H), 3.71 (d, 2H), 3.62 (d, 1H), 3.18(t, 1H), 3.09-2.98 (m, 1H), 2.89 (d, 1H), 2.26 (s, 6H), 1.67 (d, 2H), 1.57 (d, 1H), 1.48 (d, 2H), 1.43 (s, 1H), 1.32 (s, 1H), 1.27 (s, 4H), 1.20-1.11 (m, 12H).

Example 26



Step 1: In a 500 mL reaction bottle, L-alanine-3,3,3-d3 (10 g, 108.56 mmol) was dissolved in tetrahydrofuran (200 mL), then lithium aluminum hydride (4.12 g, 108.56 mmol) was added batchwise at 0°C, and then the reaction solution was stirred at 0°C for 2 hours under nitrogen protection. The reaction was stopped, quenched by slowly adding an aqueous sodium hydroxide solution (1M, 15 mL), filtered, and concentrated to obtain the target product (8 g, a yellow oil), yield: 94.3%.

Step 2: In a 500 mL reaction bottle, (S)-2-aminopropane-3,3,3-d3-1-ol (8 g, 102.39 mmol), phthalic anhydride (15.17 g, 102.39 mmol), and triethylamine(10.36 g, 102.39 mmol) were dissolved in toluene (200 mL), and then the reaction solution was placed under nitrogen protection and added into a water separator and stirred at 110°C for 12 hours. The reaction was stopped, concentrated and then recrystallized from diethyl ether to obtain the target product (17 g, a yellow oil), yield: 79.7%.

MS m/z (ESI): 209.0 [M+1].

Step 3: In a 500 mL reaction bottle, (S)-2-(1-hydroxylpropan-2-yl-3,3,3-d3)isodihydroindole-1,3-dione (17 g, 81.64 mmol) was dissolved in dichloromethane (200 mL), and at 25°C, phosphorus tribromide (22.1 g, 81.64 mmol) was added, and then the reaction solution was stirred at 25°C for 1 hour under nitrogen protection. The reaction was stopped, and quenched by adding an aqueous solution (100 mL), followed by extraction with dichloromethane (100 mL × 2); the organic phases were combined, washed with saturated sodium chloride (100 mL), dried over anhydrous sodium sulfate, filtered and concentrated to obtain the target product (19 g, yellow solid), yield: 85.8%.

MS m/z (ESI): 271.0 [M+1].

Step 4: In a 500 mL reaction bottle, (S)-2-(1-bromopropan-2-yl-3,3,3-d3)isodihydroindole-1,3-dione (19 g, 70.08 mmol) was dissolved in DMSO (200 mL), and at 25°C, sodium cyanide (3.43 g, 70.08 mmol) and potassium iodide (1.16 g, 7.01 mmol) were added, and then the reaction solution was stirred at 25°C for 12 hours under nitrogen protection. The reaction was stopped and quenched by adding an aqueous solution (200 mL), followed by extraction with dichloromethane (200 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (200 mL), dried over anhydrous sodium sulfate, filtered, and concentrated, and the resulting residue was then purified by silica gel column chromatography with an eluent system of petroleum ether and ethyl acetate to obtain the target product (11 g, yellow solid), yield: 72.2%.

MS m/z (ESI): 218.0 [M+1].

Step 5: In a 250 mL reaction bottle, (S)-3-(1,3-dicarbonylisodihydroindol-2-yl)butyronitrile-4,4,4-d3 (11 g, 50.63 mmol) was dissolved in ethanol (100 mL), and at 25°C, hydrazine hydrate (2.53 g, 50.63 mmol) was added, and then the reaction solution was stirred at 50°C for 2 hours under nitrogen protection. The reaction was stopped and cooled to room temperature, with a white solid precipitating, followed by filtration; the filtrate was concentrated and treated by adding 20 mL ethanol, with a solid precipitating, and further filtered; and the filtrate was concentrated to obtain the target product (4 g, a yellow oil), yield: 90.6%.

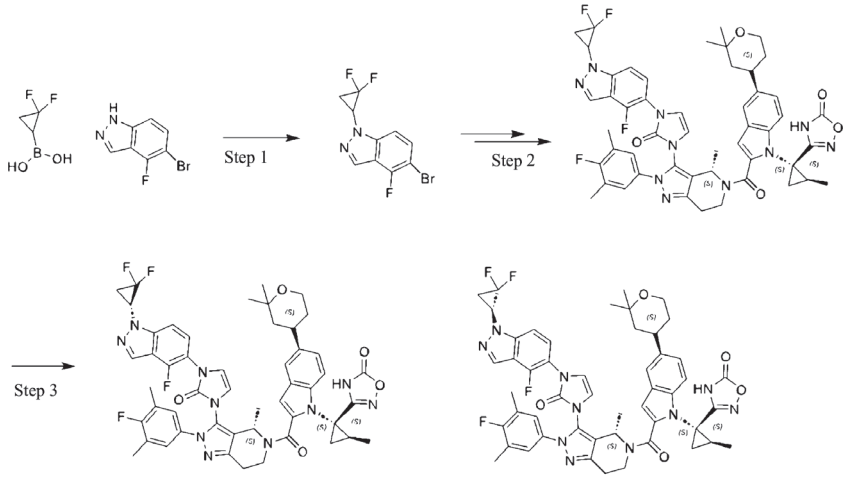
Step 6: (S)-3-aminobutyronitrile-4,4,4-d3 was used as a raw material, and the target product was obtained following the synthesis in step 1 of Example 516.

MS m/z (ESI): 141.0 [M+1].

Step 7: (S)-3-((2-cyanoethyl)amino)butyronitrile-4,4,4-d3 was used as a raw material, and the target product was obtained following the synthesis in intermediate B, intermediate E, and Example 1.

MS m/z (ESI): 912.4 [M+1].

Example 27



Step 1: in a 100 mL reaction bottle, 5-bromo-4-fluoro-1H-indazole (1 g, 4.65 mmol), (2,2-difluorocyclopropyl)boronic acid (1.13 g, 9.30 mmol), copper acetate monohydrate (928.37 mg, 4.65 mmol), sodium carbonate (985.81 mg, 9.30 mmol), and 2,2'-bipyridine (726.37 mg, 4.65 mmol) were dissolved in 1,2-dichloroethane (25.0 mL), and then the reaction solution was stirred at 25°C for 4 hours under nitrogen protection. The reaction was stopped and quenched by adding a saturated aqueous solution of ammonium chloride (60 mL), followed by extraction with dichloromethane (60 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (60 mL × 1), dried over anhydrous sodium sulfate, and filtered, and the resulting residue was purified by silica gel column chromatography with an eluent system of petroleum ether and ethyl acetate to obtain the target product (700 mg, yellow solid), yield: 51.7%.

MS m/z (ESI): 291.0,293.0 [M+1].

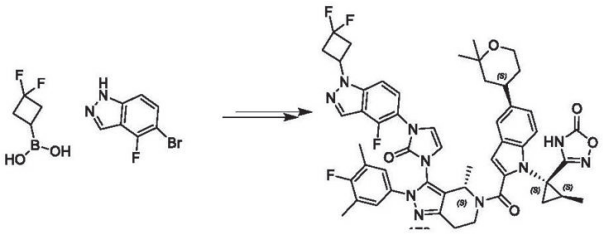
Step 2: 5-bromo-1-(2,2-difluorocyclopropyl)-4-fluoro-1H-indazole was used as a raw material, and the title product was obtained following the synthesis steps in Example 1.

MS m/z (ESI): 945.3 [M+1].

Step 3: The resulting product was chirally resolved to obtain 27-1 and 27-2.

MS m/z (ESI): 945.3 [M+1].

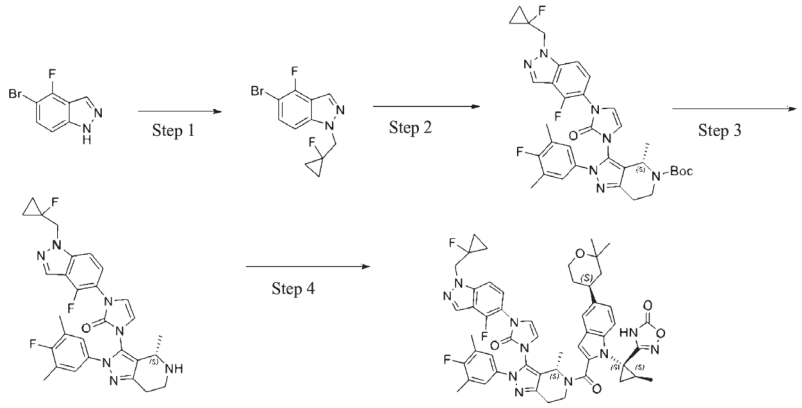
Example 28



5-bromo-4-fluoro-1H-indazole and (3,3-difluorocyclobutyl)boronic acid were used as raw materials, and the target product was obtained following the synthesis steps in Example 27.

MS m/z (ESI): 959.3 [M+1].

Example 29



Step 1: Under an ice bath, 5-bromo-4-fluoro-1H-indazole (0.43 g, 2 mmol) was dissolved in tetrahydrofuran (6 mL), followed by nitrogen replacement; then triphenylphosphine (0.79 g, 3 mmol) and diisopropyl azodicarboxylate (0.61 g, 3 mmol) were added, successively, and stirred under the ice bath for 30 minutes, and finally (1-fluorocyclopropyl)methanol was added, and stirred at room temperature for 2 hours, with LCMS indicating the completion of the reaction; the reaction solution was quenched with a saturated ammonium chloride solution (10 mL), and then extracted with ethyl acetate (15 mL × 2); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography, to obtain the target product (0.29 g, yield 50%).

MS m/z (ESI): 287.0,289.0 [M+1].

Step 2: at room temperature, tert-butyl (4S)-2-(4-fluoro-3,5-dimethyl-phenyl)-4-methyl-3-(2-carbonyl-1H-imidazol-3-yl)-6,7-dihydro-4H-pyrazolo[4,3-c]pyridine-5-carboxylate (50 mg, 0.11 mmol), 5-bromo-4-fluoro-1-((1-fluorocyclopropyl)methyl)-1H-indazole (37 mg, 0.13 mmol), cuprous iodide (11 mg, 0.06 mmol), potassium carbonate (47 mg, 0.33 mmol) and (1S, 2S)-N,N'-dimethyl-1,2-diaminocyclohexane (8 mg, 0.06 mmol) were dissolved in N-methylpyrrolidone (2 mL), subjected to nitrogen replacement, heated to 130°C for reaction for 5 hours, and cooled to room temperature, with LCMS indicating the completion of the reaction; the reaction solution was diluted with ethyl acetate (15 mL) and filtered; the filter residue was washed with ethyl acetate (10 mL); and the organic phases were combined, washed with saturated brine (15 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by thin-layer preparative chromatography (dichloromethane : methanol = 20 : 1), to obtain the target product as a yellow oil (0.043 g, yield 60%).

MS m/z (ESI): 648.2 [M+1].

Step 3: At room temperature, tert-butyl (S)-3-(3-(4-fluoro-1-((1-fluorocyclopropyl)methyl)-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (43 mg, 0.07 mmol) was dissolved in dichloromethane (2 mL), and then a hydrochloric acid/dioxane solution (4.0 M, 1 mL) was added and stirred at room temperature for 1 hour, with LCMS indicating the completion of the reaction, followed by spin-drying; and the residue was used directly in the next step (40 mg, crude product, yellow oil).

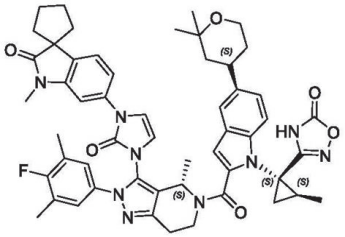
MS m/z (ESI): 548.2 [M+1].

Step 4: At room temperature, (S)-1-(4-fluoro-1-((1-fluorocyclopropyl)methyl)-1H-indazol-5-yl)-3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one hydrochloride (40 mg, 0.07 mmol) was dissolved in N,N-dimethylformamide (3 mL), and then N,N-diisopropylethylamine (0.5 mL), 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid (29 mg, 0.07 mmol) and 2-(7-azobenzotriazole)-N,N,N',N'-tetramethyluronium hexafluorophosphate (38 mg, 0.1 mmol) were added, successively, and stirred at room temperature for 14 hours, with LCMS indicating the completion of the reaction; the reaction solution was diluted with ethyl acetate (15 mL), and then washed with saturated brine (15 mL × 2); the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography and lyophilized, to obtain the target compound (10 mg, yield 15.6%).

MS m/z (ESI): 941.3 [M+1].

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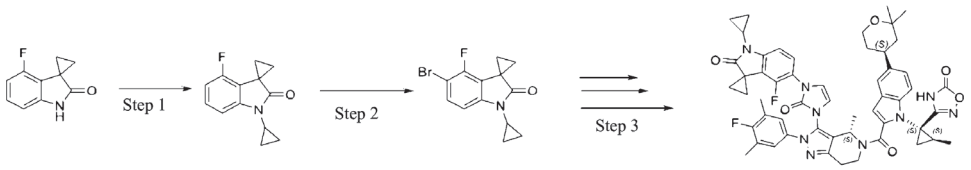
Example 30



6'-bromospiro[cyclopenta-1,3'-dihydroindole]-2'-one was used as a raw material, and a product was obtained following step 1 in Example 15, and steps 2 to 4 in Example 25.

MS m/z (ESI): 934.4 [M+1].

Example 31



Step 1: at room temperature, 4'-fluorospiro[cycloprop-1,3'-dihydroindole]-2'-one (0.35 g, 2 mmol), 2-(2-pyridyl)pyridine (0.47 g, 3 mmol), cyclopropylboronic acid (0.52 g, 6 mmol), copper acetate (0.54 g, 3 mmol) and sodium carbonate (0.64 g, 6 mmol) were dissolved in 1,2-dichloroethane (10 mL), subjected to oxygen replacement, heated to 80°C for reaction for 14 hours, and cooled to room temperature, with LCMS indicating the completion of the reaction, followed by filtration and spin-drying; and the residue was separated by Flash column chromatography (PE : EA = 10 : 1), to obtain the target product (0.15 g, yield: 35%).

MS m/z (ESI): 218.1 [M+1].

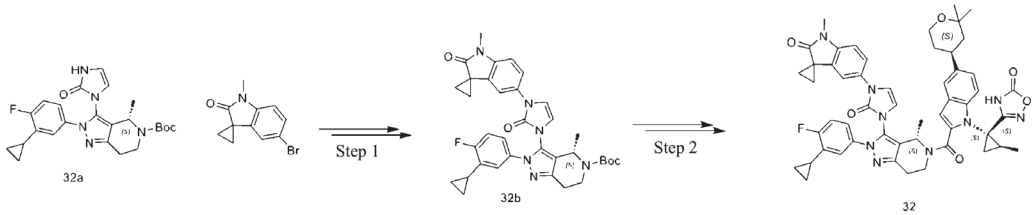
Step 2: at room temperature, 1'-cyclopropyl-4'-fluorospiro[cycloprop-1,3'-dihydroindole]-2'-one (0.15 g, 0.7 mmol) was dissolved in N,N-dimethylformamide (5 mL), and then N-bromosuccinimide (0.12 g, 0.7 mmol) was added and stirred at room temperature for 1 hour, with LCMS indicating the completion of the reaction; the reaction solution was diluted with ethyl acetate (20 mL), and then washed with saturated brine (15 mL×2); the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried; and the residue was separated by Flash column chromatography (PE : EA = 10 : 1), to obtain the target product (0.10 g, yield: 50%).

MS m/z (ESI): 296.0, 298.0 [M+1].

Step 3: 5'-bromo-1'-cyclopropyl-4'-fluorospiro[cycloprop-1,3'-dihydroindole]-2'-one was used as raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

MS m/z (ESI): 950.3 [M+1].

Example 32



Step 1: 32a and 5'-bromo-1'-methylspiro[cycloprop-1,3'-dihydroindole]-2'-one were used as raw materials, and 32b was obtained following the synthesis steps in Example 1.

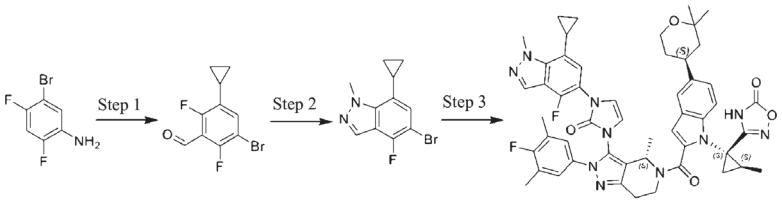
MS m/z (ESI): 625.2 [M+1].

Step 2: 32b was used as a raw material, and a product 32 was obtained following the synthesis steps 2 to 3 for intermediate C.

MS m/z (ESI): 918.4 [M+1].

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Example 33



Step 1: 5-bromo-2,4-difluoroaniline was used as a raw material, following WO 2021/76890, 2021, A1, Page/Page column 163, to obtain the target product.

MS m/z (ESI): 261.0, 263.0 [M+1].

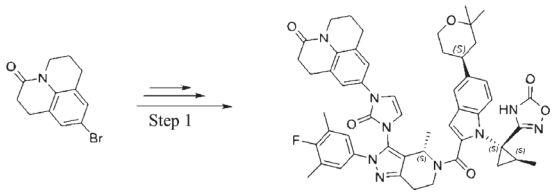
Step 2: 3-bromo-5-cyclopropyl-2,6-difluorobenzaldehyde was used as a raw material, following [Organic Letters, 2007, vol. 9, #3, p. 525-528], to obtain the target product.

MS m/z (ESI): 269.0, 271.0 [M+1].

Step 3: 5-bromo-7-cyclopropyl-4-fluoro-1-methyl-1H-indazole was used as a raw material, and the target product was obtained following Example 1.

MS m/z (ESI): 923.4 [M+1].

Example 34

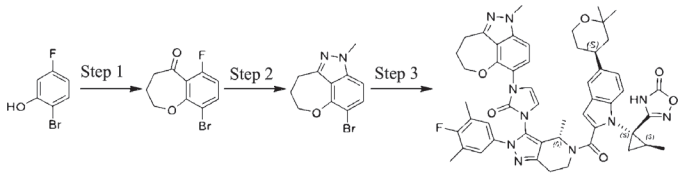


Step 1: 9-bromo-2,3,6,7-tetrahydro-1H, 5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

MS m/z (ESI): 920.3 [M+1].

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.73 (s, 1H), 7.51-7.45 (m, 1H), 7.41-7.31 (m, 3H), 7.27-7.03 (m, 4H), 6.94-6.90 (m, 1H), 6.87-6.70 (m, 1H), 5.62-5.50 (m, 1H), 4.43-4.30 (m, 1H), 3.73-3.57 (m, 5H), 3.24-3.11 (m, 1H), 3.06-3.00 (m, 1H), 2.89-2.70 (m, 5H), 2.59-2.52 (m, 2H), 2.22 (*br*, 6H), 1.85-1.75 (m, 2H), 1.73-1.58 (m, 3H), 1.55-1.48 (m, 2H), 1.39-1.34 (m, 2H), 1.27 (s, 6H), 1.18-1.11 (m, 6H),

Example 35



Step 1: 2-bromo-5-fluorophenol was used as a raw material, following Bioorganic and Medicinal Chemistry Letters, 2004, vol. 14, #10, p. 2451-2457, to obtain the target product.

MS m/z (ESI): 259.0, 261.0 [M+1].

Step 2: 9-bromo-6-fluoro-3,4-dihydrobenzo[b]oxepin-5(2H)-one was used as a raw material, and the target product was obtained following step 2 in Example 33.

MS m/z (ESI): 267.0, 269.0 [M+1].

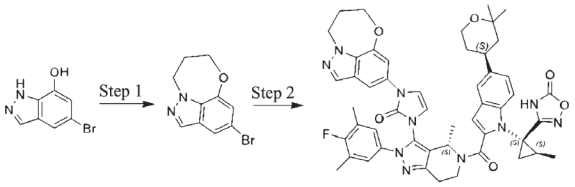
Step 3: 5-bromo-2-methyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole was used as a raw material, and the target product was obtained following Example 1.

^{1}H NMR (400 MHz, DMSO) δ [12.30(s) and 11.77(s), total 1H], 7.53 (s, 1H), 7.41-7.32 (m, 1H),

7.27-7.11 (m, 5H), 7.00-6.60 (m, 3H), 5.79-5.18 (m, 1H), 4.66-4.14 (m, 2H), 4.04-3.93 (m, 3H), 3.75-3.59 (m, 3H), 3.23-2.81 (m, 5H), 2.26-2.07 (m, 8H), 1.83-1.40 (m, 10H), 1.33-1.02 (m, 10H).

MS m/z (ESI): 921.4 [M+1].

Example 36



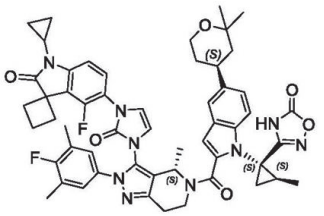
Step 1: 5-bromo-1H-indazole-7-ol was used as a raw material, following NANJING SANHOME INVESTMENT GROUP CO LTD-EP 3290419,2018, A1, Paragraph 0592; 0593; 0594, to obtain the target product.

MS m/z (ESI): 253.0, 255.0 [M+1].

Step 2: 9-bromo-3,4-dihydro-2H-[1,4]oxazepino[2,3,4-hi]indazole was used as a raw material, and the target product was obtained following Example 1.

MS m/z (ESI): 907.4 [M+1].

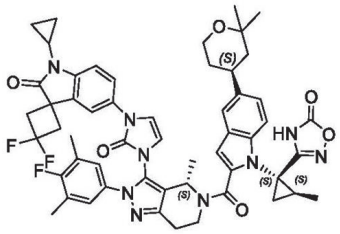
Example 37



4'-fluorospiro[cyclobuta-1,3'-dihydroindole]-2'-one was used, following the synthesis method for Example 31, to obtain the target product.

MS m/z (ESI): 964.4 [M+1].

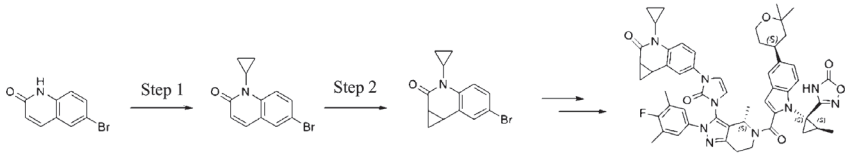
Example 38



5'-bromo-3,3-difluorospiro[cyclobuta-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 31.

MS m/z (ESI): 982.4 [M+1].

Example 39



Step 1: the target product was obtained following Example 31.

MS m/z (ESI): 264.0, 266.0 [M+1]。

Step 2: Trimethylsulfoxonium iodide (94 mg, 0.43 mmol), and NaH (20 mg, 0.84 mmol) were dispersed in DMSO (5 mL), and reacted under stirring at room temperature for 30 minutes. Subsequently, 6-bromo-1-cyclopropylquinoline-2(1H)-one (66 mg, 0.25 mmol) was added thereto, and

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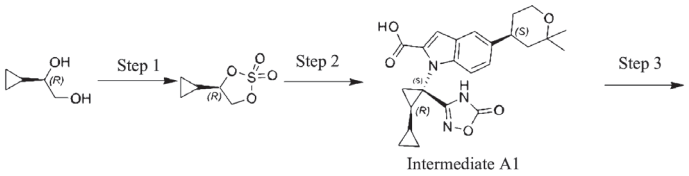
the reaction solution was heated to a temperature of 80°C, and reacted under stirring for 18 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (10 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography, to obtain the title product 6-bromo-3-cyclopropyl-1,1a,3,7b-tetrahydro-2H-cyclopropeno[c]quinoline-2-one (42 mg, yield: 60%).

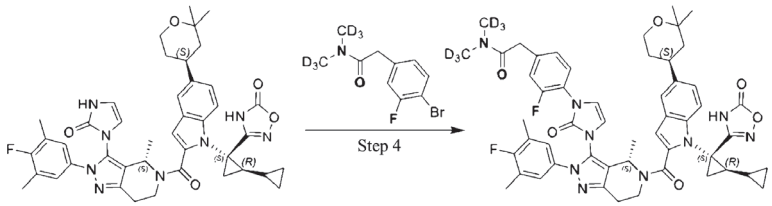
MS m/z (ESI): 278.0, 280.0 [M+1]

Step 3: 6-bromo-3-cyclopropyl-1,1a,3,7b-tetrahydro-2H-cyclopropeno[c]quinoline-2-one was used as a raw material, and the target product was obtained following Example 25.

MS m/z (ESI): 932.4 [M+1]。

Example 40





Step 1: (1R)-1-cyclopropylethan-1,2-diol (1 g, 9.79 mmol) was dissolved in tetrahydrofuran (20 mL), and under nitrogen protection and ice-water bath cooling, thionyl chloride (1.40 g, 11.75 mmol, 853.39 μL) was added. The mixture was stirred for reaction at 60°C for 1 hours. The reaction solution was evaporated to dryness to obtain a crude product. The crude product was dissolved in acetonitrile (15 mL) and water (15 mL), and under ice-water bath cooling and nitrogen protection, sodium periodate (4.19 g, 19.58 mmol) was added, followed by ruthenium trichloride (101.55 mg, 489.57μmol). The mixture was stirred for reaction at 25°C for 3 hours. The reaction solution was quenched with saturated brine (30 mL); the organic phase was separated, the aqueous phase was extracted with dichloromethane (30 mL × 2), and the organic phases were combined, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product (R)-4-cyclopropyl-1,3,2-dioxathiolane 2,2-dioxide (1.3 g). The crude product was directly used for the next step.

MS m/z (ESI): 165.0 [M+1].

Step 2: (R)-4-cyclopropyl-1,3,2-dioxathiolane 2,2-dioxide was used as a raw material, and an intermediate A1 was synthesized following steps 3 to 5 of intermediate A.

MS m/z (ESI): 438.2 [M+1].

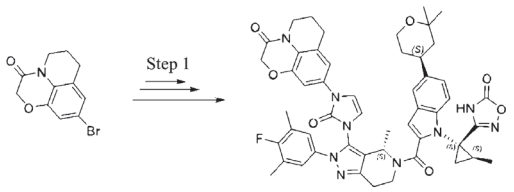
Step 3: intermediate A1 was used as a raw material, following intermediate E, to synthesize intermediate E1.

MS m/z (ESI): 761.4 [M+1].

Step 4: deuterated dimethylamine hydrochloride was used as a raw material, following Example 7, to synthesize the target product.

MS m/z (ESI): 946.5 [M+1].

Example 41



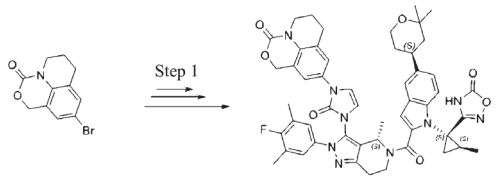
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Step 1: 9-bromo-6,7-dihydro-5H-[1,4]oxaazino[2,3,4-ij]quinoline-3(2H)-one was used as a raw material, and the target compound was obtained following Example 34.

^{1}H NMR (400 MHz, DMSO-d_6) δ [12.29(s) and 11.74(s), total 1H], 7.53-7.50 (m, 1H), 7.41-7.34 (m, 1H), 7.30-7.25 (m, 2H), 7.19-7.07 (m, 4H), 6.97-6.72 (m, 2H), [5.73-5.56(m) and 5.33-5.19(m), total 1H], 4.68-4.64 (m, 2H), 4.40-4.35 (m, 1H), 3.78-3.58 (m, 5H), 3.21-3.14 (m, 1H), 3.05-3.00 (m, 1H), 2.98-2.65 (m, 3H), 2.22(s, 6H), 1.95-1.90 (m, 2H), 1.80-1.49 (m, 7H), 1.38-1.27 (m, 7H), 1.18-1.14 (m, 5H).

MS m/z (ESI): 922.3 [M+H]+.

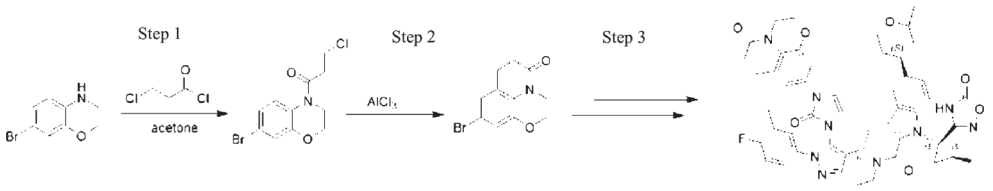
Example 42



Step 1: 9-bromo-6,7-dihydro-1H, 3H, 5H-[1,3]oxaazino[5,4,3-ij]quinoline-3-one was used as a raw material, and the target compound was obtained following Example 34.

MS m/z (ESI): 922.3 [M+H]+.

Example 43



Step 1: 7-bromo-3,4-dihydro-2H-benzo[b][1,4]oxazine (500 mg, 2.34 mmol) was dissolved in acetone (20 mL), and 3-chloropropyl chloride (444.87 mg, 3.50 mmol) was added thereto. The reaction system was stirred under an oil bath at 60°C for 4 hours. After the reaction was completed, the system was cooled to room temperature, excess solvent was concentrated, water (10 mL) was added for dilution, and the system was extracted with ethyl acetate (20 mL x 2), washed with saturated brine (20 mL x 2), dried over anhydrous sodium sulfate, filtered and concentrated, to obtain a crude product 1-(7-bromo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)-3-chloropropane-1-one (700 mg, crude). The crude product was used directly in the next-step reaction without further purification.

MS m/z (ESI): 304.0, 306.0 $[M+H]^+$.

Step 2: 1-(7-bromo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)-3-chloropropane-1-one (700 mg, 2.30 mmol) and anhydrous aluminum chloride (459.70 mg, 3.45 mmol) were mixed in a single-necked bottle, and the system was placed in an oil bath at 120°C for melting with stirring for 4 hours. After the reaction was completed, the system was cooled to room temperature, diluted with water (10 mL), extracted with dichloromethane (20 mL x 2), washed with saturated brine (20 mL x 2), dried over anhydrous sodium sulfate, filtered and concentrated, to obtain a crude product. The crude product was purified through a column (petroleum ether : ethyl acetate = 5 : 1, UV = 254 nm), to finally obtain 9-bromo-2,3,6,7-tetrahydro-5H-[1,4]oxaazino[2,3,4-ij]quinoline-5-one (300 mg, 1.12 mmol, 48.69% yield).

MS m/z (ESI): 267.9, 269.9 $[M+H]^+$.

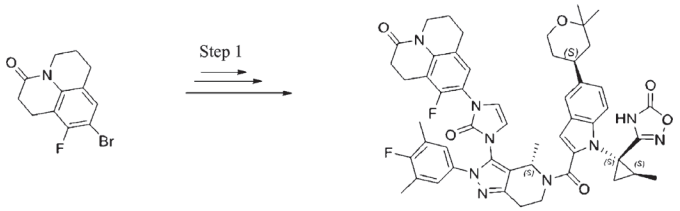
Step 3: 9-bromo-2,3,6,7-tetrahydro-5H-[1,4]oxaazino[2,3,4-ij]quinoline-5-one was used as a raw material, and the target compound was obtained finally following Example 34.

^{1}H NMR (400 MHz, DMSO) δ [12.29 (s) and 11.74 (s), total 1H], 7.53 (s, 1H), 7.40 (d, 1H), 7.28-7.25 (m, 2H), 7.17-7.08 (m, 4H), 6.97-6.93 (m, 2H), 5.56-5.54 (q, 1H), 4.39-4.36 (m, 1H), 4.24-4.22 (m, 2H), 3.87-3.82 (m, 2H), 3.73-3.70 (m, 2H), 3.62 (t, 1H), 3.18 (m, 1H), 3.06-2.98 (m, 1H), 2.95-2.86 (m, 3H), 2.60 (t, 2H), 2.22 (s, 6H), 1.78-1.49 (m, 7H), 1.36 (d, 2H), 1.27 (s, 3H), 1.24 (s, 2H), 1.18-1.13 (m, 5H)

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MS m/z (ESI): 922.3 [M+H] $^{+}$.

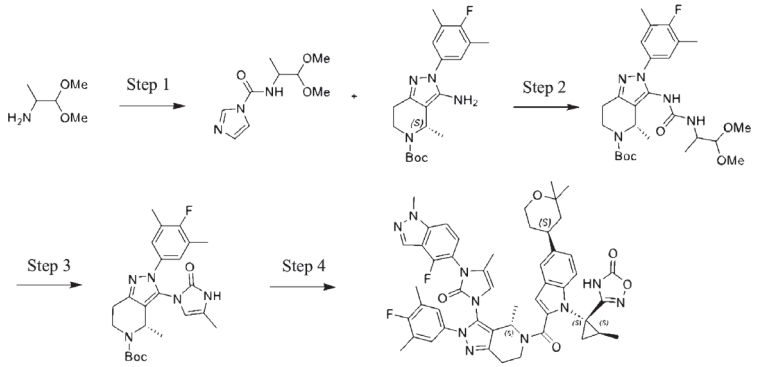
Example 44



Step 1: 9-bromo-8-fluoro-2,3,6,7-tetrahydro-1H, 5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following Example 34.

MS m/z (ESI): 938.3 [M+H]+.

Example 45



Step 1: 1,1-dimethoxy-2-propanamine (500 mg, 4.20 mmol), and carbonyldiimidazole (748 mg, 4.62 mmol) were dissolved in THF (15 mL), and stirred for reaction at room temperature for 4 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (20 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain the title product N-(1,1-dimethoxyprop-2-yl)-1H-imidazole-1-carboxamide (742 mg, yield: 82.9%).

MS m/z (ESI): 214.1 [M+1]。

Step 2: N-(1,1-dimethoxyprop-2-yl)-1H-imidazole-1-carboxamide (300 mg, 1.41 mmol), intermediate 2-4 (527 mg, 1.41 mmol), and potassium tert-butoxide (475 mg, 4.23mmol) were dissolved in DMA (10 mL), and reacted under stirring at room temperature for 4 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (20 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain a product tert-butyl (4S)-3-(3-(1,1-dimethoxyprop-2-yl)ureido)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (512 mg, yield: 70.0%).

MS m/z (ESI): 520.3 [M+1]。

Step 3: tert-butyl (4S)-3-(3-(1,1-dimethoxyprop-2-yl)ureido)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (512 mg, 0.985 mmol) was dissolved in a mixed solvent of methanesulfonic acid (1 mL) and DCM (10 mL), and reacted under stirring at room temperature for 2 hours. To the reaction solution were added a saturated potassium phosphate solution (10 mL) and di-tert-butyl dicarbonate (430 mg, 1.97 mmol), and the system was stirred for reaction at room temperature for 1 hour. The reaction solution was extracted with ethyl acetate (20 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain the title product tert-butyl ((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(4-methyl-2-oxo-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (344 mg, yield: 76.6%).

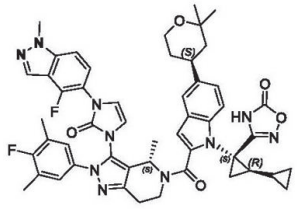
MS m/z (ESI): 456.2 [M+1]。

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Step 4: Following the synthesis methods in steps 3 to 5 in Example 23, the target product was obtained.

MS m/z (ESI): 897.4 [M+1]。

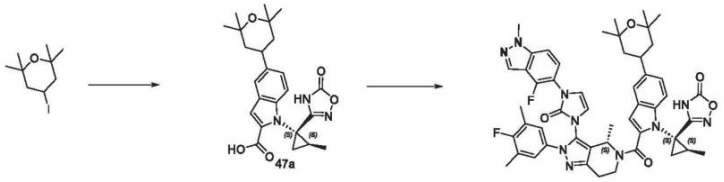
Example 46



5-bromo-4-fluoro-1-methyl-1H-indazole and intermediate E1 were used as raw materials, and the target compound was synthesized following Example 1.

MS m/z (ESI): 909.4 [M+1].

Example 47



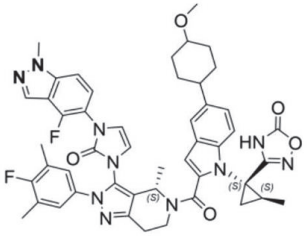
Step 1: 4-iodo-2,2,6,6-tetramethyltetrahydro-2H-pyran was used, following intermediate A, to obtain a product 47a.

MS m/z (ESI): 440.2 [M+1].

Step 2: 47a was used as a raw material, and a product was obtained following the synthesis method in step 5 of Example 23.

MS m/z (ESI): 911.4 [M+1].

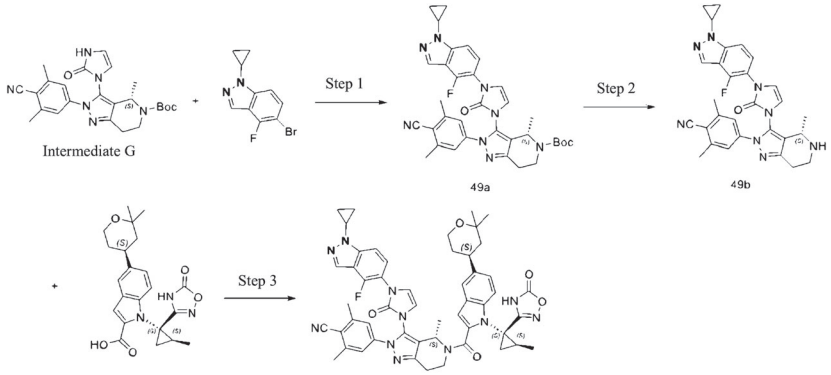
Example 48



1-iodo-4-methoxycyclohexane was used as a raw material, and a product was obtained following the synthesis method in Example 47.

MS m/z (ESI): 883.4 [M+1].

Example 49



Step 1: intermediate G (90 mg, 200.66 μmol), 5-bromo-1-cyclopropyl-4-fluoro-1H-indazole (56.30 mg, 220.73 μmol), CuI (38.22 mg, 200.66 μmol), potassium carbonate (83.20 mg, 601.98 μmol), and (1S,2S)-N,N'-dimethyl-1,2-cyclohexanediamine (28.54 mg, 200.66 μmol) were dispersed in NMP (6 mL), followed by nitrogen replacement for protection; and the reaction solution was heated to130°C and reacted under stirring for 3 hours.

The reaction solution was cooled to room temperature, quenched by adding a saturated ammonium chloride solution, and extracted twice with ethyl acetate; the organic phases were combined, washed with water once and a saturated sodium chloride solution once, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure to obtain a yellow oily crude product. The crude product was purified by silica gel column chromatography (eluent: ethyl acetate : petroleum ether = 50%, v/v) to obtain 49a (92 mg, yield: 74%).

MS m/z (ESI): 623.3 [M+1].

Step 2: 49a (92 mg, 147.75 μmol) was dissolved in a mixed solvent of HCl (4M in dioxane) (2 mL)/DCM (4 mL), and reacted under stirring at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure, to obtain a product 49b (74 mg, yield: 90%), which was used directly in the next-step reaction without purification.

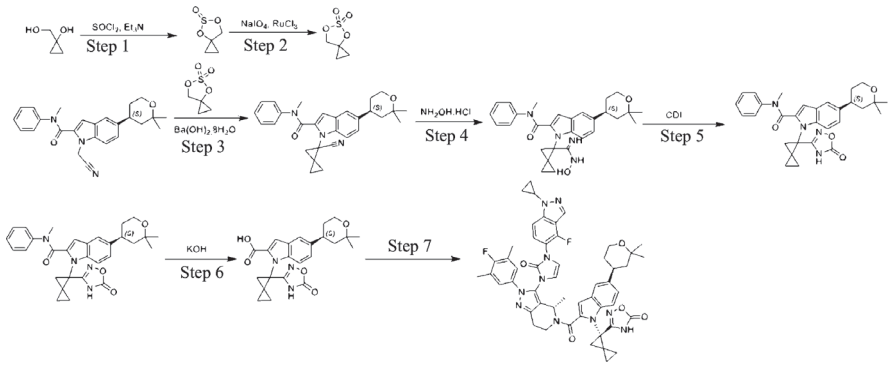
MS m/z (ESI): 523.2 [M+1].

Step 3: 49b (74 mg, 132.37 μmol), 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-methyl-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid (54.46 mg, 132.37 μmol), HATU (74.91 mg, 198.56 μmol), and DIEA (102.65 mg, 794.22 μmol, 138.34 μL) were dissolved in DMF (4 mL), and reacted under stirring at room temperature for 18 hours. The reaction solution was filtered through diatomaceous earth, and purified by preparative HPLC to obtain the target product (81 mg, yield: 67%).

MS m/z (ESI): 916.4 [M+1].

H-NMR (400 MHz, DMSO) δ 11.73 (s, 1H), 8.28 (s, 1H), 7.68 (d, 1H), 7.53 (s, 2H), 7.40 (d, 1H), 7.33 (s, 2H), 7.26 (d, 2H), 7.17 (s, 1H), 7.06 (s, 1H), 6.95 (s, 1H), 5.61 (d, 1H), 4.40 (d, 1H), 3.85(brs, 1H), 3.71 (d, 3H), 3.63 (d, 1H), 3.03(t, 1H), 2.93 (d, 1H), 1.84-1.47 (m, 8H), 1.43 (d, 3H), 1.38-1.22 (m, 7H), 1.22-1.07 (m, 10H).

Example 50



Step 1: To a mixture, at 0°C, of 1-(hydroxymethyl)cyclopropane-1-ol (4.5 g, 51.08 mmol), triethylamine (15.51 g, 153.23 mmol, 21.37 mL), and carbon tetrachloride (100 mL) was added dropwise thionyl chloride (9.11 g, 76.61 mmol, 5.56 mL), the mixture was stirred at 0°C for 1.5 hours, water was added, and the mixture was extracted with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure to obtain a pale yellow oil 4,6-dioxa-5-thiaspiro[2.4]heptane 5-oxide (6 g, crude)

Step 2: To a solution, at 0°C, of 4,6-dioxa-5-thiaspiro[2.4]heptane 5-oxide (6 g, 44.72 mmol) in carbon tetrachloride (50 mL) acetonitrile (50 mL), and water (60 mL) were added sodium periodate(14.35 g, 67.09 mmol) and ruthenium trichloride hydrate (504.15 mg, 2.24mmol), the resulting mixture was stirred at room temperature for 1.5 hours, water was added, and the mixture was extracted three times with DCM; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure and separated by column chromatography (PE/EA = 4 : 1) to obtain a colorless oil 4,6-dioxa-5-thiaspiro[2.4]heptane 5,5-dioxide (4 g, yield: 59.6%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.73 (s, 2H), 1.55-1.45 (m, 2H), 1.02-0.96 (m, 2H).

Step 3: (S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (200 mg, 0.5 mmol) and barium hydroxide octahydrate (786 mg, 0.25mmol) were added into a reaction bottle, and a solution of 4,6-dioxa-5-thiaspiro[2.4]heptane 5,5-dioxide (374 mg, 0.25 mmol) in N,N-dimethyltrimethyleneurea (8 mL) was added with stirring at room temperature; after the addition was completed, the system was stirred at room temperature for 1.5 hours, and then heated to 120°C for reaction under stirring for 1.5 hours;

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heating was stopped, and a sample was collected, diluted with acetonitrile, filtered, and then sent to LCMS for analysis, with a signal peak of the target product being observed; and the system was diluted by adding a suitable amount of acetonitrile, then filtered, directly separated by preparative liquid phase chromatography, and lyophilized to obtain a white solid 1-(1-cyanospiro[2.2]pentan-1-yl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (21 mg, yield: 9.2%).

MS m/z (ESI): 454.2 [M+1].

Step 4: a mixture of 1-(1-cyanospiro[2.2]pentan-1-yl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (80 mg, 176.38 μmol), hydroxylamine hydrochloride (28.00 mg, 402.94 μmol), triethylamine (57.11 mg, 564.41 μmol), and ethanol (5 mL) was stirred at 85°C for 12 hours, with a white solid precipitating, and LCMS showed that the reaction was completed, with MS of the target product being observed; the system was cooled, water was added, and the mixture was extracted with EtOAc; and the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered, to obtain a pale yellow oil 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(1-(N-hydroxycarbamimidoyl)spiro[2.2]pentan-1-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (80 mg, crude).

MS m/z (ESI): 487.3 [M+1].

Step 5: at room temperature, 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(1-(N-hydroxycarbamimidoyl)spiro[2.2]pentan-1-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (80 mg, 164.40 μmol) was dissolved in THF (3 mL), and then 1,1'-carbonyldiimidazole (53.32 mg, 328.81 μmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (75.09 mg, 493.21 μmol) were added successively; the system was subjected to nitrogen replacement, and heated to 55°C for reaction for 2 hours, with LCMS indicating the completion of the reaction; the system was cooled to room temperature and spin-dried; the residue was dissolved with ethyl acetate, and washed with a saturated sodium bicarbonate solution and saturated brine, successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, spin-dried and separated by column chromatography (DCM/MeOH = 10 : 1), to obtain a white solid 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-1-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)spiro[2.2]pentan-1-yl)-N-phenyl-1H-indole-2-carboxamide (80 mg, yield: 94.9%).

MS m/z (ESI): 513.2 [M+1].

Step 6: a mixture of 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-1-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)spiro[2.2]pentan-1-yl)-N-phenyl-1H-indole-2-carboxamide (80 mg, 156.07 μmol), potassium hydroxide (87.57 mg, 1.56 mmol) and polyethylene glycol (2 mL) was stirred at 165°C for 3 hours and cooled, water was added, and the mixture was adjusted to pH = 5 by adding dilute hydrochloric acid and extracted with DCM; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, filtered, concentrated, and separated by preparative chromatography (acidic), to obtain a white solid 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)spiro[2.2]pentan-1-yl)-1H-indole-2-carboxylic acid (18 mg, yield: 27.2%).

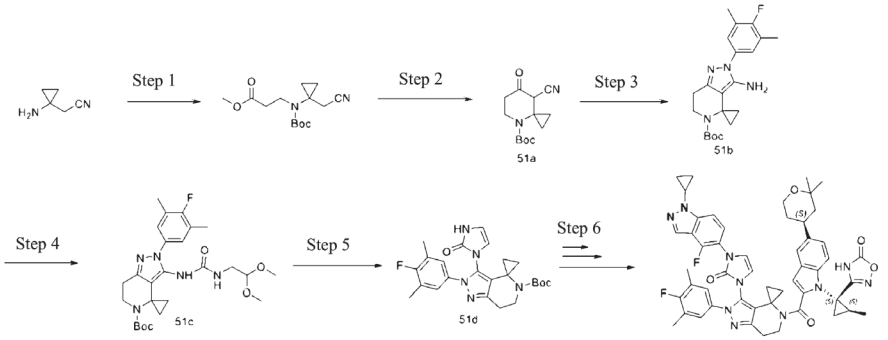
MS m/z (ESI): 424.2 [M+1].

Step 7: To a solution of 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)spiro[2.2]pentan-1-yl)-1H-indole-2-carboxylic acid (18 mg, 42.51 μmol) and 1-(1-cyclopropyl-4-fluoro-indazol-5-yl)-3-[(4S)-2-(4-fluoro-3,5-dimethyl-phenyl)-4-methyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-3-yl]imidazole-2-one (26.30 mg, 51.01μmol) in DMF (2 mL) were added HATU (32.07 mg, 85.01 μmol) and DIEA (16.48 mg, 127.52 μmol, 22.21 μL); the mixture was stirred at room temperature for 16 hours until LCMS showed that the reaction was completed, with MS of the target product being observed; water was added, and the mixture was extracted three times with DCM; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated to dryness under reduced pressure to obtain a pale yellow oil, which was separated by preparative chromatography (acidic) to obtain the target product (13 mg, yield: 33.2%).

MS m/z (ESI): 921.4 [M+1].

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Example 51



Step 1: at room temperature, 2-(1-aminocyclopropyl)acetonitrile (9.6 g, 0.1mol) was dissolved in ethanol (100 mL), and then ethyl acrylate (12 g, 0.12 mol) and triethylamine (15.2 g, 0.15 mol) were added, successively; the system was heated to 70°C for reaction for three hours, and then cooled to room temperature; to the reaction system were added N-methylpiperazine (3 g, 0.03 mol) and di-tert-butyl dicarbonate (26.2 g, 0.12 mol), and the reaction system was stirred at room temperature overnight; after the reaction was completed, the solvent was removed under reduced pressure, and the residue was dissolved with ethyl acetate (100 mL), and then washed with saturated brine (100 mL × 3); and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a crude product, which was used directly in the next step.

MS m/z (ESI): 283.1 $[M+H]^+$.

Step 2: at room temperature, methyl 3-((tert-butoxycarbonyl)(1-(cyanomethyl)cyclopropyl)amino)propanoate (28.2 g, 0.1 mol) was dissolved in tetrahydrofuran (100 mL), and then potassium tert-butoxide (11.2 g, 0.1 mol) was added and stirred at room temperature for 2 hours; then to the reaction system, dilute hydrochloric acid (2N, 80 mL) was added and stirred at room temperature for 30 minutes; then to the reaction system was added water (200 mL), and the reaction system was then extracted with ethyl acetate (100 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered and spin-dried to obtain a crude product, which was separated by Flash column chromatography to obtain the target compound 51a (7.5 g, yield 30%).

MS m/z (ESI): 251.1 $[M+H]^+$.

Step 3: at room temperature, di-tert-butyl 1-(4-fluoro-3,5-dimethylphenyl)hydrazine-1,2-dicarboxylate (2.58 g, 7.28 mmol) was dissolved in N-methylpyrrolidone (20 mL), and then methanesulfonic acid (1.40 g, 14.58 mmol) was added, and the system was heated to 80°C for reaction for 12 hours. The reaction solution was then cooled to room temperature, then added to toluene (20 mL), and then adjusted to pH 9 with an aqueous potassium carbonate solution, followed by liquid separation; the organic phase was collected, dried over anhydrous sodium sulfate, and filtered, and then 51a (1.82 g, 7.28 mmol) and pyridine hydrochloride (0.08 g, 0.73 mmol) were added to the organic phase, and the resulting mixture was heated to 90°C for reaction for 1 hour. The reaction solution was cooled to room temperature, then poured into water (40 mL), then adjusted to pH 9 with aqueous sodium hydroxide solution, and then extracted with ethyl acetate (50 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a crude product, which was separated by Flash column chromatography to obtain the target compound 51b (1.69 g, yield 60%).

MS m/z (ESI): 387.2 $[M+H]^+$.

Step 4: at room temperature, N-(2,2-dimethoxyethyl)imidazole-1-carboxamide (1.29 g, 6.47 mmol) and 51b (2.27 g, 5.88 mol) were dissolved in N,N-dimethylacetamide (30 mL), and then potassium tert-butoxide (1.98 g, 17.65 mmol) was added; the reaction solution was allowed to react at room temperature for 4 hours, then slowly poured into water (80 mL), and then extracted with ethyl acetate (50 mL × 3); the organic phases were combined, then washed with saturated brine (50 mL × 3), dried over anhydrous sodium sulfate, filtered, and spin-dried; and the residue was separated by Flash column chromatography to obtain the target compound 51c (1.22 g, yield 40%).

MS m/z (ESI): 518.3 $[M+H]^+$.

Step 5: at room temperature, 51c (20 mL), then methanesulfonic acid (0.18 g, 1.88 mmol) was then added, and the system was heated to 60°C for reaction for 2 hours. The reaction system was cooled to room temperature and then adjusted to pH 9 with an aqueous potassium phosphate solution; then di-tert-butyl dicarbonate (0.51 g, 2.35 mmol) was added and stirred at room temperature for 2 hours until LCMS indicated the completion of the reaction; then the reaction solution was poured into water (40 mL), and then extracted with ethyl acetate (30 mL × 3); and the organic phases were combined, washed with saturated brine (30 mL × 2),

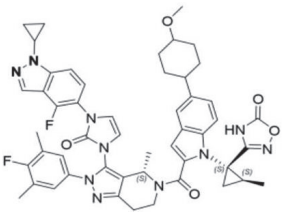
dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a crude product, which was separated by Flash column chromatography to obtain the target product 51d (0.53 g, yield 50%).

MS m/z (ESI): 454.2 $[M+H]^+$.

Step 6: 51d and 5-bromo-1-cyclopropyl-4-fluoro-1H-indazole were used as raw materials, and the target compound was obtained following steps 2, 3, and 4 in Example 29.

MS m/z (ESI): 921.4 $[M+H]^+$.

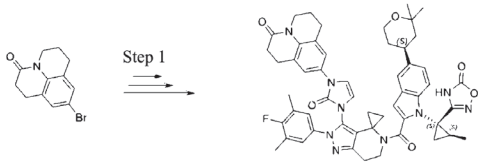
Example 52



25c was used as a raw material, and a product was obtained following the synthesis method in Example 48.

MS m/z (ESI): 909.4 [M+1].

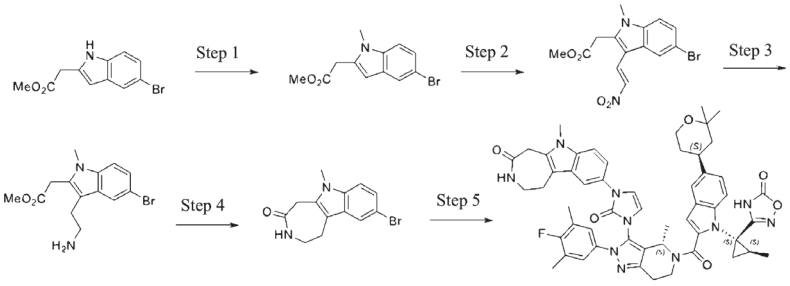
Example 53



Step 1: 9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following steps 2, 3, and 4 in Example 29.

MS m/z (ESI): 932.3 [M+H]+

Example 54



Step 1: methyl 2-(5-bromo-1H-indol-2-yl)acetate (200 mg, 0.75 mmol), sodium hydride (36 mg, 1.49 mmol), and iodomethane (127 mg, 0.90 mmol) were dispersed in DMF (10 mL) for reaction under stirring at room temperature for 4 hours. The reaction solution was quenched by adding saturated ammonium chloride solution quenched, and extracted with ethyl acetate (10 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain the title product methyl 2-(5-bromo-1-methyl-1H-indol-2-yl)acetate (174 mg, yield: 82.7%).

MS m/z (ESI): 282.0, 284.0 [M+1]。

Step 2: methyl 2-(5-bromo-1-methyl-1H-indol-2-yl)acetate (174 mg, 0.62 mmol) and (E)-N,N-dimethyl-2-nitroethen-1-amine (86 mg, 0.74 mmol) were dissolved in a mixed solvent of DCM (10 mL) and trifluoroacetic acid (5 mL) for reaction with stirring at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure, and the crude product was dissolved with dichloromethane, washed with a saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain a product methyl (E)-2-(5-bromo-1-methyl-3-(2-nitroethenyl)-1H-indol-2-yl)acetate (186 mg, yield: 85.4%).

MS m/z (ESI): 353.0, 355.0 [M+1]。

Step 3: methyl (E)-2-(5-bromo-1-methyl-3-(2-nitroethenyl)-1H-indol-2-yl)acetate (186 mg, 0.53 mmol), and palladium on carbon (19 mg, 10%wt.) were dispersed in ethanol (5 mL), and the system was stirred for reaction under hydrogen balloon pressure at room temperature for 5 hours.

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The reaction solution was filtered through diatomaceous earth, the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain a product methyl 2-(3-(2-aminoethyl)-5-bromo-1-methyl-1H-indol-2-yl)acetate (151 mg, yield: 88.2%).

MS m/z (ESI): 325.0, 327.0 [M+1]。

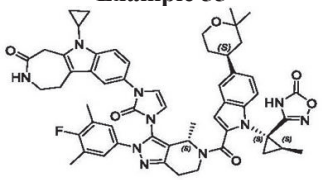
Step 4: methyl 2-(3-(2-aminoethyl)-5-bromo-1-methyl-1H-indol-2-yl)acetate (151 mg, 0.46 mmol) and p-toluenesulfonic acid (268 mg, 1.39 mmol) were dissolved in toluene (5 mL), and reacted under stirring at 80°C for 12 hours. The reaction solution was cooled to room temperature, quenched by adding a saturated sodium bicarbonate solution, and extracted with ethyl acetate (10 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography, to obtain a product 9-bromo-6-methyl-2,3,5,6-tetrahydroazepino[4,5-b]indole-4(1H)-one (92 mg, yield: 67.6%).

MS m/z (ESI): 293.0, 295.0 [M+1]。

Step 5: Following the synthesis methods in steps 3-5 of Example 23, the product 3-((1S,2S)-1-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(6-methyl-4-oxo-1,2,3,4,5,6-hexahydrogenazepino[4,5-b]indol-9-yl)-2-oxo-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-1H-indol-1-yl)-2-methylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one was obtained.

MS m/z (ESI): 947.4 [M+1]。

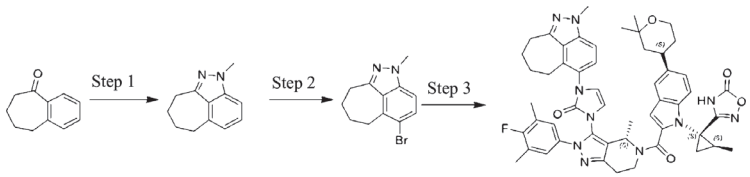
Example 55



Following the synthesis method in Example 54, the target product was obtained.

MS m/z (ESI): 973.4 [M+1]。

Example 56



Step 1: methylhydrazine hydrochloride (2.97 g, 24.97 mmol) was dissolved in N,N-dimethylformamide (30 mL), and under nitrogen protection, potassium carbonate (1.73 g, 12.48 mmol) was added. The mixture was reacted with stirring for 15 minutes at 25°C. Then, 6,7,8,9-tetrahydrobenzo[7]cycloen-5-one (1 g, 6.24 mmol) and acetic acid (374.83 mg, 6.24 mmol), and 2,2,6,6-tetramethylpiperidine oxide (3.90 g, 24.97 mmol) and copper acetate (283.43 mg, 1.56 mmol) were added, successively. The mixture was stirred for reaction at 140°C for 48 hours. The solvent in the mixture was removed under reduced pressure, and saturated brine (100 mL) was added, followed by extraction with ethyl acetate (50 mL × 2); and the organic phases were combined, washed with saturated brine (50 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure, successively. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 3 : 1), to obtain the target product (0.26 g, yield: 22.36%).

MS m/z (ESI): 187.1 [M+1].

Step 2: 2-methyl-6,7,8,9-tetrahydro-2H-cycloheptatrieno[cd]indazole (0.26 g, 1.40 mmol) was dissolved in dichloromethane (15 mL), and under nitrogen protection, N-bromosuccinimide (NBS) (273.30 mg, 1.54 mmol) was added. The mixture was stirred for reaction at room temperature for 2 hours. To the mixture, saturated brine (50 mL) was added to quench the reaction, and the organic phase was separated, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 60 : 40), to obtain the target product (0.35 g, yield: 94.56%).

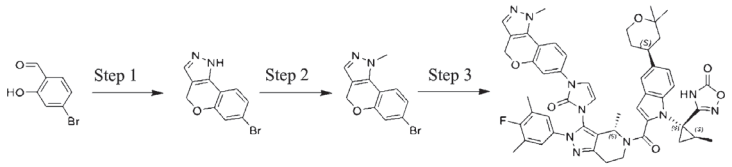
MS m/z (ESI): 265.0, 267.0 [M+1].

Step 3: following Example 1, the target product was obtained.

MS m/z (ESI): 919.4 [M+1].

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Example 57



Step 1: 4-bromo-2-hydroxybenzaldehyde was used as a raw material, following Tetrahedron Letters, 2018, vol. 59, #15, p. 1501-1505, to synthesize the target product.

MS m/z (ESI): 251.0, 253.0 [M+1].

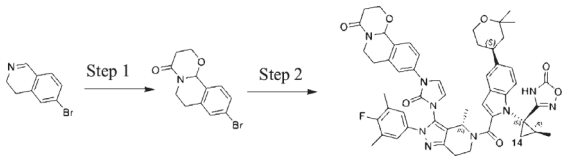
Step 2: 7-bromo-1,4-dihydrochromeno[4,3-c]pyrazole (150 mg, 597.42 μmol) was dissolved in tetrahydrofuran (10 mL), and under ice-water bath cooling and nitrogen protection, sodium hydride (28.67 mg, 716.91 μmol, 60% w/w) was added. The mixture was stirred for reaction at 0°C for 15 minutes. Iodomethane (127.20 mg, 896.13 μmol) was added. The mixture was stirred for reaction at 0°C for 1 hours. To the mixture, saturated brine (50 mL) was added to quench the reaction, followed by extraction with ethyl acetate (50 mL). The organic phases were combined, washed with saturated brine (50 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 70 : 30), to obtain the target product (0.12 g, yield: 75.77%).

MS m/z (ESI): 265.0, 267.0 [M+1].

Step 3: following Example 1, the target product was obtained.

MS m/z (ESI): 919.4 [M+1].

Example 58



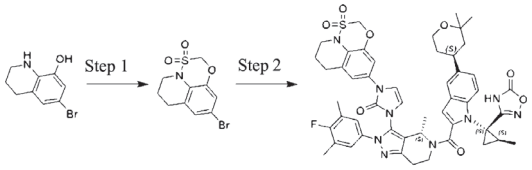
Step 1: 6-bromo-3,4-dihydroisoquinoline was used as a raw material, following Journal of Organic Chemistry, 2014, vol. 79, #3, p. 1368-1376, to synthesize the target product.

MS m/z (ESI): 282.0, 284.0 [M+1].

Step 2: following Example 1, the target product was obtained.

MS m/z (ESI): 936.4 [M+1].

Example 59



Step 1: 6-bromo-1,2,3,4-tetrahydroquinolin-8-ol was used as a raw material, following European Journal of Medicinal Chemistry, 2015, vol. 90, p. 788-796, to synthesize the target product.

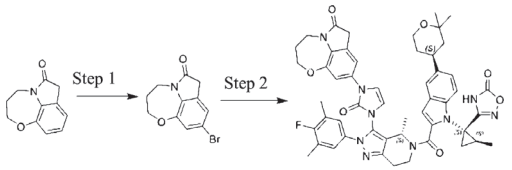
MS m/z (ESI): 304.0, 306.0 [M+1].

Step 2: following Example 1, the target product was obtained.

MS m/z (ESI): 958.4 [M+1].

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Example 60



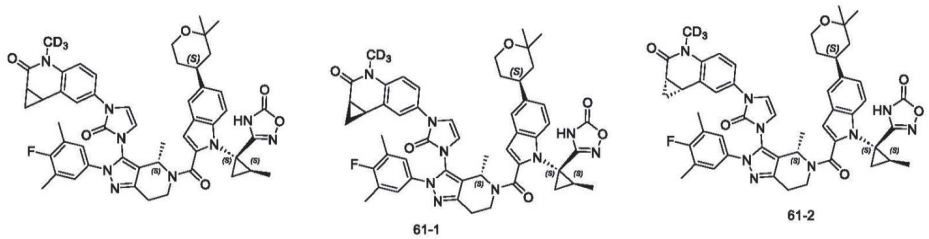
Step 1: following step 2 in Example 56, the target compound was synthesized.

MS m/z (ESI): 268.0, 270.0 [M+1].

Step 2: following Example 1, the target compound was synthesized.

MS m/z (ESI): 922.4 [M+1].

Example 61



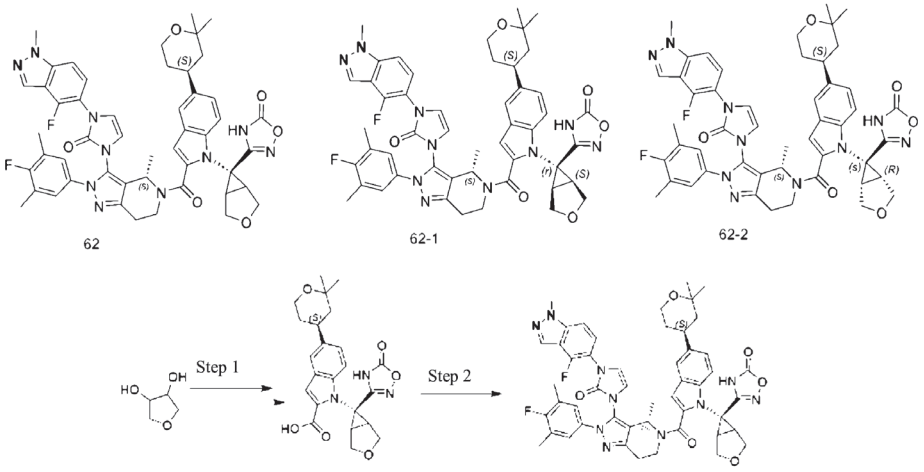
Following the synthesis method in Example 39, a product was obtained.

MS m/z (ESI): 909.4 [M+1].

Example 61 was resolved to obtain 61-1 and 61-2.

MS m/z (ESI): 909.4 [M+1].

Example 62



Step 1: 3,4-dihydroxyl tetrahydrofuran was used as a raw material, and the target compound was obtained following Example 40.

MS m/z (ESI): 440.2 [M+1].

Step 2: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(6-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-3-oxabicyclo[3.1.0]hexan-6-yl)-1H-indole-2-carboxylic acid was used as a raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

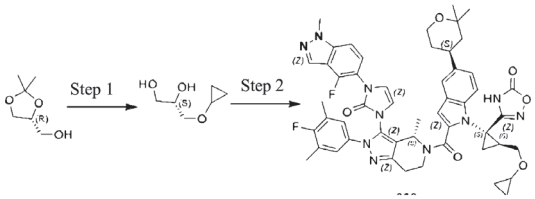
MS m/z (ESI): 911.4 [M+1].

Step 3: 62 was resolved to obtain 62-1 and 62-2.

MS m/z (ESI): 911.4 [M+1].

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Example 63



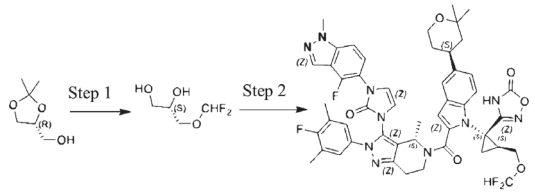
Step 1: (R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol (1 g, 7.57 mmol) and cyclopropyl bromide (1.01 g, 8.32 mmol) were dissolved in N,N-dimethylformamide (15 mL), and under nitrogen protection, potassium carbonate (3.14 g, 22.70 mmol) was added. The mixture was stirred for reaction at 25°C for 12 hours. The reaction solution was quenched with saturated brine (50 mL); the organic phase was separated, the aqueous phase was extracted with dichloromethane (30 mL × 2), and the organic phases were combined, washed with saturated brine (30 mL × 5), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product. The crude product was dissolved in MeOH (15 mL), and under nitrogen protection, p-toluenesulfonic acid monohydrate (0.144 g, 0.757 mmol) was added. The mixture was stirred for reaction at 25°C for 3 hours. The mixture was concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 10 : 90), to obtain the target product (0.3 g, yield: 30.00%).

MS m/z (ESI): 133.1 [M+1].

Step 2: following Example 40, the target product was obtained.

MS m/z (ESI): 939.4 [M+1].

Example 64

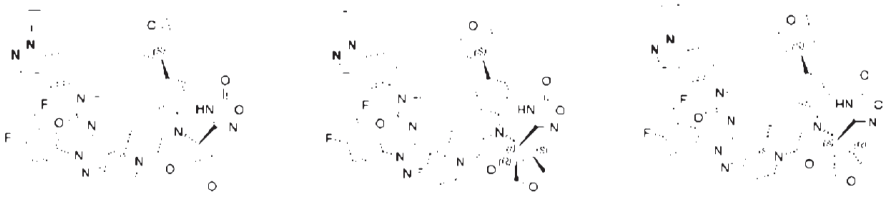


(R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol and difluoroiodomethane were used as raw materials, and the target product was obtained following Example 63.

MS m/z (ESI): 949.4 [M+1].

Example 65

3-(4-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)tetrahydro-2H-pyran-4-yl)-1,2,4-oxadiazole-5(4H)-one



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

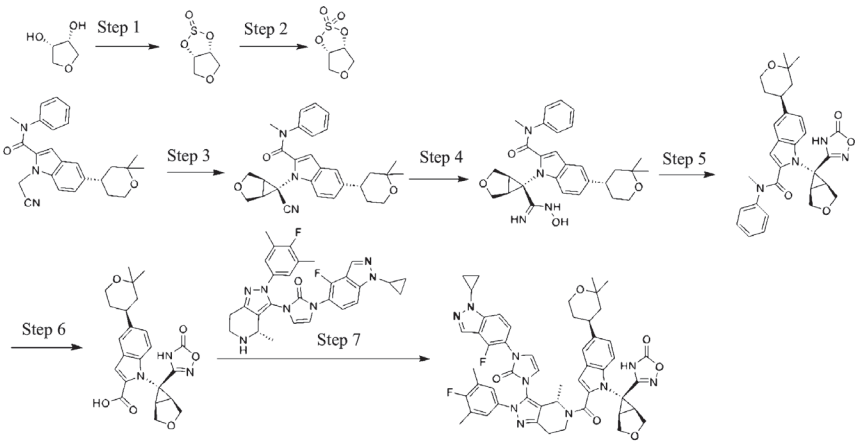
MS m/z (ESI): 937.4 [M+1].

65 was resolved to obtain 65-1 and 65-2.

MS m/z (ESI): 937.4 [M+1].

Example 65-1

3-((3R,4r,5S)-4-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)tetrahydro-2H-pyran-4-yl)-1,2,4-oxadiazole-5(4H)-one



Step 1: (3R,4S)-tetrahydrofuran-3,4-diol (8 g, 76.85 mmol) and triethylamine (31.10 g, 307.38 mmol, 42.87 mL) were dissolved in dichloromethane (150 mL), and under ice-water bath cooling and nitrogen protection, thionyl chloride (10.97 g, 92.22 mmol, 6.70 mL) was added. The mixture was stirred for reaction at 0°C for 1 hours. The reaction solution was washed with saturated brine (130 mL × 2), and the organic phase was separated, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product (11.5 g). The crude product was directly used for the next step.

Step 2: (3aR,6aS)-tetrahydrofuro[3,4-d][1,3,2]dioxothiazole 2-oxide (11.5 g, 76.59 mmol) was dissolved in dichloromethane (50 mL), acetonitrile (50 mL) and water (50 mL), and under ice-water bath cooling and nitrogen protection, were added sodium periodate (32.76 g, 153.18 mmol) and ruthenium trichloride (794.34 mg, 3.83 mmol) were added. The mixture was stirred for reaction at 0°C for 2 hours. The mixture was filtered, the resulting solid was washed with dichloromethane (50 mL), and to the liquid phase was added saturated brine (50 mL), followed by extraction with dichloromethane (50 mL × 2); and the organic phases were combined, washed with saturated brine (50 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure, successively. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 60 : 40), to obtain the target product (3aR, 6aS)-tetrahydrofuro[3,4-d][1,3,2]dioxothiazole 2,2-dioxide (4.8 g, 28.89 mmol, yield: 37.72%).

1H NMR (400MHz, CDCl3) δ 5.45-5.33 (m, 2H), 4.42-4.28 (m, 2H), 3.81-3.68 (m, 2H).

Step 3: (S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.65 g, 1.62 mmol) and (3aR,6aS)-tetrahydrofuro[3,4-d][1,3,2]dioxothiazole 2,2-dioxide (806.97 mg, 4.86 mmol) were dissolved in 1,3-dimethyl-3,4,5,6-tetrahydro-2-pyrimidinone (6 mL) and tetrahydrofuran (6 mL), and under -40°C and nitrogen protection, lithium diisopropylamide (2M, 4.86 mL) was added. The mixture was stirred for reaction at -40°C for 1 hours. To the mixture, saturated brine (50 mL) was added to quench the reaction, followed by extraction with ethyl acetate (50 mL). The organic phases were combined, and washed with saturated brine (50 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure, successively. The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 40 : 60), to obtain the target product (0.4 g, 851.84 μmol, yield: 52.62%).

MS m/z (ESI): 470.2 [M+1].

Step 4: 1-((1R,5S,6r)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.51 g, 1.09 mmol) and triethylamine (329.70 mg, 3.26 mmol, 454.45 μL) were dissolved in ethanol (10 mL), and under nitrogen protection, hydroxylamine hydrochloride (150.95 mg, 2.17 mmol) was added. The mixture was stirred for reaction at 80°C for 12 hours. The reaction solution was evaporated to dryness and quenched with saturated brine (30 mL); and the aqueous phase was extracted with ethyl acetate (30 mL × 2), and the resulting organic phase was separated, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product (0.5 g). The crude product was directly used for the next step.

MS m/z (ESI): 503.3 [M+1].

Step 5: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1R,5S,6r)-6-(N-hydroxycarbamimidoyl)-3-oxabicyclo[3.1.0]hexan-6-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.5 g, 994.82 μmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (378.62 mg, 2.49 mmol, 371.20 μL) were dissolved in tetrahydrofuran (10 mL), and

under nitrogen protection, N,N-carbonyldiimidazole (322.62 mg, 1.99 mmol) was added. The mixture was stirred for reaction at 55°C for 2 hours. The reaction solution was cooled to room temperature, saturated brine (50 mL) was added to quench the reaction, and the mixture was further stirred for 0.5 hours. The mixture was subjected to liquid separation, and the resulting aqueous phase was extracted with ethyl acetate (50 mL). The organic phases were combined, washed with saturated brine (50 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (eluting with dichloromethane : methanol = 100 : 0 to 95: 5), to obtain the target product (0.33 g, 624.29 μmol, yield: 62.75%).

1H NMR (400MHz, CDCl3) δ 10.95 (s, 1H), 7.62 (d, J = 8.5 Hz, 1H), 7.44-7.28 (m, 3H), 7.25-7.08 (m, 4H), 5.92 (s, 1H), 4.77-4.64 (m, 1H), 4.31-4.18 (m, 1H), 4.08-3.99 (m, 2H), 3.89-3.68 (m, 2H), 3.54 (s, 3H), 3.00-2.85 (m, 1H), 2.70-2.54 (m, 2H), 1.76-1.48 (m, 4H), 1.29 (s, 3H), 1.24 (s, 3H).

MS m/z (ESI): 529.2 [M+1].

Step 6: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-1-((1R,5S,6r)-6-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-3-oxabicyclo[3.1.0]hexan-6-yl)-N-phenyl-1H-indole-2-carboxamide (60 mg, 113.51 μmol) was dissolved in polyethylene glycol 400 (1 mL), and under nitrogen protection, potassium hydroxide (63.68 mg, 1.14 mmol) was added. The mixture was stirred for reaction at 160°C for 1 hours. The reaction solution was cooled and quenched with a 1N aqueous hydrochloric acid solution (1.5 mL); the aqueous phase was extracted with dichloromethane (30 mL × 2), and the resulting organic phases were combined, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product. The crude product was directly used for the next step.

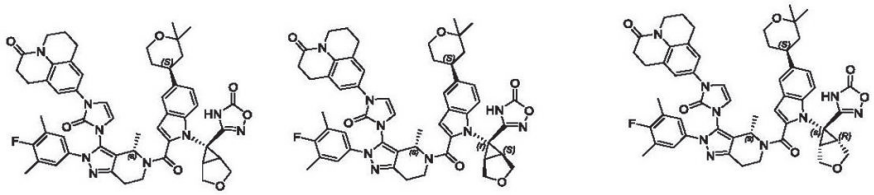
MS m/z (ESI): 440.2 [M+1].

Step 7: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1R,5S,6r)-6-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-3-oxabicyclo[3.1.0]hexan-6-yl)-1H-indole-2-carboxylic acid (19 mg, 43.23 μmol), (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one (17.83 mg, 34.59 μmol), and N,N-diisopropylethylamine (22.35 mg, 172.94 μmol, 30.12 μL) were dissolved in N,N-dimethylformamide (1.5 mL), and under nitrogen protection, 2-(7-azabenzotriazole)-N,N,N',N'-tetramethyluronium hexafluorophosphate (24.66 mg, 64.85 μmol) was added. The mixture was stirred for reaction at 15°C for 12 hours. The crude reaction solution was separated by preparative high-performance liquid chromatography to give a product (4 mg, yield: 9.68%).

^{1}H NMR (400MHz, DMSO) δ [12.17(s) and 11.53(s), total 1H], 7.73-7.49 (m, 1H), 7.48-7.35 (m, 1H), 7.27-7.18 (m, 1H), 7.18-6.98 (m, 4H), 6.87-6.60 (m, 3H), [5.80-5.39(m), 5.43-4.99(m), total 1H], 4.43-3.90 (m, 5H), 3.90-3.47 (m, 5H), 3.15-2.61 (m, 7H), 2.29-2.06 (m, 8H), 1.71-1.26 (m, 7H), 1.21 (s, 3H), 1.12 (s, 3H).

MS m/z (ESI): 937.4 [M+1].

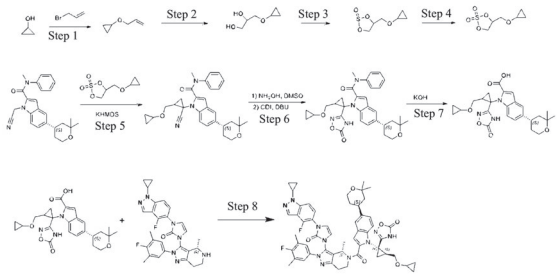
Example 66



9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

MS m/z (ESI): 948.4 [M+1].

Example 67



Step 1: at 0-5°C, cyclopropanol (2 g, 34.43 mmol) and tetrahydrofuran (40 mL) were added, and under nitrogen protection, sodium hydride (2.76 g, 68.88 mmol, 60%) was added batchwise; under an ice-water bath, the system was stirred for 35 minutes, and then 3-bromoprop-1-ene (8.32 g, 68.88 mmol) was injected and stirred for 10 minutes; and then the ice-water bath was removed, and the system was naturally brought back to room temperature, and then heated to reflux overnight. The reaction solution was cooled to room temperature, and then quenched by pouring same into an iced saturated aqueous ammonium chloride solution (40 mL), followed by layering and liquid separation, to obtain an organic phase, which was used directly in the next-step reaction.

Step 1: to the organic phase obtained in the previous step were added water (55 mL), potassium osmate dihydrate (1.26 g, 3.44 mmol), potassium ferricyanide (33.6 g, 10.32 mmol), and potassium carbonate (14 g, 10.32 mmol), and the mixture was stirred at room temperature overnight. To the reaction solution, sodium sulfite (5.3 g, 4.30 mmol) was added, and the resulting mixture was extracted with ethyl acetate, washed with a small amount of a saturated aqueous ammonium chloride solution and saturated brine, dried, and concentrated, to obtain an oily crude product. The crude product was subjected to column chromatography to obtain a yellow oil 3-cyclopropoxypropane-1,2-diol (1.07 g, yield: 23%)

MS m/z (ESI): 133.1 [M+1].

Step 3: With temperature control using an ice-water bath, to a round-bottom flask were added 3-cyclopropoxypropane-1,2-diol (876 mg, 6.61 mmol), carbon tetrachloride (20 mL), and triethylamine (2.01 g, 19.82 mmol), and thionyl chloride (1.18 g, 9.91 mmol) was added dropwise, and the system was stirred for reaction under ice-water bath for 3.5 hours. After TLC showed the completion of the reaction, to the reaction solution, water (15 mL) was added, and the mixture was extracted with dichloromethane, washed with water and saturated brine, dried, and concentrated to obtain a black oil 4-(cyclopropoxymethyl)-1,3,2-dioxathiolane 2-oxide (1.22 g, crude), and the crude product was used directly in the next-step reaction.

Step 4: under an ice-water bath, to a round-bottom flask were added 4-(cyclopropoxymethyl)-1,3,2-dioxathiolane 2-oxide (1.18 g, 6.61 mmol), carbon tetrachloride (10 mL), acetonitrile (10 mL), water (10 mL), sodium periodate (2.12 g, 9.08 mmol), and ruthenium trichloride hydrate (75 mg, 302 μmol), and the mixture was stirred for 30 minutes, and then naturally brought back to room temperature for reaction overnight. After TLC showed the completion of the reaction, to the reaction solution, water (25 mL) was added, and the mixture was extracted with dichloromethane, washed with water and saturated brine, dried and concentrated to obtain an oil, which was subjected to column chromatography to obtain a colorless oil 4-(cyclopropoxymethyl)-1,3,2-dioxathiolane 2,2-dioxide (673 mg, yield 52.3%).

Step 5: to a three-necked flask were charged (S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (130 mg, 0.324 mmol), N,N-dimethyltrimethyleneurea (3 mL), and 4-(cyclopropoxymethyl)-1,3,2-dioxathiolane 2,2-dioxide (188 mg, 0.972 mmol), and under nitrogen protection and at 0°C, potassium bis(trimethylsilyl)amide (1.3 mmol, 1.3 mL, 1M in THF) was added dropwise, and the resulting system was stirred for reaction at 0°C for 3 hours. After LCMS showed the completion of the reaction, the reaction solution was quenched by adding formic acid, water was added, and the mixture was extracted with ethyl acetate; the organic phases were combined, then washed with water twice, with saturated NaHCO3 aqueous solution once and with saturated brine, dried, and concentrated to obtain an oil. The oil was subjected to column chromatography to obtain 1-(1-cyano-2-(cyclopropoxymethyl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (127 mg, yield: 78.8%).

MS m/z (ESI): 498.3 [M+1].

Step 6: to a round-bottom flask were added 1-(1-cyano-2-(cyclopropoxymethyl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (127 mg, 255.21 μmol), ethanol (5 mL), hydroxylamine hydrochloride (35.47 mg, 510.42 μmol), and triethylamine (77.47 mg, 765.63 μmol), and under nitrogen protection, the system was heated to 90°C for reaction for 2 hours. After LCMS showed the completion of the reaction, ethyl acetate (50 mL) was added, and the system was washed with water (10 mL * 2) and saturated brine (10 mL * 2), dried and concentrated to obtain an oil. The oil above was dissolved with THF (10 mL), N,N'-carbonyldiimidazole (82.77 mg, 510.42 μmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (97.13 mg, 638.03 μmol) were added, and the system was heated to 55°C for reaction for 4 hours.

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After LCMS showed the completion of the reaction, ethyl acetate (30 mL) was added, and the system was washed with water (10 mL * 2) and saturated brine (10 mL * 2), dried and concentrated to obtain an oil, which was subjected to column chromatography to obtain an oil 1-(2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (90 mg, yield 63.3%).

MS m/z (ESI): 557.3 [M+1].

Step 7: to a round-bottom flask were added 1-(2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (90 mg, 161.68 μmol), polyethylene glycol 400 (6 mL) and potassium hydroxide (181.08 mg, 3.23 mmol), and the system was heated at an external temperature of 165°C for reaction for 3 hours. After LCMS showed the completion of the reaction, the reaction solution was cooled to room temperature, water (10 mL) was added, and hydrochloric acid (6N) was added dropwise, followed by extraction with ethyl acetate; and the organic phases were combined, then washed with water, dried, concentrated, and subjected to reverse phase preparative chromatography to obtain 1-(2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid (12 mg, yield 15.9%).

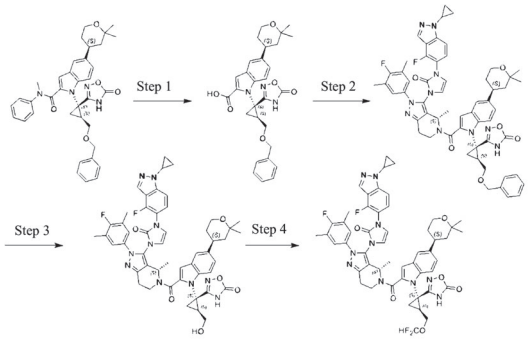
MS m/z (ESI): 468.2 [M+1].

Step 8: to a solution of (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one (15.88 mg, 30.80 μmol) and 1-(2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid (12.00 mg, 25.67 μmol) in DMF (3 mL) were added 2-(7-azobenzotriazole)-N,N,N',N'-tetramethyluronium hexafluorophosphate (19.37 mg, 51.34 μmol), and N,N-diisopropylethylamine (9.95 mg, 77.00 μmol); the reaction solution was stirred at room temperature for 12 hours until LCMS showed that the reaction was completed, with MS of the target product being observed; water was added, and the system was extracted with DCM three times; the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated to dryness under reduced pressure and separated by preparative chromatography (acidic), to obtain 3-((1S,2S)-2-(cyclopropoxymethyl)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one (6.4 mg, yield: 25.8%).

^{1}H NMR (400MHz, DMSO) δ [12.27(s) and 11.84(s), total 1H], 8.28 -8.16 (m, 1H), 7.76-7.60 (m, 1H), 7.65 -7.35 (m, 3H), 7.28 -7.09 (m, 4H), 6.96-6.92 (m, 1H), 6.76-6.54 (m, 1H), 5.78 -5.55 (m, 1H), 5.40 -5.20 (m, 1H), 4.81-4.38 (m, 1H), 4.00 -3.63 (m, 4H), 3.19 -2.67 (m, 4H), 2.26 (s, 6H), 2.03-1.95 (m, 1H), 1.85 -1.46 (m, 6H), 1.32 -1.14 (m, 14H), 0.49-0.34 (m, 4H).

MS m/z (ESI): 965.4 [M+1].

Example 68



Step 1: A mixture of 1-((1S,2S)-2-((benzyloxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (350 mg, 576.88 μmol), KOH (323.69 mg, 5.77 mmol) and polyethylene glycol (4 mL) was stirred at 165°C for 3 hours and cooled to room temperature.

With LCMS indicating the completion of the reaction, the reaction solution was neutralized with dilute hydrochloric acid (1N) and adjusted to pH 5-6, with solid precipitating; and the system was filtered, and the solid was washed with water and petroleum ether, successively, and dried to obtain a brown solid (290 mg, crude), which was used directly in the next step.

MS m/z (ESI): 518.2 [M+1]

Step 2: To a solution of 1-(1-cyclopropyl-4-fluoro-indazol-5-yl)-3-[(4S)-2-(4-fluoro-3,5-dimethyl-phenyl)-4-methyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-3-yl]imidazole-2-one (79.69 mg, 154.57 μmol) and 1-((1S, 2S)-2-((benzyloxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid (100 mg, 193.21 μmol) in DMF(5 mL) were added HATU (145.78 mg, 386.42 μmol) and DIEA(74.91 mg, 579.63 μmol, 100.96 μL); the reaction solution was stirred at room temperature for 12 hours, water was added, and the system was extracted with DCM three times; and the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated to dryness under reduced pressure to obtain a pale yellow oil, which was separated by column chromatography (DCM/MeOH = 10 : 1), to obtain a white solid (120 mg, yield: 61.2%).

MS m/z (ESI): 1015.4 [M+1]

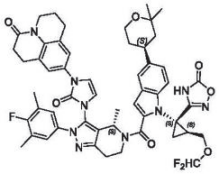
Step 3: 3-((1S,2S)-2-((benzyloxy)methyl)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one (120 mg, 0.12 mmol) was dissolved in trifluoroacetic acid (2 mL), and the reaction solution was heated to 80°C and stirred for reaction for 3 hours. The reaction solution was cooled to room temperature and concentrated under reduced pressure; the residue was dissolved with dichloromethane, washed with saturated sodium bicarbonate solution once, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure to obtain a yellow oily product (80 mg, crude).

MS m/z (ESI): 925.4 [M+1]

Step 4: To a solution of 3-((1S,2S)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)-2-(hydroxymethyl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one (50 mg, 54.05 μmol) and [bromo(difluoro)methyl]-trimethyl-silane (43.91 mg, 216.22 μmol) in DCM (1 mL) and water (1 mL) was added potassium acetate (21.22 mg, 216.22 μmol); the reaction solution was stirred at room temperature for 1 hour, water was added, and the system was extracted with DCM three times; and the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated to dryness under reduced pressure and separated by preparative chromatography (acidic) to obtain the target product (0.43 mg, yield: 0.8%).

MS m/z (ESI): 975.4 [M+1]

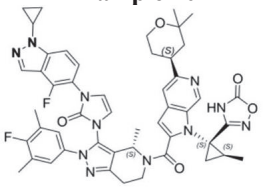
Example 69



9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target product was obtained following Example 64.

MS m/z (ESI): 986.4 [M+1].

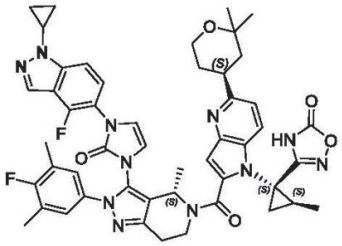
Example 70



the target compound was synthesized following Example 13.

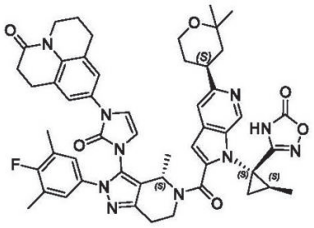
MS m/z (ESI): 910.4 [M+1].

Example 71



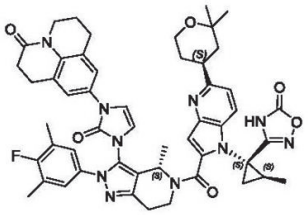
the target compound was synthesized following Example 13.
MS m/z (ESI): 910.4 [M+1].

Example 72



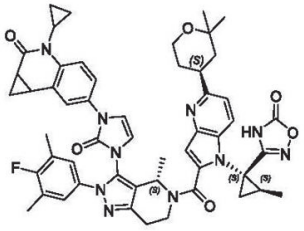
the target compound was synthesized following Example 13.
MS m/z (ESI): 921.4 [M+1].

Example 73



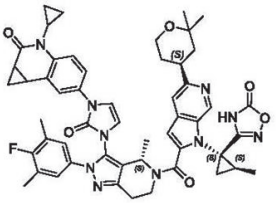
the target compound was synthesized following Example 13.
MS m/z (ESI): 921.4 [M+1].

Example 74



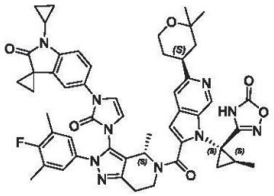
the target product was obtained following the synthesis method in Example 39.
MS m/z (ESI): 933.4 [M+1]。

Example 75



the target product was obtained following the synthesis method in Example 39.
MS m/z (ESI): 933.4 [M+1]。

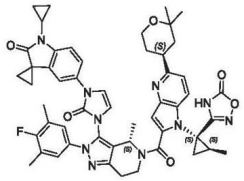
Example 76



the target product was obtained following the synthesis method in Example 31.

MS m/z (ESI): 933.4 [M+1]。

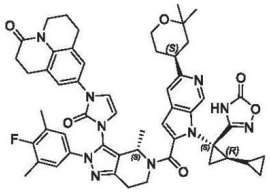
Example 77



the target product was obtained following the synthesis method in Example 31.

MS m/z (ESI): 933.4 [M+1]。

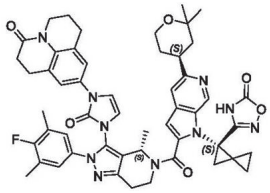
Example 78



9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following Example 46.

MS m/z (ESI): 947.3 [M+H]+

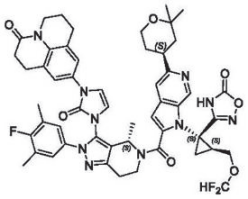
Example 79



9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following Example 50.

MS m/z (ESI): 933.3 [M+H]+

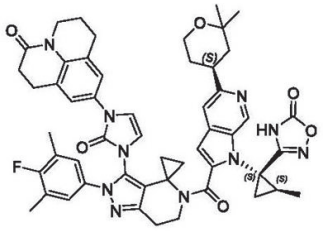
Example 80



9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following Example 64.

MS m/z (ESI): 987.3 [M+H]+

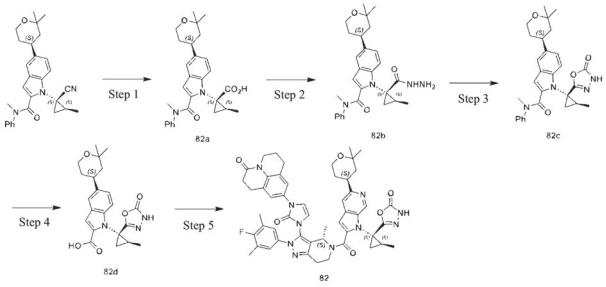
Example 81



9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following Example 51.

MS m/z (ESI): 933.4 [M+H]+

Example 82



Step 1: 1-((1S, 2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (300 mg, 0.68 mmol) and sodium hydroxide (136 mg, 3.41 mmol) were dissolved in a mixed solvent of ethanol (5 mL) and water (5 mL), and stirred at 100°C for reaction 6 hours. The reaction solution was adjusted to pH = 2 by adding hydrochloric acid, and extracted with dichloromethane (10 mL × 3); the organic phases were combined, dried over anhydrous sodium sulfate and filtered; and the filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography to obtain the target product (235 mg, yield: 75%).

MS m/z (ESI): 461.2 [M+1].

Step 2: 82a (235 mg, 0.51 mmol), HATU (291 mg, 0.77 mmol), hydrazine hydrate (33 mg, 1.02 mmol), and DIEA (196 mg, 1.53 mmol) were dissolved in DMF (10 mL), and reacted under stirring at room temperature for 3 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (10 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain the target product (184 mg, yield: 72%).

MS m/z (ESI): 475.3 [M+1]

Step 3: 82b (184 mg, 0.39 mmol) and thionyl chloride (51 mg, 0.43 mmol) were dissolved in toluene (5 mL), and stirred at 80°C for reaction for 1 hour. The reaction solution was quenched by adding a saturated sodium bicarbonate solution, and extracted with ethyl acetate (10 mL × 3); the organic phases were combined, washed with a saturated sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure, and then the resulting residue was purified by silica gel column chromatography to obtain the target product 82c (131 mg, yield: 68%).

MS m/z (ESI): 501.2 [M+1]

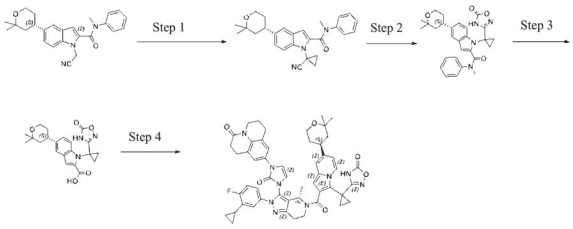
Step 4: following the synthesis method in step 5 of intermediate A, the target product 82d was obtained.

MS m/z (ESI): 412.2 [M+1]

Step 5: following the synthesis method in Example 34, the target product was obtained.

MS m/z (ESI): 921.4 [M+1]

Example 83



Step 1: Under an ice bath, (S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.80 g, 2 mmol) was dissolved in N,N-dimethylformamide (12 mL), followed by nitrogen replacement; then sodium hydride (0.24 g, 6 mmol, 60% in minerol oil) was added and stirred under the ice bath for 30 minutes, and then 1,2-dibromoethane (0.56 g, 3 mmol) was added; the reaction solution was stirred at room temperature for 2 hours until LCMS showed the completion reaction; the reaction solution was quenched with saturated ammonium chloride solution (20 mL) and then extracted with ethyl acetate (15 mL × 3); and the organic phases were combined, washed with saturated brine (15 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography (eluting with PE : EA = 10:1 - 3:1), to obtain the target product as a white solid (0.34 g, yield 40%).

MS m/z (ESI): 428.3 [M+H]+

Step 2: at room temperature, (S)-1-(1-cyanocyclopropyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.34 g, 0.8 mmol) was dissolved in ethanol (5 mL), and then triethylamine (0.24 g, 2.4 mmol) and hydroxylamine hydrochloride (0.11 g, 1.6 mmol) were added, successively, followed by nitrogen replacement; the reaction solution was heated to 90°C for reaction for 3 hours, until LCMS showed the completion of the reaction; the reaction solution was cooled to room temperature, and spin-dried, the residue was dissolved with ethyl acetate (15 mL), and then washed with saturated sodium bicarbonate solution (10 mL × 3) and saturated brine (15 mL × 3), successively; the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and then the residue was dissolved in tetrahydrofuran (5 mL); then N, N-dicarbonylimidazole (0.23 g, 1.6 mmol) and 1, 8-diazabicyclo[5.4.0]undec-7-ene (0.36 g, 2.4 mmol) were added, successively, followed by nitrogen replacement; the reaction solution was heated to 55°C for reaction for 2 hours until LCMS indicated the completion of the reaction; the reaction solution was cooled to room temperature, and spin-dried, and the residue was dissolved with ethyl acetate(30 mL), then washed with saturated sodium bicarbonate solution (15 mL × 2) and saturated brine (15 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography to obtain the target compound as a white solid (0.25 g, yield 65%).

MS m/z (ESI): 487.3 [M+H]+

Step 3: at room temperature, (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-1-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-phenyl-1H-indole-2-carboxamide (0.25 g, 0.52 mmol) was dissolved in PEG-400 (5 mL), and then potassium hydroxide (0.29 g, 5.2 mmol) was added, followed by nitrogen replacement; then the reaction solution was heated to 165°C for reaction for three hours, and cooled to room temperature, with LCMS indicating the completion of the reaction; the reaction solution was neutralized with dilute hydrochloric acid (6N) and adjusted to pH 5-6, with solid precipitating; and the system was filtered, the solid was washed with water and petroleum ether, successively, and air-dried, and the resulting solid was used directly in the next step (0.15 g, yield 75%).

MS m/z (ESI): 398.2 [M+H]+

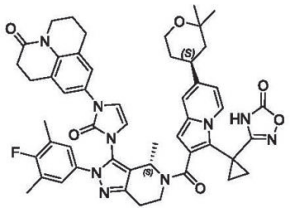
Step 4:

following step 4 in Example 29, the target product was obtained.

MS m/z (ESI): 918.4 [M+H]+

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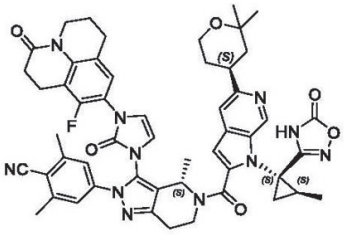
Example 84



9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target compound was obtained following Example 83.

MS m/z (ESI): 906.4 [M+H]+

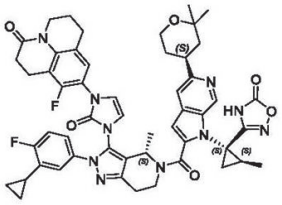
Example 85



the target compound was synthesized following Example 44.

MS m/z (ESI): 946.4 [M+1].

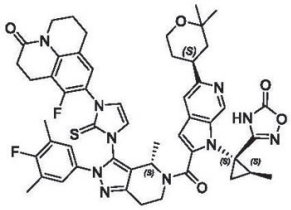
Example 86



the target compound was synthesized following Example 44.

MS m/z (ESI): 951.4 [M+1].

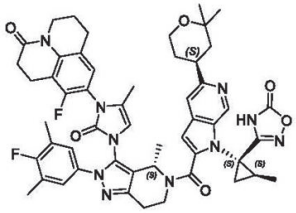
Example 87



the target compound was synthesized following Example 3.

MS m/z (ESI): 955.4 [M+1].

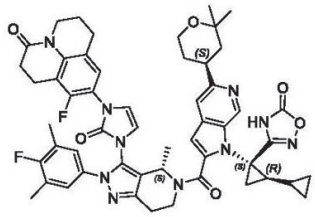
Example 88



the target compound was synthesized following Example 45.

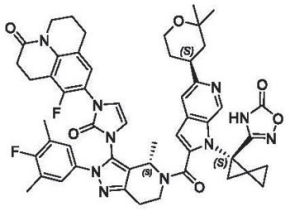
MS m/z (ESI): 953.4 [M+1].

Example 89



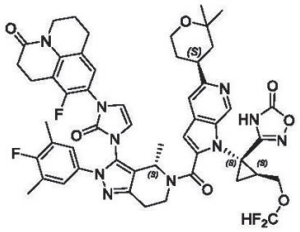
the target compound was synthesized following Example 46.
MS m/z (ESI): 965.4 [M+1].

Example 90



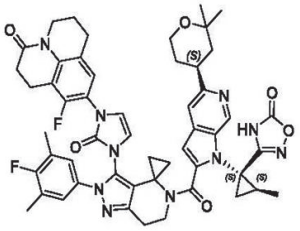
the target compound was synthesized following Example 79.
MS m/z (ESI): 951.4 [M+1].

Example 91



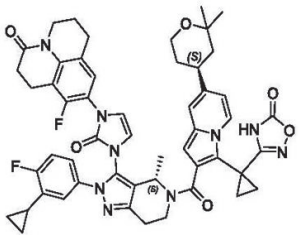
the target compound was synthesized following Example 64.
MS m/z (ESI): 1005.4 [M+1].

Example 92



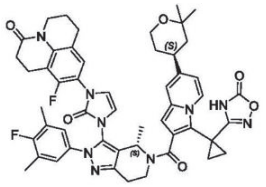
the target compound was synthesized following Example 16.
MS m/z (ESI): 951.4 [M+1].

Example 93



the target compound was synthesized following Example 44.
MS m/z (ESI): 936.4 [M+1].

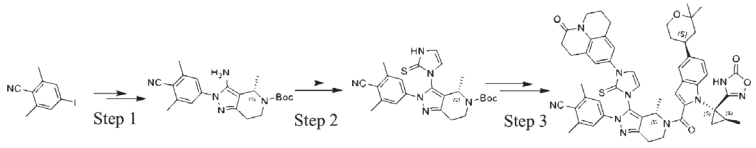
Example 94



the target compound was synthesized following Example 44.

MS m/z (ESI): 924.4 [M+1].

Example 95



Step 1

4-Iodo-2,6-dimethylbenzonitrile was used as a raw material, and the target product was obtained following the synthesis method in step 3 of intermediate B.

MS m/z (ESI): 382.2 [M+1].

Step 2

tert-Butyl (S)-3-amino-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate was used as a raw material, and the target product was obtained following the synthesis in step 1 of Example 3.

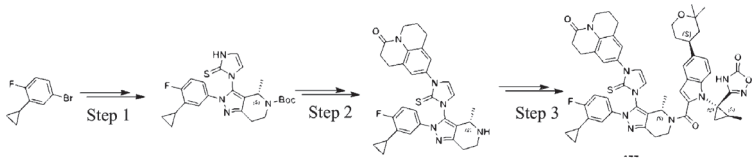
MS m/z (ESI): 465.2 [M+1].

Step 3

tert-Butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate was used as a raw material, and the target product was obtained following the synthesis in steps 2 to 4 of Example 25 (with 5-bromo-1-cyclopropyl-4-fluoroindazole being replaced with 9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2-1-ij]quinoline-5-one).

MS m/z (ESI): 943.4 [M+1].

Example 96



Step 1: 4-bromo-2-cyclopropyl-1-fluorobenzene was used as a raw material, and the target product was obtained following the synthesis method in steps 1 and 2 of Example 95.

MS m/z (ESI): 470.1 [M+1].

Step 2: tert-butyl (S)-2-(3-cyclopropyl-4-fluorophenyl)-4-methyl-3-(2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in steps 2 to 3 of Example 25 (with 5-bromo-1-cyclopropyl-4-fluoroindazole being replaced with 9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2-1-ij]quinoline-5-one).

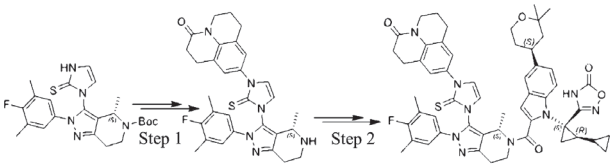
MS m/z (ESI): 555.2 [M+1].

Step 3: (S)-9-(3-(2-(3-cyclopropyl-4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target product was obtained following the synthesis method in step 4 of Example 25.

MS m/z (ESI): 948.4 [M+1].

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Example 97



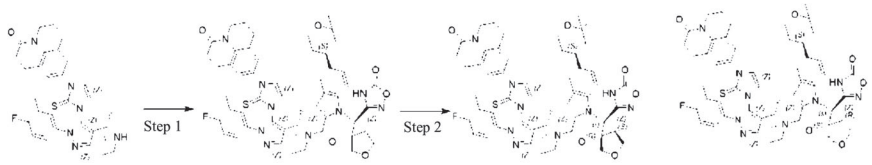
Step 1: tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in steps 2 and 3 of Example 25 (with 5-bromo-1-cyclopropyl-4-fluoroindazole being replaced with 9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2-1-ij]quinoline-5-one).

MS m/z (ESI): 543.2 [M+1].

Step 2: (S)-9-(3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1R,2S)-2-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-[1,1'-bi(cyclopropan)]-2-yl)-1H-indole-2-carboxylic acid were used as raw materials, and the target product was obtained following the synthesis method in step 4 of Example 25.

MS m/z (ESI): 962.4 [M+1].

Example 98



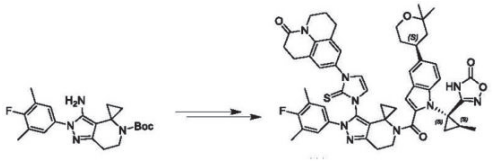
Step 1: (S)-9-(3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(6-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-3-oxabicyclo[3.1.0]hexan-6-yl)-1H-indole-2-carboxylic acid were used as raw materials, and the target product was obtained following the synthesis method in step 4 of Example 25.

MS m/z (ESI): 964.3 [M+1].

The compound 98 in step 2 was chirally resolved to obtain the title products 98-1 and 98-2.

MS m/z (ESI): 964.3 [M+1].

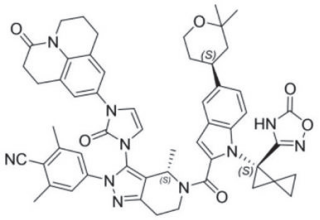
Example 99



tert-Butyl 3'-amino-2'-(4-fluoro-3,5-dimethylphenyl)-6',7'-dihydrospiro[cyclopropan-1,4'-pyrazolo[4,3-c]pyridine]-5'(2'H)-carboxylate was used as a raw material, and the target product was obtained following the synthesis in steps 2 and 3 of Example 95.

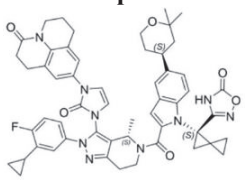
MS m/z (ESI): 948.4 [M+1].

Example 100

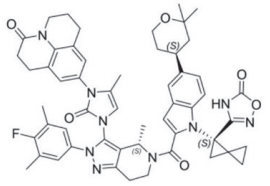


Following the synthesis in Example 403, the target product was obtained.
MS m/z (ESI): 939.4 [M+1].

Example 101

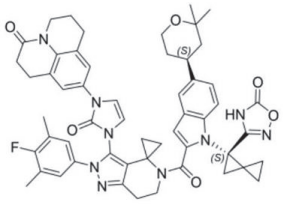


Following the synthesis in Example 22, the target product was obtained.
MS m/z (ESI): 944.4 [M+1].



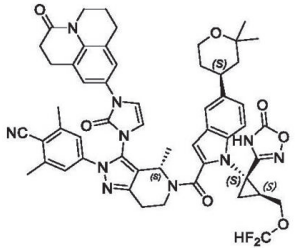
Following the synthesis in Example 406, the target product was obtained.
MS m/z (ESI): 946.4 [M+1].

Example 103



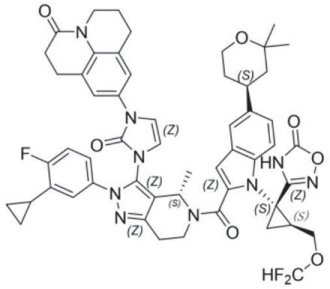
Following the synthesis in Example 51, the target compound was obtained.
MS m/z (ESI): 944.4 [M+1].

Example 104



Following the synthesis in Example 403, the target compound was obtained.
MS m/z (ESI): 993.4 [M+1].

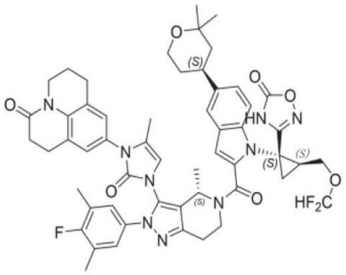
Example 105



Following the synthesis in Example 22, the target product was obtained.

MS m/z (ESI): 998.4 [M+1].

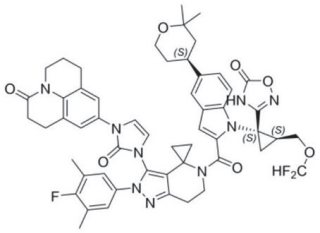
Example 106



Following the synthesis in Example 406, the target product was obtained.

MS m/z (ESI): 1000.4 [M+1].

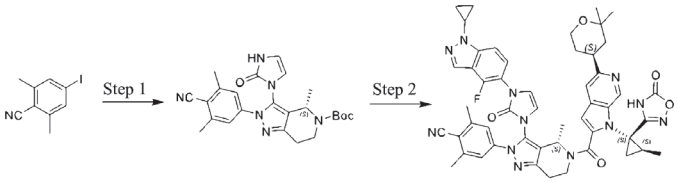
Example 107



Following the synthesis in Example 51, the target compound was obtained.

MS m/z (ESI): 998.4 [M+1].

Example 108



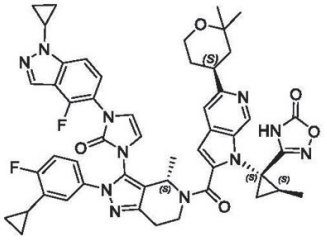
Step 1: 4-iodo-2,6-dimethylbenzonitrile was used as a raw material, and the target product was obtained following the synthesis of intermediate B.

MS m/z (ESI): 449.2 [M+1].

Step 2: following Example 25, the target product was synthesized.

MS m/z (ESI): 917.4 [M+1].

Example 109

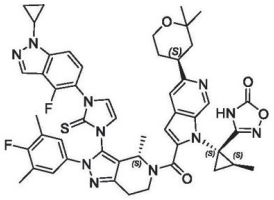


2-Cyclopropyl-1-fluoro-4-iodobenzene was used as a raw material, and the target product was synthesized following Example 108.

MS m/z (ESI): 922.4 [M+1].

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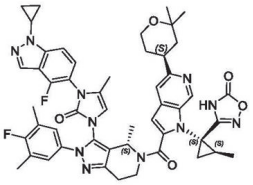
Example 110



1-Cyclopropyl-4-fluoro-1H-indazole-5-amine was used as a raw material, and the target product was synthesized following Example 3.

MS m/z (ESI): 926.4 [M+1].

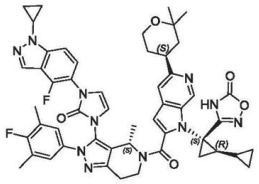
Example 111



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was synthesized following Example 45.

MS m/z (ESI): 924.4 [M+1].

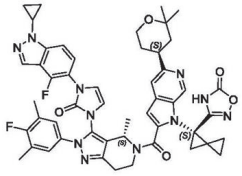
Example 112



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was synthesized following Example 40.

MS m/z (ESI): 936.4 [M+1].

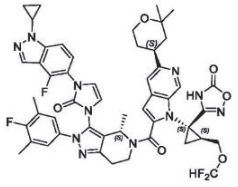
Example 113



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was synthesized following Example 5.

MS m/z (ESI): 922.4 [M+1].

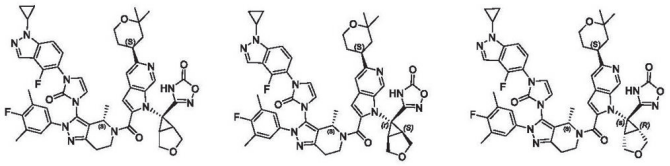
Example 114



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was synthesized following Example 64.

MS m/z (ESI): 976.4 [M+1].

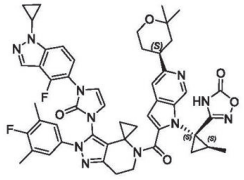
Example 115



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, following Example 62, to synthesize the target product, which was chirally resolved to obtain 115-1 and 115-2.

MS m/z (ESI): 938.4 [M+1].

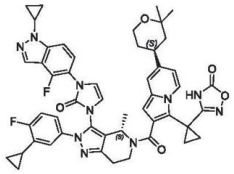
Example 116



the target product was synthesized following Example 110.

MS m/z (ESI): 922.4 [M+1].

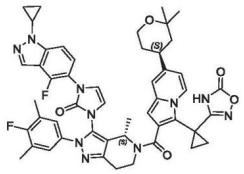
Example 117



the target product was synthesized following Examples 109 and 6.

MS m/z (ESI): 907.4 [M+1].

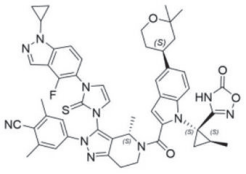
Example 118



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was synthesized following Example 6.

MS m/z (ESI): 895.4 [M+1].

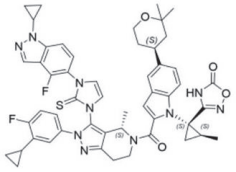
Example 119



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 4.

MS m/z (ESI): 932.4 [M+1].

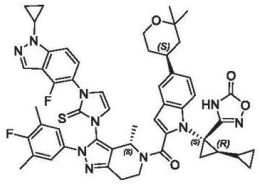
Example 120



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 4.

MS m/z (ESI): 937.3 [M+1].

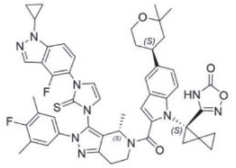
Example 121



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 46.

MS m/z (ESI): 951.4 [M+1].

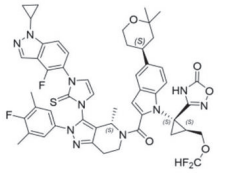
Example 122



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 46.

MS m/z (ESI): 937.4 [M+1].

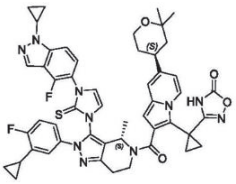
Example 123



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 64.

MS m/z (ESI): 991.4 [M+1].

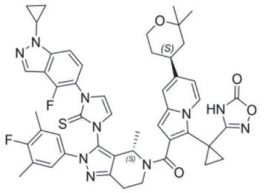
Example 124



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 47.

MS m/z (ESI): 923.3 [M+1].

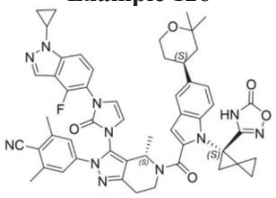
Example 125



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was finally obtained following Example 47.

MS m/z (ESI): 911.3 [M+1].

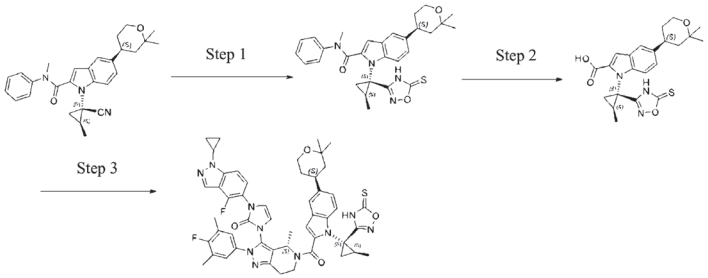
Example 126



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole, tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate, and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((S)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)spiro[2.2]pentan-1-yl)-1H-indole-2-carboxylic acid were used as raw materials, and a product was obtained following Example 29.

MS m/z (ESI): 928.4 [M+1].

Example 127



Step 1: at room temperature, 1-((1S,2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.44 g, 1 mmol) was dissolved in ethanol (6 mL), and then triethylamine (0.30 g, 3 mmol) and hydroxylamine hydrochloride (0.14 g, 2 mmol) were added, successively, followed by nitrogen replacement; the reaction solution was heated to 90°C for reaction for 3 hours, until LCMS showed the completion of the reaction; the reaction solution was cooled to room temperature, and spin-dried, the residue was dissolved with ethyl acetate (15 mL), and then washed with saturated sodium bicarbonate solution (10 mL × 3) and saturated brine (15 mL × 3), successively; the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and then the residue was dissolved in tetrahydrofuran (5 mL); then N, N-thiocarbonyldiimidazole (0.36 g, 2 mmol) and 1, 8-diazabicyclo[5.4.0]undec-7-ene (0.45 g, 3 mmol) were added, successively, followed by nitrogen replacement; the reaction solution was heated to 55°C for reaction for 2 hours until LCMS indicated the completion of the reaction; the reaction solution was cooled to room temperature, and spin-dried, and the residue was dissolved with ethyl acetate(30 mL), then washed with saturated sodium bicarbonate solution (15 mL × 2) and saturated brine (15 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography to obtain the target compound as a white solid (0.28 g, yield 55%).

MS m/z (ESI): 517.2 [M+H]+

Step 2: at room temperature, 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-1-((1S,2S)-2-methyl-1-(5-thio-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-phenyl-1H-indole-2-carboxamide (0.28 g, 0.55 mmol) was dissolved in PEG-400 (6 mL), and then potassium hydroxide (0.31 g, 5.5 mmol) was added, followed by nitrogen replacement; then the reaction solution was heated to 165°C for reaction for three hours, and

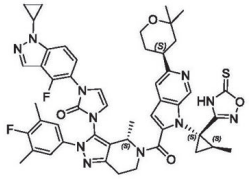
cooled to room temperature, with LCMS indicating the completion of the reaction; the reaction solution was neutralized with dilute hydrochloric acid (6N) and adjusted to pH 5-6, with solid precipitating; and the system was filtered, the solid was washed with water and petroleum ether, successively, and air-dried, and the resulting solid was used directly in the next step (0.16 g, yield 70%).

MS m/z (ESI): 428.2 [M+H]+

Step 3: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-methyl-1-(5-thio-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid was used as a raw material, and the target compound was obtained following step 4 of Example 25.

MS m/z (ESI): 925.4 [M+H]+

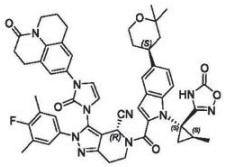
Example 128



ethyl 5-chloro-1H-pyrrolo[2,3-c]pyridine-2-carboxylate was used as a raw material, and the target compound was obtained following Examples 13 and 448.

MS m/z (ESI): 926.4 [M+H]+

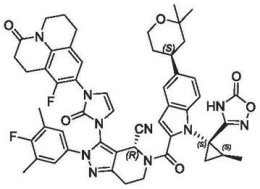
Example 129



Following the synthesis of 407, the target compound was obtained.

MS m/z (ESI): 931.4 [M+H]+。

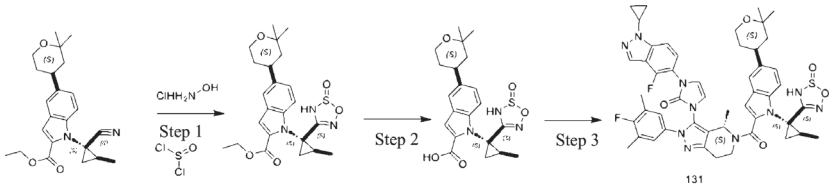
Example 130



Following the synthesis of 407, the target compound was obtained.

MS m/z (ESI): 949.4 [M+H]+

Example 131



131

Step 1: ethyl 1-((1S,2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in step 4 of intermediate A (with carbonyldiimidazole being replaced with thionyl chloride).

MS m/z (ESI): 460.1 [M+1].

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Step 2: ethyl 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-methyl-1-(2-hydroxyl-3H-1,2,3,5-oxathiadiazol-4-yl)cyclopropyl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in step 5 of intermediate A.

MS m/z (ESI): 432.1 [M+1].

Step 3: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-methyl-1-(2-hydroxyl-3H-1,2,3,5-oxathiadiazol-4-yl)cyclopropyl)-1H-indole-2-carboxylic acid and (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazol-2-one were used as raw materials, and the target was obtained following the synthesis method in step 4 of Example 25.

MS m/z (ESI): 929.3 [M+1].

Example 132

Step 1: ethyl 1-((1S,2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in step 4 of intermediate A (with carbonyldiimidazole being replaced with sulfonyl chloride).

MS m/z (ESI): 476.1 [M+1].

Step 2: ethyl 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-1-(2,2-dihydroxyl-3H-1,2,3,5-oxathiadiazol-4-yl)-2-methylcyclopropyl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in step 5 of intermediate A.

MS m/z (ESI): 448.1 [M+1].

Step 3: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-1-(2,2-dihydroxyl-3H-1,2,3,5-oxathiadiazol-4-yl)-2-methylcyclopropyl)-1H-indole-2-carboxylic acid and (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one were used as raw materials, and the target product was obtained following the synthesis method in step 4 of Example 25.

MS m/z (ESI): 945.3 [M+1].

Example 133

Ethyl 1-((1S,2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (1 g, 2.63 mmol) and ammonium acetate (202.7 mg, 2.63 mmol) were dissolved in 10 mL DMF and reacted under reflux at 100°C for 12 hours. The reaction solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel column chromatography (eluents: dichloromethane : methanol = 10 : 1), to obtain the target product (260 mg, yellow solid), yield: 24.8%.

MS m/z (ESI): 398.2 [M+1]

Step 2: ethyl 1-((1S,2S)-1-carbamimidoyl-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (260 mg, 654.06 μmol) and triethylamine (198.56 mg, 1.96 mmol) were dissolved in 5 mL DCM, then a solution of chloromethylsulfonyl chloride (97.44 g, 654.06 μmol) in dichloromethane was added slowly, and the reaction solution was stirred at room temperature for 10 hours. The reaction solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel column chromatography (eluents: dichloromethane : methanol = 10 : 1), to obtain the target product (110 mg, yellow solid), yield: 35.5%.