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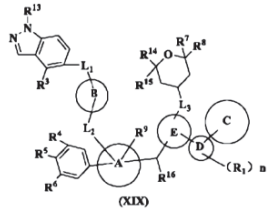
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(54) Title: BENZO NITROGEN-CONTAINING HETEROCYCLIC DERIVATIVE REGULATOR, PREPARATION METHOD THEREFOR AND USE THEREOF



(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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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.

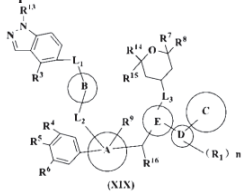
GLP-1 is a peptide hormone secreted by human intestinal L cells, and its receptors are distributed in pancreas islet cells, various gastrointestinal cells, and neurons of the central nervous system and peripheral nervous system. After activation, GLP-1 receptors have physiological effects such as promoting 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 $-(CH_2)_{n1}-$;

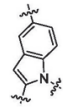
ring A is selected from C_{3-14}cycloalkyl, 3- to 14-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl;

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

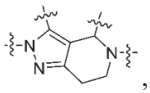
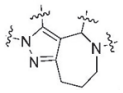
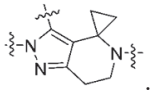
preferably, R^{13} is selected from -CD_3, hydrogen, deuterium, fluoro, chloro, bromo, methyl or cyclopropyl, wherein the methyl or cyclopropyl is optionally further substituted by one or more substituents of deuterium, halogen or C_{1-3}alkyl.

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

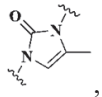
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more preferably, ring A is selected from  ,  or  .

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):

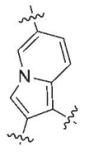
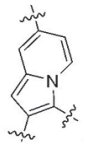
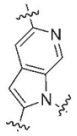
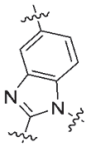
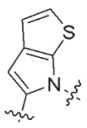
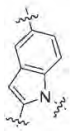
ring D is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 atoms selected from N, O or S;

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  .

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

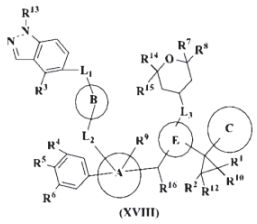
preferably, R^9 or R^{16}, respectively, is linked with the atoms to which it is connected to form cyclopropyl.

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,  ,  ,  ,  ,  ,  or  , 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.

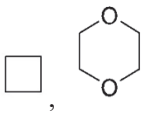
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

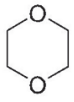
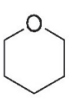
R^9 or R^{16}, respectively, is linked with the atoms to which it is connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 atoms selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 atoms selected from N, O or S; and

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

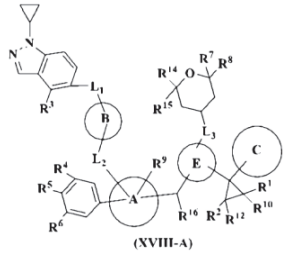
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVIII):

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.

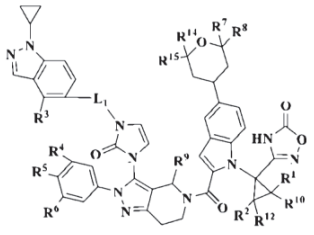
In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-A):



(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).

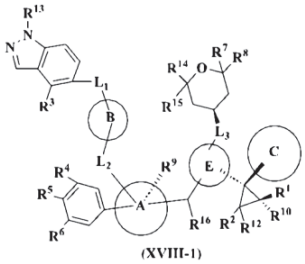
In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-B):



(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).

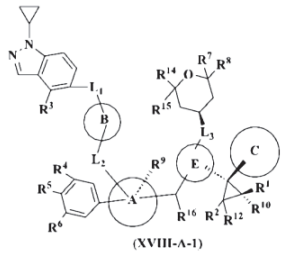
In a further preferred embodiment of the present disclosure, the compound of general formula (XVIII) is further shown as general formula (XVIII-1):



(XVIII-1)

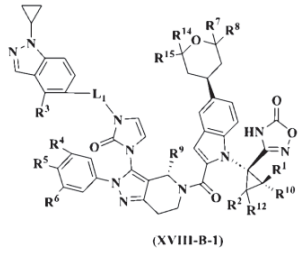
.

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



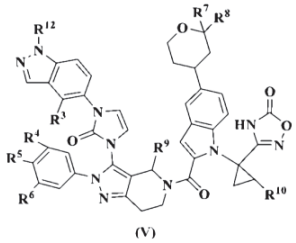
(XVIII-A-1)

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:



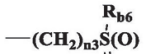
(V)

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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$,


-$NR_{a5}S(O)NR_{a4}R_{b4}$, -$(CH_2)_{n2}R_{a5}R_{b5}$ 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):

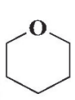
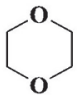
R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, cyano, C_{1-3}alkyl, C_{1-3}sulfanyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, and 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl,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

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):

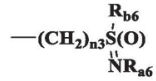
R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to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

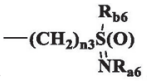
preferably, R^3 is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C6-10aryl, 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,

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

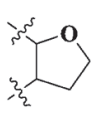
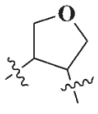
further preferably, R^{10} is linked with the atoms to which it is connected and adjacent atoms to form  .

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

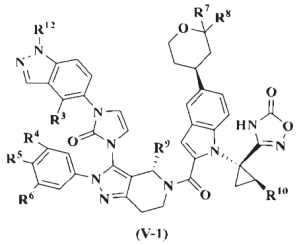
R^{10} is linked with the atoms to which it is connected and adjacent atoms to form  or  .

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  .

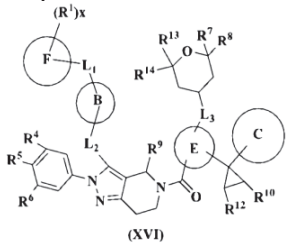
In a further preferred embodiment of the present disclosure, the compound of general formula (V) is further shown as general formula (V-1):



(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)

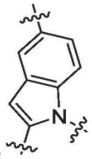
wherein

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;

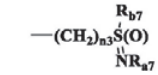
ring C is selected from C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl; optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, mercapto, thio, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl,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

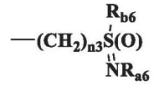
or ring E is  , optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl;

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.

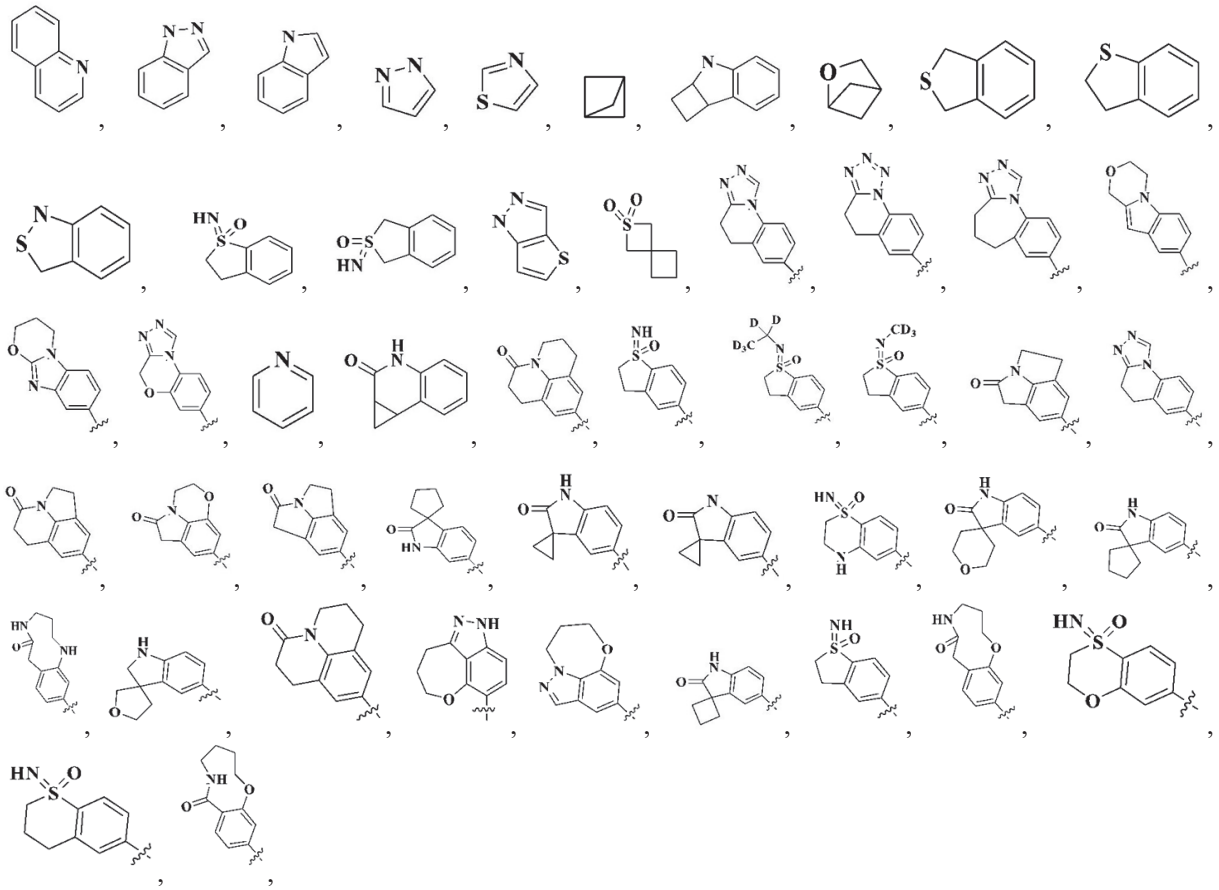
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

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;

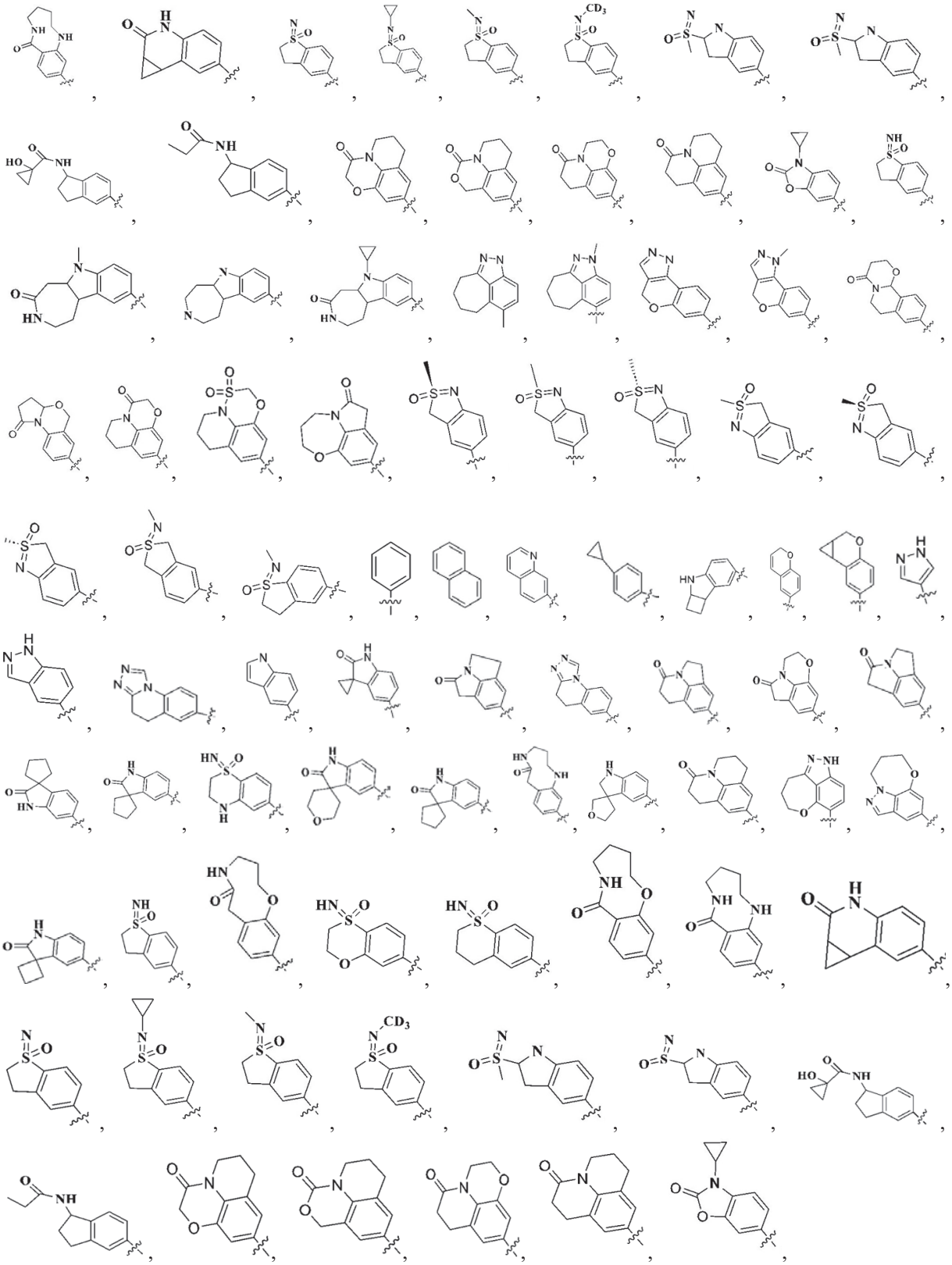
preferably, ring F is selected from C_{3-10}cycloalkyl, 5- to 14-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S;

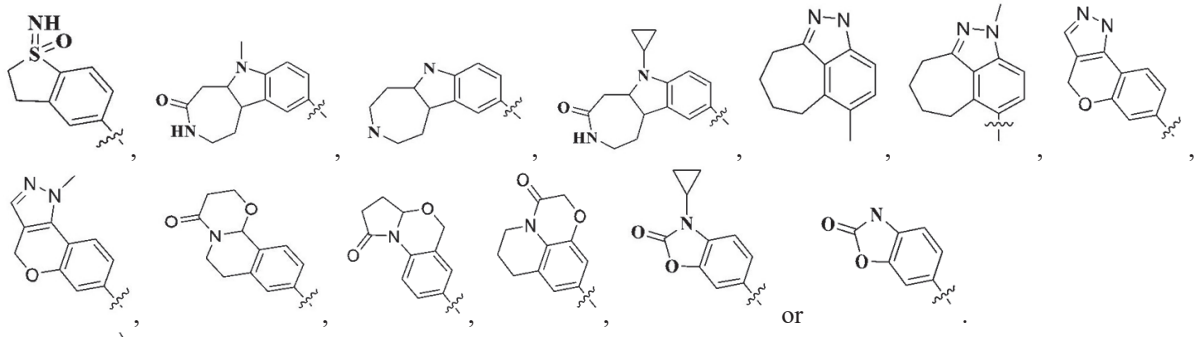
further preferably, ring F is selected from C_{3-6}bridged cycloalkyl, 8- to 14-membered tricyclic fused heterocyclyl containing 1-5 heteroatoms, 3- to 8-membered bridged heterocyclyl containing 1-3 heteroatoms, fused heterocyclyl containing 1-3 heteroatoms, bridged heterocyclyl containing 1-3 heteroatoms,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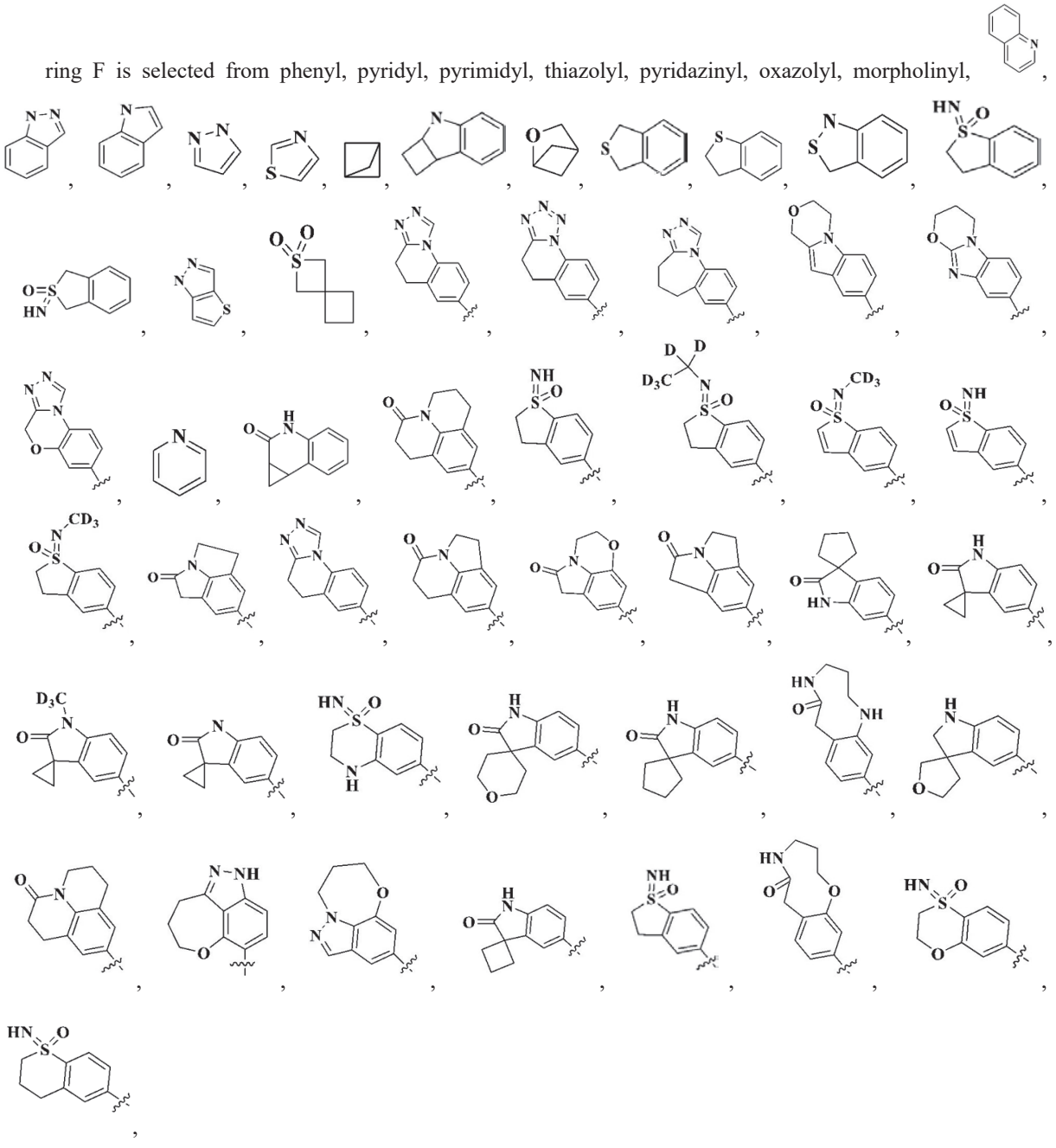


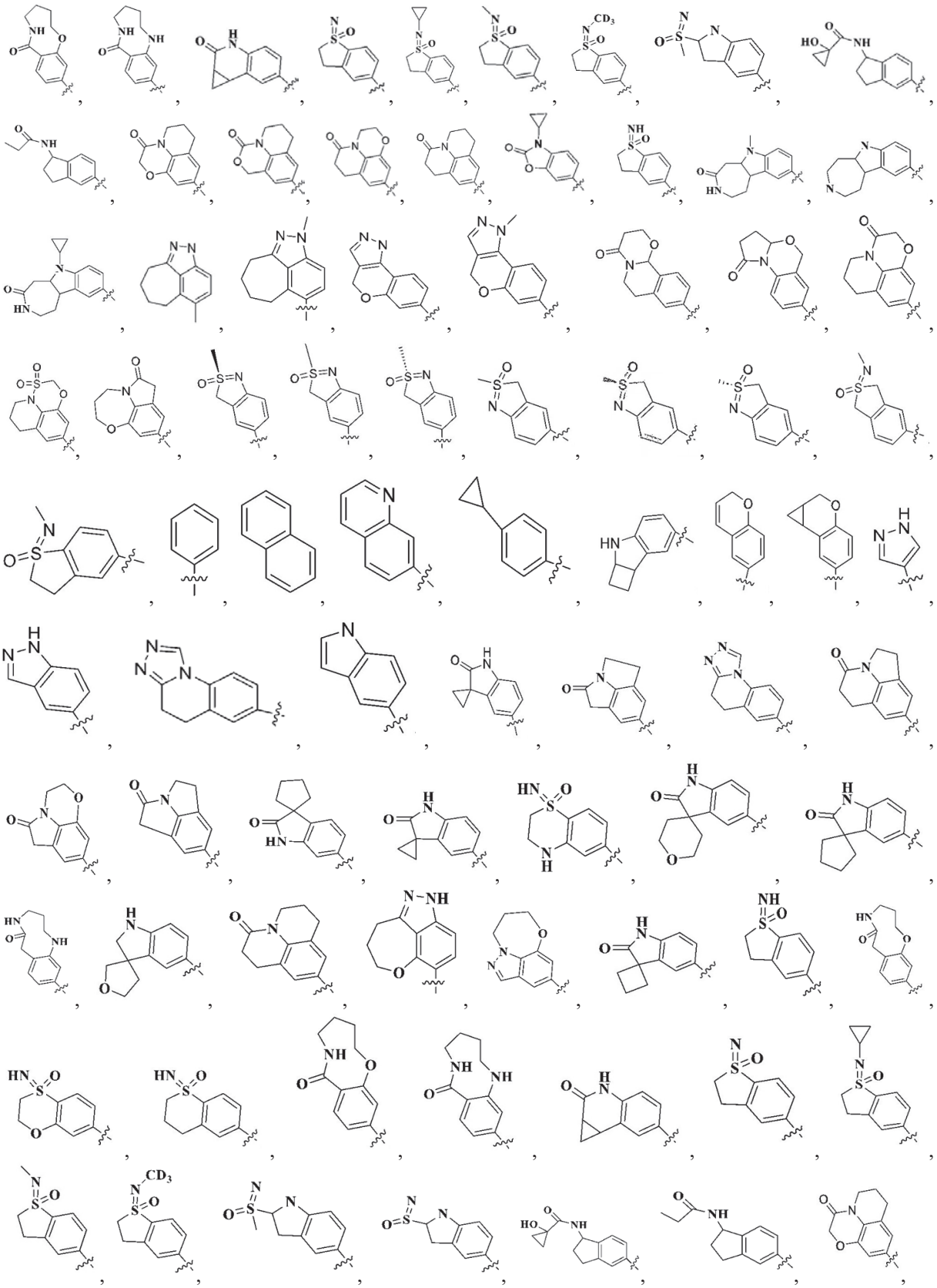


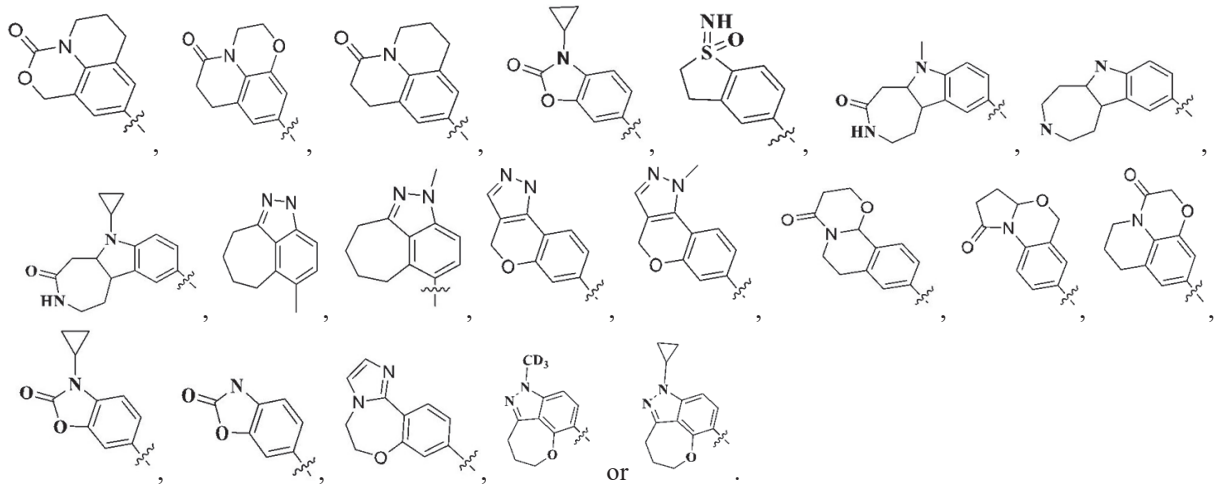
Note: " " represents connection with L_1.

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,





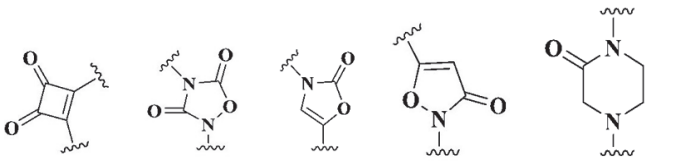


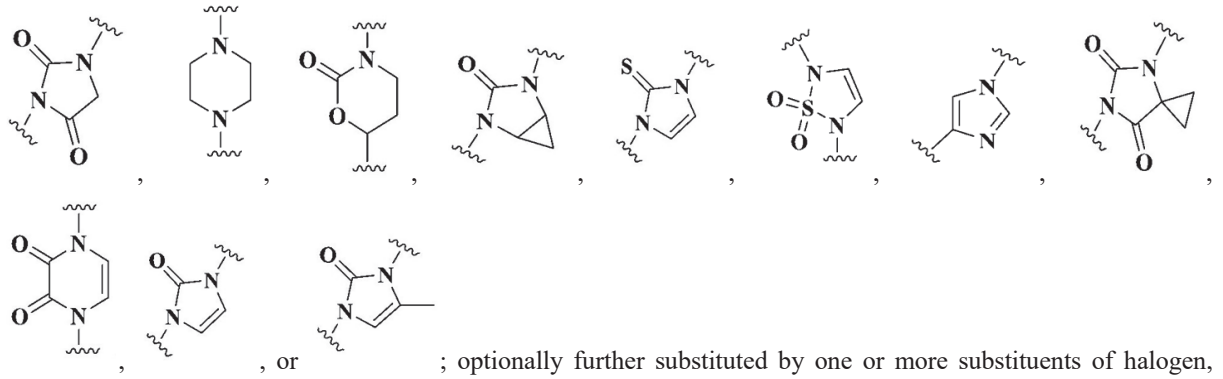
Note: "~~" represents connection with L_1.

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 

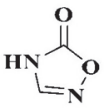
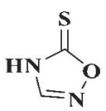
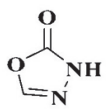
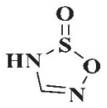


; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl.

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;

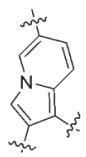
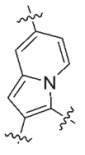
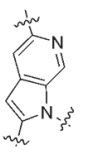
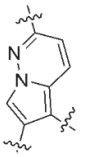
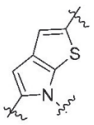
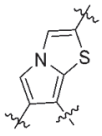
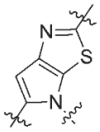
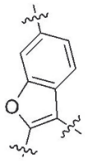
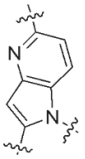
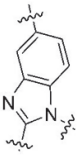
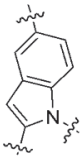
preferably, ring C is selected from C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 selected from N, O or S or 5- to 6-membered heteroaryl containing 1-3 selected from N, O or S; optionally further substituted by one or more substituents of hydroxyl, thio, oxo or C_{1-6}haloalkoxy; and

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

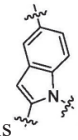
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

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;

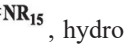
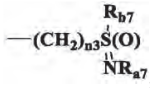
preferably, ring E is selected from C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl; and

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

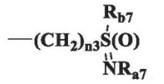
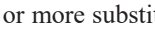
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

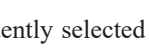
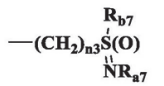
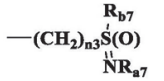
ring E is  , optionally further substituted by one or more substituents of halogen, methoxy or deuterated methyl.

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

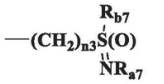
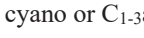
R^1 each is independently selected from  , hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy, C_{1-3}haloalkoxy, 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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$,  , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$ or $-(CH_2)_{n1}S(O)_2R_{b5}$ is optionally further substituted by one or more substituents of  , 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  , 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):

more further preferably, R^1 each is independently selected from 、hydrogen, deuterium, amino, oxo, cyano, fluoro, chloro, bromo, methyl, ethyl, cyclopropyl, $-CD_3$, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, methyl, ethyl, cyclopropyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$,  , $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ 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):

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,

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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n3}\overset{R_{b6}}{\underset{NR_{a6}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n3}\overset{R_{b6}}{\underset{NR_{a6}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$; 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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n3}\overset{R_{b6}}{\underset{NR_{a6}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$.

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  .

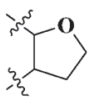
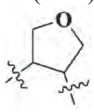
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

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;

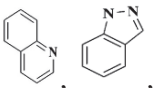
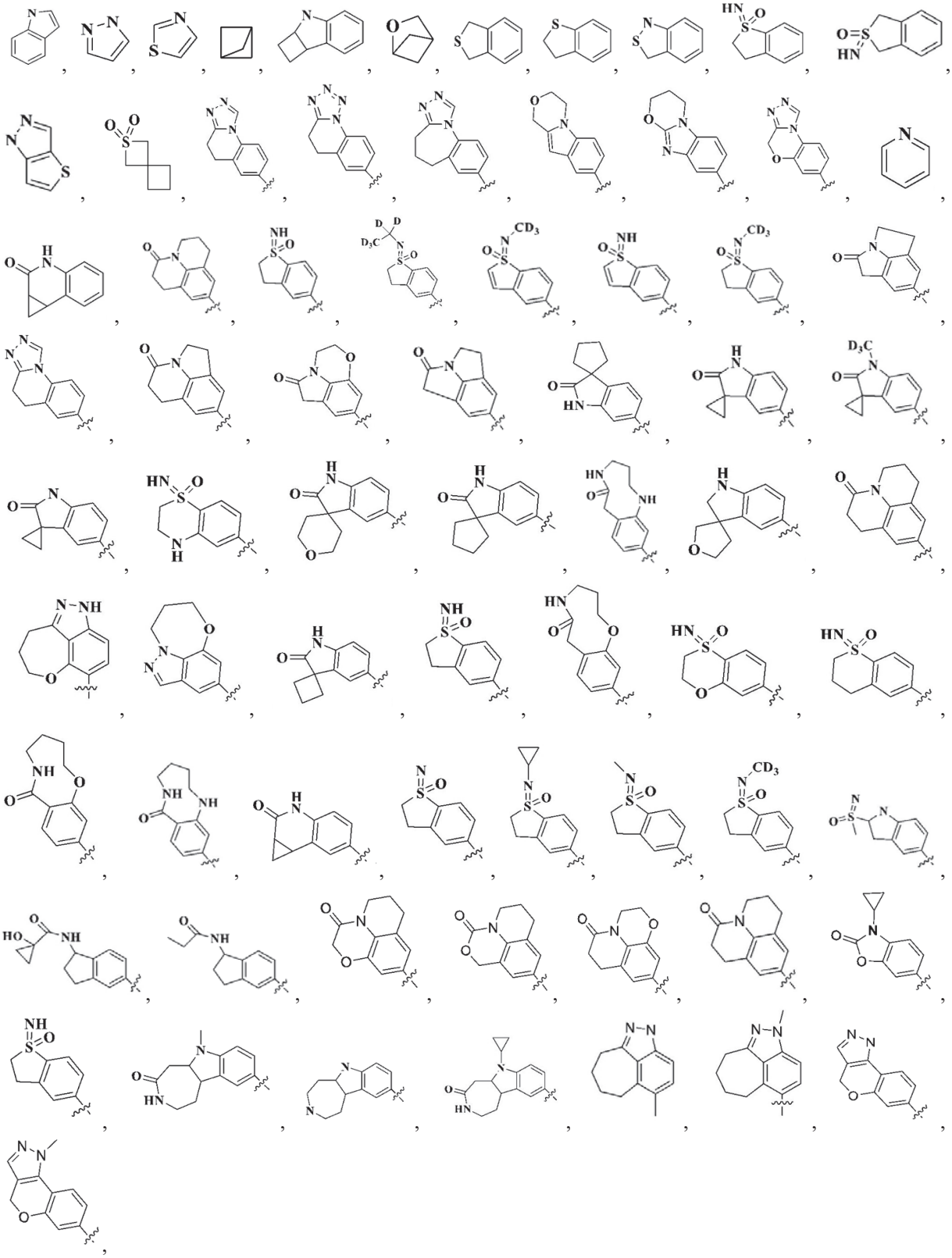
preferably, R^{10} and R^{12} are lined with the atoms to which they are connected to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; and

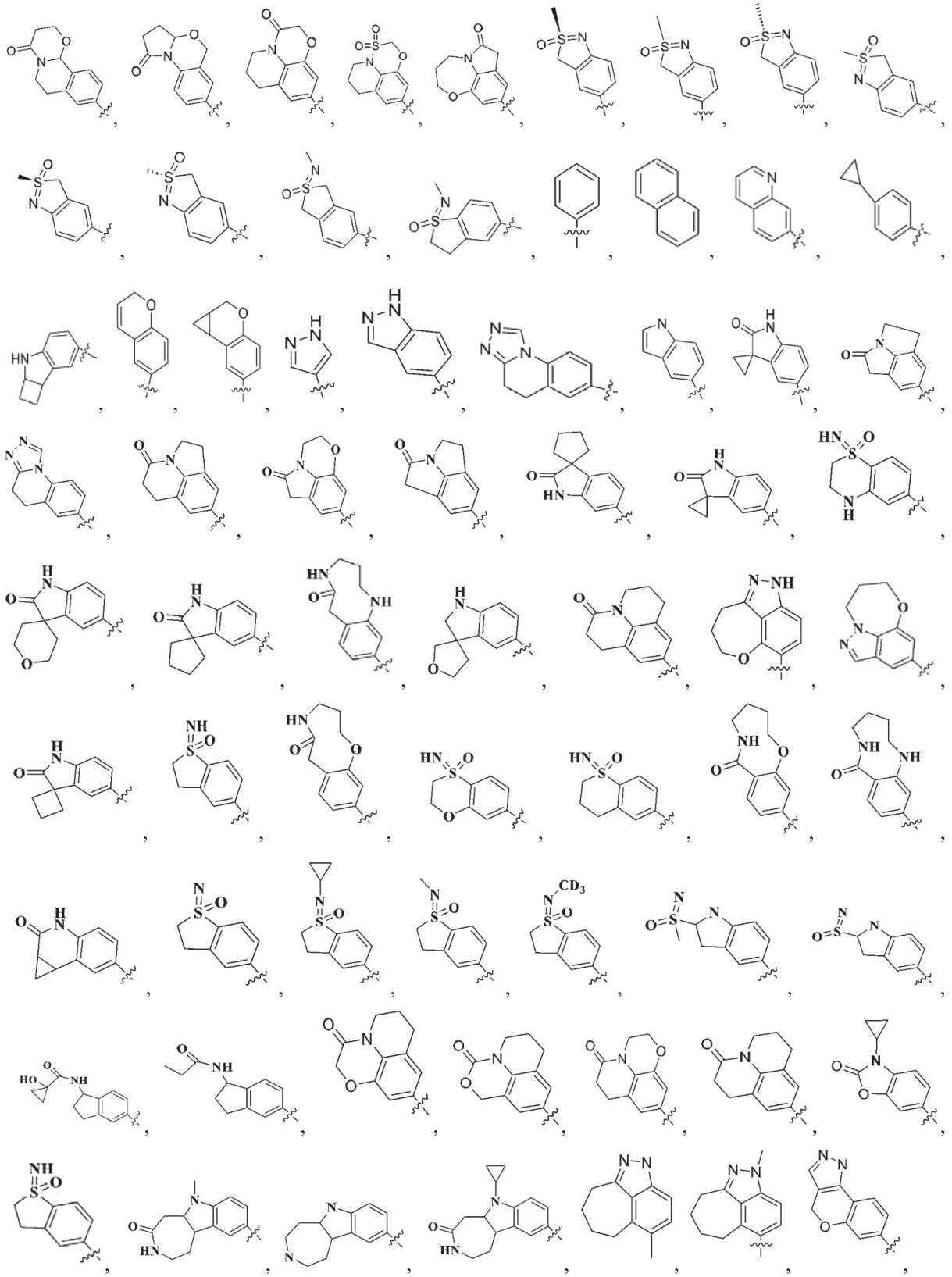
further preferably, R^{10} and R^{12} are lined with the atoms to which they are connected to form  .

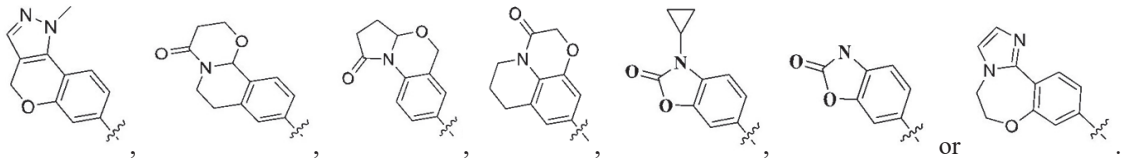
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI):

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):

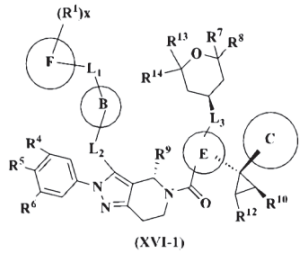
ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl,  , 





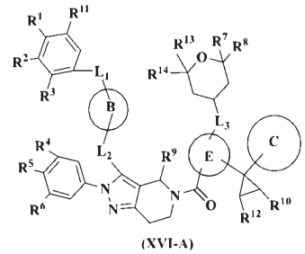
Note: “ ” represents connection with L_1.

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):



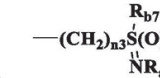
(XVI-A)

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 $=NR_{15}$, 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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n3}\overset{R_{b6}}{\underset{NR_{a6}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, wherein the amino, C_{1-6}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;

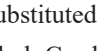
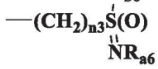
R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, 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;

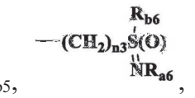
or

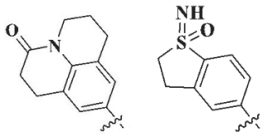
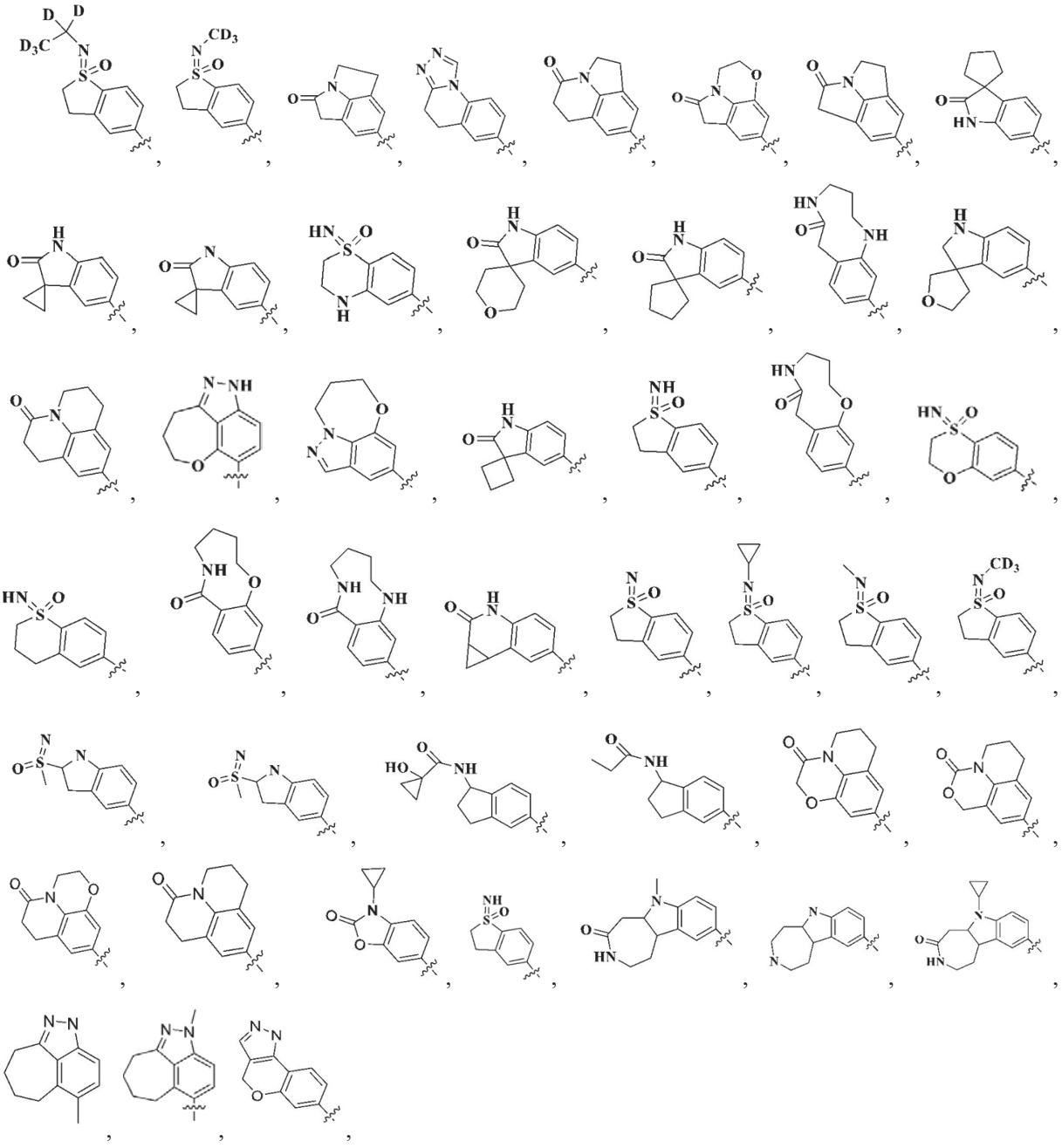
R_{a1} and R_{b1}, R_{a2} and R_{b2}, R_{a3} and R_{b3}, R_{a4} and R_{b4}, R_{a6} and R_{b6}, R_{a8} and R_{b8}, R_{a9} and R_{b9}, and R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl, 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).

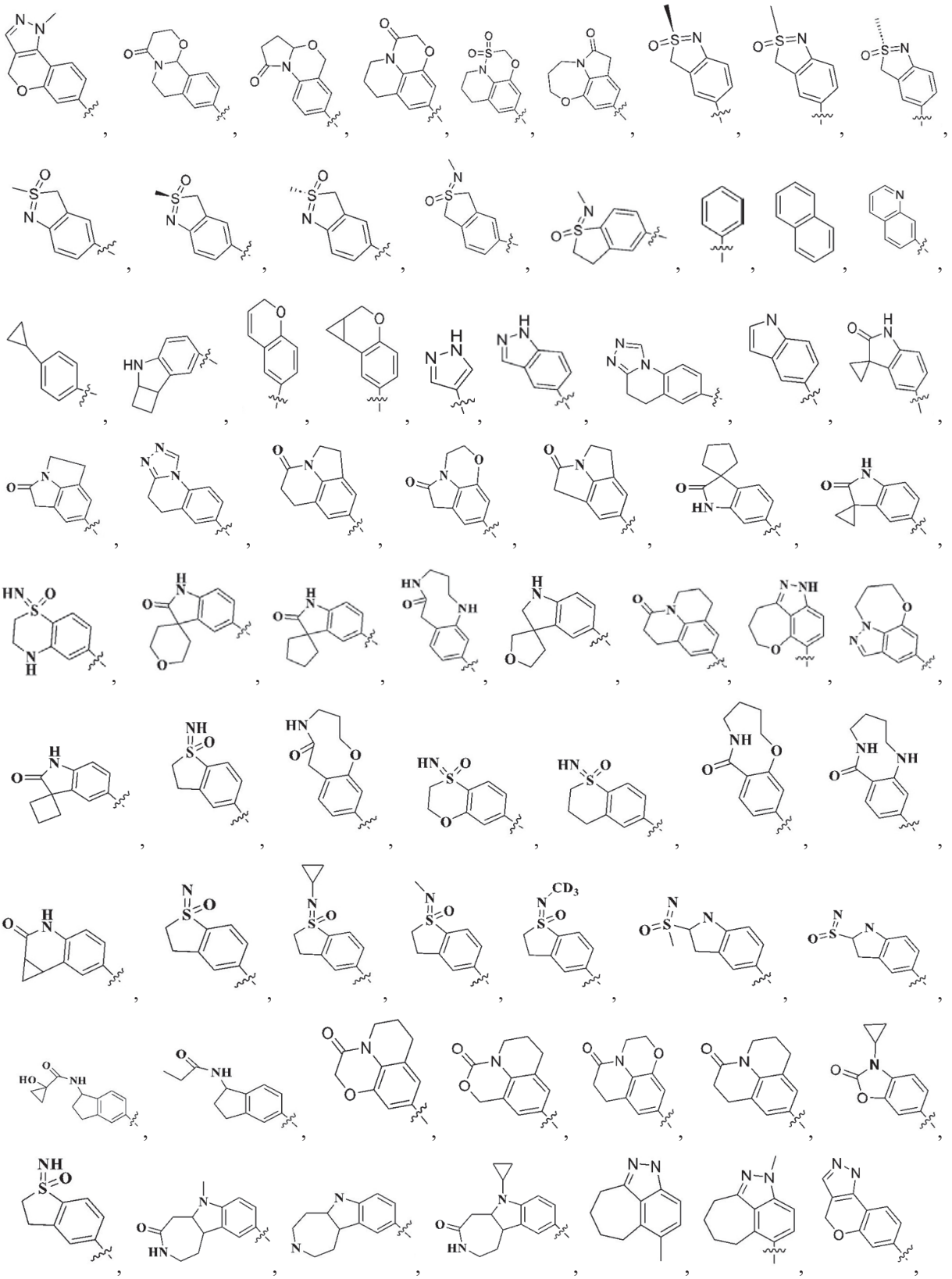
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

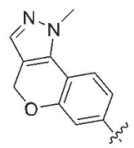
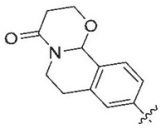
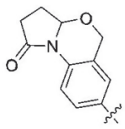
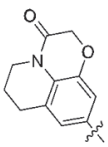
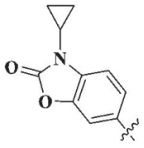
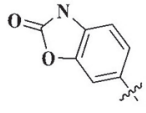
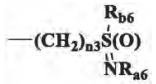
R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 selected from N, O or S, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 selected from N, O or S, optionally further substituted by one or 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  , 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 and R^2, and R^1 and R^{11} are linked with adjacent phenyl to form  , 

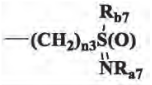
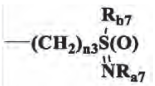
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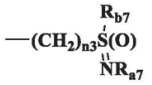


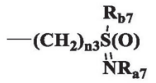
 ,  ,  ,  ,  or  ; optionally further substituted by one or more substituents of -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$,  , -$(CH_2)_{n1}NR_{a8}$C(O)R_{b8}, -$(CR_{a8}R_{b8})_{n4}$C(O)$NR_{a9}R_{b9}$, -$(CH_2)_{n1}$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):

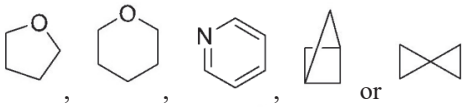
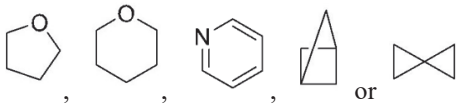
R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}deuterated alkoxy,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

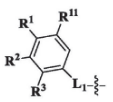
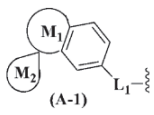
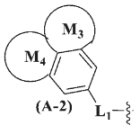
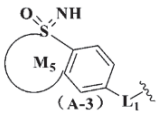
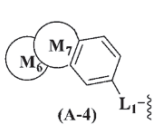
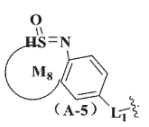
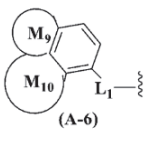
preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9}, R_{b9}, R_{a10} or R_{b10} each is independently selected from hydrogen, deuterium, halogen, methyl, ethyl, cyano, deuterated methyl, cyclopropyl, cyclopentyl, phenyl,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

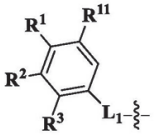
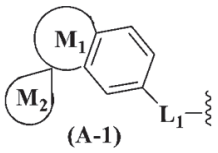
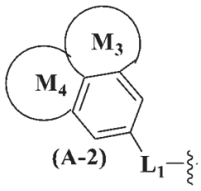
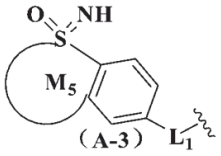
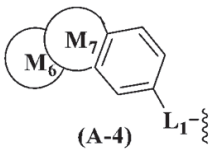
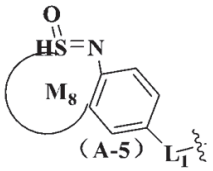
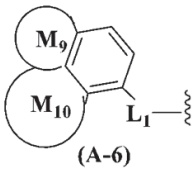
in general formula (XVI-A),  is further shown as  ,  ,  ,  ,  , or  , optionally further substituted by one or more substituents of halogen,

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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.

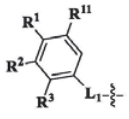
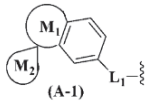
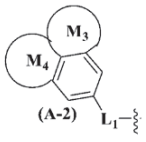
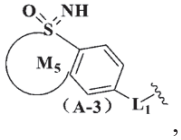
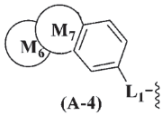
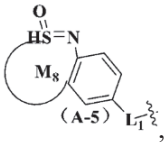
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

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.

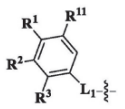
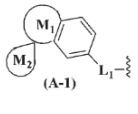
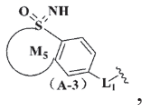
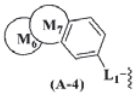
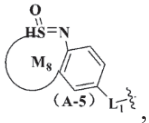
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

in general formula (XVI-A),  is further shown as  ,  ,  ,  or  , 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.

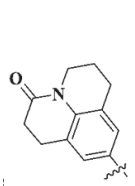
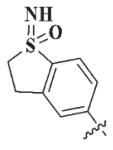
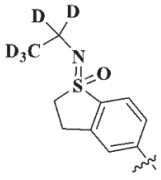
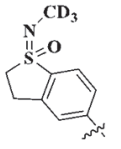
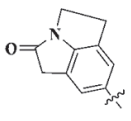
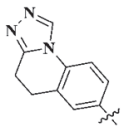
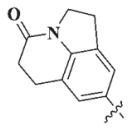
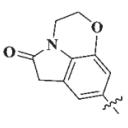
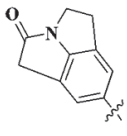
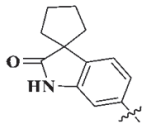
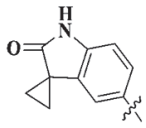
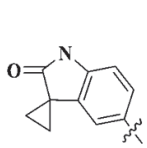
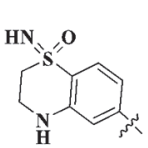
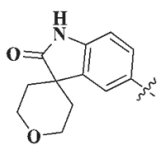
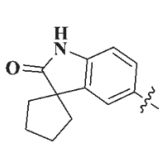
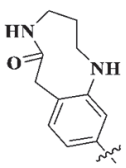
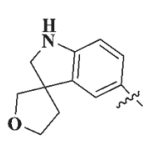
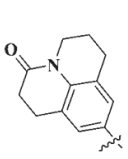
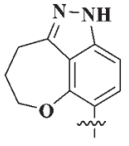
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVI-A):

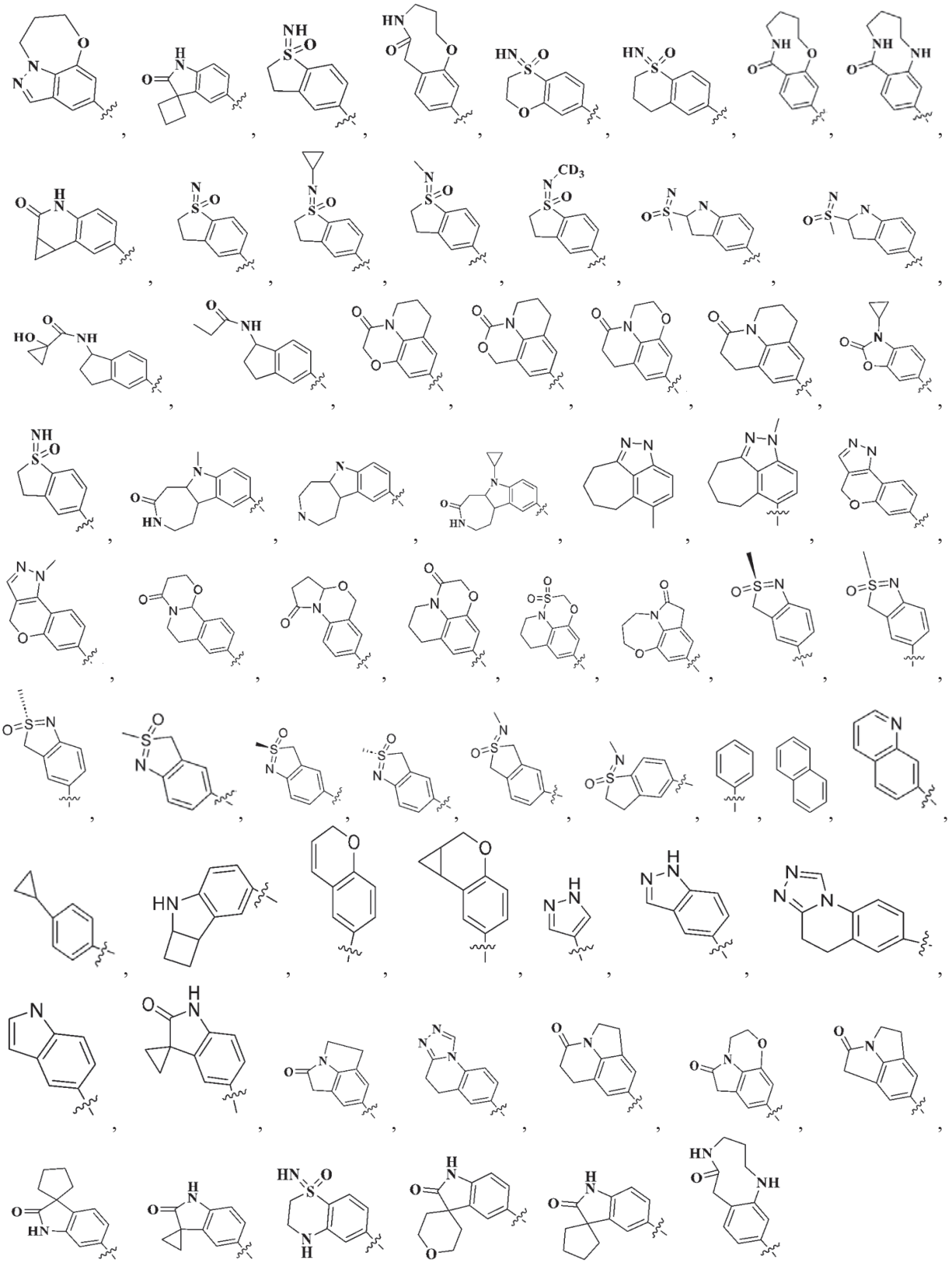
in general formula (XVI-A),  is further shown as  ,  ,  ,  or  , optionally further substituted by one or more substituents of halogen, methoxy, C_{1-3}cycloalkyl, C_{3-6}cycloalkyl or deuterated methyl;

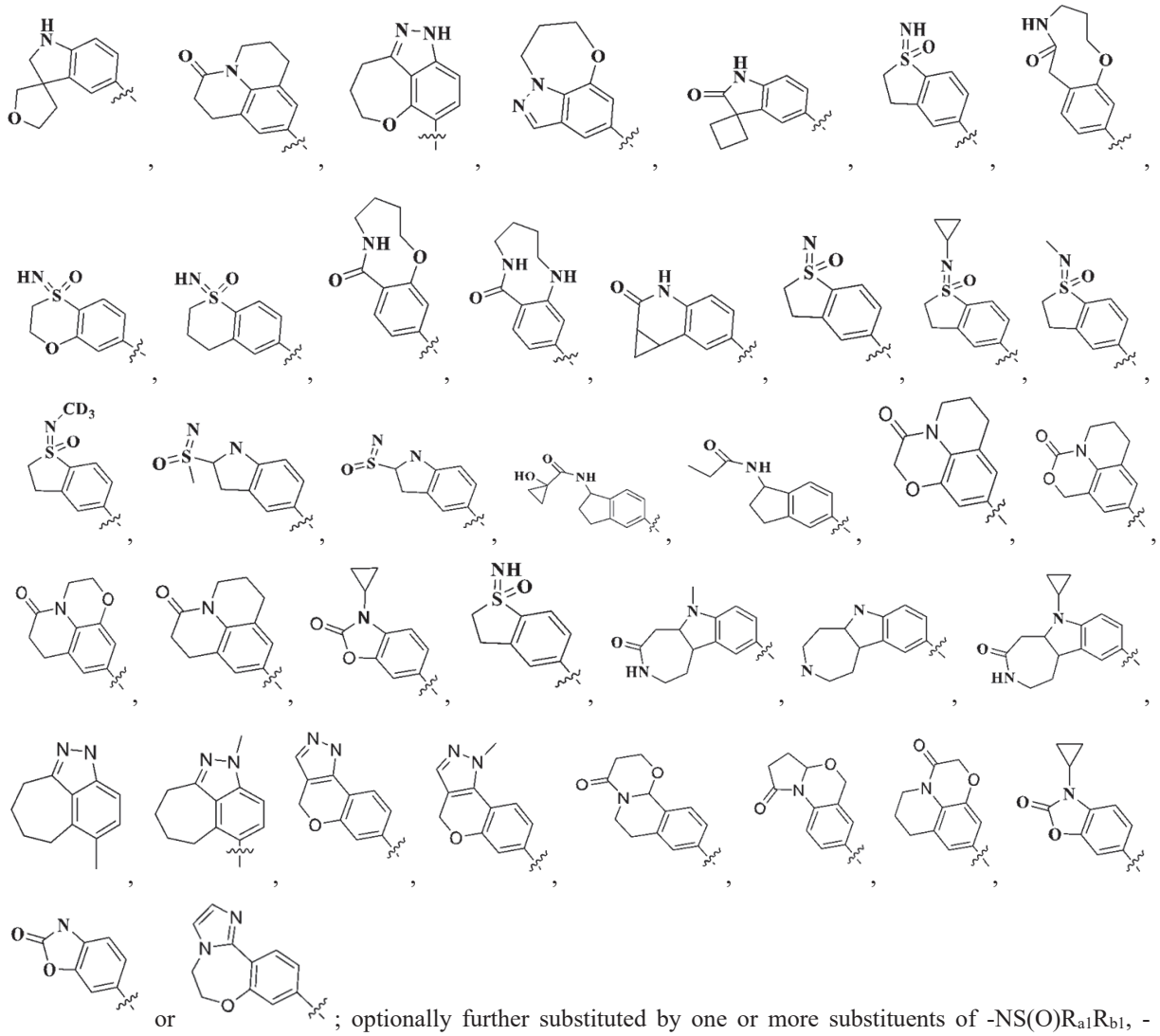
ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7 or ring M_8 each is independently selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms, optionally further substituted 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

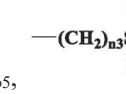
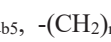
preferably, ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7 or ring M_8 each is independently selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms, optionally further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

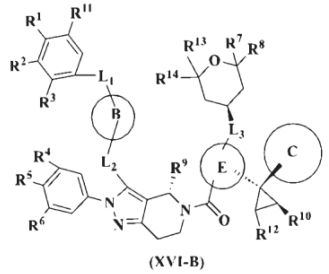




or ; optionally further substituted by one or more substituents of -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}$O$(CH_2)_{n2}R_{b5}$,  , -$(CH_2)_{n1}NR_{a8}$C(O)R_{b8}, -$(CR_{a8}R_{b8})_{n4}$C(O)$NR_{a9}R_{b9}$, -$(CH_2)_{n1}$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.

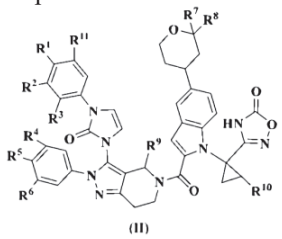
Note: "  " represents connection with L_1.

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):

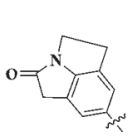
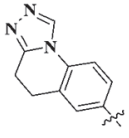
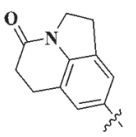
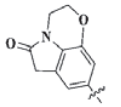
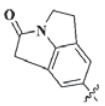
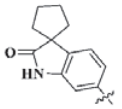
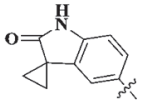
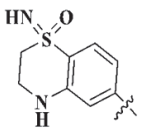
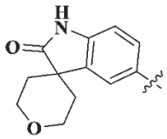
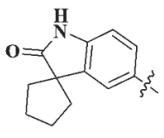
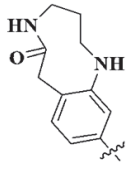
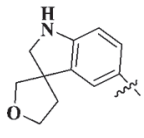
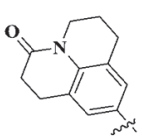
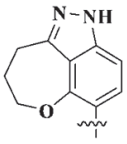
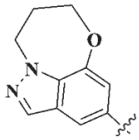
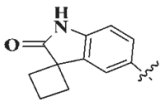
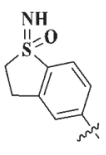
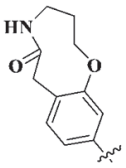
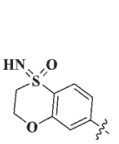
R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally 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.

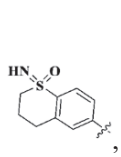
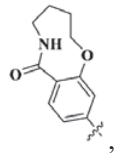
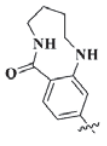
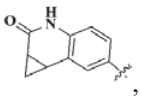
In a further preferred embodiment of the present disclosure, in the compound of general formula (II):

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  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  .

 ,  ,  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):

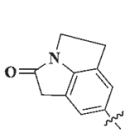
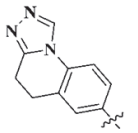
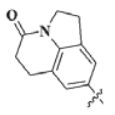
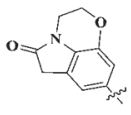
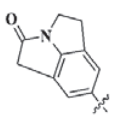
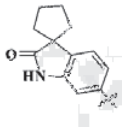
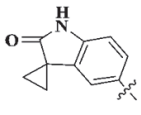
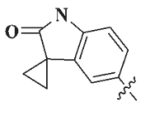
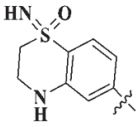
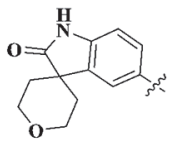
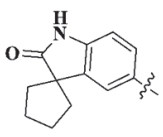
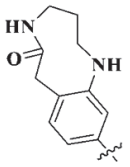
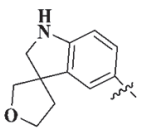
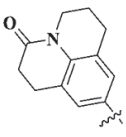
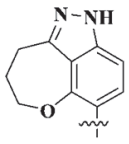
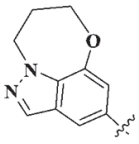
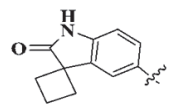
R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl or C_{1-3}haloalkyl; and

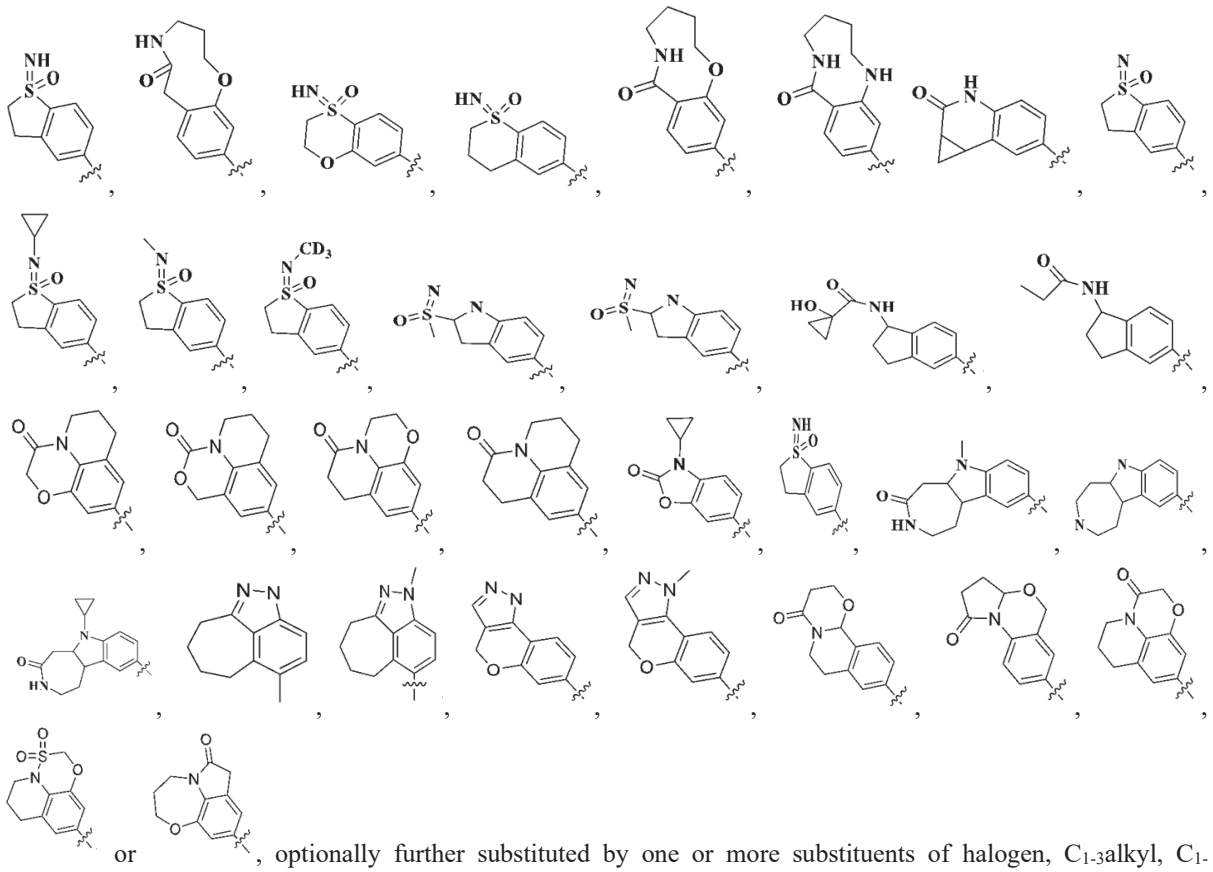
preferably, R^7, R^8, R^9or R^{10} each is independently selected from methyl.

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;

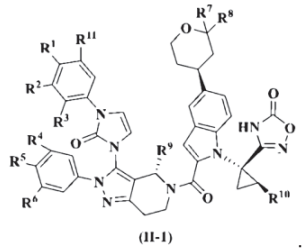
preferably, R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 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 $-(CH_2)_{m1}OR_{c1}$.

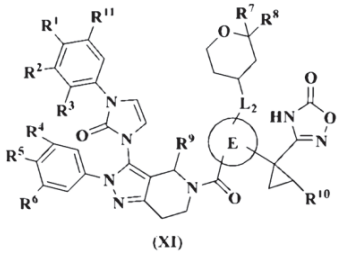
In a further preferred embodiment of the present disclosure, the compound of general formula (II) is further shown as general formula (II-1):

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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;

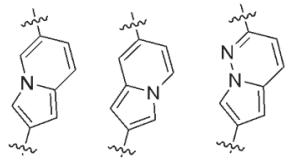
R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, 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

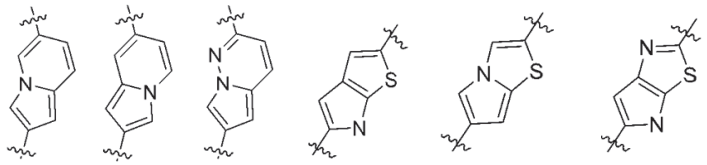
n1-n4 are an integer of 0-5.

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

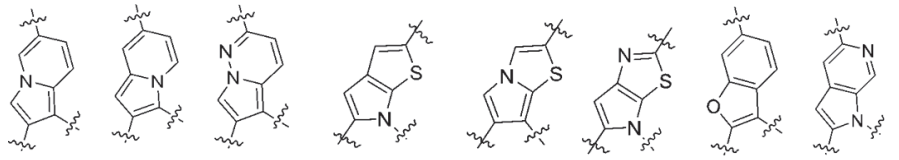
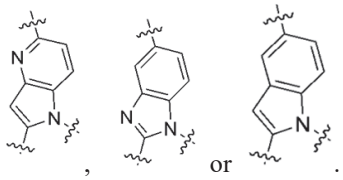
ring E is selected from C_{3-8}cycloalkyl, 3- to 10-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms; and

preferably, ring E is selected from  .

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

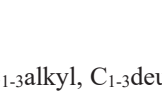
ring E is selected from  .

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

ring E is selected from   .

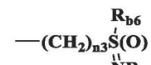
In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

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):

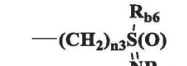
preferably, R^1, R^2, R^3 or R^{11} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 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,

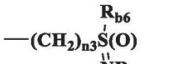
cyano, oxo, -NS(O)$R_{a1}R_{b1}$, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-3}haloalkoxy, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl.

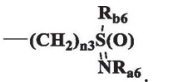
In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

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):

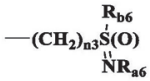
preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl,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

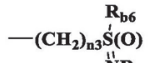
further preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form phenyl, or 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by oxo, -NS(O)$R_{a1}R_{b1}$, -$(CH_2)_{n1}$S(O)$NR_{a2}R_{b2}$, -P(O)$R_{a3}R_{b3}$,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

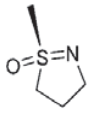
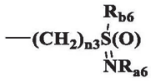
In a further preferred embodiment of the present disclosure, in the compound of general formula (XI):

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)$NR_{a2}R_{b2}$,

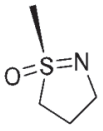
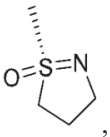
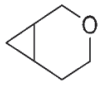
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-P(O)$R_{a3}R_{b3}$, -NR_{a5}S(O)$NR_{a4}R_{b4}$, -$(CH_2)_{n1}$S(O)$_2R_{a5}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$,  , -$(CH_2)_n$P(O)$R_{a7}R_{b7}$ or -$(CR_{a8}R_{b8})_{n4}$C(O)$NR_{a9}R_{b9}$;

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)$_2R_{a5}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$,  , -$(CH_2)_n$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)$_2R_{a5}$, -$(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$,  , -$(CH_2)_n$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

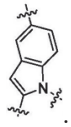
preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, R_{b8}, R_{a9} or R_{b9} each is independently selected from hydrogen, deuterium, halogen, cyano, cyclopropyl, cyclopentyl, methyl, ethyl, phenyl or  .

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):

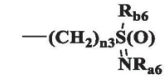
R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a7} and R_{b7}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, wherein 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,

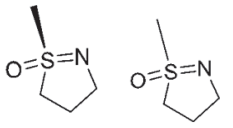
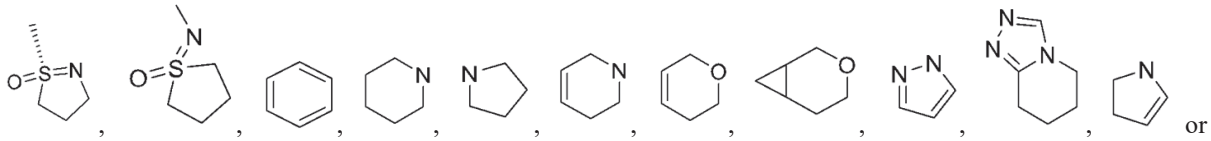
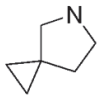
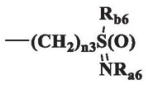
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C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl; and

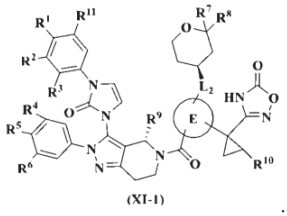
preferably, R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a7} and R_{b7}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, respectively, are linked with adjacent atoms to form cyclopropyl.

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

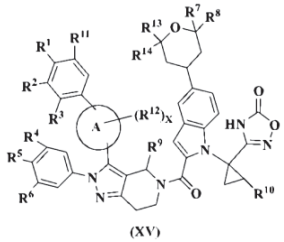
preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form  ,  ,  , optionally further substituted by one or more substituents of methyl, halogen, oxo, cyclopropyl, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$,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

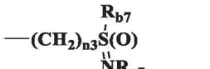


(XV)

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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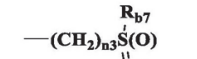
R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 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;

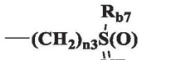
or R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14}, respectively, is linked with the atoms to which it is connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

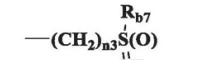
n1-n5 are an integer of 0-5; and

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

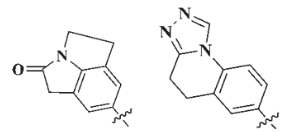
further preferably, R^1, R^2, R^3 or R^{11}each is independently selected from hydrogen, deuterium, halogen, amino, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{2-4}alkynyl, C_{3-8}bridged cycloalkyl, C_{3-8}spirocycloalkyl, 3- to 8-membered spiro heterocyclyl containing 1-3 heteroatoms, 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.

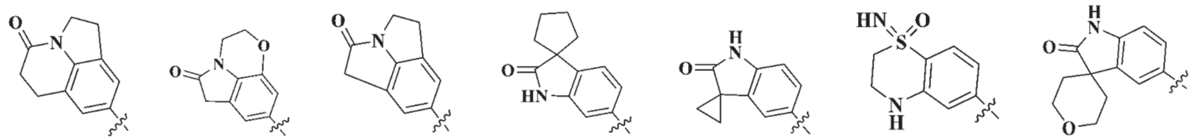
In a further preferred embodiment of the present disclosure, in the compound of general formula (XV):

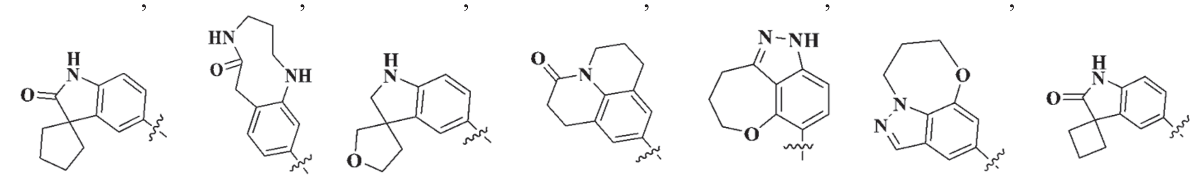
R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-6}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{3-6}cycloalkyl, amino or oxo;

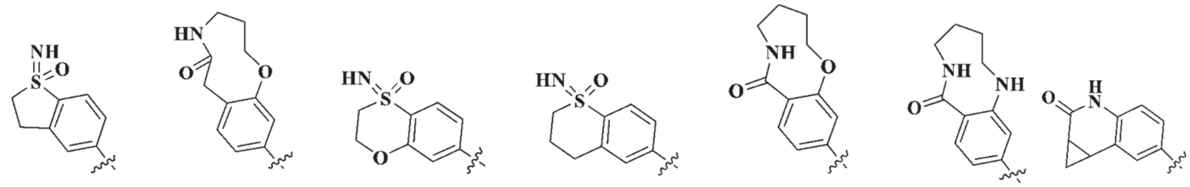
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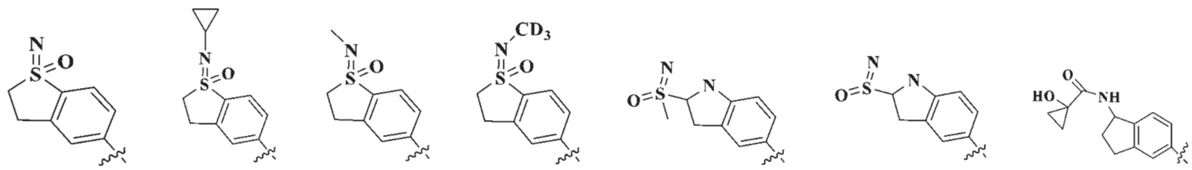
preferably, R^1 and R^2, or R^1 and R^{11}, respectively, are linked with adjacent atoms to form 5- to 7-membered heterocyclyl containing 1-3 selected from N, O or S, optionally further substituted by C_{3-6}cycloalkyl, or oxo; and

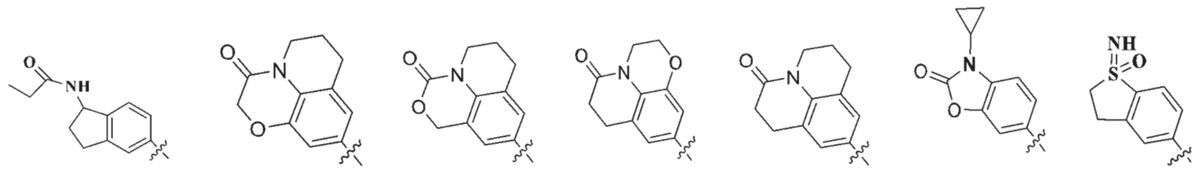
further preferably, R^1 and R^2, or R^1 and $R^{11}$are lined with adjacent phenyl to form  , ,

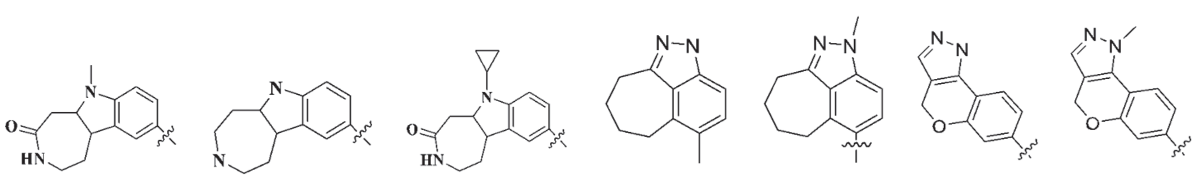
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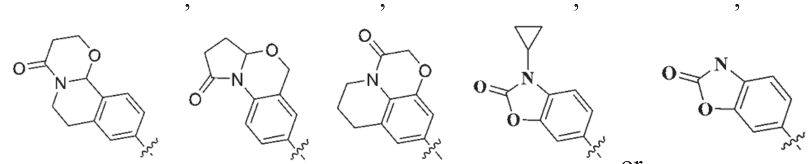
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 , , , , or , optionally further substituted by one or more substituents of halogen, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{3-6}cycloalkyl, amino or oxo.

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

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):

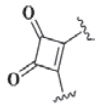
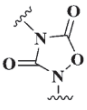
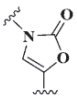
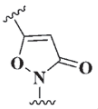
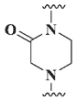
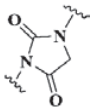
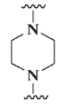
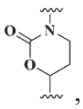
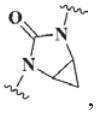
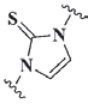
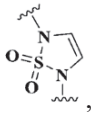
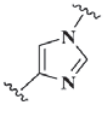
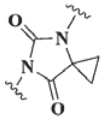
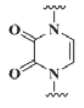
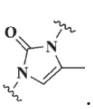
R_{a1} and R_{b1}, or R_{a2} and R_{b2}, or R_{a3} and R_{b3}, or R_{a4} and R_{b4}, or R_{a6} and R_{b6}, or R_{a8} and R_{b8}, or R_{a9} and R_{b9}, or R_{a10} and R_{b10}, respectively, are linked with adjacent atoms to form C_{3-8}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered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

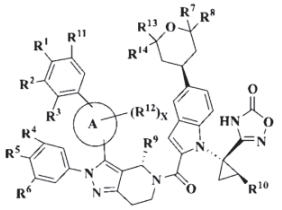
preferably, R^7, R^8, R^9, R^{10}, R^{12}, R^{13} or R^{14} each is independently selected from methyl or cyclopropyl.

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.

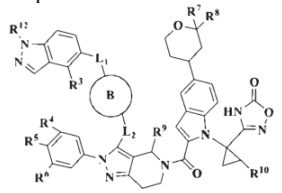
In a further preferred embodiment of the present disclosure, the compound of general formula (XV) is further shown as general formula (XV-1):



(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

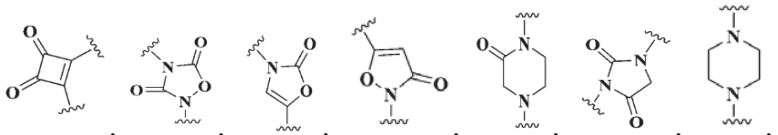
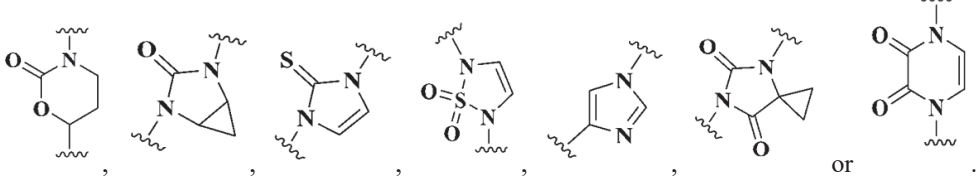
n3 is an integer of 0-5.

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):

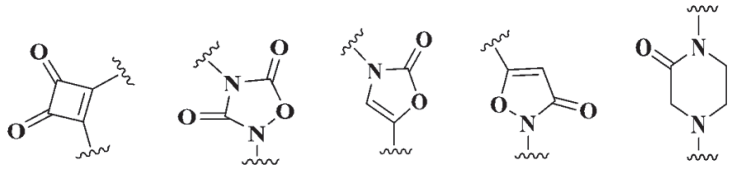
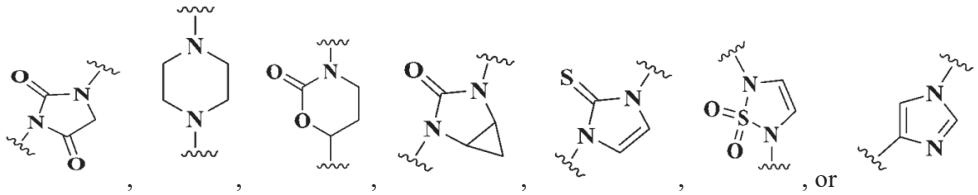
ring B is selected from C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 8-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

preferably, ring B is selected from  ,  , or .

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

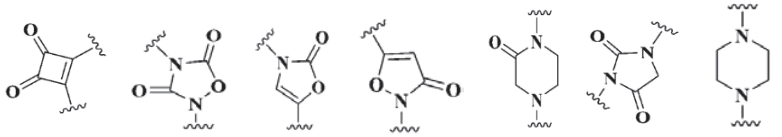
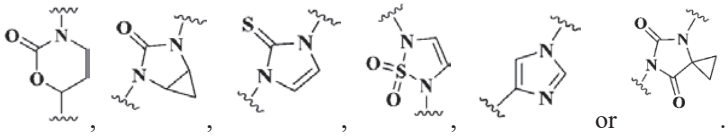
ring B is selected from C_{3-6}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms; optionally further substituted by one or more substituents of halogen, amino, oxo, thio or C_{1-3}alkyl; and

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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

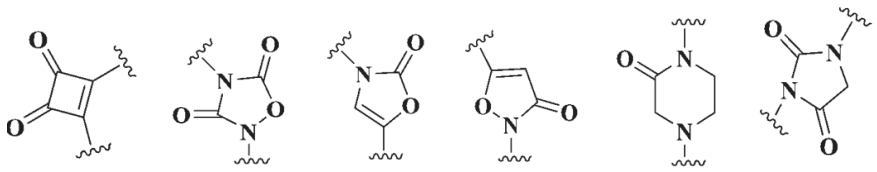
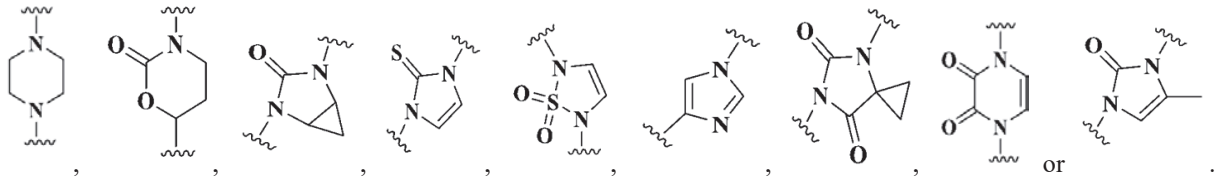
preferably, R^7, R^8, R^9or R^{10} each is independently selected from methyl.

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 .

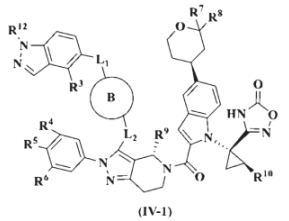
In a further preferred embodiment of the present disclosure, in the compound of general formula (IV):

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;

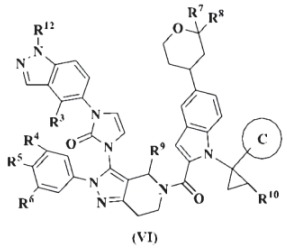
preferably, R^{12} is selected from C_{1-3}alkyl or C_{3-6}cycloalkyl; and

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)

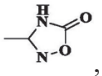
wherein

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 -$NR_{a6}S(O)_2R_{b6}$;

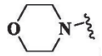
R^{10} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5-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

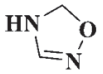
R^{12} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5-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

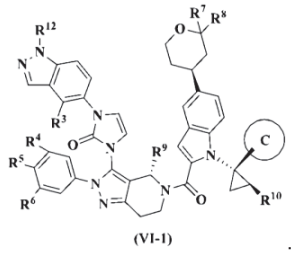
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C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

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

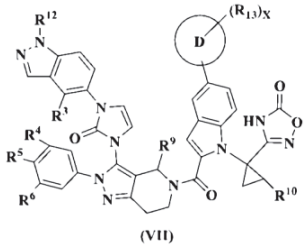
further preferably, R^{12} is selected from methyl.

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;

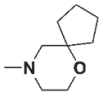
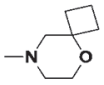
R^4, R^5 or R^6 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl,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

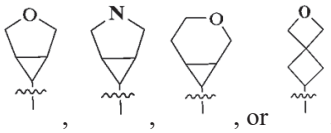
x is an integer of 0-5.

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;

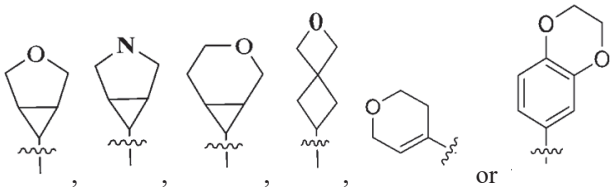
n1 is an integer of 0-5; and

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.

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

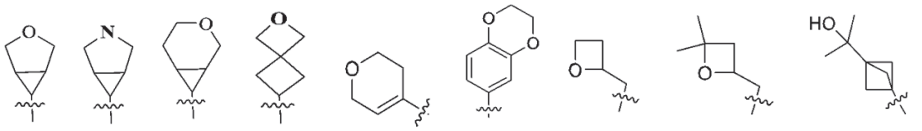
preferably, R^9 or R^{10} each is independently selected from methyl.

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  .

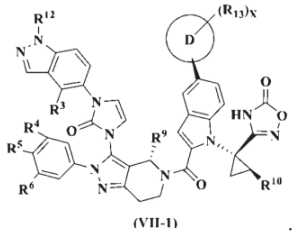
In another embodiment of the present disclosure, in the compound of general formula (VII):

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

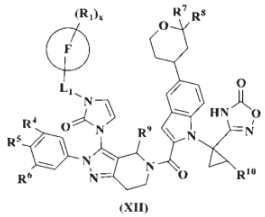
further preferably, R^{12} is selected from methyl or cyclopropyl.

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):

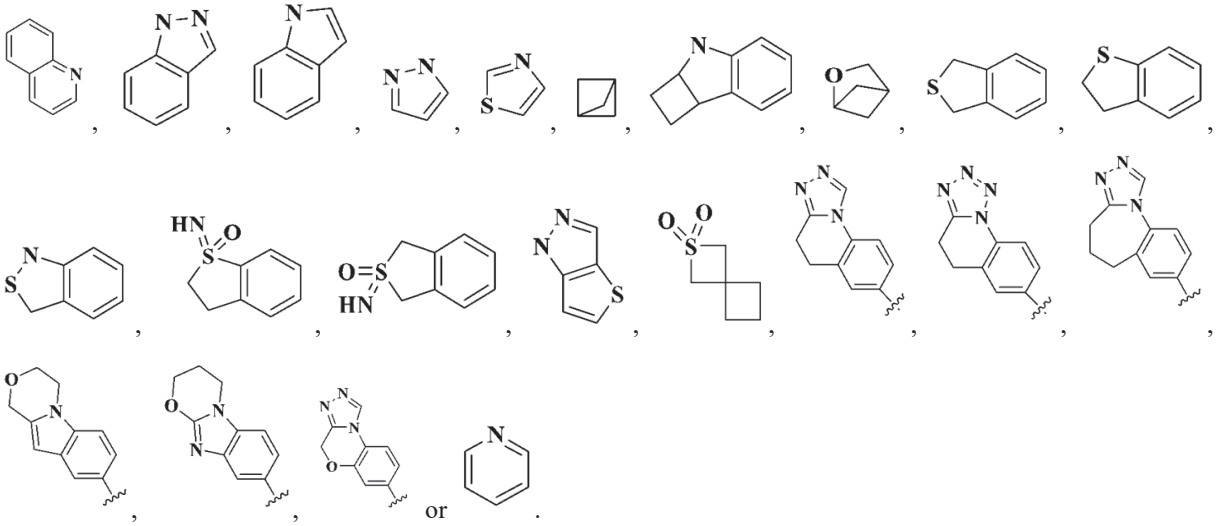
preferably, ring F is selected from C_{3-10}cycloalkyl, 5- to 14-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

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

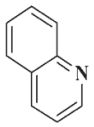
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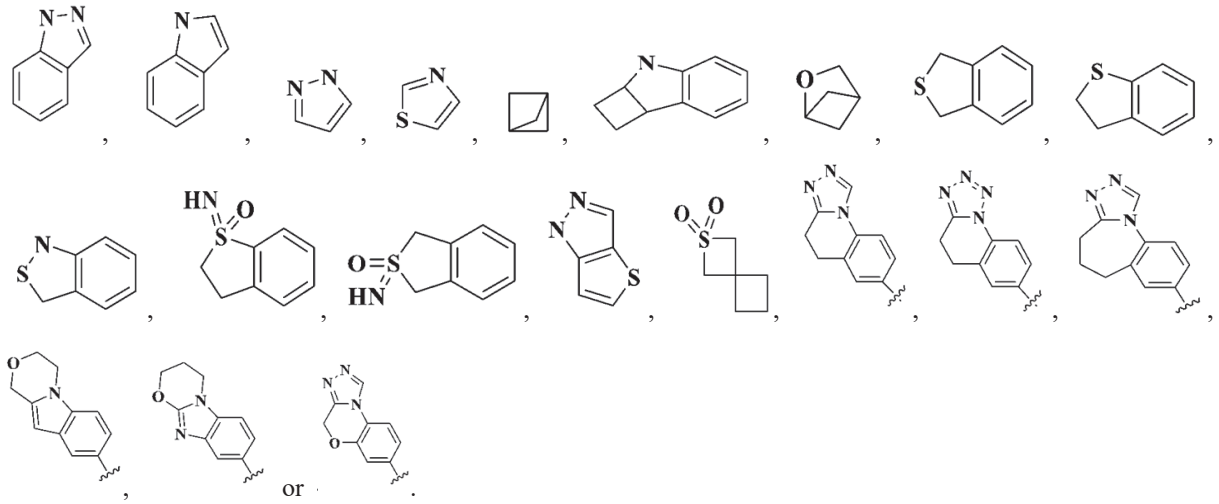
3- to 8-membered bridged heterocyclyl containing 1-3 heteroatoms, fused heterocyclyl containing 1-3 heteroatoms, bridged heterocyclyl containing 1-3 heteroatoms, C_{6-10}aryl or 5- to 10-membered fused heteroaryl containing 1-3 heteroatoms; and

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,  ,

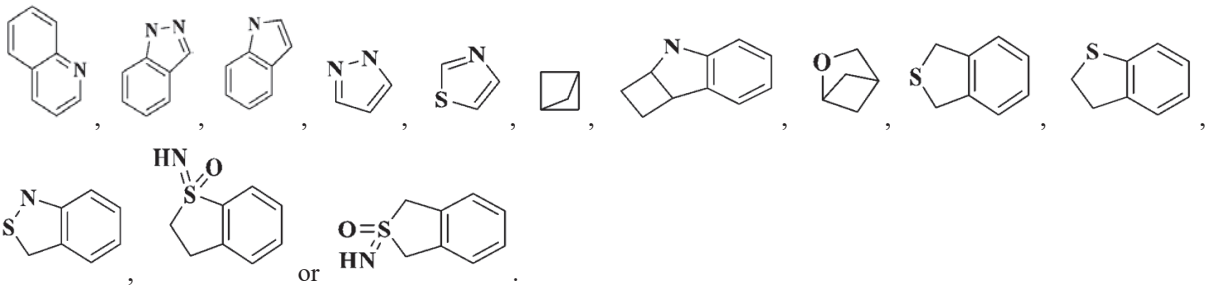


In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

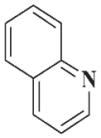
ring F is selected from C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl;

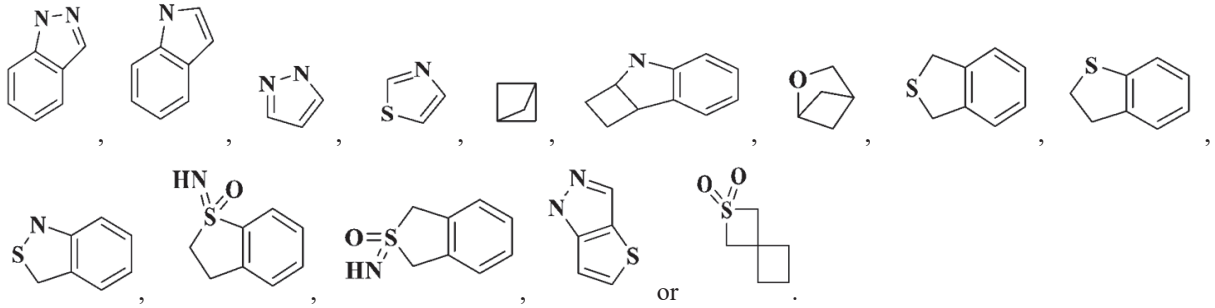
preferably, ring F is selected from C_{3-6}bridged cycloalkyl, 3- to 8-membered bridged heterocyclyl containing 1-3 heteroatoms, fused heterocyclyl containing 1-3 heteroatoms, bridged heterocyclyl containing 1-3 heteroatoms, C_{6-10}aryl or 5- to 10-membered fused heteroaryl containing 1-3 heteroatoms;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

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

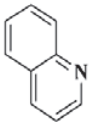


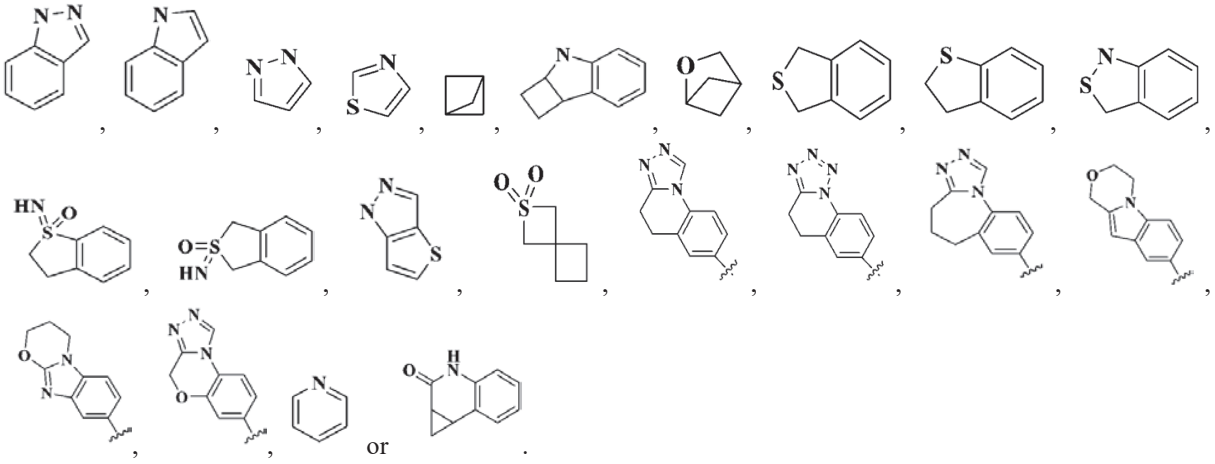
In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

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



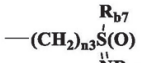
In a further preferred embodiment of the present disclosure, in the compound of general formula (XII):

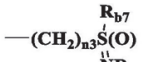
ring F is selected from phenyl, pyridyl, pyrimidyl, thiazolyl, pyridazinyl, oxazolyl, morpholinyl,  ,



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

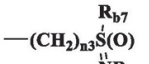
R^1 each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl,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

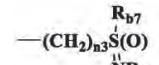
 , -$(CH_2)_{n1}NR_{a8}C(O)R_{b8}$ or -$(CH_2)_{n1}S(O)_2R_{b5}$, wherein the amino, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered 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

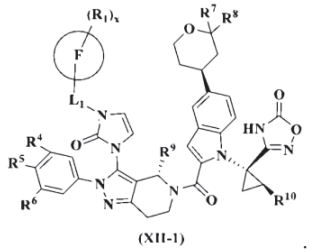
further preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{b5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, phenyl or methyl.

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

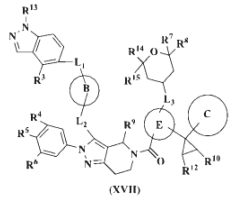
preferably, R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4}, R_{a5}, R_{a6}, R_{b6}, R_{a7}, R_{b7}, R_{a8}, or R_{b8} each is independently selected from hydrogen, deuterium, halogen, or methyl.

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;

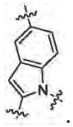
R_{c1} is selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}deuterated haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}deuterated hydroxyalkyl, C_{1-6}sulfanyl, C_{1-6}deuterated sulfanyl, C_{1-6}alkoxy, C_{1-6}deuterated 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):

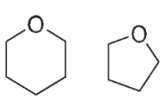
R^{10} and R^{12} are linked with the atoms to which they are connected to form C_{3-10}cycloalkyl, 3- to 10-membered heterocyclyl, C_{6-12}aryl or 5- to 12-membered heteroaryl;

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  .

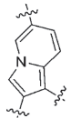
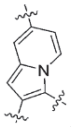
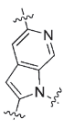
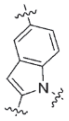
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

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

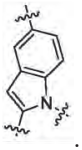
preferably, R^7 and R^8, R^{14} and R^{15}, and R^{10} and R^{12}, respectively, are linked with the atoms to which they are connected to form cyclopropyl,  ,  ,  ,  , ,  ,  , , optionally further substituted by one or more substituents of deuterium, fluoro, chloro, bromo, amino, nitro, hydroxyl, cyano,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

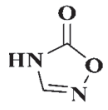
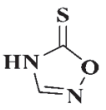
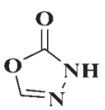
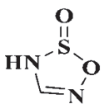
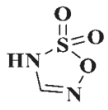
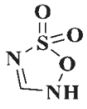
In a further preferred embodiment of the present disclosure, in the compound of general formula (XVII):

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  ,  ,  ,  ,  , 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 (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,

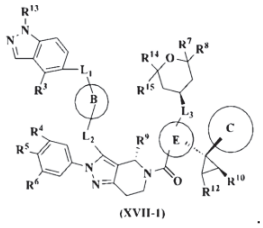
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C_{1-3}deuterated haloalkoxy, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl is optionally further substituted by one or more substituents of deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-3}alkyl, C_{1-3}deuterated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

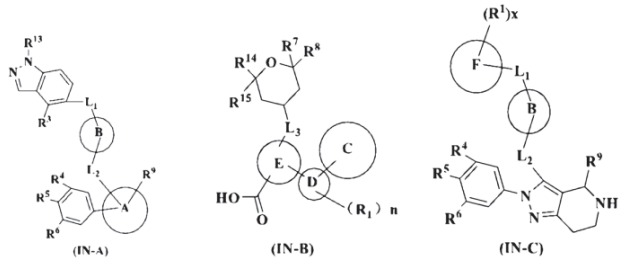
further preferably, R^{13} is selected from $-CD_3$ or cyclopropyl, wherein the $-CD_3$ or cyclopropyl is optionally further substituted by one or more substituents of deuterium, halogen or C_{1-3}alkyl; and

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):



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:



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

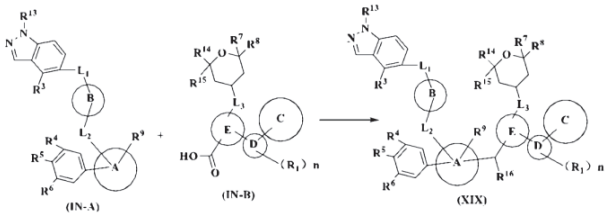
in general formula (IN-C), ring F, ring B, L_1, L_2, R^1, R^4, R^5, R^6, R^9, and x are defined as in general formula (XVI).

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);

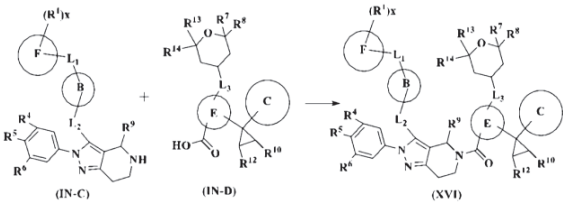
wherein the condensation agent is selected from EDC, DIC, DCC, TBTU, HATU, HBTU, HCTU, DEPBT, PyBOP or PyAOP; and

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,

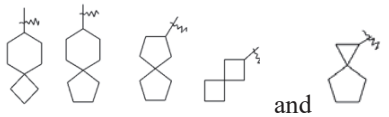
1,3-dimethylbutyl, 2-ethylbutyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2,3-dimethylbutyl, etc. Alkyl can be substituted or unsubstituted, and when substituted, the substituent can be substituted at any available connection point, and the substituent is preferably one or more groups independently 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.

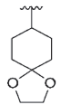
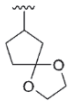
The term "alkenyl" refers to an alkyl group as defined above consisting of at least two carbon atoms and at least one carbon-carbon double bond, such as ethenyl, 1-propenyl, 2-propenyl, 1-, 2- or 3 -butenyl, etc. Alkenyl can be substituted or unsubstituted. When the alkenyl is substituted, the substituent 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.

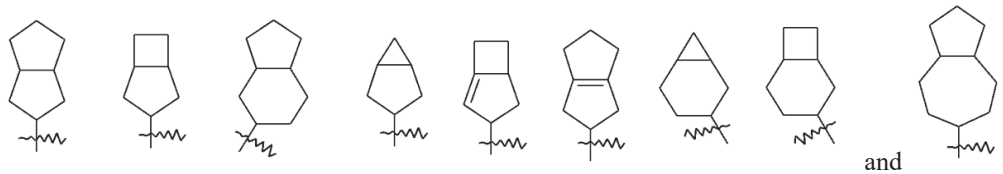
The term "spirocycloalkyl" refers to a polycyclic group with 5- to 20-membered monocyclic rings sharing one carbon atom (called a spiro atom). It may contain one or more double bonds, but no ring has a completely conjugated π electron system. Preferably, the bridged heterocyclyl is 6- to 14-membered, 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 ;

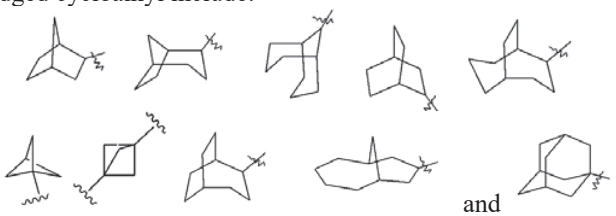
Also included are spirocycloalkyl groups in which monospirocycloalkyl and heterocycloalkyl share a spiro atom. Non-limiting examples include:

 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 .

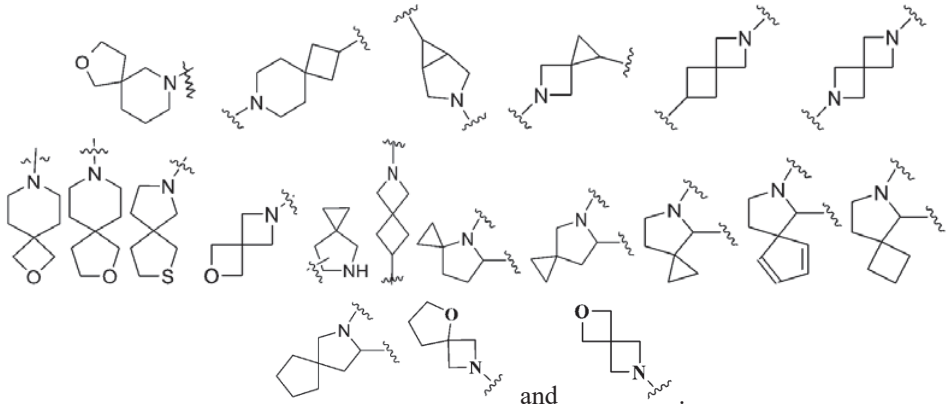
The term “bridged cycloalkyl” refers to a 5- to 20-membered all-carbon polycyclic group with any two rings sharing two carbon atoms that are not directly connected. It may contain one or more double bonds, but no ring has a fully conjugated π electron system. Preferably, the bridged heterocyclyl is 6- 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 .

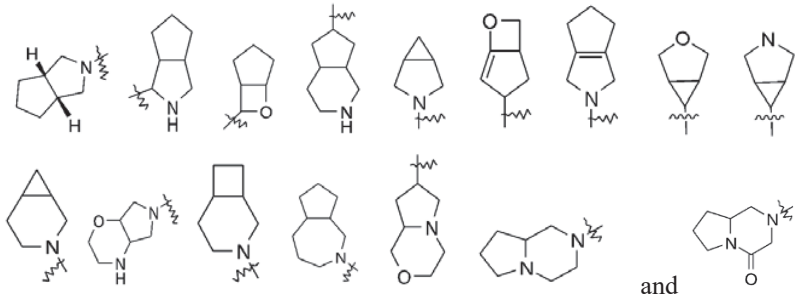
The cycloalkyl ring can be fused to an aryl, heteroaryl or heterocycloalkyl ring, wherein the ring connected to the parent structure is cycloalkyl, and non-limiting examples include indanyl, tetrahydronaphthyl, benzocycloheptanyl, etc. Cycloalkyl can be optionally substituted or unsubstituted. When the 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.

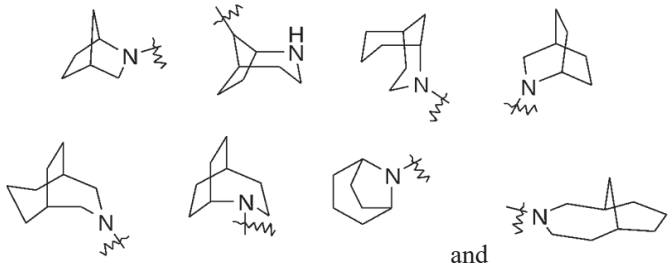
The term “spiroheterocyclyl” refers to a 5- to 20-membered polycyclic heterocyclyl with monocyclic rings sharing one atom (called a spiro atom), wherein one or more ring atoms are heteroatoms selected from nitrogen, oxygen, or $S(O)_m$ (wherein m is an integer of 0 to 2), and the remaining ring atoms 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 .

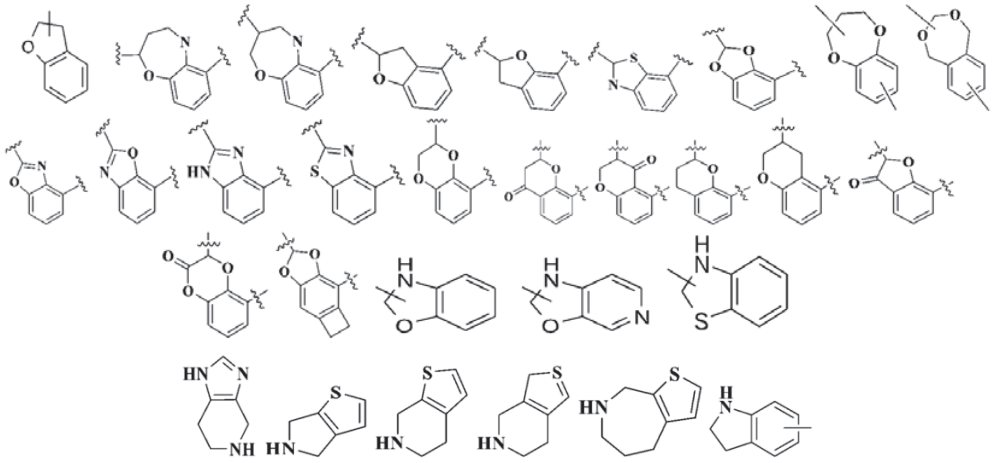
The term "fused heterocyclyl" refers to a 5- to 20-membered polycyclic heterocyclyl with each ring in the system sharing a pair of atoms neighboring other rings in the system, and one or more rings may contain one or more double bonds, but no ring has a fully conjugated π electron system, wherein one 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:

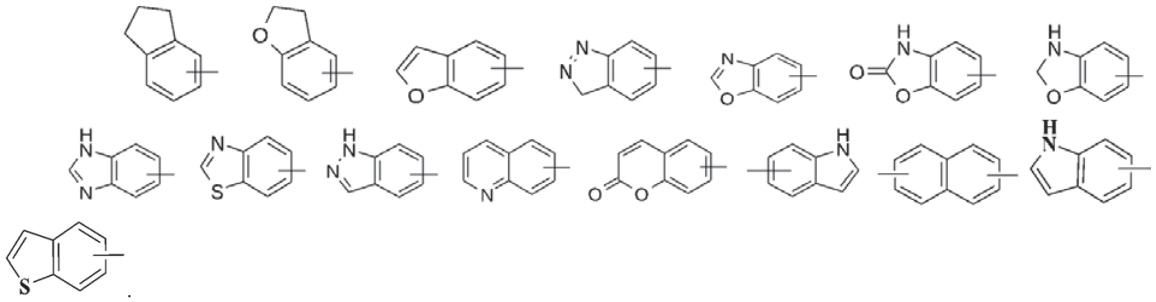

and .

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:



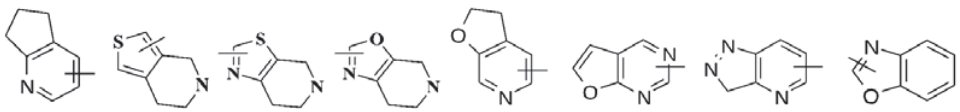
Heterocyclyl can be optionally substituted or unsubstituted. When the heterocyclyl is substituted, the substituent is preferably one or more groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, halogen, mercapto, hydroxyl, nitro, cyano, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkoxy, heterocycloalkoxy, cycloalkylthio, heterocycloalkylthio, oxo, carboxyl or a carboxylate group.

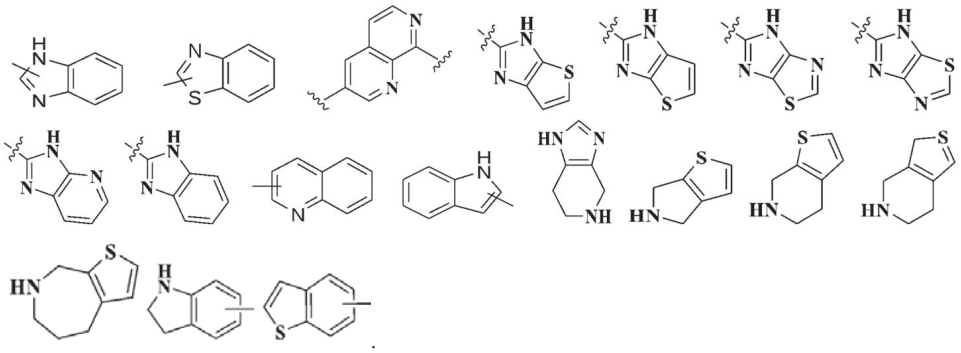
The term "aryl" refers to a 6- to 14-membered all-carbon monocyclic or fused polycyclic (i.e., rings sharing an adjacent pair of carbon atoms) group having a conjugated π electron system, preferably 6- to 10-membered, more preferably 6- to 8-membered aryl, such as phenyl and naphthyl, and more preferably 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.

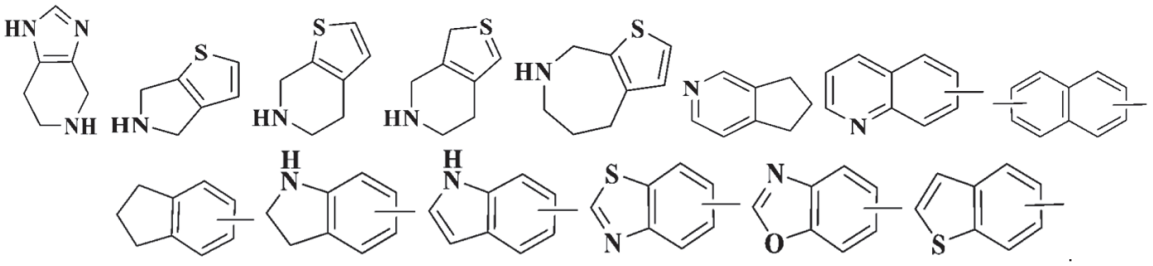
"Alkenyl" refers to a chain alkenyl group, also known as an alkene group, preferably alkyl containing 2 to 8 carbon atoms, more preferably alkyl containing 2 to 6 carbon atoms, and most preferably alkyl containing 2 to 3 carbon atoms. Moreover, the alkenyl can be further substituted with other related 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

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).

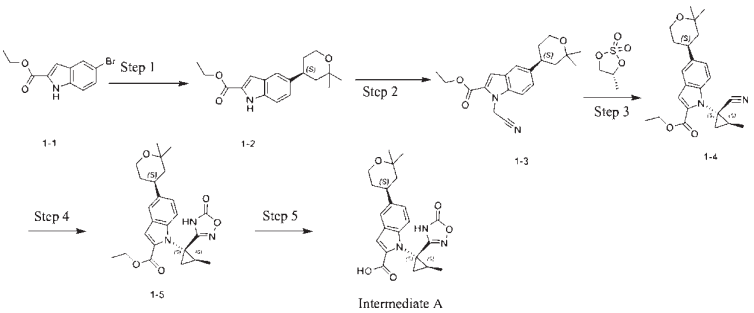
Agilent 1200 Infinity Series mass spectrometer was used for measurement by liquid chromatography-mass chromatography (LC-MS). HPLC determination used Agilent 1200DAD high-pressure liquid chromatograph instrument (Sunfire C18 150 × 4.6 mm chromatographic column) and Waters 2695-2996 high-pressure liquid 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].

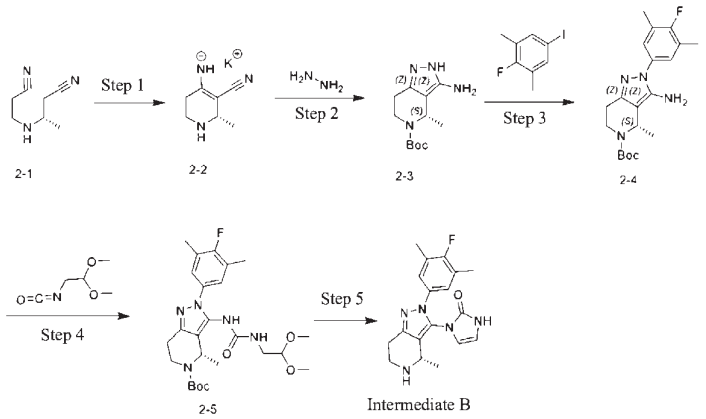
Step 4: to a solution of ethyl 1-((1S, 2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (1.20 g, 3.15 mmol) in dimethyl sulfoxide (DMSO) (10 mL) was added a 50% aqueous hydroxylamine solution (2.08 g, 31.5 mmol), and the mixture was stirred at room 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].

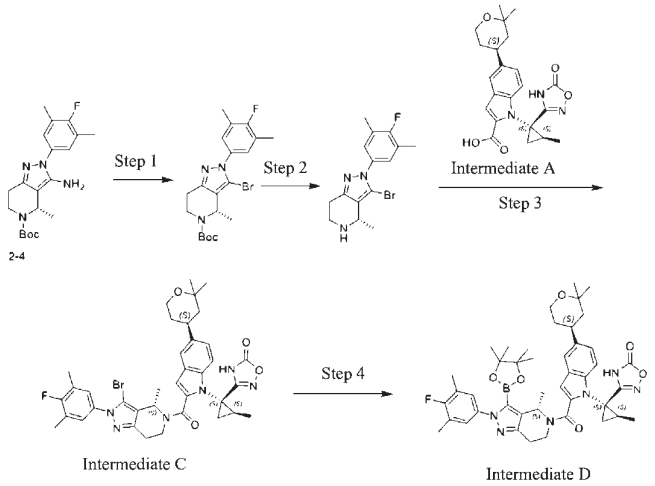
Step 4: to a solution of intermediate 2-4 (2.9 g, 7.4 mmol) in pyridine (10 mL) was added 2-isocyanato-1,1-dimethoxyethane (2.03 g, 15.49 mmol), and the mixture was stirred at room temperature. After 3 hours, diethylamine (1.13 g, 15.49 mmol) was added, and the mixture was stirred at room temperature 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].

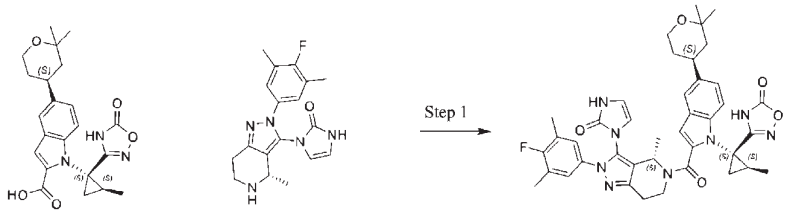
Step 3: (S)-3-bromo-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine hydrochloride (1.7 g, 4.54 mmol), intermediate A (526.84 mg, 4.54 mmol), and diisopropylethylamine (1.76 g, 13.61 mmol, 2.37 mL) were dissolved in N,N'-dimethylformamide (15 mL), and under nitrogen 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].

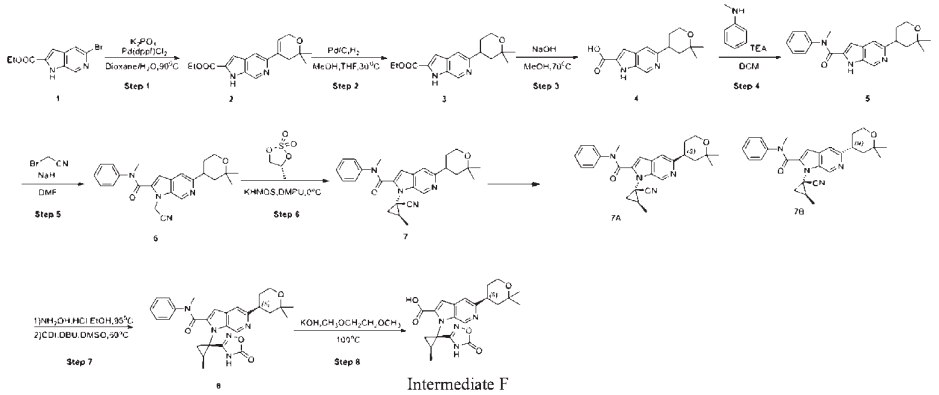
Intermediate E



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].

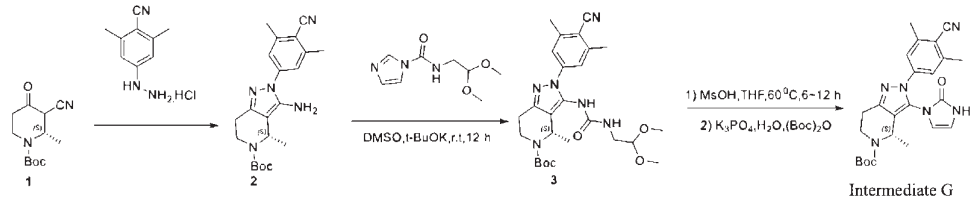
Step 7: the product 7A (450 mg, 1.02 mmol, 1.0 eq.), hydroxylamine hydrochloride (354 mg, 5.10 mmol, 5.0 eq.), K_2CO_3 (775 mg, 5.61 mmol, 5.5 eq.) and anhydrous ethanol (25 mL) were successively added to a 100 mL single-necked bottle, and the system was allowed to react at 95°C for 5 hours. The reaction 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



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%).

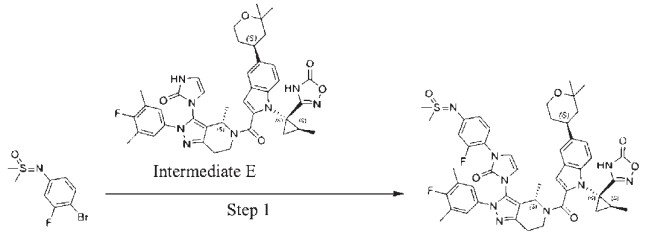
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MS m/z (ESI): 513.2 [M+1].

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].

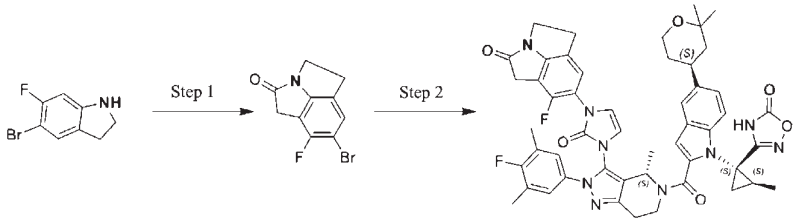
Example 1



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



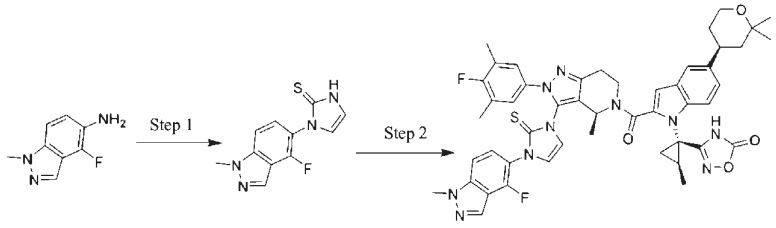
Step 1: 5-bromo-6-fluoroindoline was used as a raw material, and the target product was obtained according to Journal of Organic Chemistry, 1992, vol. 57, #8, p. 2508-2511.

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



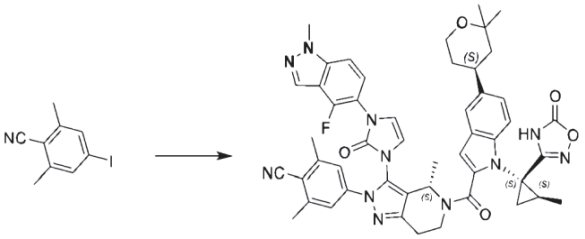
Step 1: 4-fluoro-1-methyl-1H-indazol-5-amine was used as a raw material, and the target product was obtained according to New Journal of Chemistry, 2014, vol. 38, #9, p. 4071-4082.

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].

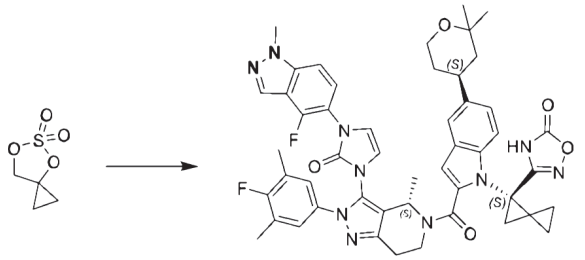
Example 4



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].

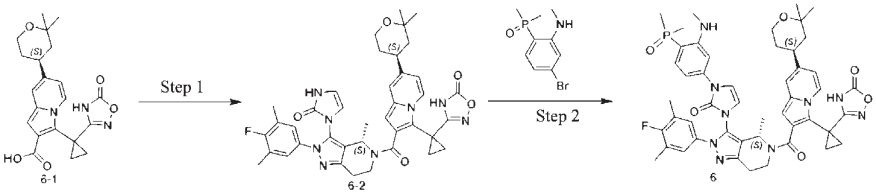
Example 5



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



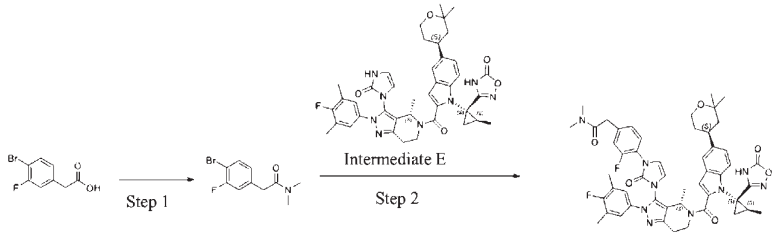
Step 1: 6-1 was used as a raw material, and 6-2 was obtained by following step 3 of intermediate C and intermediate D.

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



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Step 1: 2-(4-bromo-3-fluorophenyl)-N,N-dimethylacetamide

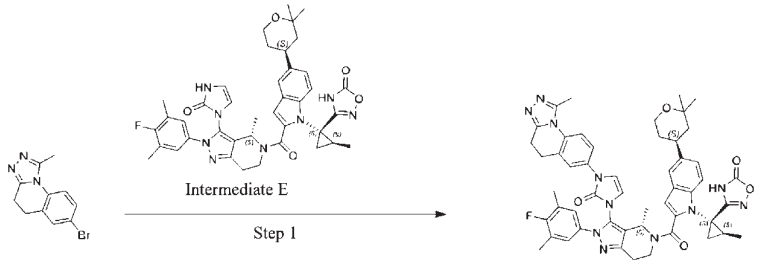
At room temperature, 2-(4-bromo-3-fluorophenyl)acetic acid (2.33 g, 10 mmol) was dissolved in N,N-dimethylformamide (30 mL), and then dimethylamine hydrochloride (0.98 g, 12 mmol) and triethylamine (4.05 g, 40 mmol), were added, followed by 2-(7-azobenzotriazole)-N,N,N',N'-tetramethyluronium hexafluorophosphate (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]+.

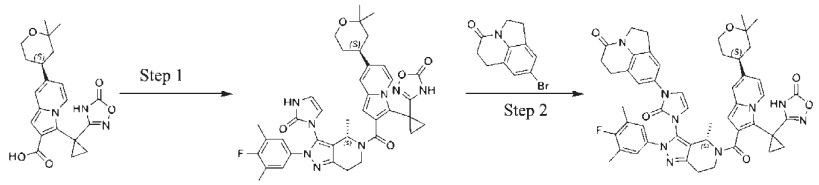
Example 8



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



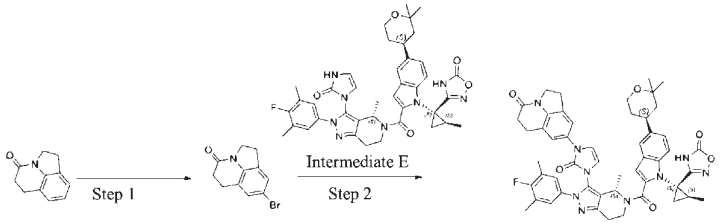
Step 1: The product was obtained by following step 3 for intermediate C and intermediate D.

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

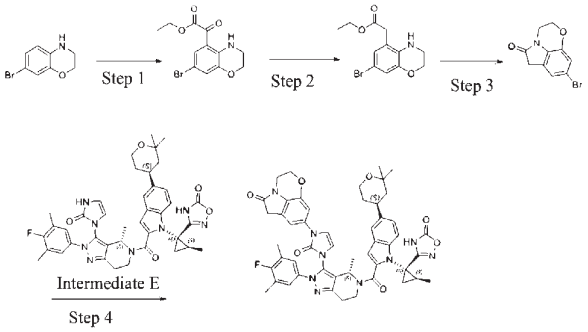
the organic phases were combined, washed with saturated brine (25 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried, and the crude product was crystallized with acetone/water, to obtain the target product as a yellow solid (1.89 g, yield 75%).

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%).

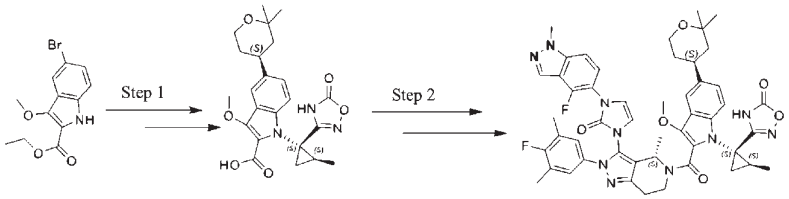
MS m/z (ESI): 254.1, 256.1 [M+H]+.

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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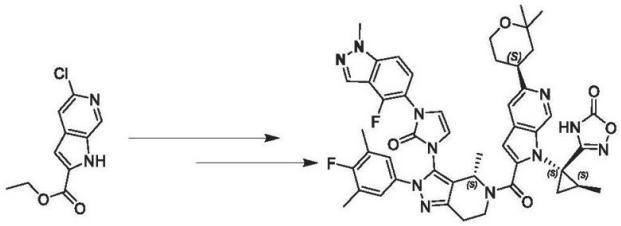
Step 1: ethyl 5-bromo-3-methoxyindole-2-carboxylate was used as a raw material, and the target product was obtained following intermediate A

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].

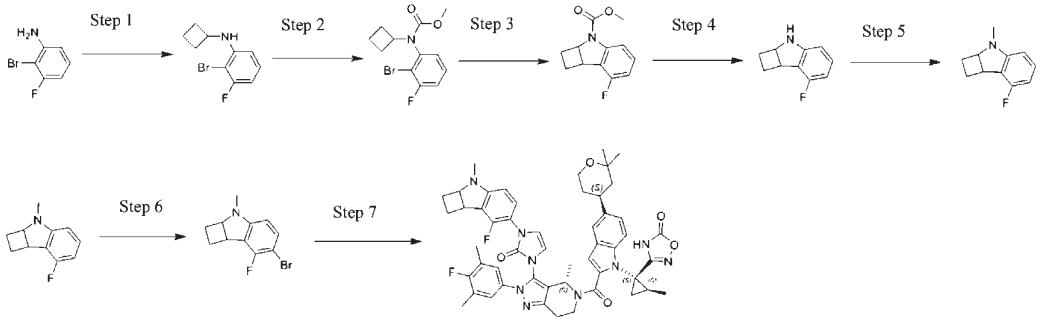
Example 13



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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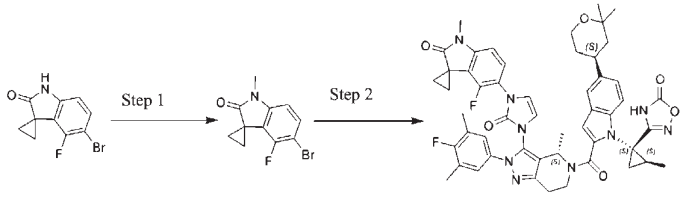
Step 6: 7-fluoro -3-methyl -2,2a,3,7b-tetrahydro-1H-cyclobutadieno[b]indole was used as a raw material to obtain the target product according to Chemistry - A European Journal, 2022, vol. 28, #2, art.no. E202103135.

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



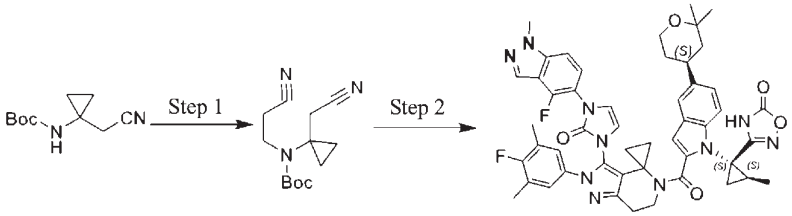
Step 1: 5'-bromo-4'-fluorospiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material to obtain the target product according to European Journal of Medicinal Chemistry, 2020, vol. 190.

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



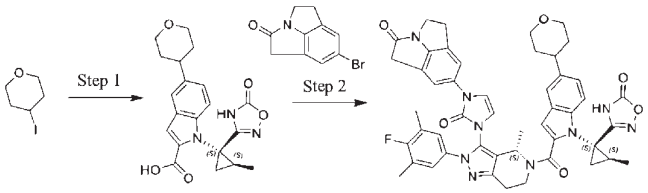
Step 1: tert-butyl (1-(cyanomethyl)cyclopropyl)carbamate (5 g, 25.48 mmol) and 3-bromopropanenitrile (3.41 g, 25.48 mmol) were dissolved in acetonitrile (100 mL), and potassium carbonate (10.56 g, 76.43 mmol) was added under nitrogen protection. The mixture was stirred for reaction at 25°C for 12 hours. 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.

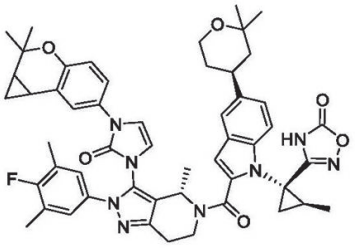
MS m/z (ESI): 384.2 [M+1].

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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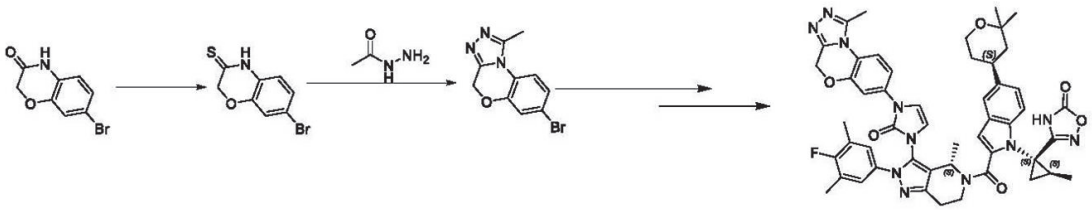
MS m/z (ESI): 864.4 [M+1].

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].

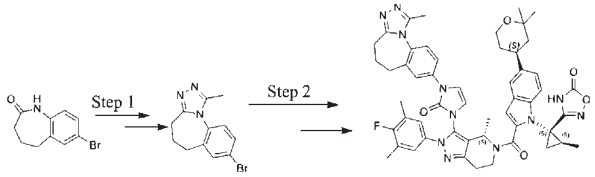
Step 2: A mixture of 7-bromo-2H-benzo[b][1,4]oxazine-3(4H)-thione (300 mg, 1.23 mmol), acetylhydrazine (109 mg, 1.47 mmol), and n-butanol (10mL) was stirred at 120°C for 24 hours, cooled, directly concentrated with silica gel, and separated by column chromatography (DCM/MeOH = 10 : 1), to obtain the 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



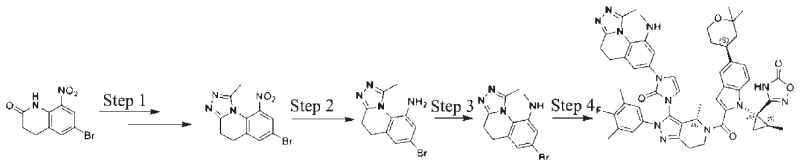
Step 1: 7-bromo-1,3,4,5-tetrahydro-2H-1-benzoazepine-2-one was used as a raw material, following steps 1 and 2 in Example 19, to obtain 8-bromo-1-methyl-5,6-dihydro-4H-benzo[f][1,2,4]triazolo[4,3-a]azepine

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].

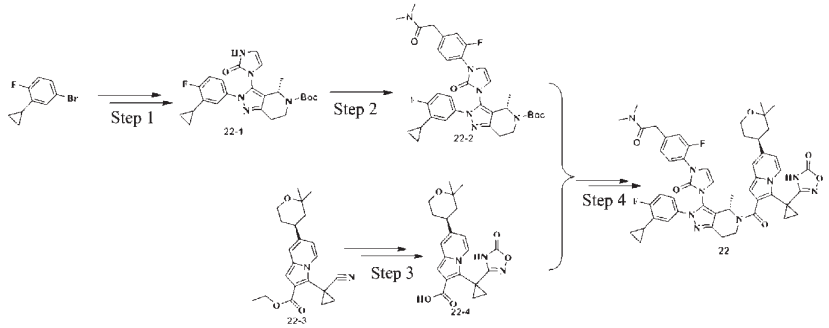
Step 3: To a solution of 7-bromo-1-methyl-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline-9-amine (600 mg, 2.16 mmol) in DMF (10 mL) was added NaH (130 mg, 3.24 mmol, 60% purity), and the mixture was stirred at room temperature for 30 minutes, and then iodomethane (457 mg, 3.24 mmol) was added dropwise and 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].

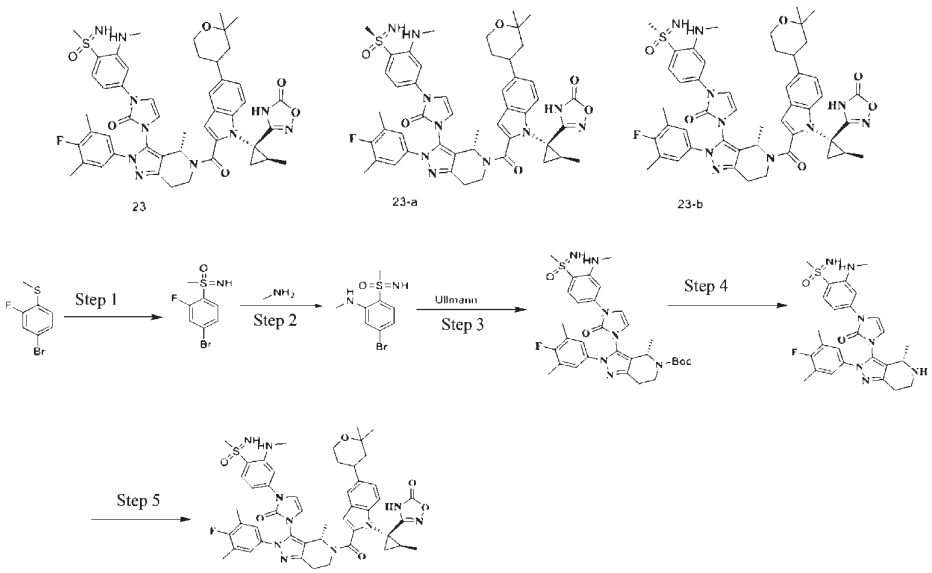
Step 4:

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

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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%)

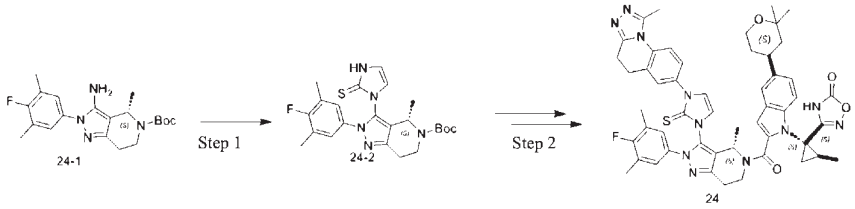
MS m/z (ESI): 917.4 [M+H]+

The product 23 was chirally resolved to obtain target products 23-a and 23-b

MS m/z (ESI): 917.4 [M+H]+.

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Example 24



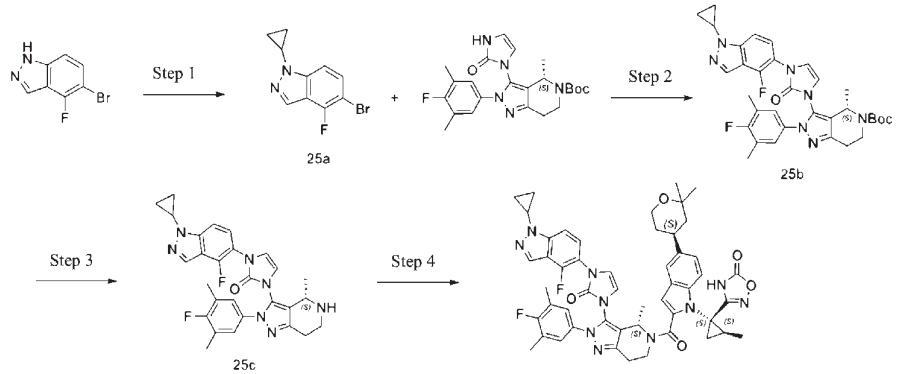
Step 1: 24-1 was used as a raw material, and a product 24-2 was obtained by following the synthesis step 1 in Example 3.

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].

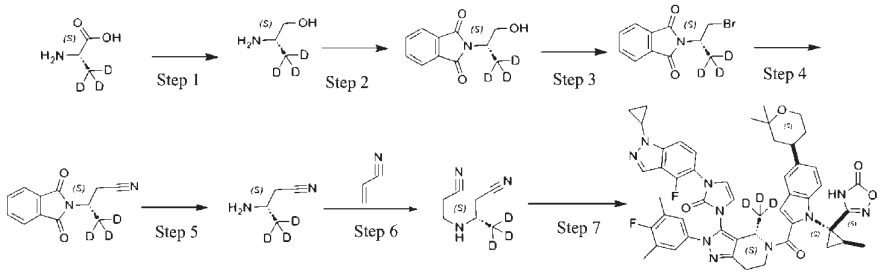
Step 4: 25c (42 mg, 81.5 μmol), intermediate A (51 mg, 0.122 mmol), HATU (46 mg, 0.122 mmol), and DIEA (53 mg, 0.407 mmol) were dissolved in DMF (3 mL), and the resulting mixture was stirred for reaction at room temperature for 3 hours. The reaction solution was quenched by adding a saturated ammonium 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.

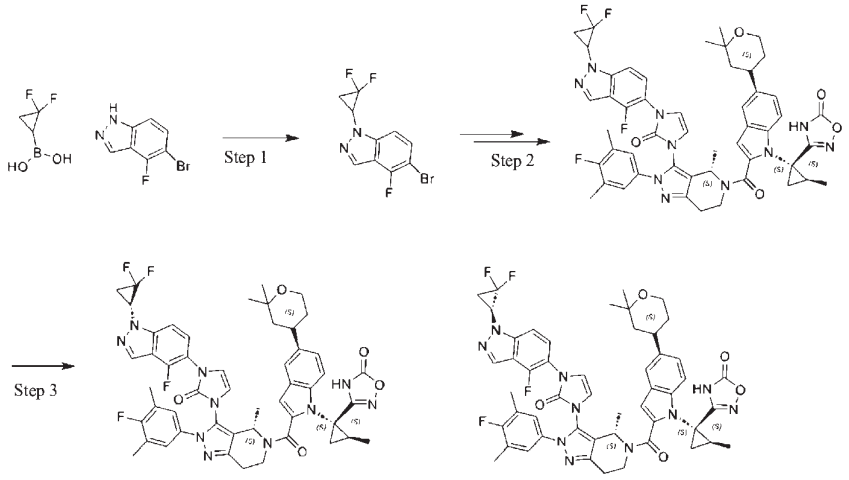
MS m/z (ESI): 141.0 [M+1].

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.

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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].

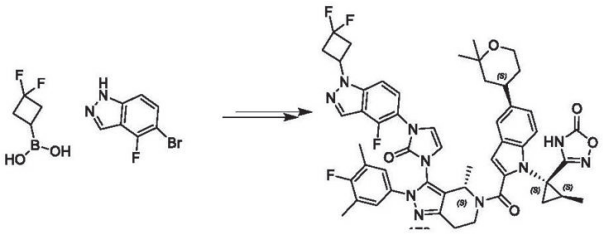
Step 2: 5-bromo-1-(2,2-difluorocyclopropyl)-4-fluoro-1H-indazole was used as a raw material, and the title product was obtained following the synthesis steps in Example 1.

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].

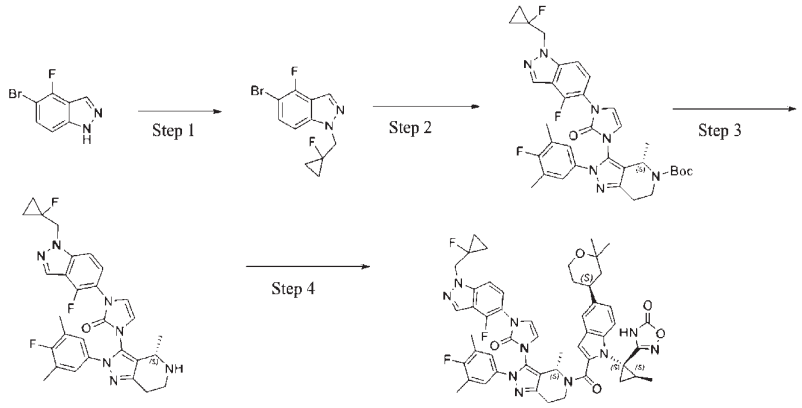
Example 28



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).

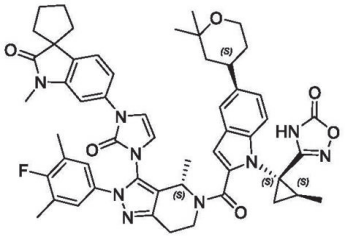
MS m/z (ESI): 548.2 [M+1].

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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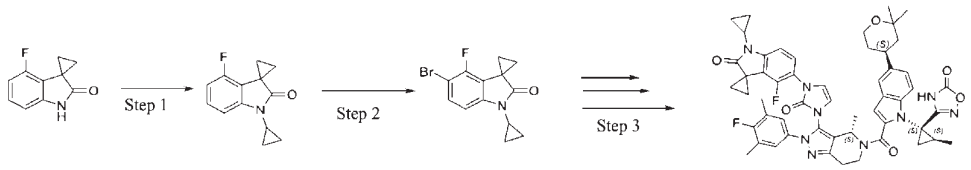
Example 30



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].

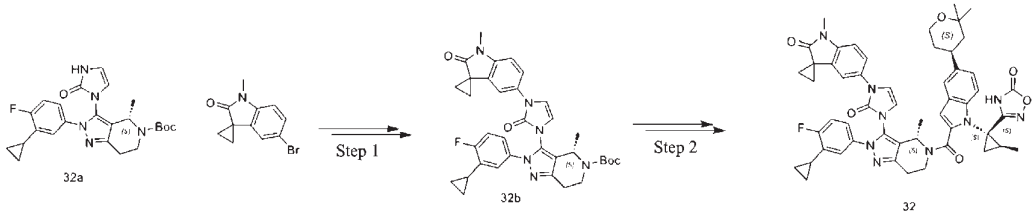
Step 2: at room temperature, 1'-cyclopropyl-4'-fluorospiro[cycloprop-1,3'-dihydroindole]-2'-one (0.15 g, 0.7 mmol) was dissolved in N,N-dimethylformamide (5 mL), and then N-bromosuccinimide (0.12 g, 0.7 mmol) was added and stirred at room temperature for 1 hour, with LCMS indicating the completion of 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.

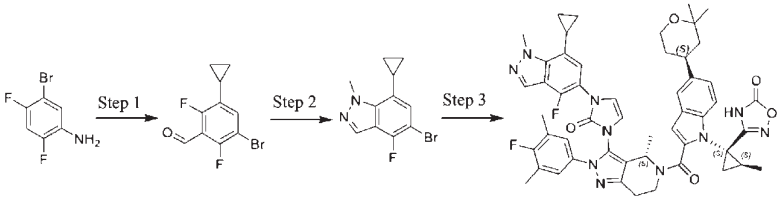
MS m/z (ESI): 625.2 [M+1].

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].

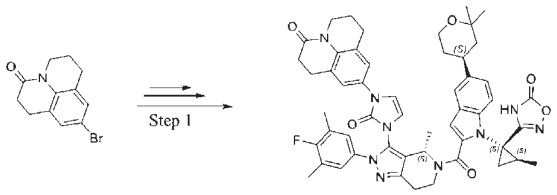
Step 2: 3-bromo-5-cyclopropyl-2,6-difluorobenzaldehyde was used as a raw material, following [Organic Letters, 2007, vol. 9, #3, p. 525-528], to obtain the target product.

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

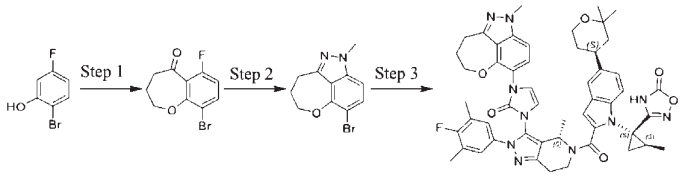


Step 1: 9-bromo-2,3,6,7-tetrahydro-1H, 5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

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].

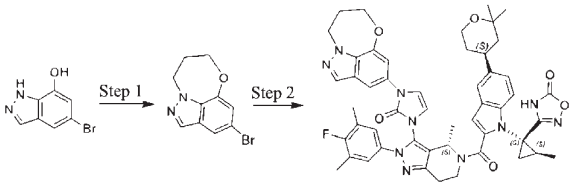
Step 3: 5-bromo-2-methyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole was used as a raw material, and the target product was obtained following Example 1.

^{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



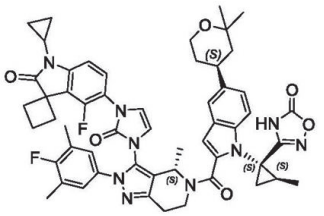
Step 1: 5-bromo-1H-indazole-7-ol was used as a raw material, following NANJING SANHOME INVESTMENT GROUP CO LTD-EP 3290419,2018, A1, Paragraph 0592; 0593; 0594, to obtain the target product.

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].

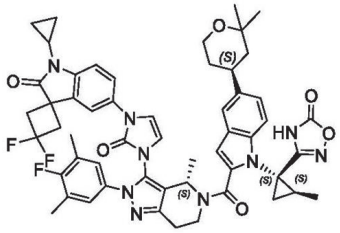
Example 37



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].

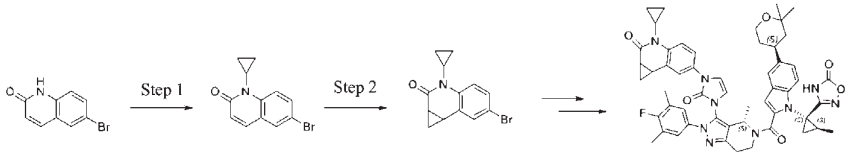
Example 38



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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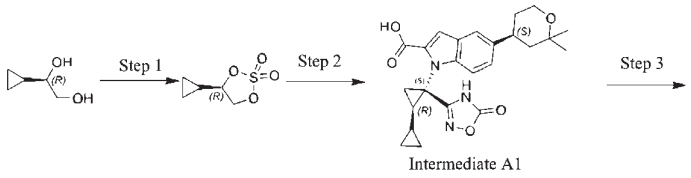
the reaction solution was heated to a temperature of 80°C, and reacted under stirring for 18 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (10 mL × 3); the organic phases were combined, washed with a saturated sodium chloride 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%).

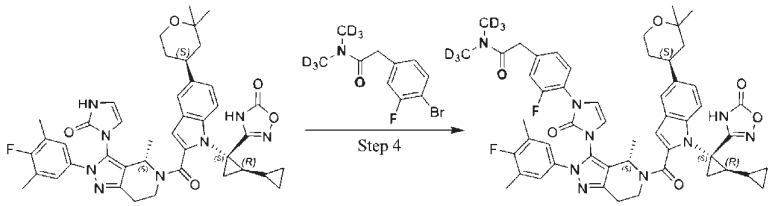
MS m/z (ESI): 278.0, 280.0 [M+1]

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].

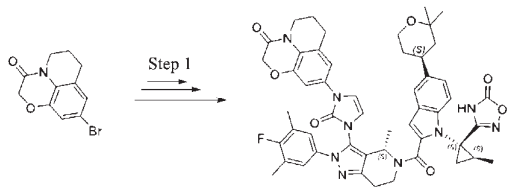
Step 3: intermediate A1 was used as a raw material, following intermediate E, to synthesize intermediate E1.

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



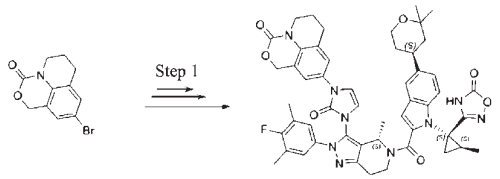
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Step 1: 9-bromo-6,7-dihydro-5H-[1,4]oxaazino[2,3,4-ij]quinoline-3(2H)-one was used as a raw material, and the target compound was obtained following Example 34.

^{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]+.

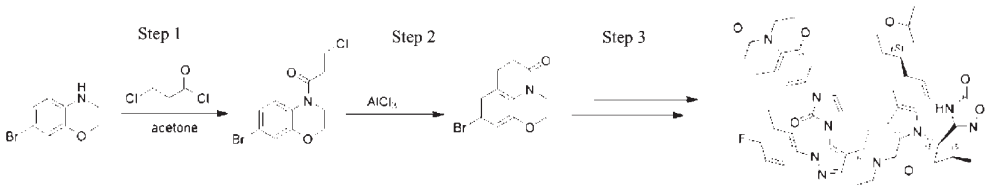
Example 42



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 $[M+H]^+$.

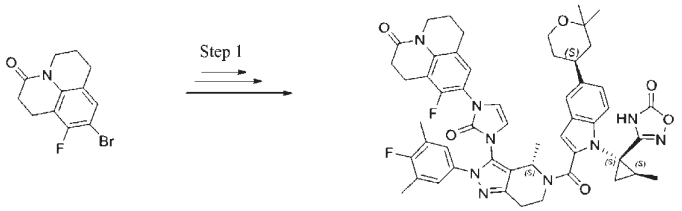
Step 3: 9-bromo-2,3,6,7-tetrahydro-5H-[1,4]oxaazino[2,3,4-ij]quinoline-5-one was used as a raw material, and the target compound was obtained finally following Example 34.

^{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] $^{+}$.

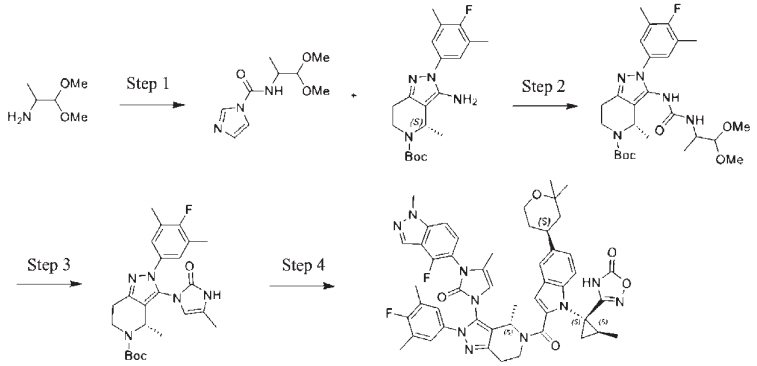
Example 44



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%).

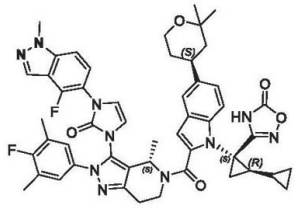
MS m/z (ESI): 456.2 [M+1]。

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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]。

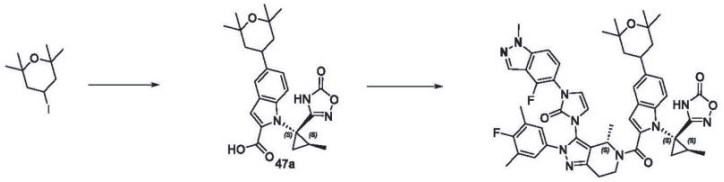
Example 46



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



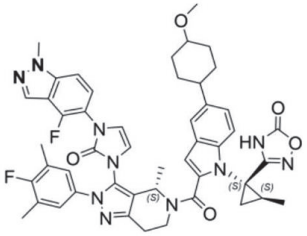
Step 1: 4-iodo-2,2,6,6-tetramethyltetrahydro-2H-pyran was used, following intermediate A, to obtain a product 47a.

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].

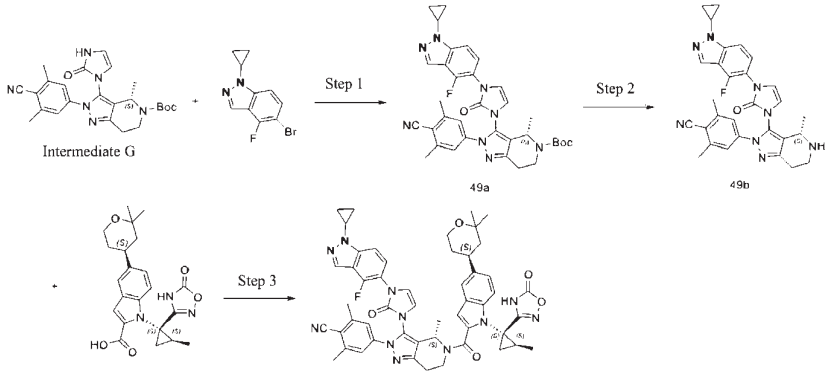
Example 48



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.

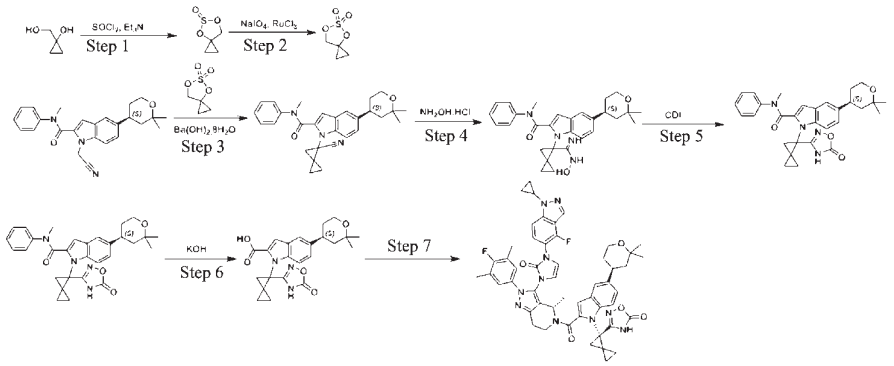
MS m/z (ESI): 523.2 [M+1].

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%).

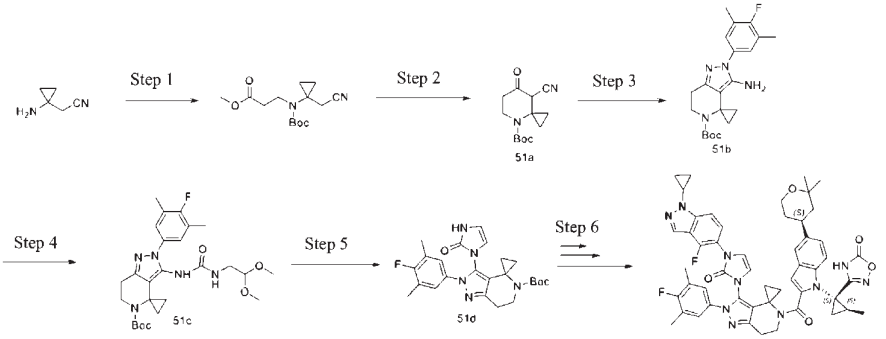
MS m/z (ESI): 424.2 [M+1].

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),

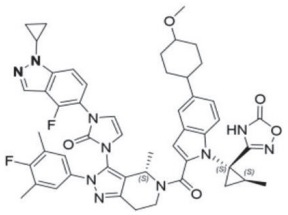
dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a crude product, which was separated by Flash column chromatography to obtain the target product 51d (0.53 g, yield 50%).

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 $[M+H]^+$.

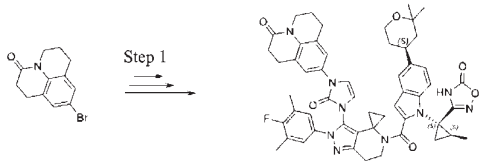
Example 52



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].

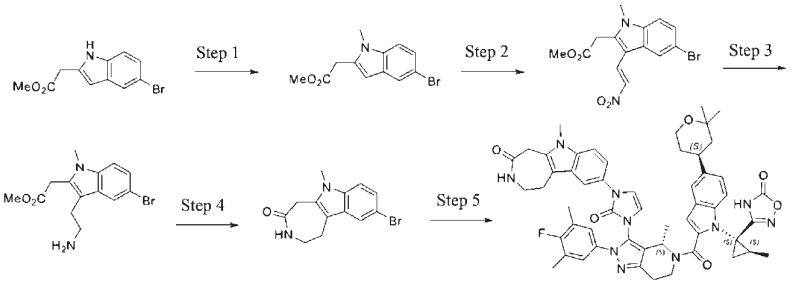
Example 53



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]。

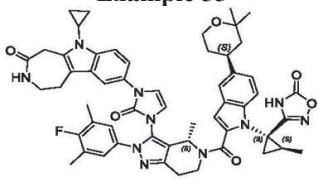
Step 4: methyl 2-(3-(2-aminoethyl)-5-bromo-1-methyl-1H-indol-2-yl)acetate (151 mg, 0.46 mmol) and p-toluenesulfonic acid (268 mg, 1.39 mmol) were dissolved in toluene (5 mL), and reacted under stirring at 80°C for 12 hours. The reaction solution was cooled to room temperature, quenched by adding a saturated 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]。

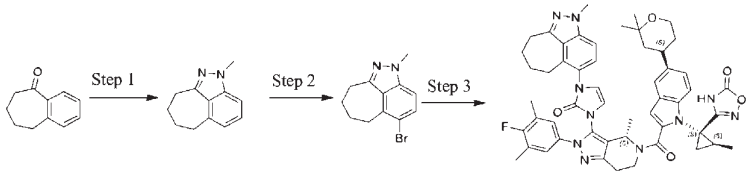
Example 55



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%).

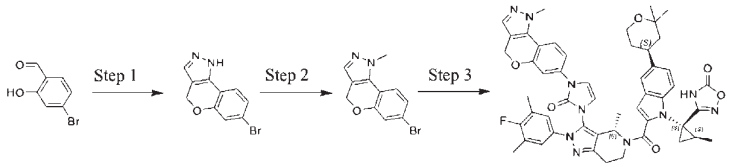
MS m/z (ESI): 265.0, 267.0 [M+1].

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].

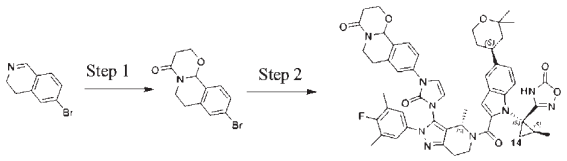
Step 2: 7-bromo-1,4-dihydrochromeno[4,3-c]pyrazole (150 mg, 597.42 μmol) was dissolved in tetrahydrofuran (10 mL), and under ice-water bath cooling and nitrogen protection, sodium hydride (28.67 mg, 716.91 μmol, 60% w/w) was added. The mixture was stirred for reaction at 0°C for 15 minutes. Iodomethane (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



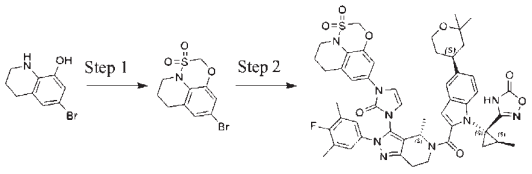
Step 1: 6-bromo-3,4-dihydroisoquinoline was used as a raw material, following Journal of Organic Chemistry, 2014, vol. 79, #3, p. 1368-1376, to synthesize the target product.

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.

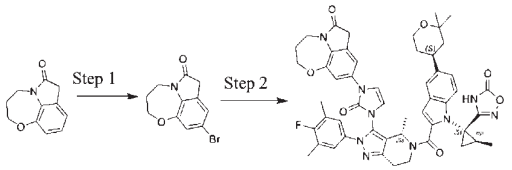
MS m/z (ESI): 304.0, 306.0 [M+1].

Step 2: following Example 1, the target product was obtained.

MS m/z (ESI): 958.4 [M+1].

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Example 60



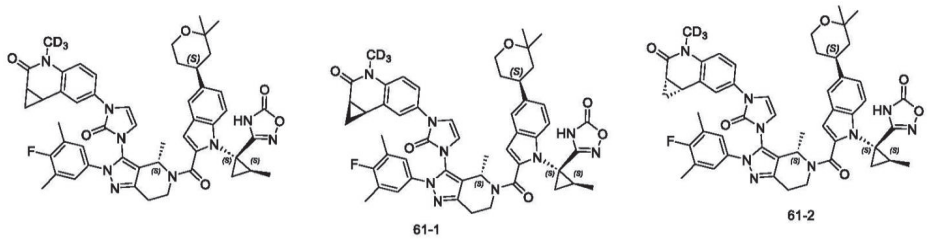
Step 1: following step 2 in Example 56, the target compound was synthesized.

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



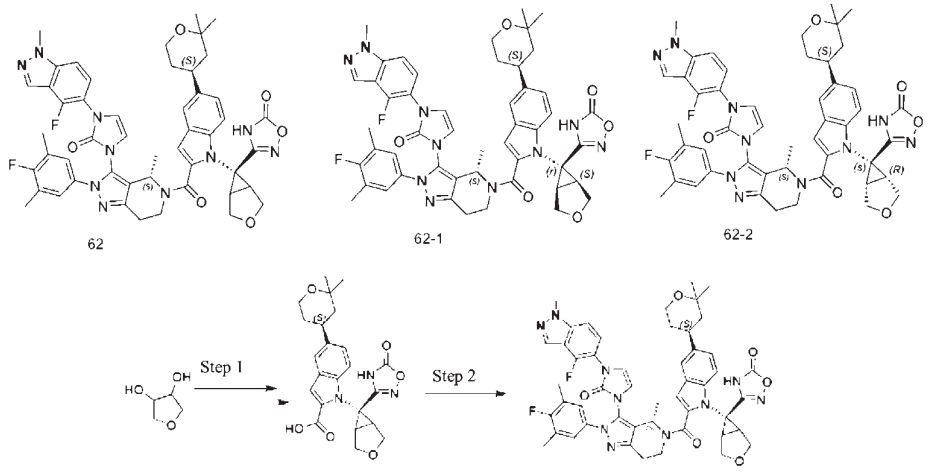
Following the synthesis method in Example 39, a product was obtained.

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.

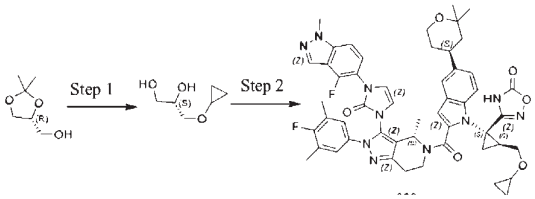
MS m/z (ESI): 911.4 [M+1].

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



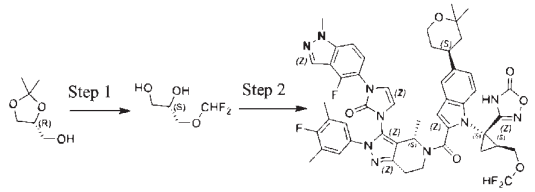
Step 1: (R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol (1 g, 7.57 mmol) and cyclopropyl bromide (1.01 g, 8.32 mmol) were dissolved in N,N-dimethylformamide (15 mL), and under nitrogen protection, potassium carbonate (3.14 g, 22.70 mmol) was added. The mixture was stirred for reaction at 25°C for 12 hours. 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

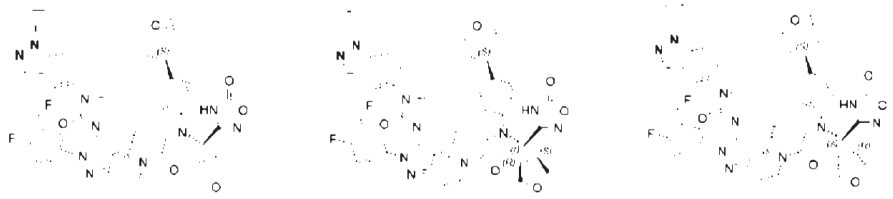


(R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol and difluoroiodomethane were used as raw materials, and the target product was obtained following Example 63.

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.

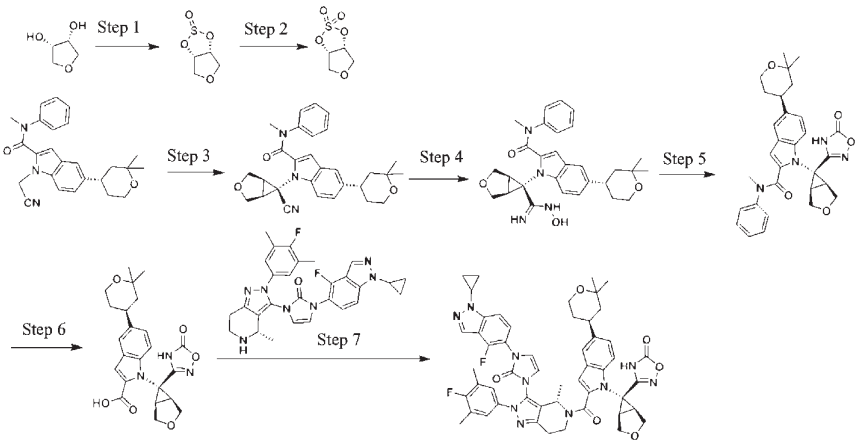
MS m/z (ESI): 937.4 [M+1].

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

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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.

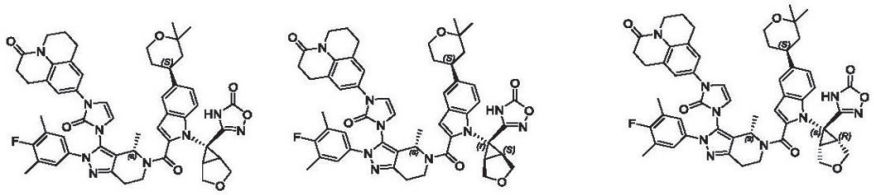
MS m/z (ESI): 440.2 [M+1].

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

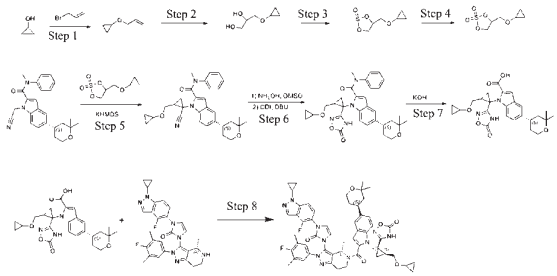


9-bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one was used as a raw material, and the target product was obtained following steps 2, 3, and 4 in Example 29.

MS m/z (ESI): 948.4 [M+1].

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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%).

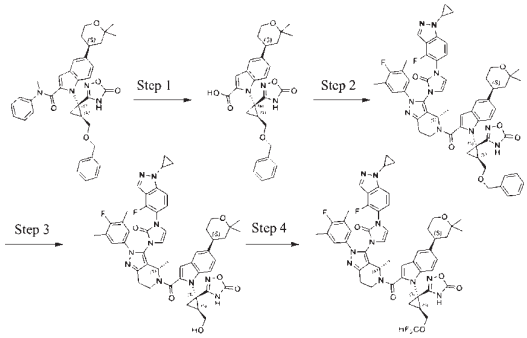
MS m/z (ESI): 468.2 [M+1].

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]

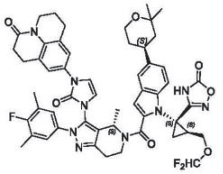
Step 3: 3-((1S,2S)-2-((benzyloxy)methyl)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one (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]

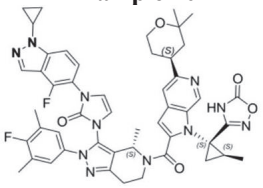
Example 69



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].

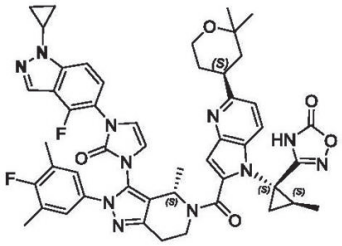
Example 70



the target compound was synthesized following Example 13.

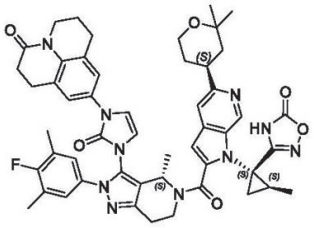
MS m/z (ESI): 910.4 [M+1].

Example 71



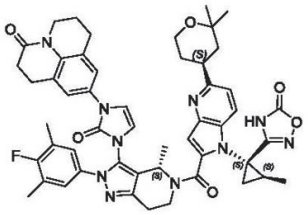
the target compound was synthesized following Example 13.
MS m/z (ESI): 910.4 [M+1].

Example 72



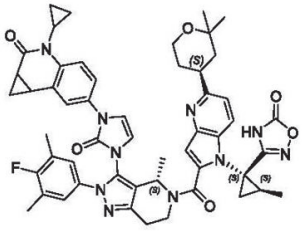
the target compound was synthesized following Example 13.
MS m/z (ESI): 921.4 [M+1].

Example 73



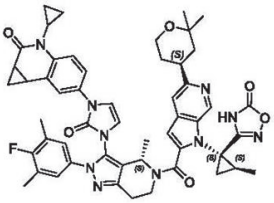
the target compound was synthesized following Example 13.
MS m/z (ESI): 921.4 [M+1].

Example 74



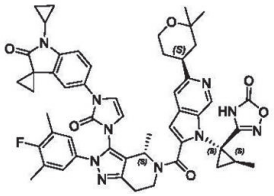
the target product was obtained following the synthesis method in Example 39.
MS m/z (ESI): 933.4 [M+1]。

Example 75



the target product was obtained following the synthesis method in Example 39.
MS m/z (ESI): 933.4 [M+1]。

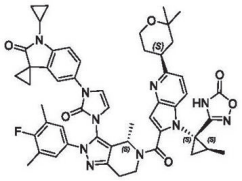
Example 76



the target product was obtained following the synthesis method in Example 31.

MS m/z (ESI): 933.4 [M+1]。

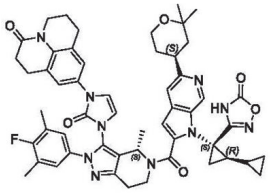
Example 77



the target product was obtained following the synthesis method in Example 31.

MS m/z (ESI): 933.4 [M+1]。

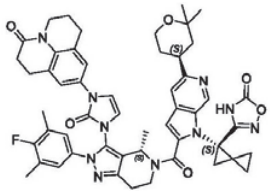
Example 78



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]+

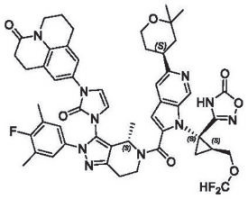
Example 79



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]+

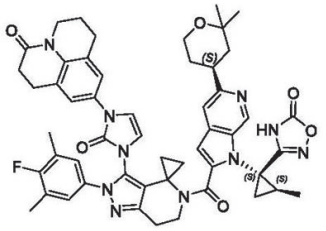
Example 80



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]+

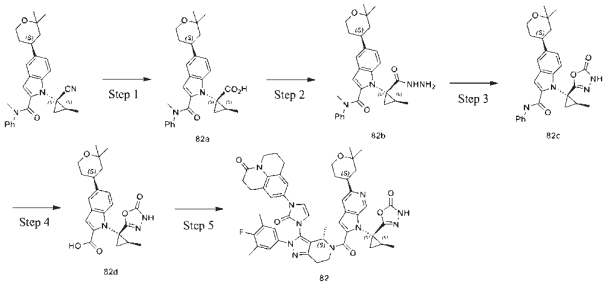
Example 81



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]

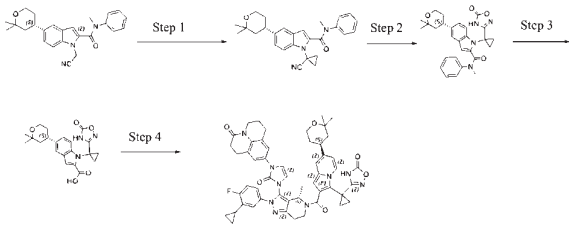
Step 4: following the synthesis method in step 5 of intermediate A, the target product 82d was obtained.

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]+

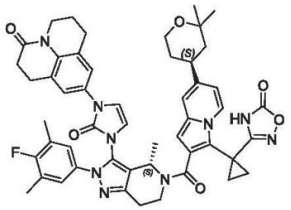
Step 4:

following step 4 in Example 29, the target product was obtained.

MS m/z (ESI): 918.4 [M+H]+

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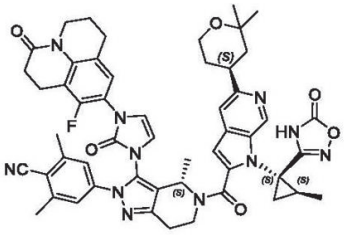
Example 84



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]+

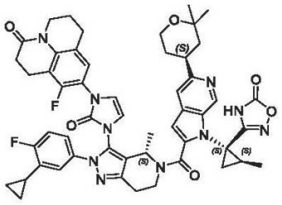
Example 85



the target compound was synthesized following Example 44.

MS m/z (ESI): 946.4 [M+1].

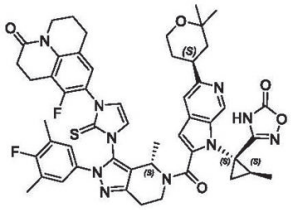
Example 86



the target compound was synthesized following Example 44.

MS m/z (ESI): 951.4 [M+1].

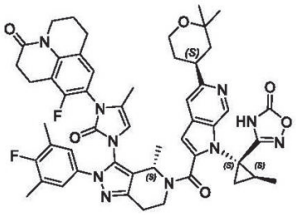
Example 87



the target compound was synthesized following Example 3.

MS m/z (ESI): 955.4 [M+1].

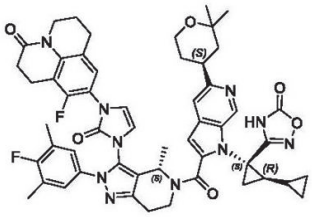
Example 88



the target compound was synthesized following Example 45.

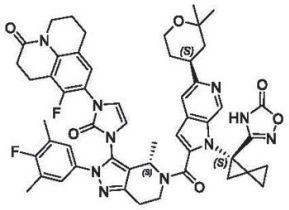
MS m/z (ESI): 953.4 [M+1].

Example 89



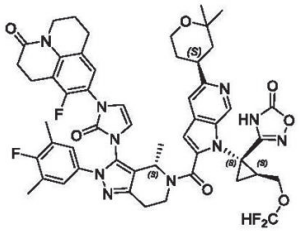
the target compound was synthesized following Example 46.
MS m/z (ESI): 965.4 [M+1].

Example 90



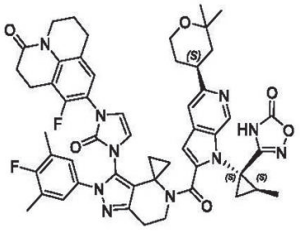
the target compound was synthesized following Example 79.
MS m/z (ESI): 951.4 [M+1].

Example 91



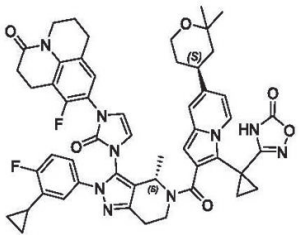
the target compound was synthesized following Example 64.
MS m/z (ESI): 1005.4 [M+1].

Example 92



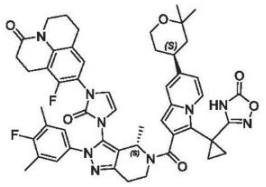
the target compound was synthesized following Example 16.
MS m/z (ESI): 951.4 [M+1].

Example 93



the target compound was synthesized following Example 44.
MS m/z (ESI): 936.4 [M+1].

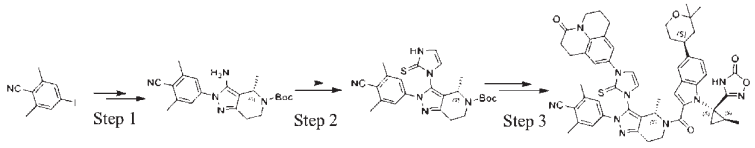
Example 94



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.

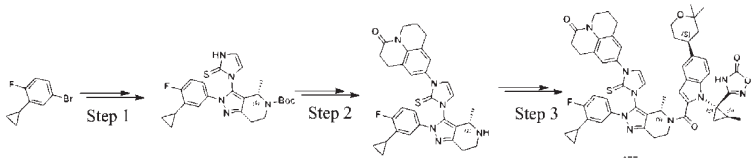
MS m/z (ESI): 465.2 [M+1].

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).

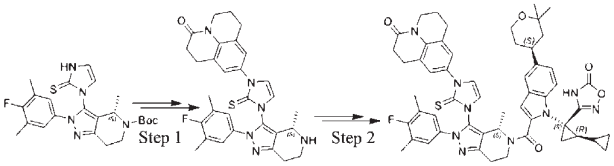
MS m/z (ESI): 555.2 [M+1].

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



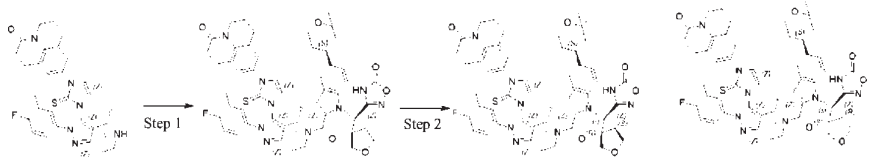
Step 1: tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in steps 2 and 3 of Example 25 (with 5-bromo-1-cyclopropyl-4-fluoroindazole 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



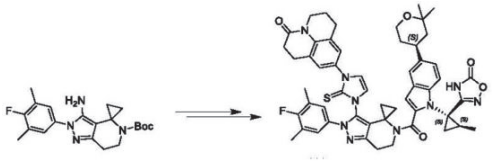
Step 1: (S)-9-(3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-(6-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-3-oxabicyclo[3.1.0]hexan-6-yl)-1H-indole-2-carboxylic 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].

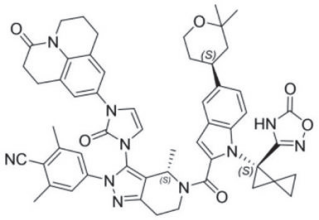
Example 99



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.

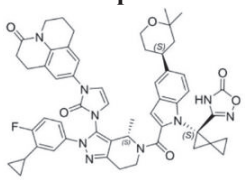
MS m/z (ESI): 948.4 [M+1].

Example 100

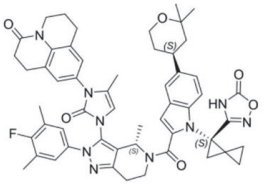


Following the synthesis in Example 403, the target product was obtained.
MS m/z (ESI): 939.4 [M+1].

Example 101

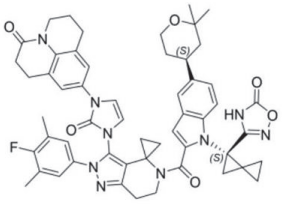


Following the synthesis in Example 22, the target product was obtained.
MS m/z (ESI): 944.4 [M+1].



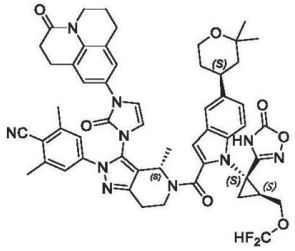
Following the synthesis in Example 406, the target product was obtained.
MS m/z (ESI): 946.4 [M+1].

Example 103



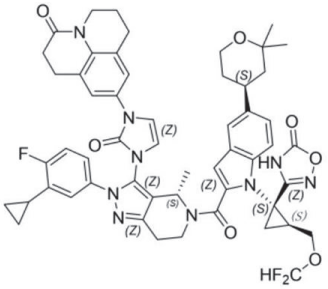
Following the synthesis in Example 51, the target compound was obtained.
MS m/z (ESI): 944.4 [M+1].

Example 104



Following the synthesis in Example 403, the target compound was obtained.
MS m/z (ESI): 993.4 [M+1].

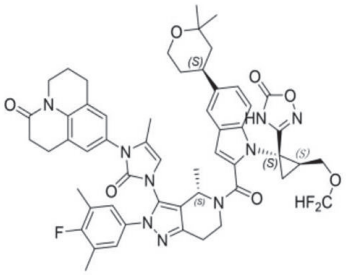
Example 105



Following the synthesis in Example 22, the target product was obtained.

MS m/z (ESI): 998.4 [M+1].

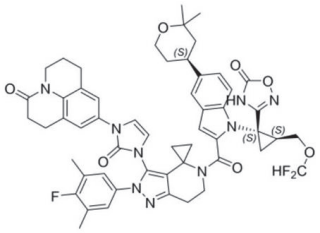
Example 106



Following the synthesis in Example 406, the target product was obtained.

MS m/z (ESI): 1000.4 [M+1].

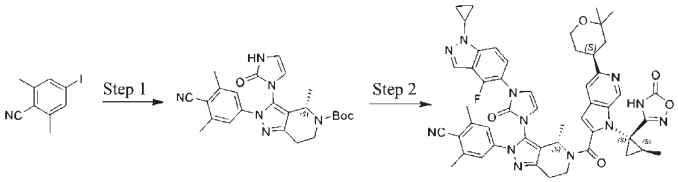
Example 107



Following the synthesis in Example 51, the target compound was obtained.

MS m/z (ESI): 998.4 [M+1].

Example 108



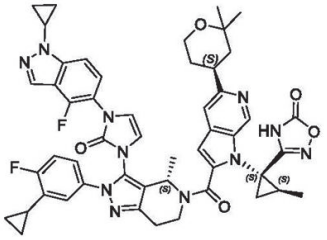
Step 1: 4-iodo-2,6-dimethylbenzonitrile was used as a raw material, and the target product was obtained following the synthesis of intermediate B.

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].

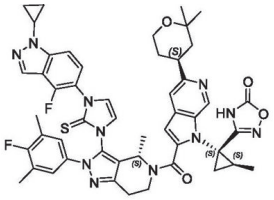
Example 109



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].

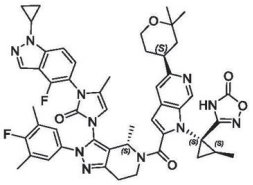
Example 110



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].

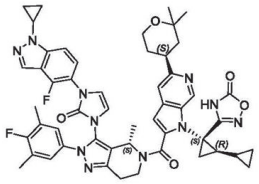
Example 111



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].

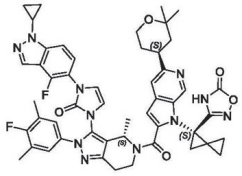
Example 112



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].

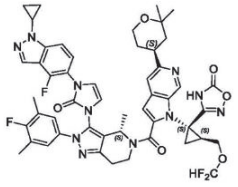
Example 113



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].

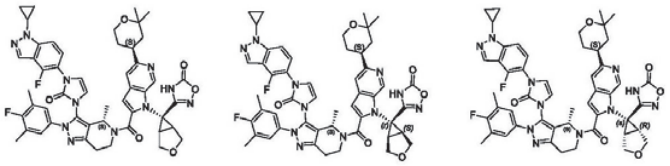
Example 114



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].

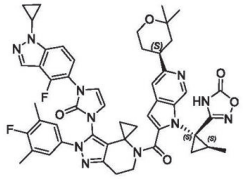
Example 115



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].

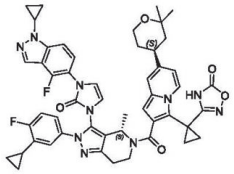
Example 116



the target product was synthesized following Example 110.

MS m/z (ESI): 922.4 [M+1].

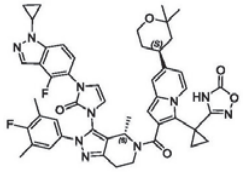
Example 117



the target product was synthesized following Examples 109 and 6.

MS m/z (ESI): 907.4 [M+1].

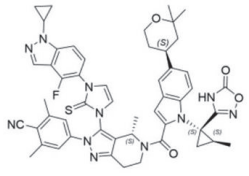
Example 118



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].

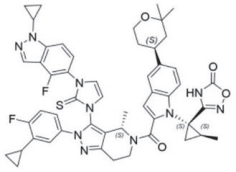
Example 119



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].

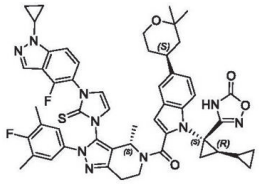
Example 120



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].

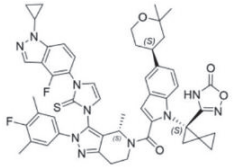
Example 121



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].

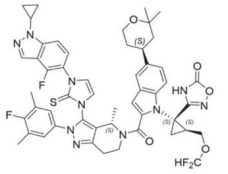
Example 122



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].

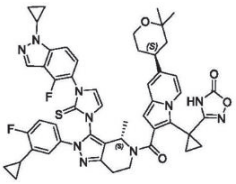
Example 123



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].

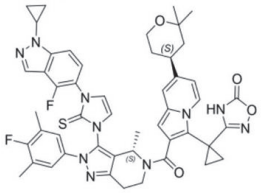
Example 124



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].

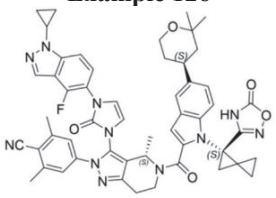
Example 125



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].

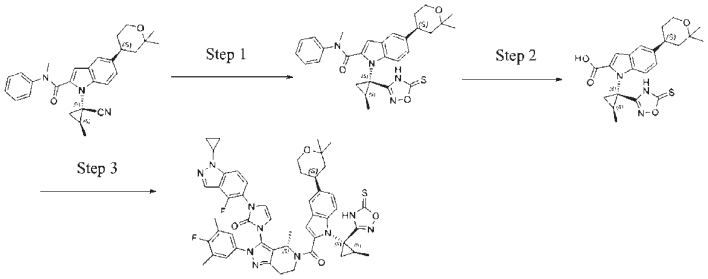
Example 126



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

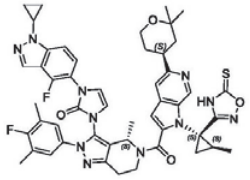
cooled to room temperature, with LCMS indicating the completion of the reaction; the reaction solution was neutralized with dilute hydrochloric acid (6N) and adjusted to pH 5-6, with solid precipitating; and the system was filtered, the solid was washed with water and petroleum ether, successively, and 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]+

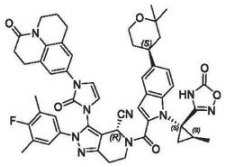
Example 128



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]+

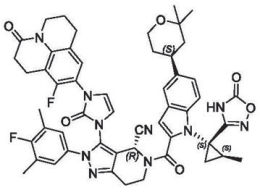
Example 129



Following the synthesis of 407, the target compound was obtained.

MS m/z (ESI): 931.4 [M+H]+。

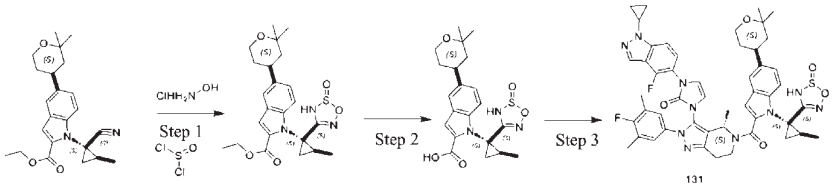
Example 130



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].

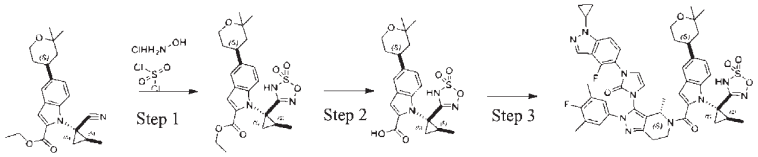
Step 2: ethyl 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-methyl-1-(2-hydroxyl-3H-1,2,3,5-oxathiadiazol-4-yl)cyclopropyl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in step 5 of intermediate A.

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].

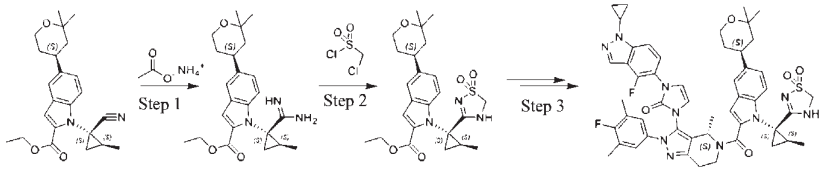
Step 2: ethyl 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-1-(2,2-dihydroxyl-3H-1,2,3,5-oxathiadiazol-4-yl)-2-methylcyclopropyl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in step 5 of intermediate A.

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]

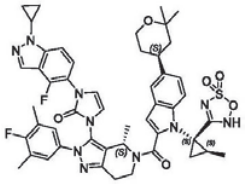
Step 2: ethyl 1-((1S,2S)-1-carbamimidoyl-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylate (260 mg, 654.06 μmol) and triethylamine (198.56 mg, 1.96 mmol) were dissolved in 5 mL DCM, then a solution of chloromethylsulfonyl chloride (97.44 g, 654.06 μmol) in dichloromethane 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%.

MS m/z (ESI): 474.2 [M+1]

Step 3: ethyl 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-1-(1,1-dihydroxyl-4,5-dihydro-1,2,4-thiadiazol-3-yl)-2-methylcyclopropyl)-1H-indole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method in Example 25.

MS m/z (ESI): 943.3 [M+1].

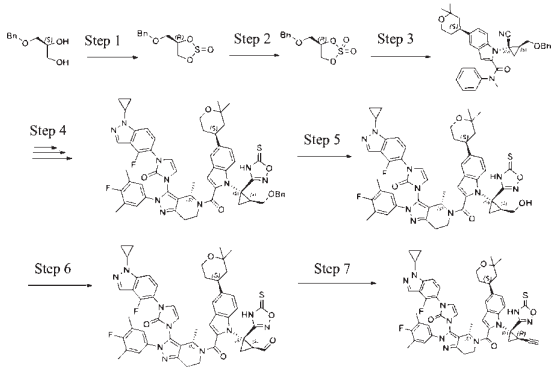
Example 134



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 Example 132.

MS m/z (ESI): 945.3 [M+1].

Example 135



Step 1: under an ice bath, (2S)-3-benzyloxypropane-1,2-diol (5 g, 27.44 mmol) was dissolved in dichloromethane (100 mL), then triethylamine (11.11 g, 109.76 mmol, 15.31 mL) was added, then thionyl chloride (4.90 g, 41.16 mmol, 2.99 mL) was slowly added dropwise, and the reaction solution was stirred under an ice bath for one hour, with LCMS showing the completion of the reaction; the reaction solution was quenched by adding water (150 mL) and then extracted with dichloromethane (100 mL × 3); and the organic phases were combined, washed with saturated brine (100 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain the target product (6 g, crude).

Step 2: under an ice bath, (4R)-4-((benzyloxy)methyl)-1,3,2-dioxathiolane 2-oxide (6 g, 26.29 mmol) was dissolved in acetonitrile (90 mL) and water (10 mL), then sodium periodate (8.43 g, 39.43 mmol) and ruthenium chloride hydrate (296.29 mg, 1.31 mmol) were added, and the reaction solution was stirred at room temperature for three hours, with LCMS indicating the completion of the reaction; the reaction solution was quenched by adding water (150 mL) and then extracted with dichloromethane (100 mL × 3); and the organic phases were combined, washed with saturated brine (100 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a crude product, which was separated by Flash column chromatography (PE/EA = 4 : 1). to obtain the target compound (5 g, yield 55%).

Step 3: under an ice bath, 1-(cyanomethyl)-5-[(4S)-2,2-dimethyltetrahydropyran-4-yl]-N-methyl-N-phenyl-indole-2-carboxamide (0.5 g, 1.25 mmol) was dissolved in DMPU (15 mL), and (R)-4-((benzyloxy)methyl)-1,3,2-dioxathiolane 2,2-dioxide (1.06 g, 4.36 mmol) was then added, followed by nitrogen replacement; then potassium bis(trimethylsilyl)amide (1.0M, 5.6 mL) was slowly added dropwise, and after addition, the reaction solution was stirred under an ice bath for 2 hours, with LCMS indicating the completion of the reaction; the reaction solution was quenched with saturated ammonium chloride solution (20 mL), and then saturated brine (20 mL) was added; the reaction solution was extracted with ethyl acetate (30 mL × 3); 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 compound as pale yellow solid (0.48 g, yield 70.4%).

Step 4: the target product was obtained following steps 1, 2, and 3 in Example 127.

MS m/z (ESI): 1031.4 [M+H]+.

Step 5: at room temperature, 1-((S)-5-(1-((1S,2S)-2-((benzyloxy)methyl)-1-(5-thio-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carbonyl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-1,3-dihydro-2H-imidazole-2-one (0.20 g, 0.19 mmol) was dissolved in dichloromethane (5 mL), then boron trichloride (1.0M, 1 mL) was added dropwise, and the reaction solution was stirred at room temperature for one hour, with LCMS indicating the completion of the reaction; the reaction solution was quenched with a saturated sodium bicarbonate solution (10 mL) and extracted with dichloromethane (15 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography to obtain the target product (0.10 g, yield 55%).

MS m/z (ESI): 941.4 [M+H]+.

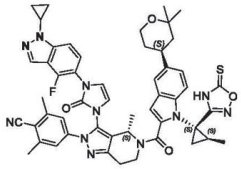
Step 6: at room temperature, 1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-((S)-5-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-(hydroxymethyl)-1-(5-thio-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carbonyl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one (0.10 g, 0.11 mmol) was dissolved in dichloromethane (5 mL), then Dess-Martin (0.09 g, 0.22 mmol) was then added, and the reaction solution was stirred at room temperature for 14 hours, with LCMS indicating the completion of the reaction; the reaction solution was diluted with dichloromethane (20 mL), and 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 (0.06 g, yield 60%).

MS m/z (ESI): 939.4 [M+H]+.

Step 7: at room temperature, (1S,2S)-2-(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-(5-thio-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carbaldehyde (0.06 g, 0.06 mmol) was dissolved in methanol (3 mL), then 1-diazo-1-dimethoxyphospho-propane-2-one (0.02 g, 0.1 mmol) and potassium carbonate (0.02 g, 0.14 mmol) were added, and the reaction solution was stirred at room temperature for 5 hours, with LCMS indicating the completion of the reaction; the reaction solution was quenched with saturated brine (20 mL), and then extracted with ethyl acetate (15 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography to obtain the target compound (0.02 g, yield 35.7%).

MS m/z (ESI): 935.4 [M+H]+.

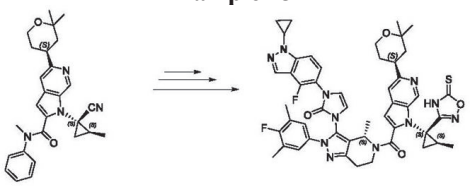
Example 136



Intermediate G was used as a raw material, and the target product was obtained following Example 25 and Example 127.

MS m/z (ESI): 932.4 [M+H]+.

Example 137

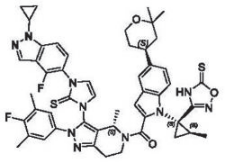


1-((1S,2S)-1-cyano-2-methylcyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-pyrrolo[2,3-c]pyridine -2-carboxamide was used as a raw material, and

the target product was obtained following Example 127.

MS m/z (ESI): 926.2 [M+H]+.

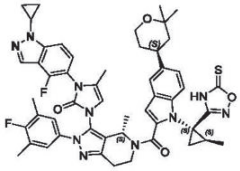
Example 138



the target product was obtained following Example 3 and Example 127.

MS m/z (ESI): 941.4 [M+H]+.

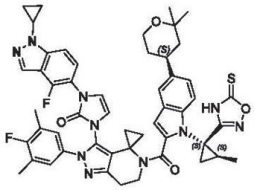
Example 139



the target product was obtained following Example 45 and Example 127.

MS m/z (ESI): 939.4 [M+H]+.

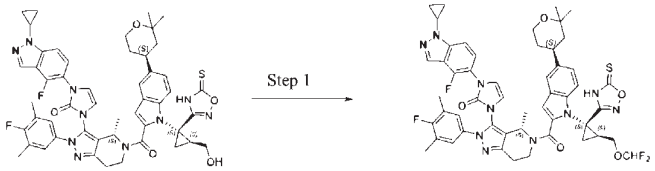
Example 140



the target product was obtained following Example 51 and Example 127.

MS m/z (ESI): 937.4 [M+H]+.

Example 141

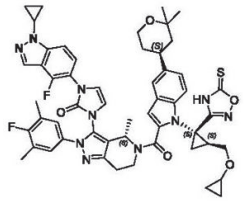


Step 1: 1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-((S)-5-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-(hydroxymethyl)-1-(5-thio-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carbonyl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one (0.05 g, 0.053 mmol) was dissolved in dichloromethane (2 mL), then potassium acetate (0.02 g, 0.212 mmol) was added, then (bromodifluoromethyl)trimethylsilane (0.022 g, 0.11 mmol) was added dropwise, and the reaction solution was stirred at room temperature for 12 hours, with LCMS indicating the completion of the reaction; the reaction solution was quenched by adding water (5 mL), and then extracted with dichloromethane (10 mL × 3); and the organic phases were combined, washed with saturated brine (10 mL × 2), dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography to obtain the target compound (0.01 g, yield 19%).

MS m/z (ESI): 991.4 [M+H]+.

Example 142

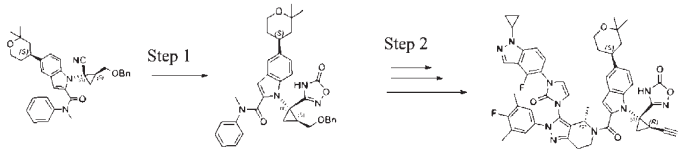
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the target product was obtained following Example 63 and Example 135.

MS m/z (ESI): 981.4 [M+H]+.

Example 143



Step 1: 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

at room temperature, 1-((1S,2S)-2-((benzyloxy)methyl)-1-cyanocyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.55 g, 1 mmol) was dissolved in ethanol (8 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-carbonyldiimidazole (0.32 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 (0.42 g, yield 70%).

MS m/z (ESI): 607.3 [M+H]+.

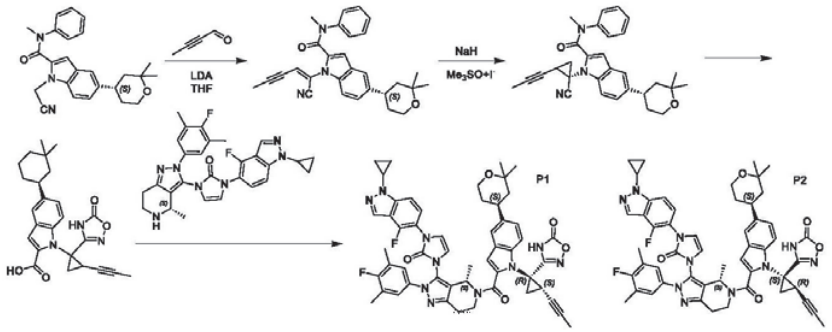
Step 2: 3-((1S,2R)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one

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 was used as a raw material, and the target compound was obtained following steps 2 and 3 of Example 127, and steps 5, 6 and 7 of Example 135.

^{1}H NMR (400MHz, DMSO-d_6) δ [12.49(s) and 11.96(s), total 1H], 8.29 (s, 1H), 7.68-7.60 (m, 1H), 7.54-7.27 (m, 4H), 7.20-7.08 (m, 3H), 6.98-6.74 (m, 2H), [5.77-5.60(m) and 5.33-5.17(m), total 1H], [4.82-4.69(m) and 4.51-4.35(m), total 1H], 3.88-3.78 (m, 1H), 3.72-3.47 (m, 3H), 3.22-3.16 (m, 1H), 3.17-3.01 (m, 1H), 2.91-2.76 (m, 2H), 2.33-2.28 (m, 1H), 2.26 (s, 6H), 2.01-1.95 (m, 1H), 1.67-1.49 (m, 6H), 1.38-1.27 (m, 5H), 1.18-1.13 (m, 7H).

MS m/z (ESI): 919.4 [M+H]+.

Example 144



Step 1: (S)-1-(1-cyanopent-1-en-3-yn-1-yl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide

(S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (1.8 g, 4.48 mmol) and but-2-ynal (915.56 mg, 13.45 mmol) were dissolved in anhydrous tetrahydrofuran (18 mL), and under nitrogen protection and -40°C, lithium diisopropylamide (2M, 4.48 mL) was added. The mixture was stirred for reaction at -40°C for 2 hours. The reaction solution was slowly heated to room temperature. LCMS showed the generation of the target product. Th crude reaction solution was used directly in the next step.

MS m/z (ESI): 452.2 [M+1].

Step 2: 1-(1-cyano-2-(prop-1-yn-1-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide

Trimethylsulfoxonium iodide (1.46 g, 6.64 mmol) was dissolved in dimethyl sulfoxide (8 mL), and under nitrogen protection, sodium hydride (265.72 mg, 6.64 mmol, w/w 60%) was added. The mixture was stirred for reaction at 18°C for 3 hours. Then, at 0°C, the reaction solution was added to the crude solution in step 1. Then, the system was stirred at room temperature overnight. To the mixture, saturated brine (50 mL) was added to quench the reaction, and the system was extracted with ethyl acetate (30 mL × 2); and the organic phases were combined, and washed with saturated brine (50 mL × 4), 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 a crude product. The crude product was separated by preparative high-performance liquid phase chromatography to obtain a product (0.26 g, 558.44 μmol, yield: 12.61%) as a white solid.

MS m/z (ESI): 466.2 [M+1].

Step 3: 5-((S)-3,3-dimethyl cyclohexyl)-1-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indole-2-carboxylic acid

the target compound was synthesized following steps 4 and 5 of intermediate A.

MS m/z (ESI): 434.2 [M+1].

Step 4: 3-((1S,2R)-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-(prop-1-yn-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one

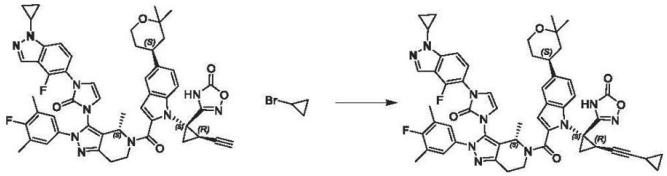
A crude product was synthesized following step of intermediate C and intermediate D, and the crude product was separated by preparative high-performance liquid phase chromatography to obtain P1 and P2, which P2 was the target compound, i.e., Example 144.

^{1}H NMR (400MHz, DMSO) δ , [12.42(s) and 11.92(s), total 1H], 8.28 (s, 1H), 7.77-7.59 (m, 1H), 7.58-7.23 (m, 4H), 7.23-7.02 (m, 3H), 7.02-6.85 (m, 2H), [5.83-5.53(m), 5.38-5.05(m), total 1H], [4.88-4.61(m), 4.56-4.23(m), total 1H], 3.93-3.78 (m, 1H), 3.78-3.41 (m, 3H), 3.23-2.96 (m, 2H), 2.96-2.64 (m, 2H), 2.26 (s, 6H), 2.04-1.87 (m, 1H), 1.87-1.40 (m, 9H), 1.40-0.96 (m, 12H).

MS m/z (ESI): 933.4 [M+1].

Example 145

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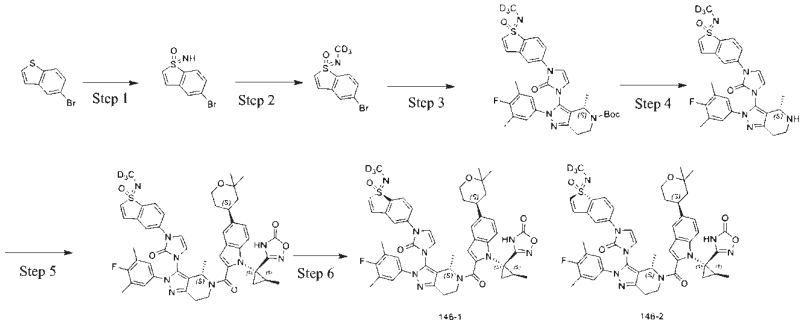


3-((1S,2R)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one (100 mg, 108.81 umol), [μ2-N2,N2'-bis(sodium 3-formyl-4-oxidobenzylidenesulfonato)benzene-1,3-dicarbohydrazidato]bis[aqua-copper(II)] monohydrate (7.79 mg, 10.88 umol), potassium carbonate (30.07 mg, 217.63 umol), and cyclopropyl bromide (26.33 mg, 217.63 umol) were dissolved in ethanol (5 mL), and the reaction solution was stirred for reaction at 80°C under nitrogen protection for 10 hours. To the reaction solution, water (5 mL) was added to quench the reaction, and the reaction solution was extracted with ethyl acetate (5 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (5 mL), dried over anhydrous sodium sulfate, filtered, and concentration, and the resulting residue was purified by silica gel column chromatography using a eluent system of petroleum ether and ethyl acetate to obtain the target product (10 mg), yield: 9.58%.

^{1}H NMR (400MHz, DMSO) δ [12.36(s) and 11.93(s), total 1H], 8.28 (s, 1H), 7.73-7.56 (m, 1H), 7.56-7.23 (m, 4H), 7.22-6.97 (m, 3H), 6.98-6.67 (m, 2H), [5.84-5.53(m), 5.35-5.05(m), total 1H], 4.87-4.23 (m, 1H), 3.92-3.43 (m, 4H), 3.21-2.64 (m, 4H), 2.26 (s, 6H), 2.09-1.43 (m, 8H), 1.38-0.99 (m, 12H), 0.85-0.69 (m, 2H), 0.60-0.37 (m, 2H).

MS m/z (ESI): 959.4 [M+1].

Example 146



Step 1: 5-bromobenzo[b]thiophene (453 mg, 2.13 mmol) and ammonium carbamate (664.10 mg, 8.51 mmol) were dissolved in methanol (15 mL), and under nitrogen protection, iodobenzenediacetic acid (2.05 g, 6.38 mmol) was added. The mixture was stirred for reaction at 25°C for 12 hours. The mixture was evaporated to dryness under reduced pressure, saturated brine (100 mL) was added to quench the reaction, and the system was extracted with ethyl acetate (30 mL × 2); and the organic phases were combined, and 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 0 : 100), to obtain the target product (410 mg, white solid), yield: 79.0%.

MS m/z (ESI): 243.9,245.9 [M+1].

Step 2: 5-bromo-1-imino-1H-1l4-benzo[b]thiophene 1-oxide (410 mg, 1.68 mmol) was dissolved in tetrahydrofuran (10 mL), and under nitrogen protection, sodium hydride (100.77 mg, 2.52 mmol, 60% w/w) was added. The mixture was stirred for reaction at 25°C for 0.5 hours. Under nitrogen protection, iodomethane (486.94 mg, 3.36 mmol) was added. The mixture was stirred for reaction at 25°C for 12 hours. To the reaction solution, saturated brine (50 mL) was added to quenched the reaction, and the mixture was subjected to liquid separation; the organic phase was dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure to obtain a crude product, which was purified by flash silica gel chromatographic column (petroleum ether:ethyl acetate = 1 : 1), to obtain the target product (260 mg, white solid), yield: 59.2%.

MS m/z (ESI): 261.0, 263.0 [M+1].

Step 3: 5-bromo-1-((methyl-d3)imino)-1H-1l4-benzo[b]thiophene 1-oxide was used as a raw material, and the target product was obtained following step 2 of Example 25.

MS m/z (ESI): 622.2 [M+1].

Step 4: tert-butyl (4S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(1-((methyl-d3)imino)-1-hydroxyl-1H-1l4-benzo[b]thiophen-5-yl)-2-carbonyl-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 step 3 of Example 25.

MS m/z (ESI): 522.2 [M+1].

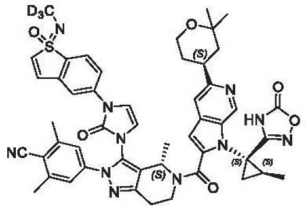
Step 5: tert-butyl (4S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(1-((methyl-d3)imino)-1-hydroxyl-1H-1l4-benzo[b]thiophen-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate was used as a raw material, and the target product was obtained following steps 3 to 4 of Example 25.

MS m/z (ESI): 915.3 [M+1].

Step 6: The resulting product was chirally resolved to obtain 146-1 and 146-2.

MS m/z (ESI): 915.3 [M+1].

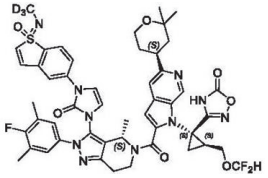
Example 147



5-bromobenzo[b]thiophene and intermediate G were used as starting raw materials, and the target product was finally obtained following Example **146**.

MS m/z (ESI): 923.4 [M+1].

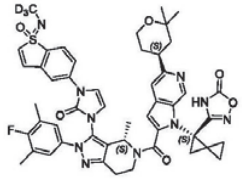
Example 148



5-bromobenzo[b]thiophene was used as a starting raw material, and the target product was finally obtained following Examples **135** and **146**.

MS m/z (ESI): 982.4 [M+1].

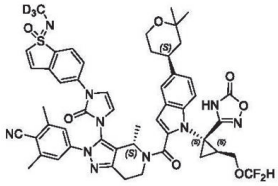
Example 149



5-bromobenzo[b]thiophene was used as a starting raw material, and the target product was finally obtained following Examples **135** and **146**.

MS m/z (ESI): 928.4 [M+1].

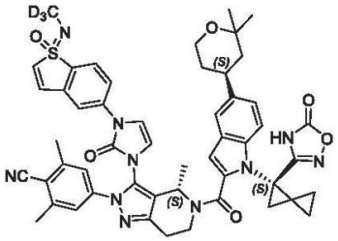
Example 150



5-bromobenzo[b]thiophene and intermediate G were used as starting raw materials, and the target product was finally obtained following Examples **146** and **135**.

MS m/z (ESI): 988.4 [M+1].

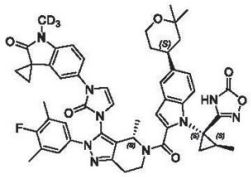
Example 151



5-bromobenzo[b]thiophene and intermediate G were used as starting raw materials, and the target product was finally obtained following Examples **146** and **135**.

MS m/z (ESI): 934.4 [M+1].

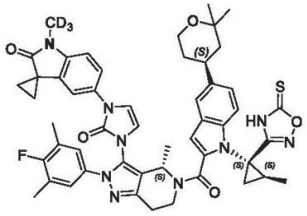
Example 152



5'-bromospiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a starting raw material, and the target product was finally obtained following Example **146**.

MS m/z (ESI): 909.4 [M+1].

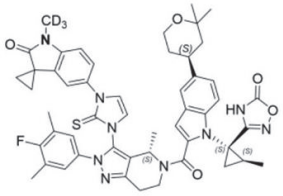
Example 153



5'-bromospiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a starting raw material, and the target product was finally obtained following Example **146** and intermediate F.

MS m/z (ESI): 925.4 [M+1].

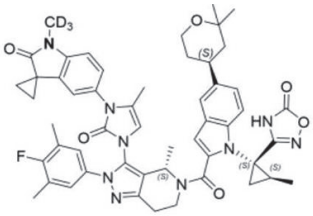
Example 154



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target compound was synthesized following Example 3 and Example 127.

MS m/z (ESI): 925.4 [M+1].

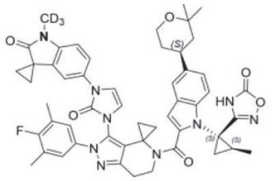
Example 155



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 45 and Example 127.

MS m/z (ESI): 923.4 [M+1].

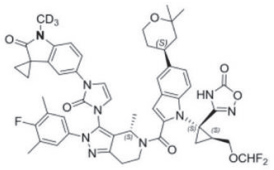
Example 156



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 51 and Example 127

MS m/z (ESI): 921.4 [M+1].

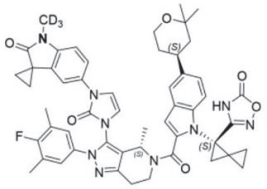
Example 157



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target compound was synthesized following Example 141.

MS m/z (ESI): 975.4 [M+1].

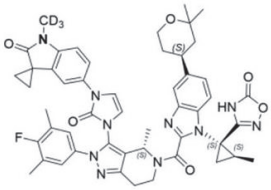
Example 158



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target compound was synthesized following Example 79.

MS m/z (ESI): 921.4 [M+1].

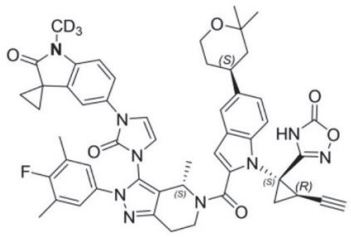
Example 159



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target compound was synthesized following Example 364.

MS m/z (ESI): 910.4 [M+1].

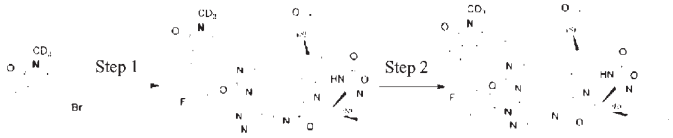
Example 160



5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target compound was synthesized following Example 143.

MS m/z (ESI): 919.4 [M+1].

Example 161



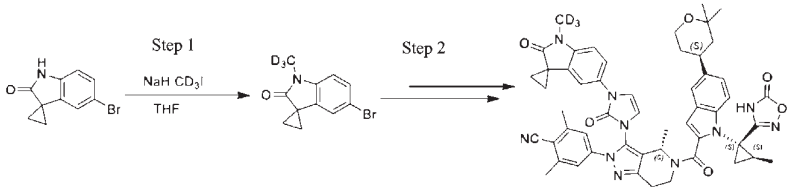
Step 1: 5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 135.

MS m/z (ESI): 919.4 [M+1].

Step 2: following Example 145, the target product was obtained.

MS m/z (ESI): 959.4 [M+1].

Example 162



Step 1: 5'-bromospiro[cycloprop-1,3'-dihydroindole]-2'-one (200 mg, 840.05 μmol) was dissolved in anhydrous tetrahydrofuran (10 mL), and at room temperature 20°C, sodium hydride (67.20 mg, 1.68 mmol, 60% purity) was added thereto; and the reaction solution was stirred at room temperature for 0.5 hours, and then deuterated iodomethane (243.54 mg, 1.68 mmol) was added dropwise. The reaction system was further stirred at room temperature 20°C for 3.5 hours. After the reaction was completed, saturated ammonium chloride solution (10 mL) was added dropwise to quench the reaction, and the mixture was extracted with ethyl acetate (20 mL × 2), followed by washing with saturated brine (20 mL × 2), drying over anhydrous sodium sulfate, filtration and concentration to obtain a crude product 5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one (210 mg, crude). The crude product was used directly in the next-step reaction without further purification.

MS m/z (ESI): 255.0, 257.0 [M+1].

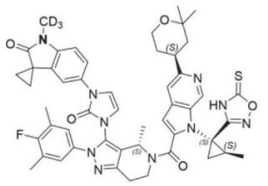
Step 2: 5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example **147**.

^{1}H NMR (400MHz, DMSO) δ [11.97(s) and 11.74(s), total 1H], 7.50 (d, 2H), 7.38(t, 2H), 7.29-7.24 (m, 4H), 7.16 (d, 1H), 6.96 (s, 1H), 6.76 (s, 1H), 5.59-5.57(q, 1H), 4.41-4.38 (m, 1H), 3.70-3.60 (m, 5H), 3.50-3.46 (m, 1H), 3.25-3.17 (m, 1H), 3.03-2.89 (m, 3H), 2.47 (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)

MS m/z (ESI): 917.4 [M+1].

Example 163

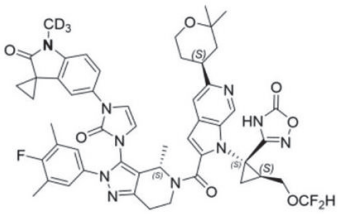
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5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 137.

MS m/z (ESI): 926.4 [M+1].

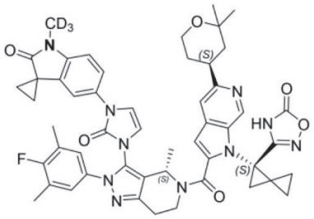
Example 164



5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 148.

MS m/z (ESI): 976.4 [M+1].

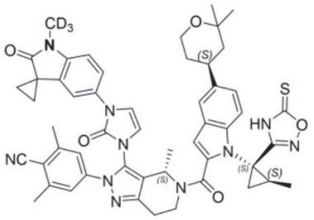
Example 165



5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 149.

MS m/z (ESI): 922.4 [M+1].

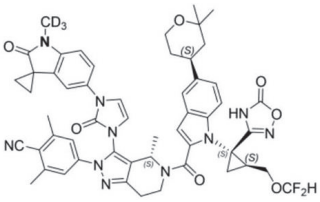
Example 166



5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 136.

MS m/z (ESI): 932.4 [M+1].

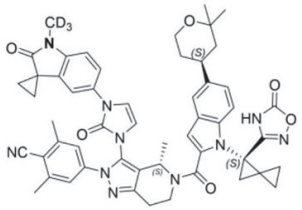
Example 167



5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 150.

MS m/z (ESI): 982.4 [M+1].

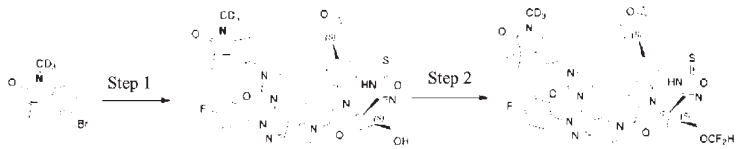
Example 168



5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 151.

MS m/z (ESI): 928.4 [M+1].

Example 169



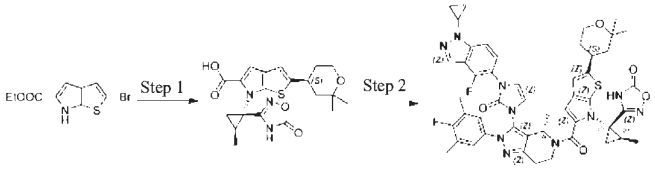
Step 1: 5'-bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 135.

MS m/z (ESI): 941.4 [M+1].

Step 2: following Example 141, the target product was obtained.

MS m/z (ESI): 991.4 [M+1].

Example 170



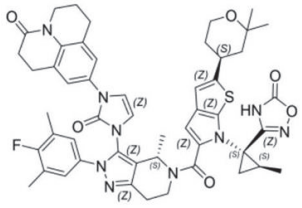
Step 1: ethyl 2-bromo-6H-thieno[2,3-b]pyrrole-5-carboxylate was used as a raw material, and the target product was obtained following intermediate F.

MS m/z (ESI): 418.1 [M+1].

Step 2: Following step 4 of Example 25, the target product was obtained.

MS m/z (ESI): 915.4 [M+1].

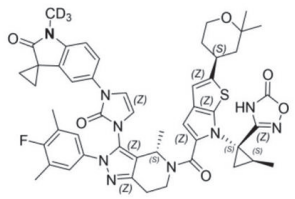
Example 171



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 170.

MS m/z (ESI): 926.4 [M+1].

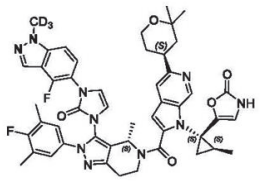
Example 172



5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one was used as a raw material, and the target product was obtained following Example 170.

MS m/z (ESI): 915.4 [M+1].

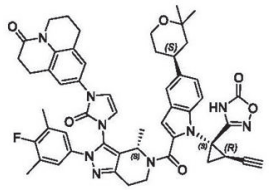
Example 173



Following the synthesis method in Example 370, the target product was obtained.

MS m/z (ESI): 886.4 [M+1]

Example 174

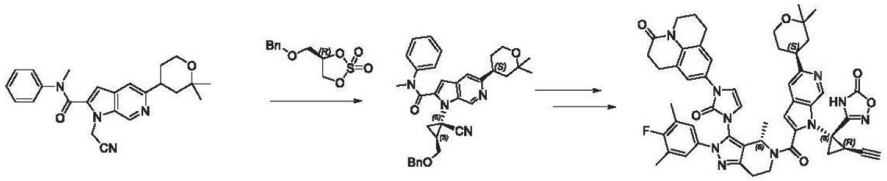


Following the synthesis method in Example 143, the target product was obtained.

^{1}H NMR (400MHz, DMSO-d_6) δ [12.47(s) and 11.94(s), total 1H], 7.54-7.51 (m, 1H), 7.43-7.09 (m, 7H), 6.98-6.70 (m, 2H), [5.72-5.58(m) and 5.32-5.14(m), total 1H], [4.81-4.67(m) and 4.49-4.35(m), total 1H], 3.75-3.47 (m, 5H), 3.21-3.01 (m, 2H), 2.99-2.73 (m, 6H), 2.56-2.51 (m, 2H), 2.28-2.15 (m, 7H), 1.96-1.92 (m, 1H), 1.90-1.78 (m, 2H), 1.73-1.41 (m, 6H), 1.28-1.14 (m, 8H).

MS m/z (ESI): 930.4 [M+1].

Example 175



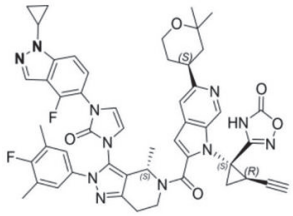
Step 1: 1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-pyrrolo[2,3-c]pyridine-2-carboxamide and (R)-4-((benzyloxy)methyl)-1,3,2-dioxathiolane 2,2-dioxide were used as raw materials, and the target compound was obtained following step 6 of intermediate F, followed by resolution.

MS m/z (ESI): 549.2 [M+1].

Step 2: 1-((1S,2S)-2-((benzyloxy)methyl)-1-cyanocyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-pyrrolo[2,3-c]pyridine-2-carboxamide and tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-3-(3-carbonyl-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate were used as raw materials, and the target compound was obtained following Example 143.

MS m/z (ESI): 931.4 [M+1].

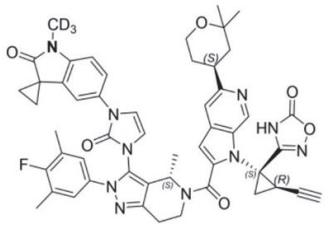
Example 176



tert-Butyl (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-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 Example 175.

MS m/z (ESI): 920.4 [M+1].

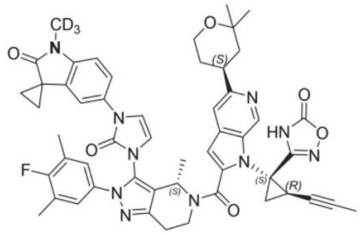
Example 177



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(1'-(methyl-d3)-2'-carbonylspiro[cycloprop-1,3'-dihydroindol]-5'-yl)-2-carbonyl-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 Example 176.

MS m/z (ESI): 920.4 [M+1].

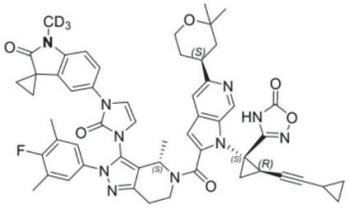
Example 178



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(1'-(methyl-d3)-2'-carbonylspiro[cycloprop-1,3'-dihydroindol]-5'-yl)-2-carbonyl-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 Example 465.

MS m/z (ESI): 934.4 [M+1].

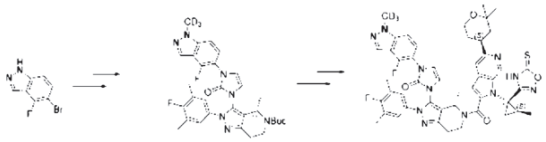
Example 179



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(1'-(methyl-d3)-2'-carbonylspiro[cycloprop-1,3'-dihydroindol]-5'-yl)-2-carbonyl-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 Example 471.

MS m/z (ESI): 960.4 [M+1].

Example 180



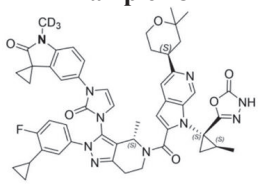
Step 1: 5-bromo-4-fluoro-1H-indazole was used as a raw material, and the target product was obtained following steps 2 and 3 of Example 145.

MS m/z (ESI): 593.2 [M+1].

Step 2: 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-pyrrolo[2,3-c]pyridine-2-carboxylic acid and tert-butyl (S)-3-(3-(4-fluoro-1-(methyl-d3)-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 were used as raw materials, and the target product was obtained following steps 3 and 4 of Example 25

MS m/z (ESI): 903.4 [M+1].

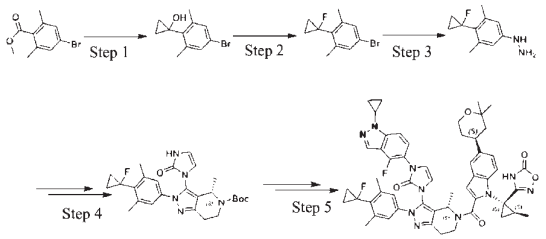
Example 181



-Butyl (S)-2-(3-cyclopropyl-4-fluorophenyl)-4-methyl-3-(3-(1'-(methyl-d3)-2'-carbonylspiro[cycloprop-1,3'-dihydroindol]-5'-yl)-2-carbonyl-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 Example 478.

MS m/z (ESI): 922.4 [M+1].

Example 182



Step 1: in a 100 mL reaction bottle, methyl 4-bromo-2,6-dimethylbenzoate (3 g, 12.34 mmol) and titanium(IV) isopropionate (5.26 g, 18.51mmol) were dissolved in tetrahydrofuran (30 mL), then at 80°C, ethylmagnesium bromide (37.02 mL, 37.02 mmol, 1 M) was added slowly, and the reaction solution was stirred at 80°C for 1 hour. The reaction was stopped and quenched by adding a saturated aqueous solution of ammonium chloride (30 mL), followed by extraction with ethyl acetate (30 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (30 mL), 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 (1.1 g, yellow solid), yield: 37.0%.

MS m/z (ESI): 241.0 [M+1].

Step 2: 1-(4-bromo-2,6-dimethylphenyl)cyclopropane-1-ol (1.1 g, 4.56 mmol) was dissolved in dichloromethane (10 mL), and then at 0°C, DAST (1.10 g, 6.84 mmol) was added. The reaction solution was stirred at 25°C for 2 hours. The reaction was stopped and quenched by adding an water (10 mL), followed by extraction with dichloromethane (10 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (10 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, 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 (800 mg, yellow solid), yield: 72.1%.

MS m/z (ESI): 243.0 [M+1].

Step 3: in a 50 mL reaction bottle, 5-bromo-2-(1-fluorocyclopropyl)-1,3-dimethylbenzene (800 mg, 3.29 mmol), cuprous iodide (125.34 mg, 658.11 μmol),

sodium phosphate (1.08 g, 16.58 mmol), and 85% hydrazine hydrate (1 mL) were dissolved in PEG-400 (10 mL), and the reaction solution was stirred at 120°C under nitrogen protection for 6 hours.

The reaction was stopped and quenched by adding a saturated aqueous solution of ammonium chloride (30 mL), followed by extraction with ethyl acetate (30 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (30 mL), 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 (400 mg, yellow solid), yield: 62.5%.

MS m/z (ESI): 195.1 [M+1].

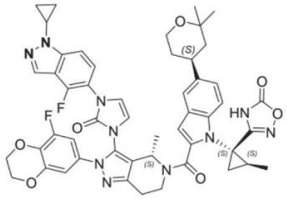
Step 4: (4-(1-fluorocyclopropyl)-3,5-dimethylphenyl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method for intermediate G.

MS m/z (ESI): 482.3 [M+1].

Step 5: tert-butyl (S)-2-(4-(1-fluorocyclopropyl)-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 was used as a raw material, and the target product was obtained following the synthesis method in Example 25.

MS m/z (ESI): 949.4 [M+1].

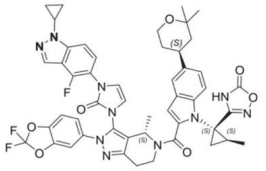
Example 183



(8-Fluoro-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)hydrazine was used as a starting raw material, and the target product was obtained following intermediate G and Example 136.

MS m/z (ESI): 939.4 $[M+H]^+$.

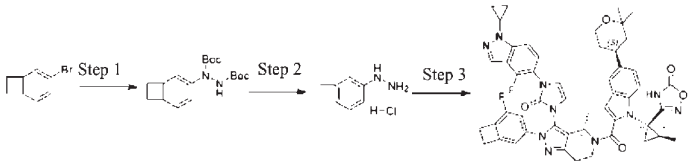
Example 184



(2,2-Difluorobenzo[d][1,3]dioxazole-5-yl)hydrazine was used as a starting raw material, following intermediate G and Example 136, to obtain 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-(2,2-difluorobenzo[d][1,3]dioxazol-5-yl)-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.

MS m/z (ESI): 943.3 $[M+H]^+$.

Example 185



Step 1: 3-bromobicyclo[4.2.0]oct-1(6), 2,4-triene (1 g, 5.46 mmol) was dissolved in tetrahydrofuran (20 mL), and under nitrogen protection and cooling with a dry ice-ethanol bath, n-butyllithium (2.5M, 2.40 mL) was added. The mixture was stirred for reaction at -78°C for 0.5 hours. Then, under cooling with a dry ice-ethanol bath, a solution of di-tert-butyl azodicarboxylate (1.26 g, 5.46 mmol) in tetrahydrofuran (4 mL) was added. The reaction solution was slowly heated to room temperature and stirred for 12 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, successively.

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The residue was purified by flash silica gel chromatography (eluting with petroleum ether : ethyl acetate = 100 : 0 to 80 : 20), to obtain the target product (1.5 g, 4.49 mmol, yield: 82.11%) as a pale brown solid.

1H NMR (400MHz, CDCl3) δ 7.24-7.14 (m, 1H), 7.14-7.02 (m, 1H), 7.02-6.93 (m, 1H), 6.81-6.59 (m, 1H), 3.13 (s, 4H), 1.49 (s, 18H).

MS m/z (ESI): 335.2 [M+H]

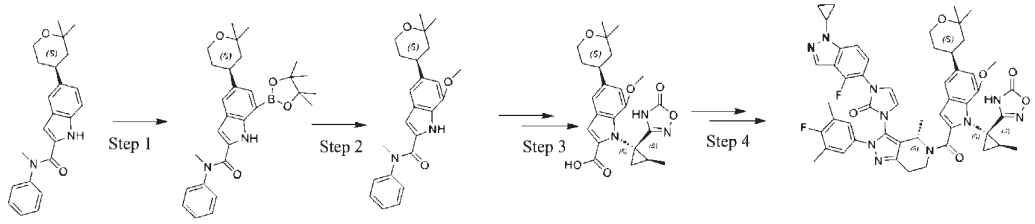
Step 2: di-tert-butyl 1-(bicyclo[4.2.0]oct-1(6), 2,4-trien-3-yl)hydrazine-1,2-dicarboxylate (1 g, 6 3 mmol) was dissolved in NMP (8 mL), methanesulfonic acid (0.65 g, 6.6 mmol) was added thereto, and the mixture was stirred at an external temperature of 80°C for 7 hours. The reaction solution was cooled to room temperature, then toluene (15 mL), potassium carbonate (0.46g) and water (6g) were added thereto, and the reaction solution was stirred at room temperature for 10 minutes. The aqueous layer was removed, and then the organic phase was used directly in the next step.

MS m/z (ESI): 135.1 [M+H]

Step 3: 5-bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was obtained following steps 1 and 2 in Example 515.

MS m/z (ESI): 907.4 [M+H]

Example 186



Step 1: in a 50 mL reaction bottle, 5-[(4S)-2,2-dimethyltetrahydro pyran-4-yl]-N-methyl-N-phenyl-1H-indole-2-carboxamide (1 g, 2.76mmol) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (1.05 g, 4.14mmol) were dissolved in THF(10 mL), and at 25°C, 4,4'-di-tert-butyl-2,2'-dipyridyl (74.05 mg, 275.89μmol) and Di-μ-methylcarbonyldi(1,5-cyclooctadiene)diiridium(I) (180.65 mg, 275.89μmol) were added; and the reaction solution was placed under nitrogen protection and stirred at 60°C for 1 hour. The reaction was stopped and quenched by adding an aqueous solution (10 mL), followed by extraction with dichloromethane (10 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (10 mL), 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 (900 mg, yellow solid), yield: 66.7%.

MS m/z (ESI): 489.3 [M+1].

Step 2: in a 50 mL reaction bottle, (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole-2-carboxamide (900 mg, 1.84mmol), DMAP(450.22 mg, 3.69mmol), and copper acetate (183.94 mg, 921.33μmol) were dissolved in MeOH (5 mL) and DCM (25 mL), 4A molecular sieves (5g) were added, and then the reaction solution was placed under nitrogen protection and stirred at 25°C for 1 hour. The reaction was stopped and quenched by adding an aqueous solution (10 mL), followed by extraction with dichloromethane (10 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (10 mL), 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 (500 mg, yellow solid), yield: 69.1%.

MS m/z (ESI): 393.2 [M+1].

Step 3: (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target product was obtained following the synthesis method in steps 5 to 8 of intermediate F.

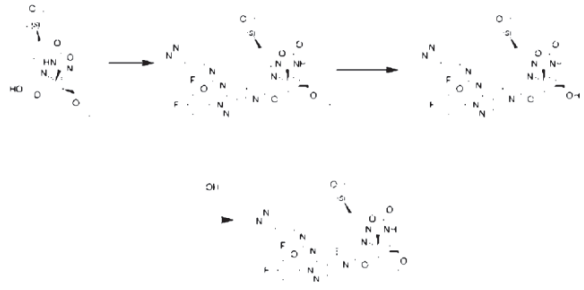
MS m/z (ESI): 442.2 [M+1].

Step 4: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-1-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid 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): 939.4 [M+1].

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Example 187



Step 1: following step 4 of Example 25, the target compound was obtained.

MS m/z (ESI): 1015.4 [M+1].

Step 2:

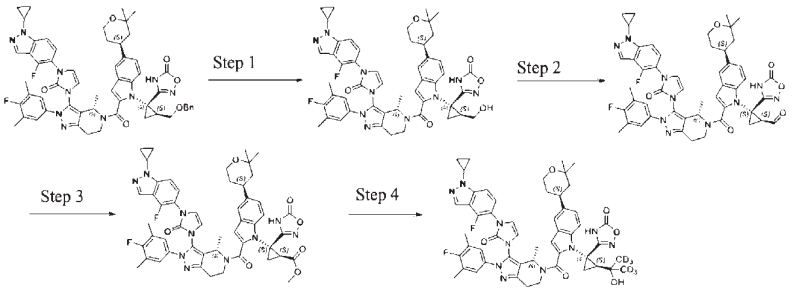
at room temperature, 3-((1S, 2S)-2-((benzyloxy)methyl)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one (0.51 g, 0.5 mmol) was dissolved in trifluoroacetic acid (20 mL) and heated to 80°C for reaction for 14 hours, followed by spin-drying; the residue was dissolved with ethyl acetate (30 mL), and then washed with saturated sodium bicarbonate solution (20 mL × 2) and saturated brine (20 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 (eluting with dichloromethane : methanol = 95 : 5), to obtain the target compound as a white solid (0.26 g, yield 55%).

MS m/z (ESI): 925.4 [M+H]+.

Step 3: used as a raw material, following the document [Chemical Communications, 2016, vol. 52, #8, p. 1665-1668], to obtain the target product

MS m/z (ESI): 1001.4 [M+1].

Example 188



Step 1: at room temperature, 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 (0.51 g, 0.5 mmol) was dissolved in trifluoroacetic acid (20 mL) and heated to 80°C for reaction for 14 hours, with LCMS indicating the completion of the reaction, followed by spin-drying; the residue was dissolved with ethyl acetate (30 mL), and then washed with saturated sodium bicarbonate solution (20 mL × 2) and saturated brine (20 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 (eluting with dichloromethane : methanol = 95 : 5), to obtain the target compound as a white solid (0.26 g, yield 55%).

MS m/z (ESI): 925.4 [M+H]+.

Step 2: at room temperature, 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 (0.26 g, 0.28 mmol) was dissolved in dichloromethane (10 mL),

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then a Dess-Martin reagent (0.24 g, 0.56mmol) was added, and the reaction solution was stirred at room temperature for 2 hours, with LCMS indicating the completion of the reaction; the reaction solution was diluted with dichloromethane (20 mL), and then washed with saturated sodium bicarbonate solution (20 mL × 2) and saturated brine (20 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 (0.25 g, crude)

MS m/z (ESI): 923.4 [M+H]+.

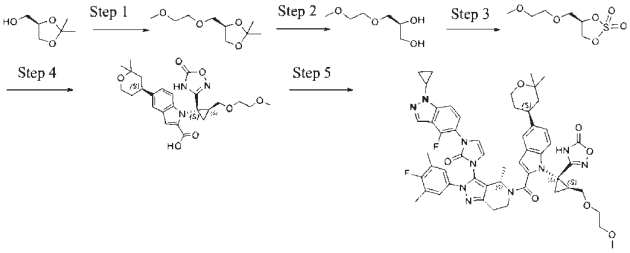
Step 3: at room temperature, (1S, 2S)-2-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indol-1-yl)-2-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carbaldehyde (0.25 g, 0.27 mmol) was dissolved in tertiary butanol (10 mL), and then 2-methylbuta-2-ene (0.38 g, 5.4 mmol), sodium dihydrogen phosphate (0.12 g, 1.03 mmol) and a solution of sodium chlorite (0.098 g, 1.08 mmol) in water (1 mL), successively; the reaction solution was stirred at room temperature for one hour, with LCMS indicating the completion of the reaction; the reaction solution was diluted with ethyl acetate (30 mL), and washed with saturated brine (20 mL × 2); and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried. The resulting crude carboxylate product was then dissolved in methanol (10 mL) and cooled to 0°C, and then a (trimethylsilyl)diazomethane solution (2.0M/diethyl ether, 0.34 mL, 0.68 mmol) was added dropwise; the reaction solution was stirred under an ice bath for half an hour, with LCMS indicating the completion of the reaction, followed by spin-drying; and the residue was separated by Flash column chromatography to obtain the target compound (0.19 g, yield 71%).

MS m/z (ESI): 953.4 [M+H]+.

Step 4: at -78°C, methyl (1S, 2S)-2-(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-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carboxylate (0.19 g, 0.2 mmol) was dissolved in tetrahydrofuran (5 mL), followed by nitrogen replacement; then (methyl-d3)magnesium bromide (1.0/tetrahydrofuran, 1 mL, 1 mmol) was added dropwise and reacted at -78°C for one hour, with LCMS indicating the completion of the reaction; the reaction solution was quenched with saturated ammonium chloride solution (10 mL), and then washed with saturated brine (20 mL × 3); 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 (0.086 g, yield 45%).

MS m/z (ESI): 959.2 [M+H]+.

Example 189



Step 1: at room temperature, (R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol (1.38 g, 10.44mmol), 1-bromo-2-methoxy-ethane (2.90 g, 20.88mmol) and tetrabutylammonium iodide (385.70 mg, 1.04 mmol) were dissolved in toluene (10 mL), then a solution of sodium hydroxide (4.18 g, 104.42 mmol) in water (10 mL) was added, and the reaction solution was heated to 80°C for reaction for 14 hours and cooled to room temperature, with TLC indicating the generation of new spots; the reaction solution was extracted with ethyl acetate (20 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was separated by Flash column chromatography (eluting with PE : EA = 10 : 1-2 : 1), to obtain the target product as a colorless oil (1.40 g, yield 70.5%).

MS m/z (ESI): 191.1 [M+H]+.

Step 2: at room temperature, (R)-4-((2-methoxyethoxy)methyl)-2,2-dimethyl-1,3-dioxolane (1.4 g, 7.36mmol) was dissolved in acetone (15 mL), then dilute hydrochloric acid (1.0M, 15 mmol, 15 mL) was added, and the reaction solution was stirred at room temperature for 2 hours, with TLC indicating the completion of the reaction; and acetone was removed by rotary evaporation, and the aqueous phase was lyophilized to obtain the target compound as a colorless oil (0.80 g, yield 72%).

MS m/z (ESI): 151.0 [M+H]+.

Step 3: (S)-3-(2-methoxyethoxy)propane-1,2-diol was used as a raw material, and the target product was obtained following steps 1 and 2 of Example 135.

MS m/z (ESI): 213.0 [M+H]+.

Step 4: (R)-4-((2-methoxyethoxy)methyl)-1,3,2-dioxathiolane 2,2-dioxide was used as a raw material, and the target product was obtained following steps 6, 7, 8 and 9 of intermediate F.

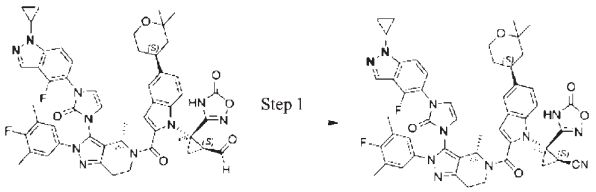
MS m/z (ESI): 486.2 [M+H]+.

Step 5: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2S)-2-((2-methoxyethoxy)methyl)-1-(5-carbonyl-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.

^{1}H NMR (400MHz, DMSO-d_6) δ 12.11 (s, 1H), 8.28 (s, 1H), 7.68-7.66 (m, 1H), 7.53-7.48 (m, 2H), 7.21-7.07 (m, 5H), 6.98-6.74 (m, 2H), [5.54-5.43(m) and 5.22-5.11(m), total 1H], [4.60-4.48(m) and 4.37-4.25(m), total 1H], 3.93-3.80 (m, 2H), 3.73-3.68 (m, 2H), 3.60-3.48 (m, 6H), 3.28 (s, 3H), 3.16-3.09 (m, 1H), 2.94-2.72 (m, 2H), 2.30-2.22 (m, 7H), 2.03-1.94 (m, 1H), 1.76-1.49 (m, 6H), 1.38-1.27 (m, 5H), 1.19-1.13 (m, 7H).

MS m/z (ESI): 983.2 [M+H]+.

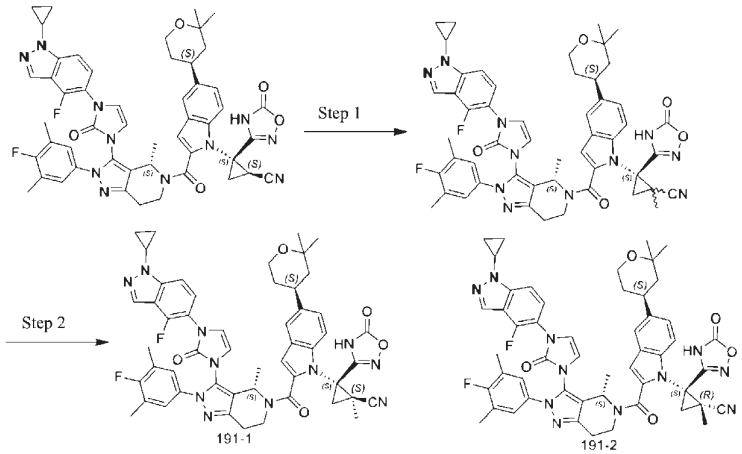
Example 190



Step 1: (1S, 2S)-2-(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-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carbaldehyde (0.1 g, 108.35 μmol) and hydroxylamine hydrochloride (9.79 mg, 140.85 μmol) were dissolved in acetonitrile (3 mL), and under nitrogen protection and ice-water bath cooling, iodosodium (16.24 mg, 108.35 μmol) was added. The mixture was stirred for reaction at 90°C for 1 hour. The reaction solution was evaporated to dryness and separated by preparative HPLC to obtain a product (23 mg, 25.00 μmol, yield: 23.08%).

MS m/z (ESI): 920.4 [M+H]

Example 191



Step 1: (0.1 g, 108.70 μmol) and iodomethane (20.06 mg, 141.31 μmol, 8.80 μL) were dissolved in acetonitrile (3 mL), and under nitrogen protection, potassium carbonate (45.07 mg, 326.10 μmol) was added.

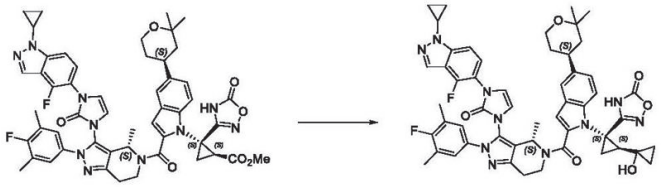
The mixture was stirred for reaction at 80°C for 3 hours. The reaction solution was evaporated to dryness, to obtain a product (15 mg, yield: 14.77%).

MS m/z (ESI): 934.4 [M+H]

Step 2: The product was chirally resolved to obtain 191-1 and 191-2.

MS m/z (ESI): 934.4 [M+H]

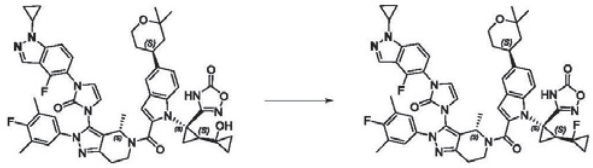
Example 192



Methyl (1S,2S)-2-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-oxo-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-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carboxylate (200 mg, 0.210mmol) and tetraisopropyl titanate (179 mg, 0.630 mmol) were dissolved in THF (10 mL). At 0°C, to the reaction solution, ethylmagnesium bromide (053 mL, 0.525 mmol, 1M in THF) was added and stirred for reaction. After 1 hour, the reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted twice with ethyl acetate; the organic phases were combined, 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 to obtain the target product (104 mg, yield: 52%).

MS m/z (ESI): 951.4 [M+1]

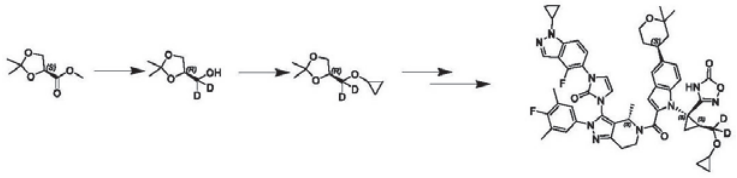
Example 193



3-((1S, 2S)-2-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-oxo-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)-1'-hydroxyl-[1,1'-bis(cyclopropan)]-2-yl)-1,2,4-oxadiazole-5(4H)-one (100 mg, 0.105 mmol) and BAST (1 mL) was dissolved in dichloromethane (5 mL). The mixture was stirred for reaction at 0°C for 1 hour. The reaction solution was quenched by adding a saturated sodium bicarbonate solution, and extracted twice with ethyl acetate; the organic phases were combined, 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 to obtain the target product (36 mg, yield: 36%).

MS m/z (ESI): 953.4 [M+1]

Example 194



Step 1: to a solution of methyl (*S*)-(-)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (5 g, 31.25 mmol) in methanol (50 mL) was added sodium borodeuteride (3.94 g, 93.75), and the system was allowed to react at room temperature for 12 hours, with TLC indicating the generation of new spots; the reaction solution was quenched by adding saturated ammonium chloride and extracted with ethyl acetate (50 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain the target product as a colorless oil (1.40 g, crude).

MS m/z (ESI): 135.1 [M+1].

Step 2: following step 1 of Example 189, the target product was obtained.

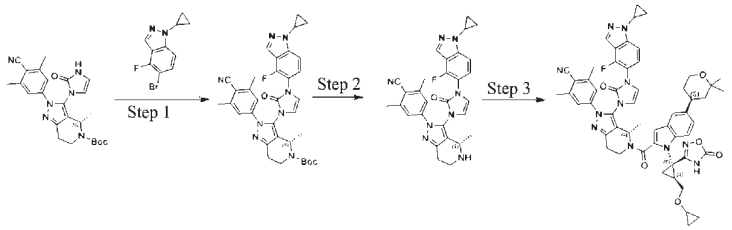
MS m/z (ESI): 175.1 [M+1].

Step 3: following Example 189, the target product was obtained.

^{1}H NMR (400MHz, DMSO) δ [12.25(s) and 11.82(s), total 1H], 8.26-8.16 (m, 1H), 7.81-7.60 (m, 1H), 7.60-7.33 (m, 3H), 7.28-7.09 (m, 4H), 6.95-6.92 (m, 1H), 6.75 (s, 1H), 5.75-5.58 (m, 1H), 5.2-4.65 (m, 1H), 4.42-4.39 (m, 1H), 3.88-3.83 (m, 1H), 3.72-3.48 (m, 3H), 3.17-2.65 (m, 4H), 2.40-2.26 (m, 6H), 2.07-1.77 (m, 2H), 1.76-1.42 (m, 6H), 1.35-1.10 (m, 11H), 0.49-0.31 (m, 4H).

MS m/z (ESI): 967.4 [M+1].

Example 195



Step 1: a mixture of intermediate G (1.5 g, 3.34 mmol), 5-bromo-1-cyclopropyl-4-fluoro-1H-indazole (1.28 g, 5.02 mmol), CuI (509.55 mg, 2.68 mmol), (1S, 2S)-N1,N1-dimethylcyclohexane-1,2-diamine (475.70 mg, 3.34 mmol), potassium carbonate (1.38 g, 10.03 mmol) and NMP (20 mL) was stirred for reaction at 130°C under nitrogen protection for 4 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 EtOAc; and the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and separated by column chromatography (DCM/MeOH = 10 : 1), to obtain the target product (2 g, yield 96%)

MS m/z (ESI): 623.3 [M+1].

Step 2: to a solution of (S)-4-(3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)-2,6-dimethylbenzonitrile (2 g, 3.21 mmol) in DCM (30 mL) was added dropwise HCl (4M, 15 mL), and the reaction solution was stirred at room temperature for 0.5 hours until LCMS showed that the reaction was completed, with MS of the target product being observed, followed by spin-drying, to obtain a pale yellow solid (1.6 g, crude)

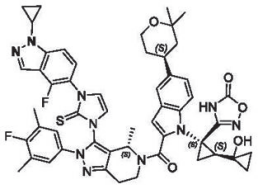
MS m/z (ESI): 523.2 [M+1].

Step 3: to a solution of (S)-4-(3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)-2,6-dimethylbenzonitrile (215.24 mg, 385.02 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 (150.00 mg, 320.85 μmol) in DMF (5 mL) were added HATU (242.09 mg, 641.69 μmol) and DIEA (165.86 mg, 1.28 mmol), and the reaction solution was stirred at room temperature for 12 hours; water was added, and the system was extracted three times with DCM; 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 (188 mg, yield: 60.2%)

MS m/z (ESI): 972.4 [M+1].

^{1}H NMR (400MHz, DMSO) δ [12.20(s) and 11.75(s), total 1H], 8.22-8.15 (m, 1H), 7.70-7.60 (m, 1H), 7.54-7.40 (m, 1H), 7.31-7.24 (m, 3H), 7.20-6.84 (m, 3H), 6.83-6.34 (m, 2H), 5.60-5.22 (m, 1H), 4.72 (d, *J* = 13.1 Hz, 1H), 3.83-3.56 (m, 4H), 2.98-2.92 (m, 1H), 2.67-2.60 (m, 2H), 2.39 (s, 3H), 2.03-1.81 (m, 3H), 1.69-1.29 (m, 6H), 1.26-1.02 (m, 16H), 0.84-0.74 (m, 1H), 0.33-0.25 (m, 4H).

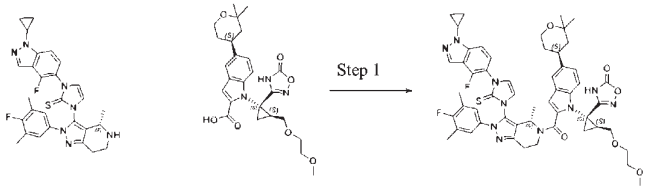
Example 196



Following the synthesis method in Example 192, the target product was obtained.

MS m/z (ESI): 967.4 [M+1]

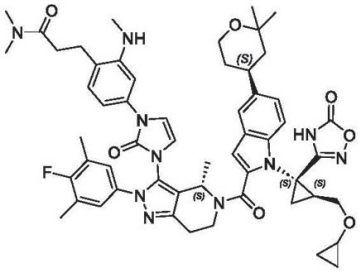
Example 197



Step 1: following step 4 of Example 25, the target compound was obtained.

MS m/z (ESI): 999.4 [M+H]+.

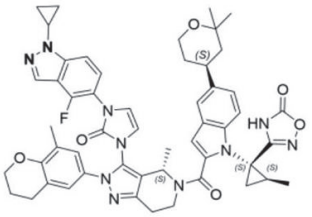
Example 198



Following Examples 25, 63 and 135, the title product was obtained.

MS m/z (ESI): 995.5 [M+H]+.

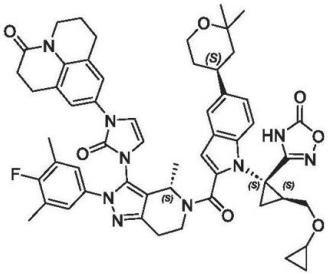
Example 199



(8-Methylchroman-6-yl)hydrazine was used as a starting raw material, and the target product was obtained following intermediate G and Example 136.

MS m/z (ESI): 933.4 $[M+H]^+$.

Example 200



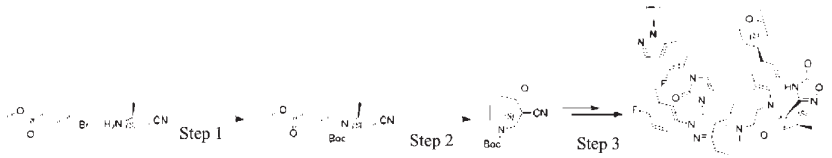
Following Examples 25, 63 and 135, the title product was obtained.

^{1}H NMR (400MHz, DMSO-d_6) δ [12.27(s) and 11.83(s), total 1H], 7.77-7.32 (m, 3H), 7.28-7.20 (m, 2H),

7.17-7.05 (m, 3H), 6.96-6.89 (m, 1H), 6.76-6.70 (m, 1H), [5.72-5.57(m) and 5.24-5.14(m), total 1H], [4.79-4.63(m) and 4.46-4.38(m), total 1H], 3.97-3.59 (m, 5H), 3.47-3.37 (m, 1H), 3.26-3.00 (m, 3H), 2.90-2.65 (m, 5H), 2.62-2.53 (m, 2H), 2.43-2.29 (m, 1H), 2.22 (s, 6H), 2.08-1.93 (m, 1H), 1.90-1.75 (m, 3H), 1.73-1.50 (m, 5H), 1.42-1.38 (m, 1H), 1.27-1.18 (m, 8H), 0.48-0.21 (m, 4H).

MS m/z (ESI): 976.4 [M+H]+.

Example 201



Step 1: in a 50 mL reaction bottle, ethyl 4-bromobutyrate (1 g, 5.13 mmol) and (S)-3-aminobutyronitrile (431.27 mg, 5.13 mmol) were dissolved in THF (10 mL), and at 25°C, triethylamine (5.19 g, 51.27 mmol) was added, and then the reaction solution was placed under nitrogen protection and stirred at 60°C for 10 hours. The reaction solution was cooled to room temperature, and Di-tert-butyl dicarbonate (1 g, 5.13 mmol) was added and further stirred for 2 h. The reaction was stopped and quenched by adding an aqueous solution (10 mL), followed by extraction with dichloromethane (10 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (10 mL), 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 (500 mg, yellow liquid), yield: 32.6%.

MS m/z (ESI): 299.2 [M+1].

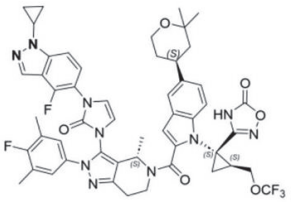
Step 2: in a 50 mL reaction bottle, ethyl (S)-4-((1-cyanopropan-2-yl)amino)butyrate (500 mg, 1.68 mmol) and potassium tert-butoxide (188.04 mg, 1.68 mmol) were dissolved in tetrahydrofuran (5 mL), and then the reaction solution was placed under nitrogen protection and stirred at 25°C for 2 hours. Then, to the reaction solution was added 2N hydrochloric acid (1 mL, 2.0 mmol). The reaction was stopped and quenched by adding an aqueous solution (10 mL), followed by extraction with ethyl acetate (10 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (10 mL), 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 (300 mg, yellow solid), yield: 70.9%.

MS m/z (ESI): 253.2 [M+1].

Step 3: tert-butyl (2S)-3-cyano-2-methyl-4-carbonylazepane-1-carboxylate was used as a raw material, and the target product was obtained following the synthesis method of intermediate G and Example 25.

MS m/z (ESI): 923.4 [M+1].

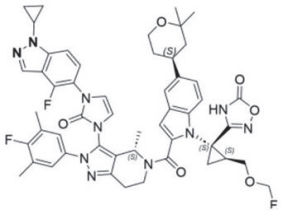
Example 202



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 was used as a raw material, following the document [Journal of Organic Chemistry, 1964, 29, 11-15], to obtain the target product.

MS m/z (ESI): 993.4 [M+1].

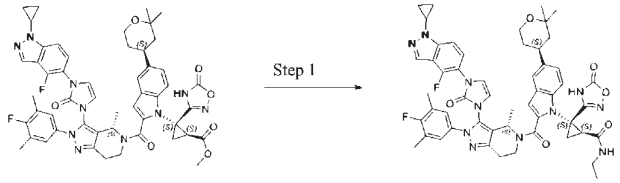
Example 203



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 was used as a raw material, following the document [Journal of Organic Chemistry, 2017, 82, 16, 8604-8610], to obtain the target product.

MS m/z (ESI): 957.4 [M+1].

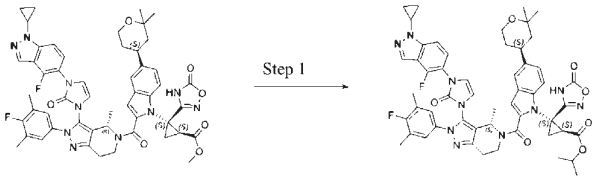
Example 204



At room temperature, methyl (1S,2S)-2-(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-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carboxylate (0.095 g, 0.1 mmol) was dissolved in tetrahydrofuran (10 mL), then ethylamine hydrochloride (0.016 g, 0.2 mmol) and triethylamine (0.03 g, 0.3 mmol) were added, and the reaction solution was stirred at room temperature overnight, with LCMS indicating the completion of the reaction; the reaction solution was diluted with ethyl acetate (30 mL), and then washed with saturated sodium bicarbonate solution (20 mL × 2) and saturated brine (20 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography to obtain the target compound (0.029 g, yield 30%).

MS m/z (ESI): 966.4 [M+H]+.

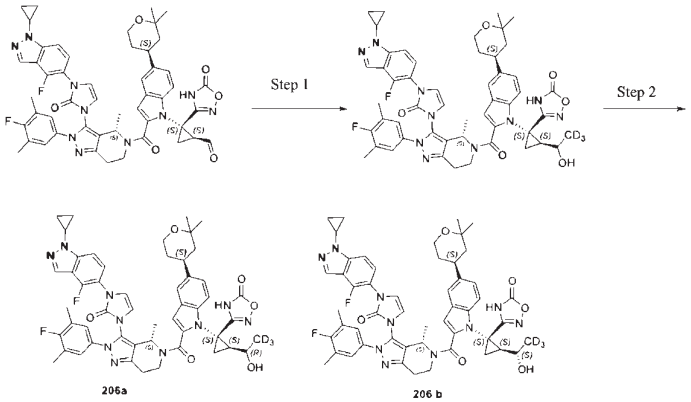
Example 205



At room temperature, methyl (1S,2S)-2-(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-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carboxylate (0.095 g, 0.1mmol) was dissolved in isopropanol (10 mL), then concentrated hydrochloric acid (0.015 g, 0.15 mmol) was added dropwise, followed by nitrogen replacement, and the reaction solution was heated for refluxing for 14 hours, with LCMS indicating the completion of the reaction; the reaction solution was cooled to room temperature, isopropanol was removed by means of spin-drying, and the residue was dissolved with ethyl acetate (10 mL) and then washed with saturated sodium bicarbonate solution (20 mL × 2) and saturated brine (20 mL × 2), successively; and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography to obtain the target compound (0.02 g, yield 20%).

MS m/z (ESI): 981.4 [M+H]+.

Example 206



Step 1: at -78°C, (1S, 2S)-2-(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-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropane-1-carbaldehyde (0.092 g, 0.1 mmol) was dissolved in tetrahydrofuran (10 mL), followed by nitrogen replacement, then (methyl-d3)magnesium bromide (1.0M, 0.3 mmol, 0.3 mL) was added dropwise, and the reaction solution was stirred at -78°C for 2 hours, with LCMS indicating the completion of the reaction; the reaction solution was quenched with saturated ammonium chloride solution (50 mL) and then extracted with ethyl acetate (20 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried, and the residue was purified by reverse phase preparative chromatography to obtain the target compound (0.047 g, yield 50%).

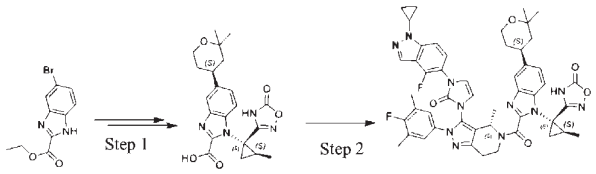
MS m/z (ESI): 942.4 [M+H]+.

Step 2:

compound 206 was resolved to obtain compound 206a and compound 206b.

MS m/z (ESI): 942.4 [M+H]+.

Example 207



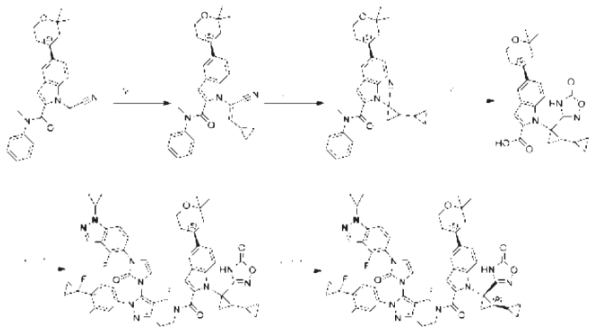
Step 1: ethyl 5-bromo-1H-benzo[d]imidazole-2-carboxylate was used as a raw material, and the target product was obtained following the synthesis method for intermediate F.

MS m/z (ESI): 413.2 [M+1].

Step 2: (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 and 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-benzo[d]imidazole-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): 910.4 [M+1].

Example 208



Step 1: to a reaction bottle were added (S)-1-(cyanomethyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (300 mg, 0.75), cyclopropane carboxaldehyde (262 mg, 3.74 mmol) and potassium hydroxide (3.0 eq., 126 mg, 2.24 mmol), tetrahydrofuran (6 mL) was added, and the reaction solution was stirred at room temperature for reaction for 2 h; the system was quenched by adding an appropriate amount of ammonium chloride (10 mL), and extracted with ethyl acetate (15 mL); and the organic phases were combined, dried and then concentrated to dryness to obtain a pale yellow solid crude product (320mg), which was directly used in the next-step reaction.

MS m/z (ESI): 454.2 [M+H]

Step 2: to a reaction bottle were added potassium tert-butoxide (1.1 eq., 6.2 mg) and trimethylsulfoxonium iodide (1.1 eq., 12.1 mg), dimethyl sulfoxide (0.2 mL) was added, and the reaction solution was heated to 50°C for reaction for 1 h; a solution of (S, E)-1-(1-cyano-2-cyclopropylethenyl)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.05 mmol, 1.0 eq., 23 mg) in dimethyl sulfoxide (0.2 mL) was added, and the system was further held at 50°C for reaction for 3 h; the reaction solution was cooled, and saturated brine (15 mL) was added, followed by extraction with ethyl acetate (10 mL), saturated brine (15 mL × 3), and separated by preparative TLC to obtain the target product (7 mg, yield: 29.5%).

MS m/z (ESI): 468.3 [M+H]

Step 3: following steps 7 and 8 of intermediate F, the target product was synthesized.

MS m/z (ESI): 438.2 [M+H]

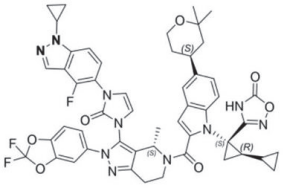
Step 4: following Example 182, the target product was synthesized.

MS m/z (ESI): 961.4 [M+H]

Step 5: the product was chirally resolved to obtain the target product.

MS m/z (ESI): 961.4 [M+H]

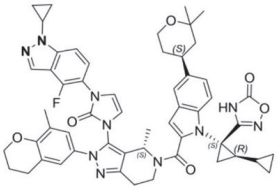
Example 209



5-Bromo-2,2-difluorobenzo[d][1,3]dioxazole was used as a raw material, and the target product was synthesized following Example 208.

MS m/z (ESI): 969.4 [M+H]

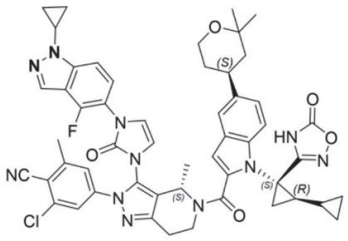
Example 210



6-Bromo-8-methylchromane was used as a raw material, and the target product was synthesized following Example 208.

MS m/z (ESI): 959.4 [M+H]

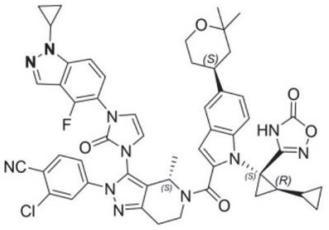
Example 211



4-Bromo-2-chloro-6-methylbenzonitrile was used as a raw material, and the target product was synthesized following Example 208.

MS m/z (ESI): 962.4 [M+H]

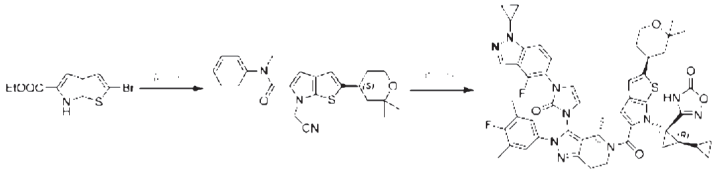
Example 212



4-Bromo-2-chlorobenzonitrile was used as a raw material, and the target product was synthesized following Example 208.

MS m/z (ESI): 948.3 [M+H]

Example 213



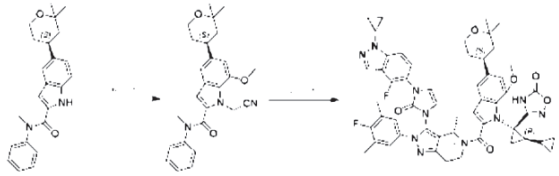
Step 1: ethyl 2-bromo-6H-thieno[2,3-b]pyrrole-5-carboxylate was used as a raw material, and the target product was obtained following intermediate F.

MS m/z (ESI): 408.2 [M+1].

Step 2: following Example 208, the target product was synthesized.

MS m/z (ESI): 941.4 [M+H]

Example 214



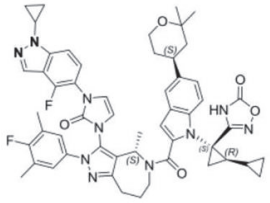
Step 1: (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target product was synthesized following Example 186.

MS m/z (ESI): 432.2 [M+1].

Step 2: following Example 208, the target product was synthesized.

MS m/z (ESI): 965.4 [M+H]

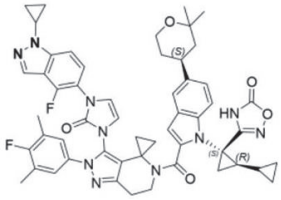
Example 215



used as a raw material, and the target product was synthesized following Examples 201 and 208.

MS m/z (ESI): 949.4 [M+H]

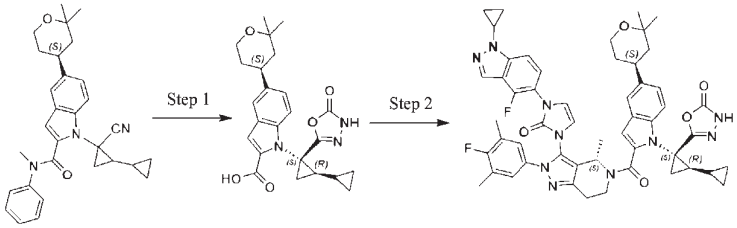
Example 216



used as a raw material, and the target product was synthesized following Examples 51 and 208.

MS m/z (ESI): 947.4 [M+H]

Example 217



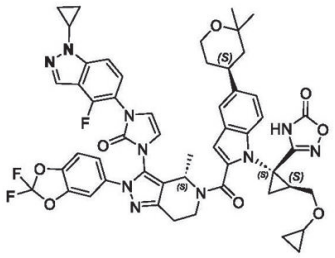
Step 1: 1-(2-cyano-[1,1'-bi(cyclopropan)]-2-yl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target product was synthesized following steps 1 to 4 of Example 237.

MS m/z (ESI): 438.2 [M+1].

Step 2: (4-fluoro-3,5-dimethylphenyl)hydrazine hydrochloride was used as a raw material, and the target product was synthesized following intermediate G and Example 208.

MS m/z (ESI): 935.4 [M+H]

Example 218

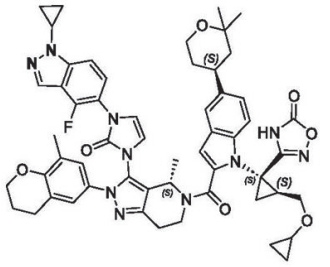


Following Example 184, the title product was obtained.

MS m/z (ESI): 999.4 [M+1].

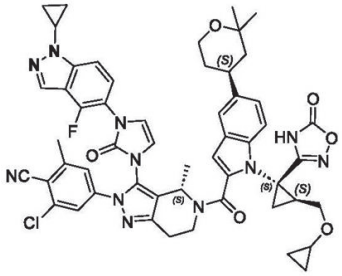
Example 219

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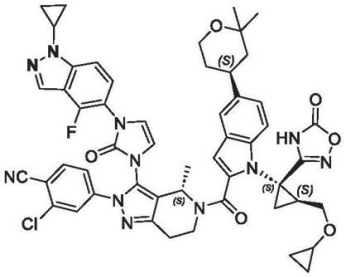
Following Example 199, the title product was obtained.
MS m/z (ESI): 989.4 [M+1].

Example 220



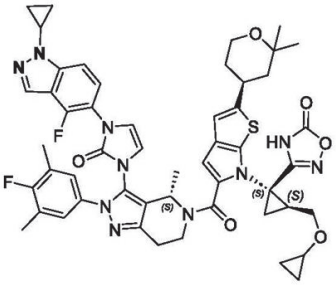
Following Example 484, the title product was obtained.
MS m/z (ESI): 992.4 [M+1].

Example 221



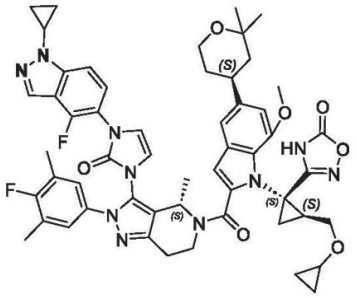
Following Example 485, the title product was obtained.
MS m/z (ESI): 978.4 [M+1].

Example 222



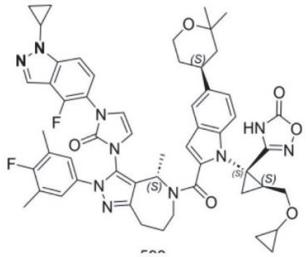
Following Example 213, the title product was obtained.
MS m/z (ESI): 971.4 [M+1].

Example 223



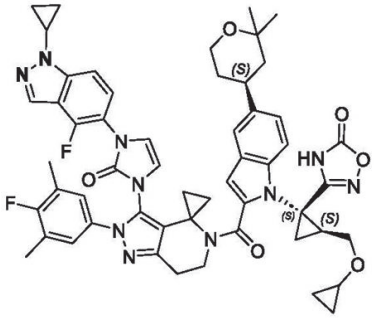
Following Example 186, the title product was obtained.
MS m/z (ESI): 995.4 [M+1].

Example 224



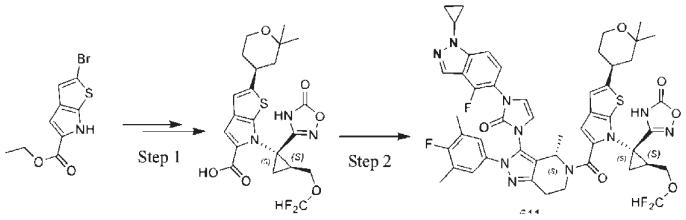
Following Example 215, the title product was obtained.
MS m/z (ESI): 979.4 [M+1].

Example 225



Following the synthesis in Example 51, the target compound was obtained.
MS m/z (ESI): 977.4 [M+1].

Example 226



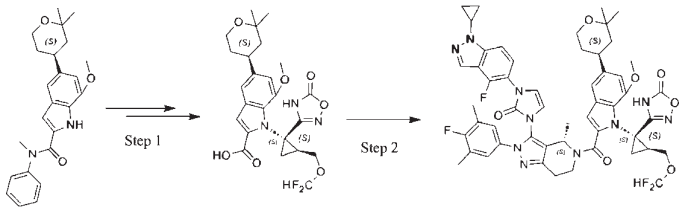
Step 1: ethyl 2-bromo-6H-thieno[2,3-b]pyrrole-5-carboxylate was used as a raw material, and the target product was obtained following the synthesis method for intermediate F (with (R)-4-methyl-1,3,2-dioxathiane 2,2-dioxide being replaced with (R)-4-((difluoromethoxy)methyl)-1,3,2-dioxathiolane 2,2-dioxide).

MS m/z (ESI): 484.1 [M+1].

Step 2: (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 and 6-((1S, 2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-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): 981.3 [M+1].

Example 227



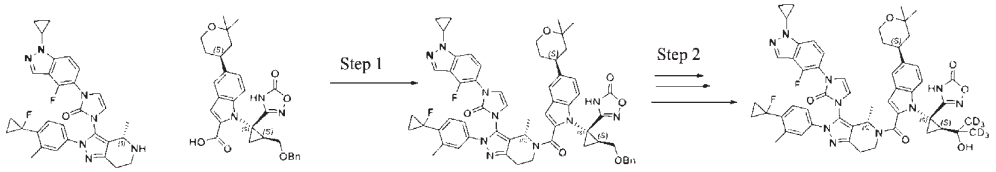
Step 1: (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target product was obtained following the synthesis method for intermediate F (with (R)-4-methyl-1,3,2-dioxathiane 2,2-dioxide being replaced with (R)-4-((difluoromethoxy)methyl)-1,3,2-dioxathiolane 2,2-dioxide).

MS m/z (ESI): 508.1 [M+1].

Step 2: (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 and 1-((1S, 2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-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): 1005.4 [M+1].

Example 228



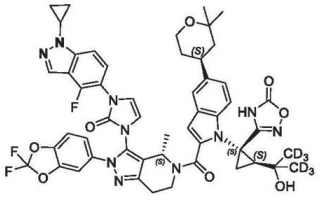
Step 1: (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one and 1-((1S, 2S)-2-((benzyloxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid were used as raw materials, and the target compound was obtained following step 4 of Example 25.

MS m/z (ESI): 1041.2 [M+H]+.

Step 2: 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-(1-fluorocyclopropyl)-3-methylphenyl)-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 was used as a raw material, and the target compound was obtained following steps 1, 2, 3 and 4 of Example 188.

MS m/z (ESI): 985.5 [M+H]+.

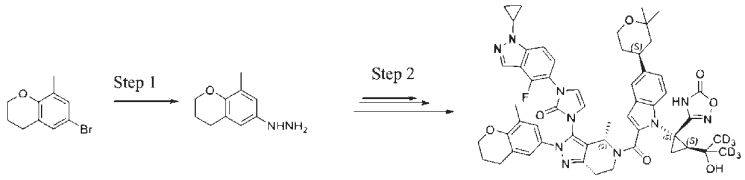
Example 229



(2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine was used as a raw material, and the target compound was obtained following intermediate G and Example 228.

MS m/z (ESI): 993.4 [M+H]+.

Example 230



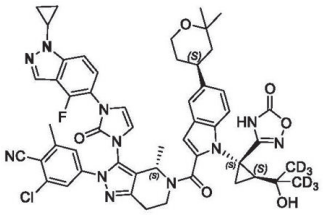
Step 1: 6-bromo-8-methylchromane was used as a raw material, and the target compound was obtained following step 3 of Example 182.

MS m/z (ESI): 179.1 [M+H]+.

Step 2: (8-methylchroman-6-yl)hydrazine was used as a raw material, and the target compound was obtained following intermediate G and Example 228.

MS m/z (ESI): 983.5 [M+H]+.

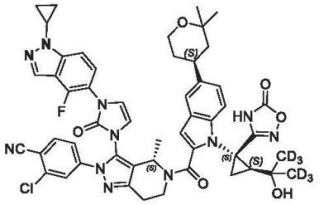
Example 231



4-bromo-2-chloro-6-methylbenzonitrile was used as a raw material, and the target compound was obtained following steps 3 to 5 of Example 182, and Example 228.

MS m/z (ESI): 986.4 [M+H]+.

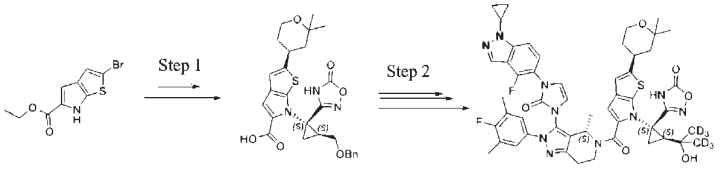
Example 232



4-Bromo-2-chlorobenzonitrile was used as a raw material, and the target compound was obtained following steps 3 to 5 of Example 182, and Example 228.

MS m/z (ESI): 972.4 [M+H]+.

Example 233



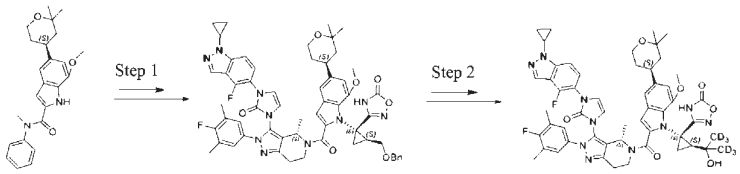
Step 1: ethyl 2-bromo-6H-thieno[2,3-b]pyrrole-5-carboxylate was used as a raw material, and the target compound was obtained following the synthesis steps 1 and 2 of Example 135, and intermediate F.

MS m/z (ESI): 524.2 [M+H]+.

Step 2: 6-((1S, 2S)-2-((benzyloxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid was used as a raw material, and the target compound was obtained following Example 228.

MS m/z (ESI): 965.2 [M+H]+.

Example 234



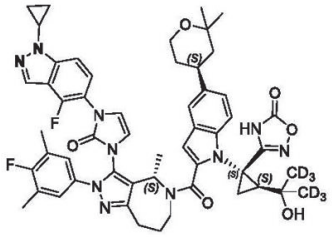
Step 1: (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target compound was obtained following the synthesis in steps 1 and 2 of Example 135, and intermediate F.

MS m/z (ESI): 1045.2 [M+H]+.

Step 2: 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)-7-methoxy-1H-indol-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)-one was used as a raw material, and the target compound was obtained following Example 228.

MS m/z (ESI): 989.4 [M+H]+.

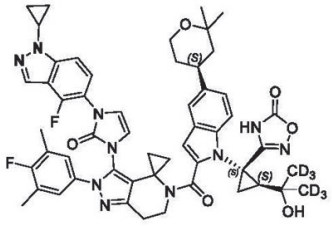
Example 235



the target product was obtained following Example 201 and Example 228.

MS m/z (ESI): 973.4 [M+H]+.

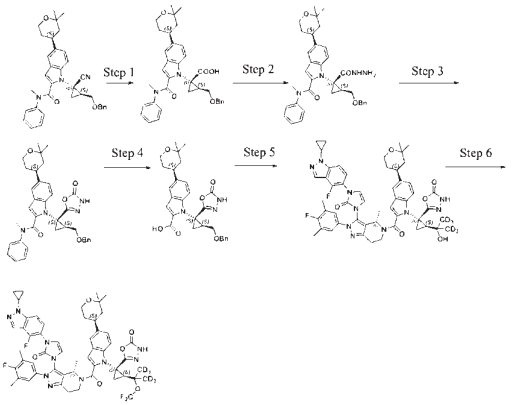
Example 236



the target product was obtained following Example 51 and Example 228.

MS m/z (ESI): 971.4 [M+H]+.

Example 237



Step 1: 1-((1S, 2S)-2-((benzyloxy)methyl)-1-cyanocyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.30 g, 0.55 mmol) was dissolved in a mixed solvent of concentrated sulfuric acid (2 mL) and HCl (2M in EtOH, 6 mL), and the reaction solution was heated to 80°C for reaction under stirring. After 18 hours, heating was stopped, and the reaction solution was cooled to room temperature, with LCMS indicating the completion of the reaction; the reaction solution was slowly added dropwise to ice water (20 mL) for quenching, and then extracted with ethyl acetate (20 mL × 3); and the organic phases were combined, washed with water (20 mL × 1) once and saturated sodium bicarbonate solution (20 mL × 1) once, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated under reduced pressure to obtain a colorless oily crude product. The crude product was purified by silica gel column chromatography (eluent: ethyl acetate : petroleum ether = 50%, v/v) to obtain a mixture of amide and ester (0.15g).

The mixture of ester and amide (0.15g) was dissolved in a mixed solvent of ethanol (3 mL) and water (3 mL), then lithium hydroxide (0.10 g, 4.2 mmol) was added, and the reaction solution was heated to 85°C for reaction under stirring. After 32 hours, heating was stopped, and the reaction solution was cooled to room temperature, with LCMS indicating the completion of the reaction; the reaction solution was adjusted to pH = 1 by adding dilute hydrochloric acid (1M) and extracted with ethyl acetate (20 mL × 3); and the organic phases were combined, washed with water (20 mL × 1) once, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated under reduced pressure to obtain a colorless oily crude product (130 mg), which was used directly in the next-step reaction without purification.

MS m/z (ESI): 567.2 [M+H]+.

Step 2: (1S, 2S)-2-((benzyloxy)methyl)-1-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-(methyl(phenyl)carbamoyl)-1H-indol-1-yl)cyclopropane-1-carboxylic acid

(0.13 g, 0.23mmol) was dissolved in a mixed solvent of dichloromethane (3 mL) and N,N-dimethylformamide (0.1 mL), chloride (0.058 g, 0.46 mmol) was added, and the reaction solution was stirred for reaction at room temperature for one hour. When LCMS detected that the reaction was completed, the system was spin-dried to obtain a yellow oily crude product (0.13 g), which was used directly in the next-step reaction without purification. The resulting acyl chloride crude product above (0.13 mg, 0.22 mmol) and triethylamine (0.067 g, 0.66 mmol) were dissolved in a mixed solvent of water and 50% hydrazine (1 mL) and tetrahydrofuran (2 mL), and the reaction solution was stirred at room temperature for reaction for one hour. After the reaction was completed as detected by LCMS, the reaction was quenched with saturated ammonium chloride solution (5 mL), and the resulting solution was extracted with dichloromethane (20 mL × 3); and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a yellow oily crude product. The crude product was purified by preparative TLC (developing solvent: methanol : dichloromethane = 10%, v/v) to obtain the target product (0.13 g, yield 97%).

MS m/z (ESI): 581.3 [M+H]+.

Step 3: 1-((1S, 2S)-2-((benzyloxy)methyl)-1-(hydrazinecarbonyl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (0.13 g, 0.22 mmol), N,N'dicarbonylimidazole (0.07 g, 0.44 mmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.17 g, 1.1 mmol) were dissolved in tetrahydrofuran (3 mL), followed by nitrogen replacement to protect the reaction, and the reaction solution was heated to 55°C for reaction under stirring for 2 hours. After LCMS indicated the completion of the reaction, the reaction solution was spin-dried, and the residue was dissolved with ethyl acetate (20 mL), and then washed with saturated brine (20 mL × 3); and the organic phase was dried over anhydrous sodium sulfate, filtered, and spin-dried to obtain a crude product, which was purified by preparative TLC (developing solvent: methanol : ethyl acetate = 10%, v/v), to obtain the target product (0.093 g, yield 70%).

MS m/z (ESI): 607.3 [M+H]+.

Step 4: following step 8 of intermediate F, the target compound was obtained.

MS m/z (ESI): 518.3 [M+H]+.

Step 5:

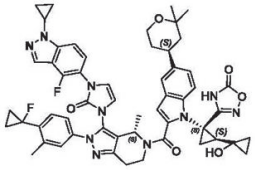
1-((1S, 2S)-2-((benzyloxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid was used as a raw material, and the target compound was obtained following steps 1, 2, 3 and 4 of Example 188.

MS m/z (ESI): 959.4 [M+H]+.

Step 6: 5-((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-(2-hydroxyl propane-2-yl-1,1,1,3,3,3-d6)cyclopropyl)-1,3,4-oxadiazole-2(3H)-one was used as a raw material, and the target compound was obtained following step 1 of Example 141.

MS m/z (ESI): 1008.4 [M+H]+.

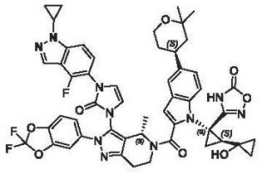
Example 238



Following the synthesis method in Example 192, the target product was obtained.

MS m/z (ESI): 977.4 [M+1]

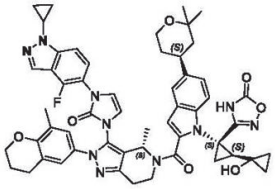
Example 239



Following the synthesis method in Example 192, the target product was obtained.

MS m/z (ESI): 985.4 [M+1]

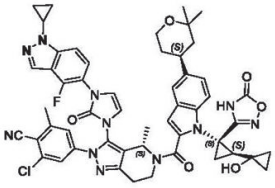
Example 240



Following the synthesis method in Example 192, the target product was obtained.

MS m/z (ESI): 975.4 [M+1]

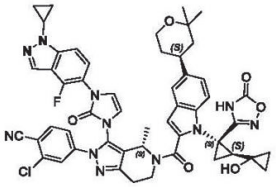
Example 241



Following the synthesis method in Example 192, the target product was obtained.

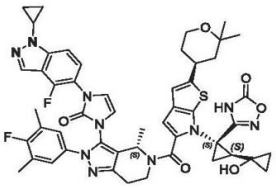
MS m/z (ESI): 978.4 [M+1]

Example 242



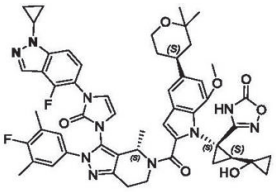
Following the synthesis method in Example 192, the target product was obtained.
MS m/z (ESI): 964.3 [M+1]

Example 243



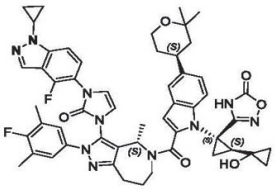
Following the synthesis method in Example 192, the target product was obtained.
MS m/z (ESI): 957.4 [M+1]

Example 244



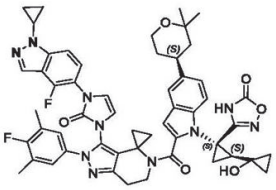
Following the synthesis method in Example 192, the target product was obtained.
MS m/z (ESI): 981.4 [M+1]

Example 245



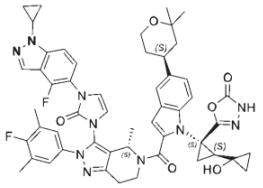
Following the synthesis method in Example 192, the target product was obtained.
MS m/z (ESI): 965.4 [M+1]

Example 246



Following the synthesis method in Example 192, the target product was obtained.
MS m/z (ESI): 963.4 [M+1]

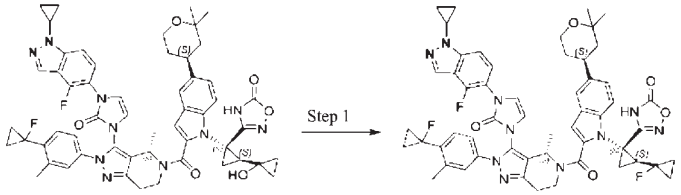
Example 247



Following the synthesis method in Example 192, the target product was obtained.

MS m/z (ESI): 951.4 [M+1]

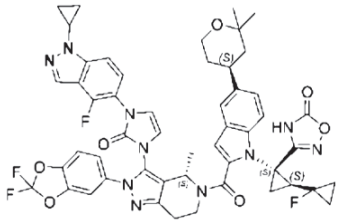
Example 248



Step 1: 3-((1S, 2S)-2-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-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)-1'-hydroxyl-[1,1'-bi(cyclopropan)]-2-yl)-1,2,4-oxadiazole-5(4H)-one (0.44 g, 0.456 mmol) was dissolved in dichloromethane (10 mL), and then DAST was added dropwise at 0°C (0.11 g, 0.684 mmol). The reaction solution was stirred at 25°C for 2 hours. The reaction was stopped and quenched by adding an water (10 mL), followed by extraction with dichloromethane (10 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (10 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, 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 (0.21 g), yield: 47.6%.

MS m/z (ESI): 979.4 [M+1].

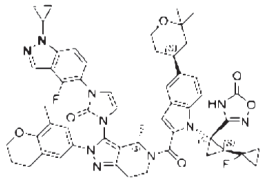
Example 249



The final product of Example 239 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 987.4 [M+H]

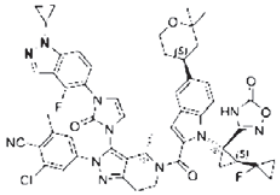
Example 250



The final product of Example 240 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 977.4 [M+H]

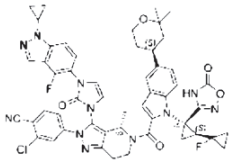
Example 251



The final product of Example 241 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 980.4 [M+H]

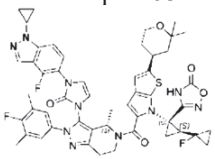
Example 252



The final product of Example 242 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 966.3 [M+H]

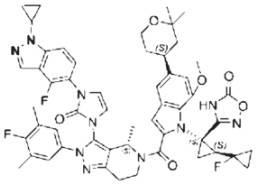
Example 253



The final product of Example 243 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 959.4 [M+H]

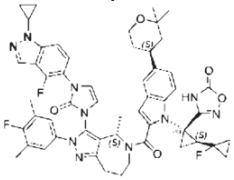
Example 254



The final product of Example 244 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 983.4 [M+H]

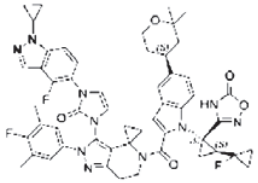
Example 255



The final product of Example 245 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 967.4 [M+H]

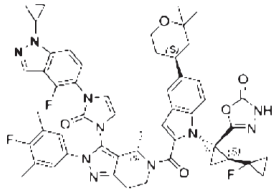
Example 256



The final product of Example 246 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 965.4 [M+H]

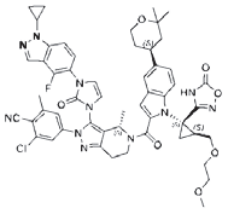
Example 257



The final product of Example 247 was used as a raw material, and the target product was synthesized following Example 248.

MS m/z (ESI): 953.4 [M+H]

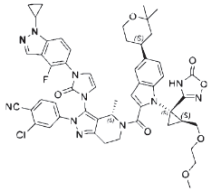
Example 258



4-Bromo-2-chloro-6-methylbenzonitrile was used as a raw material, and the target compound was obtained following steps 3 to 5 of Example 182, and Example 189.

MS m/z (ESI): 1010.3 [M+H]+.

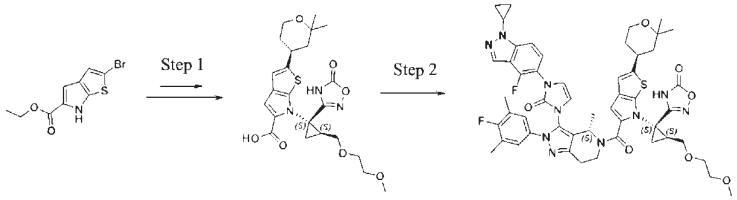
Example 259



4-Bromo-2-chlorobenzonitrile was used as a raw material, and the target compound was obtained following steps 3 to 5 of Example 182, and Example 189.

MS m/z (ESI): 996.3 [M+H]+.

Example 260



Step 1: ethyl 2-bromo-6H-thieno[2,3-b]pyrrole-5-carboxylate was used as a raw material, and the target compound was obtained following the synthesis steps 1, 2 and 3 of Example 189, and intermediate F.

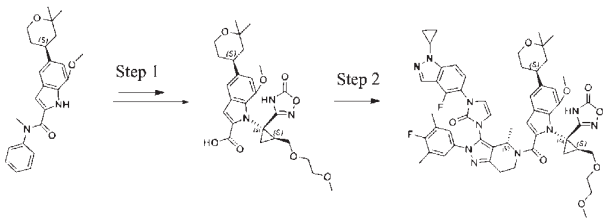
MS m/z (ESI): 492.2 [M+H]+.

Step 2: (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 and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2S)-2-((2-methoxyethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid were used as raw materials, and the target compound was obtained following step 4 of Example 25.

MS m/z (ESI): 989.3 [M+H]+.

Example 261

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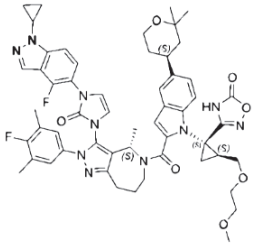
Step 1: (S)-5-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target compound was obtained following the synthesis in steps 1, 2 and 3 of Example 189, and intermediate F.

MS m/z (ESI): 516.2 [M+H]+.

Step 2: (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 and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-1-((1S, 2S)-2-((2-methoxyethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid were used as raw materials, and the target compound was obtained following Example 25.

MS m/z (ESI): 1013.4 [M+H]+.

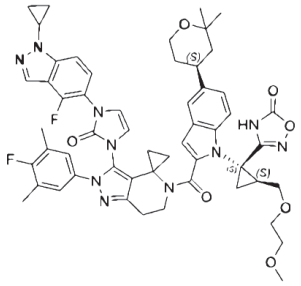
Example 262



the target product was obtained following Example 201 and Example 189.

MS m/z (ESI): 997.4 [M+H]+.

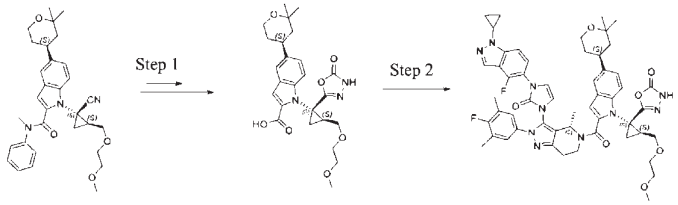
Example 263



the target product was obtained following Example 51 and Example 189.

MS m/z (ESI): 995.4 [M+H]+.

Example 264



Step 1: 1-((1S, 2S)-1-cyano-2-((2-methoxyethoxy)methyl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-1H-indole-2-carboxamide was used as a raw material, and the target compound was obtained following steps 1, 2, 3, and 4 of Example 237.

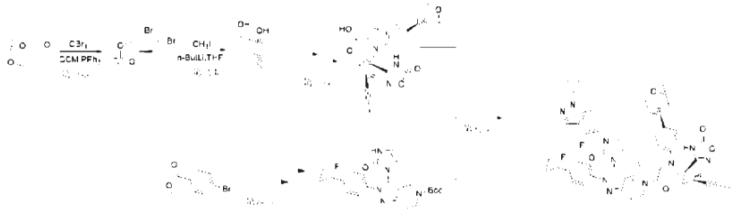
MS m/z (ESI): 486.2 [M+H]+.

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Step 2: (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 and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2S)-2-((2-methoxyethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)cyclopropyl)-1H-indole-2-carboxylic acid were used as raw materials, and the target compound was obtained following step 4 of Example 25.

MS m/z (ESI): 983.4 [M+H]+

Example 265



Step 1: at room temperature, triphenylphosphine (48.6 g, 185 mmol) was dissolved in dichloromethane (150 mL), and at 0°C, carbon tetrabromide (30.6 g, 92.3 mmol) was added, and the system was allowed to react at room temperature for 30 minutes. At 0°C, a solution of (S)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (6 g, 46.1 mmol) in dichloromethane (10 mL) was added, and the system was allowed to react at room temperature for 3 h. At 0°C, 250 mL of n-hexane was added and stirred for 1 h. The resulting solution was filtered and spin-dried, and the residue was separated by Flash column chromatography to obtain the target product (12 g, yield 91%).

MS m/z (ESI): 286.9, 284.9 [M+H]+.

Step 2: at -78°C, n-butyllithium (2.5M, 12.4 mL, 31.0 mmol) was added to a solution of (R)-4-(2,2-dibromoethenyl)-2,2-dimethyl-1,3-dioxolane (4.0 g, 13.99 mmol) in THF (700 mL), and the reaction solution was stirred at -78°C for 1 h and heated slowly to room temperature; and at room temperature, iodomethane (1.31 mL, 21.04 mmol) was added, and stirred at room temperature for 4 h. 30 mL of water was added, the reaction solution was extracted with ethyl acetate (50 mL × 3), and the organic phases were combined, dried over anhydrous sodium sulfate, filtered, and spin-dried. 30 mL of methanol and p-toluenesulfonic acid (133 mg, 0.7 mmol) were added, the reaction solution was stirred at room temperature for 18 h and spin-dried, and the residue was separated by Flash column chromatography to obtain the target product (700 mg, yield 50%).

Step 3: (R)-pent-3-yn-1,2-diol was used as a raw material, and the target product was obtained following the synthesis method of intermediate F.

MS m/z (ESI): 436.2 [M+H]+.

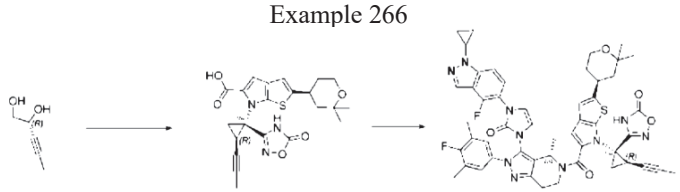
Step 4: methyl 4-bromo-2-methyl benzoate was used as a raw material, and the target product was obtained following the synthesis methods of steps 1 to 4 of Example 182.

MS m/z (ESI): 468.2 [M+H]+.

Step 5: 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indole-2-carboxylic acid and tert-butyl (S)-2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-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 were used as raw materials, and the target product was obtained following the synthesis methods in Example 25.

MS m/z (ESI): 959.4 [M+H]+.

Example 266



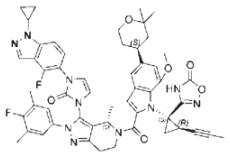
Step 1: (R)-pent-3-yn-1,2-diol and ethyl 2-bromo-6H-thieno[2,3-b]pyrrole-5-carboxylate were used as raw materials, and a product was obtained following the synthesis method of intermediate F.

MS m/z (ESI): 442.1 [M+H]+.

Step 2: 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid was used as a raw material, and the product was obtained following the synthesis method of Example 25.

MS m/z (ESI): 939.4 [M+H]+.

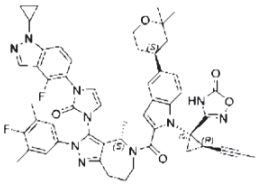
Example 267



(R)-pent-3-yn-1,2-diol was used as a raw material, and a product was obtained following the synthesis method of Example 214.

MS m/z (ESI): 963.4 [M+H]+.

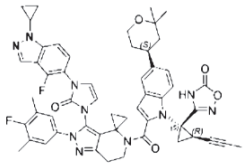
Example 268



(R)-pent-3-yn-1,2-diol was used as a raw material, and a product was obtained following the synthesis method of Example 215.

MS m/z (ESI): 947.4 [M+H]+.

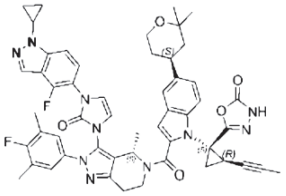
Example 269



(R)-pent-3-yn-1,2-diol was used as a raw material, and a product was obtained following the synthesis method of Example 216.

MS m/z (ESI): 945.4 [M+H]+.

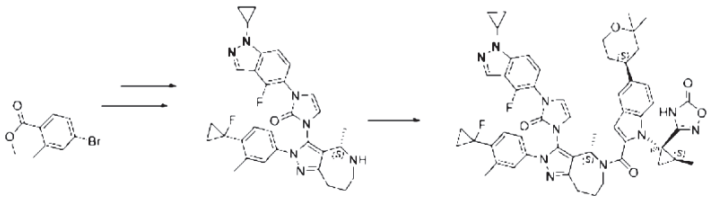
Example 270



(R)-pent-3-yn-1,2-diol was used as a raw material, and a product was obtained following the synthesis method of Example 217.

MS m/z (ESI): 933.4 [M+H]+.

Example 271



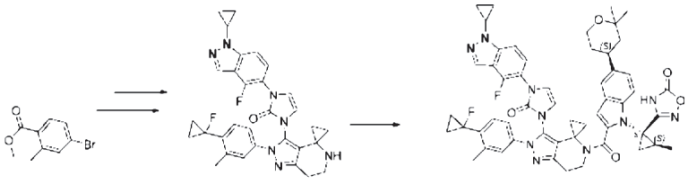
Step 1: methyl 4-bromo-2-methyl benzoate was used as a raw material, and the target product was obtained following the synthesis methods of Examples 208 and 215.

MS m/z (ESI): 556.3 [M+H]+.

Step 2: (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-4-methyl-2,4,5,6,7,8-hexahydropyrazolo[4,3-c]azepin-3-yl)-1,3-dihydro-2H-imidazole-2-one was used as a raw material, and the target product was obtained following the synthesis method of Example 25.

MS m/z (ESI): 949.4 [M+H]+.

Example 272



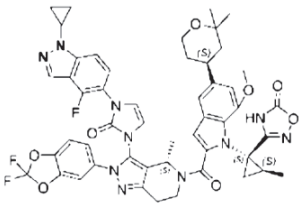
Step 1: methyl 4-bromo-2-methyl benzoate was used as a raw material, and the target product was obtained following the synthesis method of Examples 208 and 206.

MS m/z (ESI): 554.2 [M+H]+.

Step 2: 1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2'-(4-(1-fluorocyclopropyl)-3-methylphenyl)-2',5',6',7'-tetrahydrospiro[cyclopropane-1,4'-pyrazolo[4,3-c]pyridine]-3'-yl)-1,3-dihydro-2H-imidazole-2-one was used as a raw material, and the target product was obtained following the synthesis method of Example 25.

MS m/z (ESI): 947.4 [M+H]+.

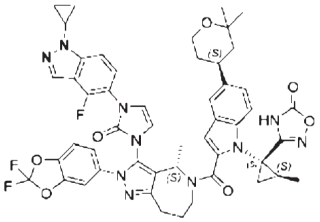
Example 273



(2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method in Example 186.

MS m/z (ESI): 973.3 [M+1].

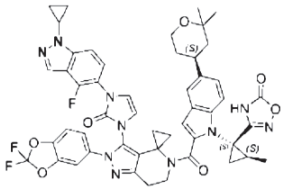
Example 274



(2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method in Example 201.

MS m/z (ESI): 957.3 [M+1].

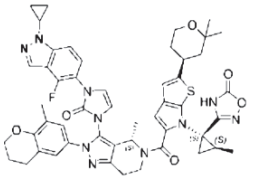
Example 275



(2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method in Example 51.

MS m/z (ESI): 955.3 [M+1].

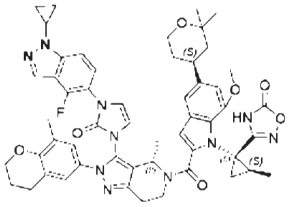
Example 276



(8-Methylchroman-6-yl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method in Example 226.

MS m/z (ESI): 939.3 [M+1].

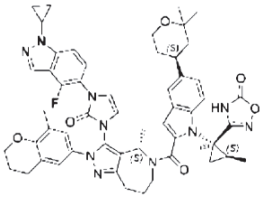
Example 277



(8-Methylchroman-6-yl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method in Example 186.

MS m/z (ESI): 963.4 [M+1].

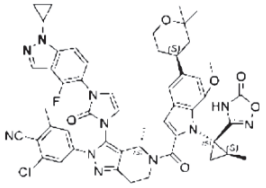
Example 278



(8-Methylchroman-6-yl)hydrazine was used as a raw material, and the target product was obtained following the synthesis method in Example 201.

MS m/z (ESI): 947.4 [M+1].

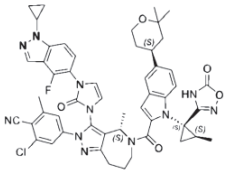
Example 279



Following Example 485, the title product was obtained.

MS m/z (ESI): 966.4 [M+1].

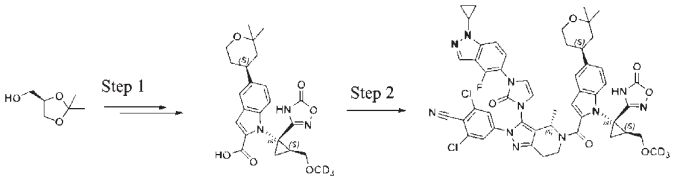
Example 280



Following Example 215, the title product was obtained.

MS m/z (ESI): 950.4 [M+1].

Example 281



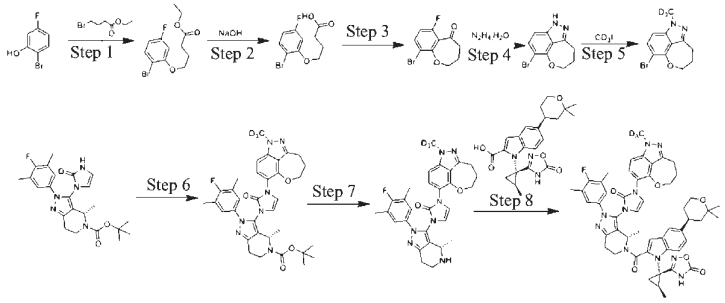
Step 1: (R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol was used as a raw material, and the target product was obtained following the synthesis method of Example 189 (with 1-bromo-2-methoxy-ethane being replaced with deuterated iodomethane).

MS m/z (ESI): 445.2 [M+1].

Step 2: (S)-2,6-dichloro-4-(3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2S)-2-((methoxy-d3)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-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): 989.3 [M+1].

Example 282



Step 1: ethyl 4-(2-bromo-5-fluorophenoxy)butyrate

A mixture of 2-bromo-5-fluorophenol (5 g, 26.18 mmol), ethyl 4-bromobutyrate (10.21 g, 52.36mmol), DMF (50 mL), and potassium carbonate (10.85 g, 78.54 mmol) was stirred at 100°C for 1 hour until LCMS showed that the reaction was completed, with MS of the target product being observed; the reaction was stopped, water was added to quench the reaction, and the system was extracted with dichloromethane (100 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (50 mL), dried over anhydrous sodium sulfate, filtered, concentrated, and separated by column chromatography (PE/EA = 4 : 1), to obtain a colorless oil (7 g, yield: 87.6%)

MS m/z (ESI): 305.0 307.0 [M+1].

Step 2: 4-(2-bromo-5-fluorophenoxy)butyric acid

To a mixture of ethyl 4-(2-bromo-5-fluorophenoxy)butyrate (5 g, 16.39 mmol) in THF(30 mL), water (30 mL), and methanol (30 mL) was added sodium hydroxide (1.97 g, 49.16mmol), and the reaction solution was stirred at room temperature for 2 hours until LCMS showed that the reaction was completed, with MS of the target product being observed; the system was adjusted to pH = 3 by adding dilute hydrochloric acid, and extracted three times with DCM; 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 white solid (4 g, crude)

MS m/z (ESI): 277.0 279.0 [M+1].

Step 3: 9-bromo-6-fluoro-3,4-dihydrobenzo[b]oxepin-5(2H)-one

A mixture of 4-(2-bromo-5-fluorophenoxy)butyric acid (2.6 g, 9.38 mmol), polyphosphoric acid (3.17 g, 9.38 mmol, 20 mL), and toluene (60 mL) was stirred at 120°C for 12 hours, water was added to quench the reaction, and the system was extracted with dichloromethane (50 mL × 2); the organic phases were combined, washed with saturated sodium chloride (50 mL), dried over anhydrous sodium sulfate, filtered, concentrated, and separated by column chromatography (PE/EtOAc = 2 : 1), followed by concentration, to obtain the title product (500 mg, yield: 20.6%)

MS m/z (ESI): 259.0 261.0 [M+1].

Step 4: 5-bromo-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole

A mixture of 9-bromo-6-fluoro-3,4-dihydrobenzo[b]oxepin-5(2H)-one (500 mg, 1.93 mmol), hydrazine hydrate (727.60 mg, 19.30 mmol, 85% purity), and 1,4-dioxane (10 mL) was stirred at 110°C for 12 hours until LCMS showed that the reaction was completed, with MS of the target product being observed; water was added to quench the reaction, and the system was extracted with dichloromethane (50 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (50 mL), dried over anhydrous sodium sulfate, filtered, concentrated, and separated by preparative chromatography (PE/EA = 1 : 1), followed by concentration to obtain the title product (400 mg, yield: 81.9%)

MS m/z (ESI): 253.0 255.0 [M+1].

Step 5: To a solution of 5-bromo-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole (100 mg, 395.11 μmol) in DMF (5 mL) was added sodium hydride (23.70 mg, 592.66 μmol, 60% purity), and the reaction solution was stirred at room temperature for 0.5 hours; deuterated iodomethane (85.94 mg, 592.66μmol) was added dropwise, and then the reaction solution was stirred at room temperature for 0.5 hours until LCMS showed that the reaction was completed, with MS of the target product being observed; water was added to quench the reaction, and the system was extracted with dichloromethane (50 mL × 2); and the organic phases were combined, washed with saturated sodium chloride (50 mL), dried over anhydrous sodium sulfate, filtered, concentrated, and separated by preparative chromatography (PE/EtOAc = 1 : 1), followed by concentration to obtain a product 5-bromo-2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole (60 mg, yield: 56.2%)

MS m/z (ESI): 270.0 272.0 [M+1].

Step 6: a mixture of 5-bromo-2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole (64.25 mg, 237.83 μmol), tert-butyl (S)-2-(4-fluoro-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 (70 mg, 158.55 μmol), cuprous iodide (24.16 mg, 126.84 μmol), (1S, 2S)-N,N'-dimethyl-1,2-cyclohexanediamine (22.55 mg, 158.55 μmol), potassium carbonate (65.64 mg, 475.65 μmol) and NMP (3 mL) was stirred at 130°C under N2 protection for 16 hours until LCMS showed that the reaction was completed, with MS of the target product being observed; water was added, followed by extraction with EtOAc; and the organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, separated by column chromatography (DCM/MeOH = 10 : 1), to obtain tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo [4,3-c]pyridine -5-carboxylate (40 mg, yield: 40.0%)

MS m/z (ESI): 631.1 [M+1].

Step 7: to a solution of tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate (40 mg, 63.42 μmol) in DCM(2 mL) was added dropwise TFA (7.23 mg, 63.42 μmol, 1 mL), and the reaction solution was stirred at room temperature for 0.5 hours until LCMS showed that the reaction was completed, with MS of the target product being observed, followed by spin-drying; the system was adjusted to pH = 10 by adding saturated $NaHCO_3$, and 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 (S)-1-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-1,3-dihydro-2H-imidazole-2-one (30 mg, crude)

MS m/z (ESI): 531.3 [M+1].

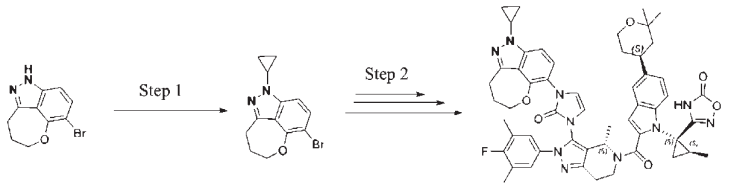
Step 8: to a solution of (S)-1-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-1,3-dihydro-2H-imidazole-2-one (15 mg, 28.27 μmol) and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid (17.45 mg, 42.40 μmol) in DMF (2 mL) were added HATU (21.33 mg, 56.54 μmol) and DIEA (10.96 mg, 84.81 μmol, 14.77 μL), and

the reaction solution 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 , followed by extraction 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 preparative chromatography (acidic), to obtain 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-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-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 (5.8 mg, yield: 22.1%).

^{1}H NMR (400MHz, DMSO) δ [12.30(s) and 11.77(s), total 1H], 7.54 (s, 1H), 7.43-7.31 (m, 1H), 7.28-7.05 (m, 5H), 6.99-6.60 (m, 3H), 5.76-5.20 (m, 1H), 4.62-4.16 (m, 2H), 3.80-3.57 (m, 3H), 3.22-2.76 (m, 5H), 2.25-2.07 (m, 8H), 1.81-1.41 (m, 10H), 1.35-1.15 (m, 10H).

MS m/z (ESI): 924.4 [M+1].

Example 283



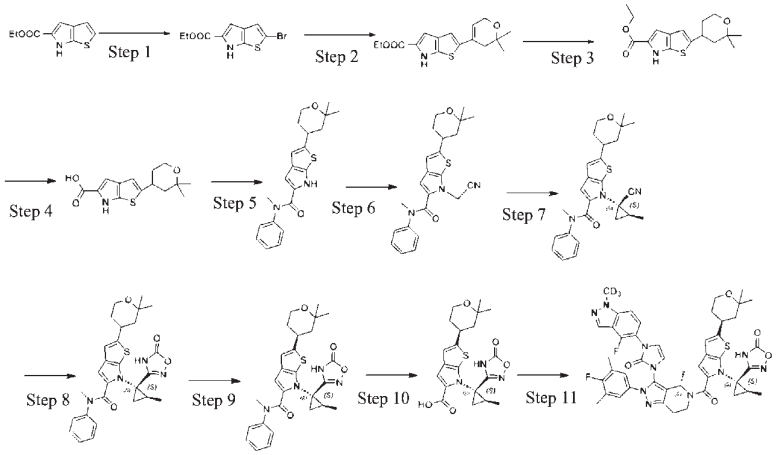
Step 1: at room temperature, 5-bromo-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole (2.53 g, 10 mmol) was dissolved in 1,2-dichloroethane (30 mL), and cyclopropyl boronic acid (1.29 g, 15mmol), copper acetate (0.91 g, 5 mmol), 2,2-dibipyridine (0.78 g, 5 mmol) and sodium carbonate (3.18 g, 30 mmol) were then added, followed by oxygen replacement, and the system was heated to 80°C for reaction for 16 hours, with LCMS indicating the completion of the reaction; the reaction solution was cooled to room temperature, filtered using diatomaceous earth, and then washed with dichloromethane; and the organic phases were combined, and then spin-dried, and the residue was purified by Flash column chromatography (petroleum ether : ethyl acetate: 1 : 1), to obtain the target compound as a white solid (2.05 g, yield 70%).

MS m/z (ESI): 293.1, 295.1 [M+H]+.

Step 2: 5-bromo-2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole was used as a raw material, and the target compound was obtained following steps 6, 7, and 8 of Example 282.

MS m/z (ESI): 947.4 [M+H]+.

Example 284



Step 1: ethyl 6*H*-thieno[2,3-*b*]pyrrole-5-carboxylate (9 g, 46.10 mmol) was dissolved in $CHCl_3$ (100 mL), and at 0°C, NBS (8.20 g, 46.10 mmol) was added in three batches, and the reaction solution was stirred for 0.5 hours. As monitored by LCMS, the raw materials disappeared. 500 mL water and DCM (300 mL X 3) were added for extraction; and the organic phase was dried over anhydrous sodium sulfate and concentrated under vacuum, and the crude product was separated by column chromatography (PE : EtOAc = 96 : 4) to obtain ethyl 2-bromo-6*H*-thieno[2,3-*b*]pyrrole-5-carboxylate (9 g, yellow solid), yield: 71.22%.

MS m/z (ESI): 273.9, 275.9 [M+1].

Step 2: ethyl 2-bromo-6*H*-thieno[2,3-b]pyrrole-5-carboxylate (9 g, 32.83 mmol) and 2-(6,6-dimethyl-2,5-dihydropyran-4-yl)-4,4,5-5-tetramethyl-1,3,2-dioxaborane (10.16 g, 42.68 mmol) were dissolved in H_2O (20 mL) and 1'4-Dioxane (100 mL), and at room temperature, $Pd(dppf)CI_2$ (2.40 g, 3.28 mmol) and K_3PO_4 (13.94 g, 65.66 mmol) were added. After nitrogen replacement three times, the reaction solution was stirred at 90°C for 8 hours. As monitored by LCMS, the raw materials disappeared. The reaction solution was extracted by adding 500 mL water and EtOAC (300 mL X 3); and the organic phase was dried by adding anhydrous sodium sulfate, and concentrated under vacuum, and the crude product was subjected to column chromatography (PE : EA = 90 : 10) to obtain the target product (4.1 g, yellow solid), yield: 40.89%.

MS m/z (ESI): 306.1 [M+1].

Step 3: ethyl 2-(6,6-dimethyl-2,5-dihydro pyran-4-yl)-6*H*-thieno[2,3-*b*]pyrrole-5-carboxylate (4.1 g, 13.43 mmol) was dissolved in TFA (40 mL), and at room temperature, Et_3SiH (1.56 g, 13.43 mmol) was added; and the reaction was stirred for 10 min, and as monitored by LCMS, the raw materials disappeared. To the reaction solution, ice cubes were added, and saturated aqueous solution of sodium bicarbonate was added to adjust PH to 7-8, and the system was extracted by adding EtOAc (200 mL X 3); and the organic phase was dried over anhydrous sodium sulfate and concentrated under vacuum, and the crude product was subjected to column chromatography to obtain the target product (2.8 g, yellow solid), yield: 67.82%

MS m/z (ESI): 308.1 [M+1].

Step 4: ethyl 2-[2,2-dimethyltetrahydro pyran-4-yl]-6*H*-thieno[2,3-*b*]pyrrole-5-carboxylate (2.8 g, 9.11 mmol) was dissolved in MeOH (20 mL) and H_2O (10 mL), and at room temperature, NaOH (801.49 mg, 20.04 mmol) was added, and the reaction solution was stirred at 70°C for 3 hours. As monitored by LCMS, the raw materials disappeared. The reaction solution was cooled to room temperature and extracted by adding 200 mL EtOAc to obtain an organic phase, and the aqueous phase was adjusted to PH 5-6 by adding hydrochloric acid and then extracted by adding EtOAc (200 mL X 3) to obtain an organic phase; the organic phases were dried over anhydrous sodium sulfate, and concentrated under vacuum, and the crude product was subjected to column chromatography (DCM : MeOH = 96 : 4) to obtain a product 2-[2,2-dimethyltetrahydropyran-4-yl]-6*H*-thieno[2,3-*b*]pyrrole-5-carboxylic acid (2.2 g, yellow solid), yield: 86.46%.

MS m/z (ESI): 280.0 [M+1].

Step 5: 2-[2,2-dimethyltetrahydropyran-4-yl]-6*H*-thieno[2,3-*b*]pyrrole-5-carboxylic acid (2.2 g, 7.88 mmol) was dissolved in Tol. (20 mL), followed by nitrogen replacement three times. At room temperature, DMF (57.56 mg, 787.53 μmol, 60.98 μL) and oxalyl chloride (2.00 g, 15.75 mmol) were added, and the reaction solution was stirred at 100°C for 2 hours. The reaction solution was directly concentrated under vacuum, followed by draining. The mixture was dissolved in DCM (20 mL), and triethylamine (1.59 g, 15.75 mmol, 2.20 mL) and N-methylaniline (1.69 g, 15.75 mmol) were added, successively, followed by nitrogen replacement three times, and the system was allowed to react at 30°C for 8 hours. The reaction solution was concentrated under vacuum, and the crude product was subjected to column chromatography (PE : EA = 80 : 20) to obtain the target product (1.9 g, yellow solid), yield: 65.47%.

MS m/z (ESI): 369.1 [M+1].

Step 6: 2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-*N*-phenyl-6*H*-thieno[2,3-b]pyrrole-5-carboxamide (1.9 g, 5.16 mmol) was dissolved in DMF (15 mL), followed by nitrogen replacement three times; at 0°C, NaH (371.21 mg, 15.47 mmol) was added slowly and stirred for 0.5 hours; and then 2-bromoacetonitrile (1.86 g, 15.47mmol) was added, and the reaction was stirred at 30°C for 8 hours. As monitored by LCMS, there was still a small amount of raw material left, and the product was generated. To the reaction solution were added H_2O (300 mL) and EtOAc (200 mL X 3) for extraction, the organic phase was dried over anhydrous sodium sulfate, and concentrated under vacuum, and the crude product was subjected to column chromatography (PE : EtOAc = 74 : 26) to obtain the target product (2 g, yellow solid), yield: 95.18%

MS m/z (ESI): 408.1 [M+1].

Step 7: 6-(cyanomethyl)-2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-*N*-phenylthieno[2,3-*b*]pyrrole-5-carboxamide and (4*R*)-4-methyl-1,3,2-dioxathiane 2,2-dioxide (2.37 g, 17.18 mmol) were dissolved in DMPU (20 mL), and cooled to 0°C with an ice bath; KHMDS (9.79 g, 49.08 mmol) was slowly added dropwise; and after addition, the system was allowed to react at 0°C for 5 hours. As monitored by LCMS, the raw materials disappeared; formic acid was added to adjust PH to acidic; and the system was stirred for 5min, and then extracted by adding 300 mL water and EtOAc (300 mL X 3). The organic phase was dried over anhydrous sodium sulfate and concentrated under vacuum, and the crude product was subjected to column chromatography (PE : EA = 55 : 45) to obtain the target product (450 mg, yellow solid), yield: 20.49%.

MS m/z (ESI): 448.2 [M+1].

Step 8: (6R)-6-[(1S,2S)-1-cyano-2-methyl-cyclopropyl]-2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-*N*-phenyl-thieno[2,3-*b*]pyrrole-5-carboxamide (450 mg, 1.01 mmol), K_2CO_3 (764.25 mg, 5.53 mmol) and hydroxylamine hydrochloride (349.32 mg, 5.03 mmol) were dissolved in THF (20 mL) and stirred at 90°C for 2 hours, after which as LCMS monitored, an intermediate formed, and raw materials disappeared. The reaction solution was concentrated to dryness, and anhydrous EtOH (20 mL) was added until the solution was clear, the insoluble matter was filtered off; and to the filtrate were added DBU (459.17 mg, 3.02 mmol, 450.17 μL) and CDI (318.40 mg, 2.21 mmol) dissolved in 1 ml THF (20 mL), and the reaction solution was stirred for 3 hours. As monitored by LCMS, a product was formed, and the intermediate disappeared. The reaction solution was directly stirred with silica gel and spin-dried, and the crude product was subjected to column chromatography (DCM : MeOH = 98 : 2) to obtain the target product (390 mg, yellow solid), yield: 76.57%.

MS m/z (ESI): 507.2 [M+1].

Step 9: 2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-6-[(1*S*, 2*S*)-2-methyl-1-(5-oxo-4H-1,2,4-oxadiazol-3-yl)cyclopropyl]-*N*-phenylthieno[2,3-*b*]pyrrole-5-carboxamide was chirally resolved to obtain the title product 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-6-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-phenyl-6H-thieno[2,3-b]pyrrole-5-carboxamide.

MS m/z (ESI): 507.2 [M+1].

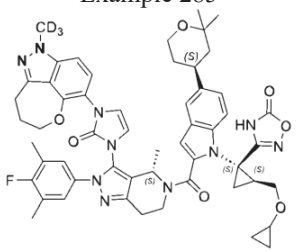
Step 10: 2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-6-[(1*S*,2*S*)-2-methyl-1-(5-oxo-4H-1,2,4-oxadiazol-3-yl)cyclopropyl]-N-phenylthieno[2,3-*b*]pyrrole-5-carboxamide (390 mg, 769.81 μmol) was dissolved in ethylene glycol dimethyl ether (10 mL), and at room temperature, KOH (345.53 mg, 6.16 mmol) was added, followed by nitrogen replacement three times, and the reaction solution was stirred at 100°C for 8 hours. As monitored by LCMS, the raw materials disappeared, and a product was generated. The reaction solution was extracted by adding H_2O (200 mL) and EtOAc (100 mL X 3) to obtain an organic phase; the aqueous phase was adjusted to about PH 5-6 by adding hydrochloric acid and extracted by adding EA (100 mL X 3) to obtain an organic phase; the organic phases were dried over anhydrous sodium sulfate, and concentrated under vacuum; and the crude product was subjected to reverse phase column (H_2O : ACN = 55 : 45) to obtain the target product (168 mg, yellow solid), yield: 52.27%.

MS m/z (ESI): 418.1 [M+1].

Step 11: (S)-1-(4-fluoro-1-(methyl-d3)-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 and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-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): 892.3 [M+1].

Example 285

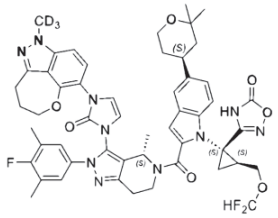


Following the synthesis method in Example 282, the title product 3-((1S, 2S)-2-(cyclopropoxymethyl)-1-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-1H-indol-1-yl)cyclopropyl)-1,2,4-oxadiazole-5(4H)- one was obtained.

MS m/z (ESI): 980.5 [M+1].

^{1}H NMR (400MHz, DMSO) δ 11.59 (s, 1H), 7.81-7.64 (m, 1H), 7.53-7.35 (m, 1H), 7.29-7.05 (m, 5H), 6.93-6.59 (m, 3H), 5.69-5.59 (m, 1H), 5.34-5.31 (m, 1H), 4.41 (s, 2H), 3.93-3.82 (m, 1H), 3.75 -3.41 (m, 3H), 3.11 -2.89 (m, 2H), 2.77 -2.64 (m, 1H), 2.33-2.19 (m, 6H), 2.11-1.90 (m, 2H), 1.73-1.43 (m, 6H), 1.30-1.18 (m, 14H), 0.47-0.33 (m, 4H).

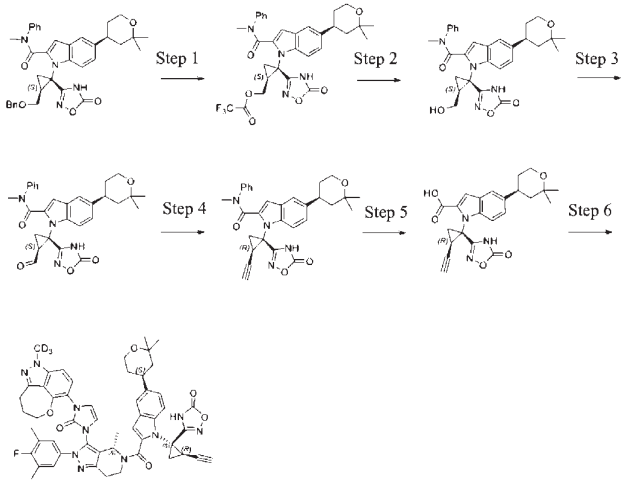
Example 286



Following the synthesis method in Example 282, the target product was obtained.

MS m/z (ESI): 990.4 [M+1].

Example 287



Step 1 ((1S,2S)-2-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-(methyl(phenyl)carbamoyl)-1H-indol-1-yl)-2-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)methyl 2,2,2-trifluoroacetate

1-((1S,2S)-2-((benzyloxy)methyl)-1-(5-oxo-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 (2.44 g, 4.02 mmol) was dissolved in trifluoroacetic acid (9 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 2.31 g (yield: 93.8%).

MS m/z (ESI): 613.2 [M+1]

Step 2 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-(hydroxymethyl)-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-methyl-N-phenyl-1H-indole-2-carboxamide

((1S,2S)-2-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-(methyl(phenyl)carbamoyl)-1H-indol-1-yl)-2-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)methyl 2,2,2-trifluoroacetate (2.31 g, 3.77 mmol), and potassium carbonate (1.56 g, 11.31 mmol) were dispersed in MeOH (15 mL), and stirred for reaction at room temperature for 1 hour. The reaction solution was filtered through diatomaceous earth, and the filtrate was concentrated under reduced pressure to obtain a yellow oily crude product, which was purified by silica gel column chromatography (eluent: methanol : ethyl acetate = 5%, v/v) to obtain the title product 1.81g (yield: 92.9%).

MS m/z (ESI): 517.2 [M+1]

Step 3 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-formyl-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-methyl-N-phenyl-1H-indole-2-carboxamide

((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-(hydroxymethyl)-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (1.81 g, 3.50 mmol) and Dess-martin Periodinane (2.97 g, 7.00 mmol) were dissolved in DCM (30 mL) and reacted under stirring at room temperature for 1 hour.

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The reaction solution was quenched by adding saturated sodium sulfite solution, and extracted with dichloromethane (30 mL × 2); and the organic phases were combined, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated under reduced pressure to obtain a colorless oily crude product. The crude product was purified by silica gel column chromatography (eluent: methanol : ethyl acetate = 5%, v/v) to obtain the title product 1.42g (yield: 78.8%).

MS m/z (ESI): 515.2 [M+1]

Step 4 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-2-ethynyl-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-methyl-N-phenyl-1H-indole-2-carboxamide

5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-formyl-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (1.42 g, 2.76 mmol), potassium carbonate (1.14 g, 8.28 mmol), and dimethyl (1-azo-2-oxopropyl)phosphonate (1.59 g, 8.28 mmol) were dispersed in methanol (20 mL), and reacted under stirring at room temperature for 2 hours. The reaction solution was quenched by adding a saturated ammonium chloride solution, and extracted with ethyl acetate (20 mL× 2); the organic phases were combined, dried over anhydrous sodium sulfate, and filtered; and the filtrate was concentrated under reduced pressure to obtain a colorless oily crude product. The crude product was purified by silica gel column chromatography (eluent: ethyl acetate) to obtain the title product 964 mg (yield: 74.2%).

MS m/z (ESI): 511.2 [M+1]

Step 5 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-2-ethynyl-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-N-methyl-N-phenyl-1H-indole-2-carboxamide (964 mg, 1.89 mmol) and potassium hydroxide (1.06 g, 18.90mmol) were dissolved in DME (20 mL) and reacted at 100°C under stirring for 2 hours. The reaction solution was cooled to room temperature, adjusted to pH = 1 by adding dilute hydrochloric acid (1M), and extracted with dichloromethane (20 mL × 5); and the organic phases were combined, dried over anhydrous sodium sulfate, and filtered, and the filtrate was concentrated under reduced pressure to obtain a colorless oily crude product. The crude product was purified by preparative HPLC to obtain the title product 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-2-ethynyl-1-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid 355 mg(yield: 44.6%).

MS m/z (ESI): 422.2 [M+1]

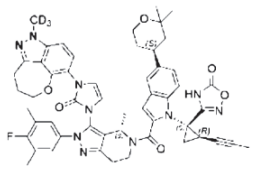
Step 6 3-((1S, 2R)-1-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-1H-indol-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one

Following the synthesis method in Example 282, the title product was obtained.

^{1}H NMR (400MHz, DMSO-d_6) δ [12.46(s) and 11.94(s), total 1H], 7.54-7.45 (m, 1H), 7.41-7.32 (m, 1H), 7.29-7.06 (m, 5H), 6.96-6.63 (m, 3H), [5.78-5.60(m) and 5.33-5.16(m), total 1H], [4.81-4.70(m) and 4.21-4.14(m), total 1H], 4.40-4.32 (m, 2H), 3.72-3.58 (m, 3H), 3.13-2.96 (m, 4H), 2.89-2.67 (m, 2H), 2.33-2.14 (m, 8H), 2.12-1.96 (m, 2H), 1.67-1.47 (m, 6H), 1.30-1.18 (m, 8H).

MS m/z (ESI): 934.4 [M+1].

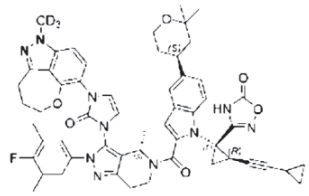
Example 288



Following the synthesis method in Example 282, the target product was obtained.

MS m/z (ESI): 948.4 [M+1].

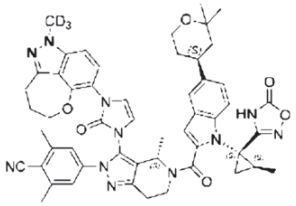
Example 289



Following the synthesis method in Example 282, the target product was obtained.

MS m/z (ESI): 974.5 [M+1].

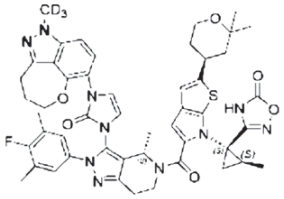
Example 290



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 was used as a raw material, and the target product was obtained following the synthesis method in Example 282.

MS m/z (ESI): 931.4 [M+1].

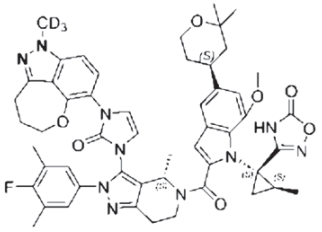
Example 291



Following the synthesis method in Example 282, the target product was obtained.

MS m/z (ESI): 930.4 [M+1].

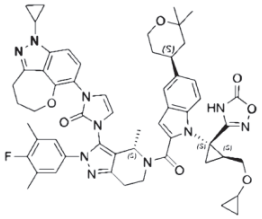
Example 292



Following the synthesis method in Example 282, the target product was obtained.

MS m/z (ESI): 954.4 [M+1].

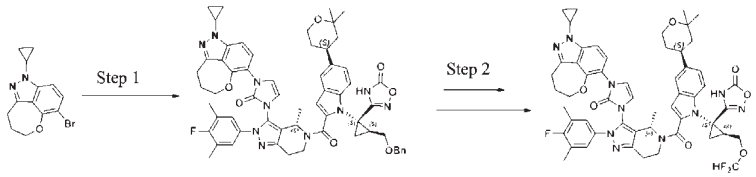
Example 293



Following Example 285, the target compound was obtained.

MS m/z (ESI): 1003.2 [M+H]+.

Example 294



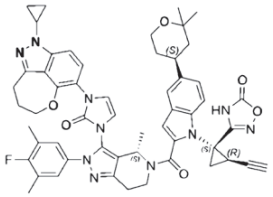
Step 1: 5-bromo-2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole was used as a raw material, and the target compound was obtained following steps 6, 7, and 8 of Example 282.

MS m/z (ESI): 1053.5 [M+H]+.

Step 2: 3-((1S, 2S)-2-((benzyloxy)methyl)-1-(2-((S)-3-(3-(2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]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 was used as a raw material, and the target compound was obtained following step 1 of Example 188, and step 1 of Example 141.

MS m/z (ESI): 1013.4 [M+H]+.

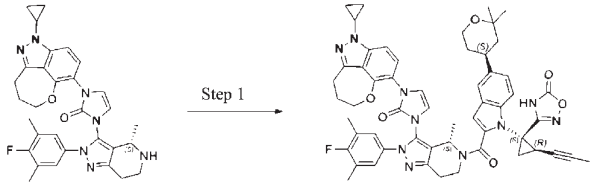
Example 295



Following Example 287, the target compound was obtained.

MS m/z (ESI): 957.4 [M+H]+.

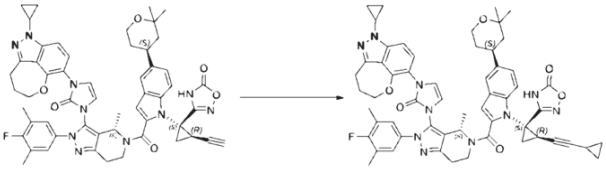
Example 296



Following step 8 of Example 282, the target compound was obtained.

MS m/z (ESI): 971.4 [M+H]+.

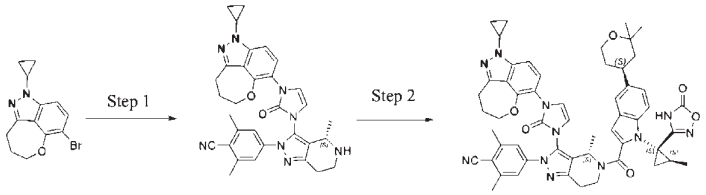
Example 297



Following step 1 of Example 145, the target compound was obtained.

MS m/z (ESI): 997.4 [M+H]+.

Example 298



Step 1: 5-bromo-2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole was used as a raw material, and the target compound was obtained following steps 6 and 7 of Example 282.

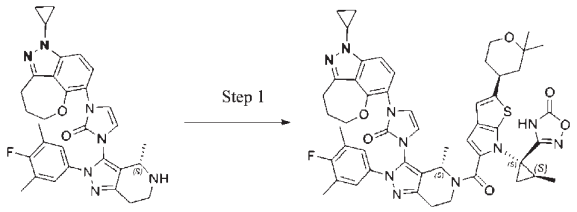
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MS m/z (ESI): 561.2 [M+H]+.

Step 2: Following step 8 of Example 282, the target compound was obtained.

MS m/z (ESI): 954.4 [M+H]+.

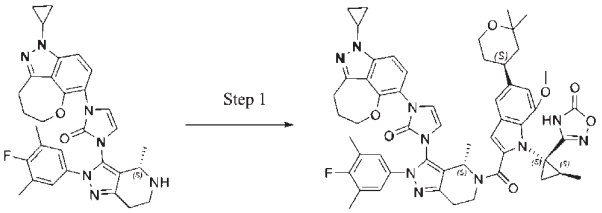
Example 299



Following step 8 of Example 282, the target compound was obtained.

MS m/z (ESI): 953.4 [M+H]+.

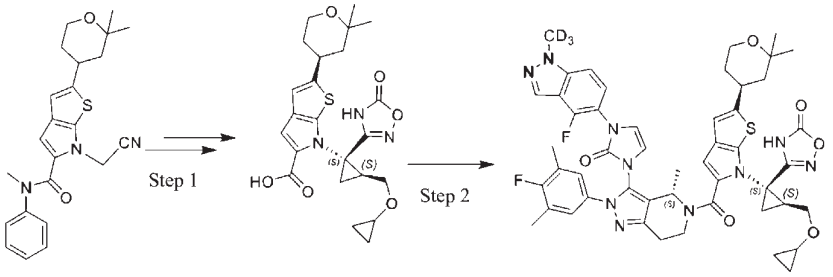
Example 300



Following step 8 of Example 282, the target compound was obtained.

MS m/z (ESI): 977.4 [M+H]+.

Example 301



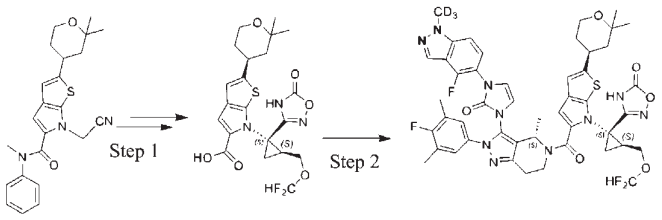
Step 1: 6-(cyanomethyl)-2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-*N*-phenylthieno[2,3-*b*]pyrrole-5-carboxamide was used as a raw material, following the synthesis method in steps 6 to 10 of Example 284 (with (R)-4-methyl-1,3,2-dioxathiane 2,2-dioxide being replaced with (R)-4-(cyclopropoxymethyl)-1,3,2-dioxathiolane 2,2-dioxide), to obtain a title product 6-((1S, 2S)-2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid.

MS m/z (ESI): 474.1 [M+1].

Step 2: (S)-1-(4-fluoro-1-(methyl-d3)-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 and 6-((1S, 2S)-2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-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): 948.3 [M+1].

Example 302



Step 1

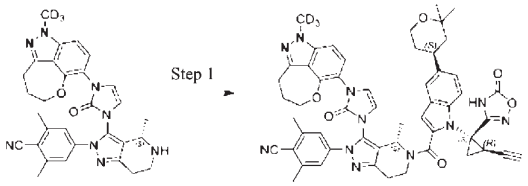
6-(cyanomethyl)-2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-*N*-phenylthieno[2,3-*b*]pyrrole-5-carboxamide was used as a raw material, and the target product was obtained following the synthesis method in steps 6 to 10 of Example 284 (with (R)-4-methyl-1,3,2-dioxathiane 2,2-dioxide being replaced with (R)-4-((difluoromethoxy)methyl)-1,3,2-dioxathiolane 2,2-dioxide).

MS m/z (ESI): 484.1 [M+1].

Step 2: (S)-1-(4-fluoro-1-(methyl-d3)-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 and 6-((1S,2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-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): 958.3 [M+1].

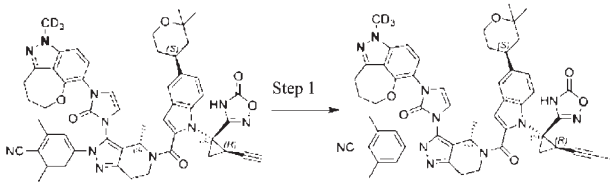
Example 303



Step 1: (S)-2,6-dimethyl-4-(4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile was used as a raw material, and the target compound was synthesized following Example 143.

MS m/z (ESI): 941.4 [M+H]

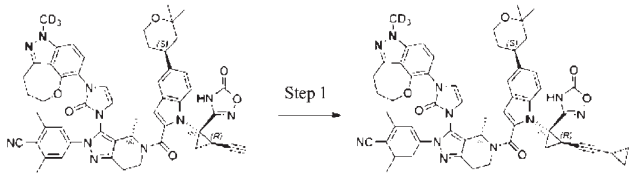
Example 304



Step 1: 4-((S)-5-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2R)-2-ethynyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carbonyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo [4,3-c]pyridin-2-yl)-2,6-dimethylbenzonitrile was used as a raw material, and the target compound was synthesized following Example 144.

MS m/z (ESI): 955.4 [M+H]

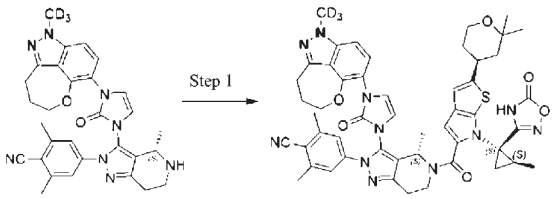
Example 305



Step 1: 4-((S)-5-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2R)-2-ethynyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carbonyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo [4,3-c]pyridin-2-yl)-2,6-dimethylbenzonitrile was used as a raw material, and the target compound was synthesized following Example 145.

MS m/z (ESI): 981.5 [M+H]

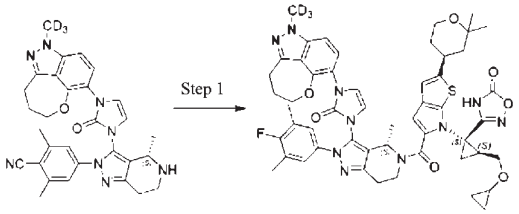
Example 306



Step 1: (S)-2,6-dimethyl-4-(4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile was used as a raw material, and the target compound was synthesized following Example 170.

MS m/z (ESI): 937.4 [M+H]

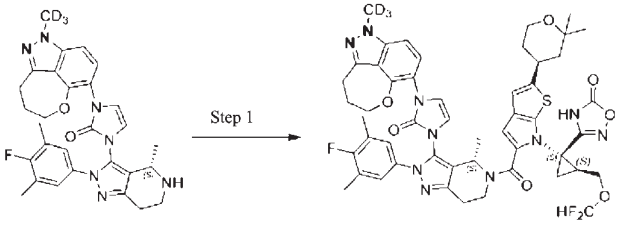
Example 307



Step 1: (S)-2,6-dimethyl-4-(4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile was used as a raw material, and the target compound was synthesized following Example 222.

MS m/z (ESI): 986.4 [M+H]

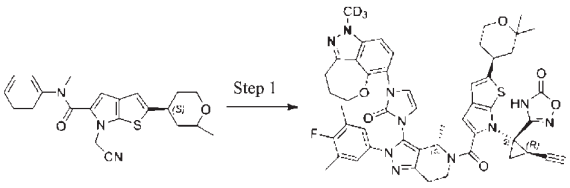
Example 308



Step 1: (S)-1-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-1,3-dihydro-2H-imidazole-2-one was used as a raw material, and the target compound was synthesized following Example 226.

MS m/z (ESI): 996.4 [M+H]

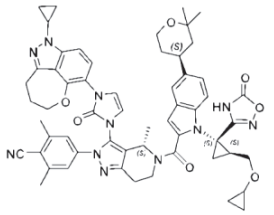
Example 309



Step 1: (S)-6-(cyanomethyl)-2-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-6H-thieno[2,3-b]pyrrole-5-carboxamide was used as a raw material, and the target compound was synthesized following Example 135.

MS m/z (ESI): 940.4 [M+H]

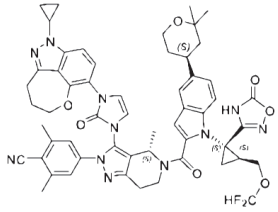
Example 310



Following the synthesis method in Example 293, the target product was obtained.

MS m/z (ESI): 1010.5 [M+1]

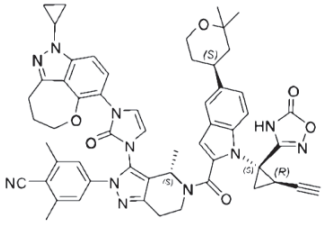
Example 311



Following the synthesis method in Example 294, the target product was obtained.

MS m/z (ESI): 1020.4 [M+1]

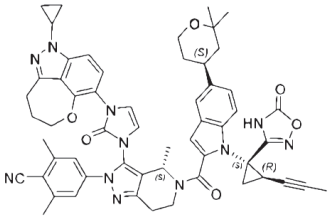
Example 312



Following the synthesis method in Example 287, the title product was obtained.

MS m/z (ESI): 964.4 [M+1]

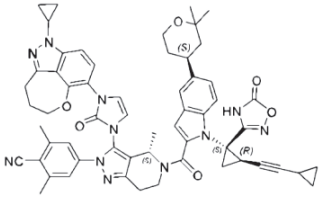
Example 313



Following the synthesis method in Example 296, the target product was obtained.

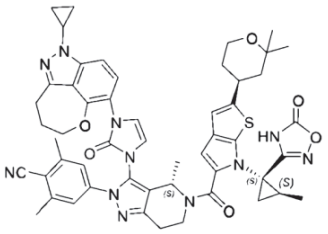
MS m/z (ESI): 978.4 [M+1]

Example 314



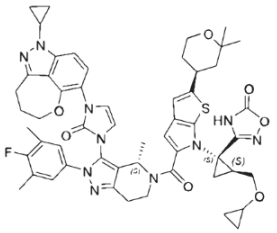
Following the synthesis method in Example 297, the target product was obtained.
MS m/z (ESI): 1004.5 [M+1]

Example 315



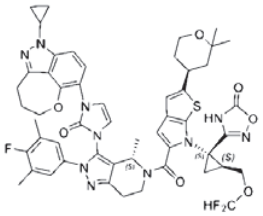
Following the synthesis method in Example 284, the target product was obtained.
MS m/z (ESI): 960.4 [M+1]

Example 316



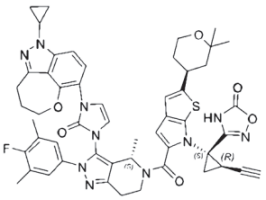
Following the synthesis method in Example 301, the target product was obtained.
MS m/z (ESI): 1009.4 [M+1]

Example 317



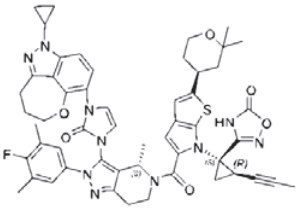
Following the synthesis method in Example 302, the target product was obtained.
MS m/z (ESI): 1019.4 [M+1]

Example 318



Following the synthesis method in Example 460, the target product was obtained.
MS m/z (ESI): 963.4 [M+1]

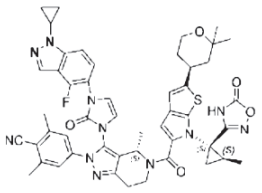
Example 319



Following the synthesis method in Example 466, the target product was obtained.

MS m/z (ESI): 977.4 [M+1]

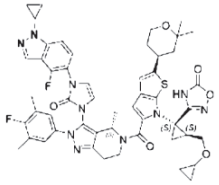
Example 320



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was obtained following the synthesis method of Example **282**.

MS m/z (ESI): 922.3 [M+1].

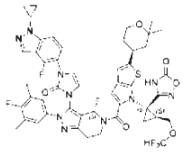
Example 321



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was obtained following the synthesis method of Example **67**.

MS m/z (ESI): 971.4 [M+1].

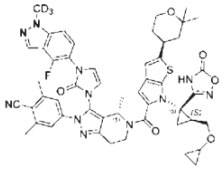
Example 322



5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole was used as a raw material, and the target product was obtained following the synthesis method of Example **286**.

MS m/z (ESI): 981.3 [M+1].

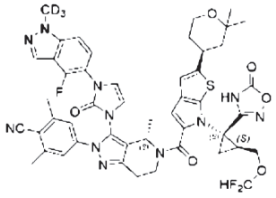
Example 323



5-Bromo-4-fluoro-1-(methyl-d3)-1H-indazole was used as a raw material, and the target product was obtained following the synthesis method of Example **67**.

MS m/z (ESI): 955.3 [M+1].

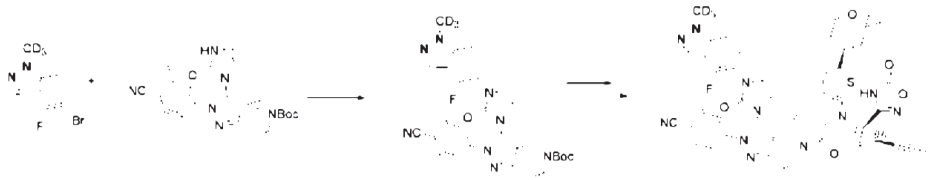
Example 324



5-Bromo-4-fluoro-1-(methyl-d3)-1H-indazole was used as a raw material, and the target product was obtained following the synthesis method of Example **286**.

MS m/z (ESI): 965.3 [M+1].

Example 325



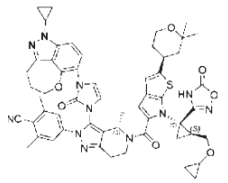
Step 1: 5-bromo-4-fluoro-1-(methyl-d3)-1H-indazole and tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate were used as raw materials, and a product was obtained following step 2 of Example 25.

MS m/z (ESI): 600.2 [M+1].

Step 2: tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-3-(3-(4-fluoro-1-(methyl-d3)-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylate were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 923.3 [M+1].

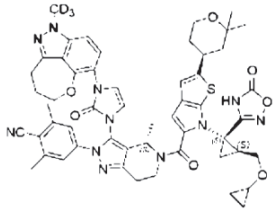
Example 326



tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-3-(3-(2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 6-((1S, 2S)-2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 1016.4 [M+1].

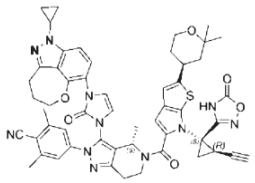
Example 327



tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 6-((1S, 2S)-2-(cyclopropoxymethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 993.4 [M+1].

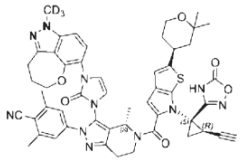
Example 328



tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-3-(3-(2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2R)-2-ethynyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 970.3 [M+1].

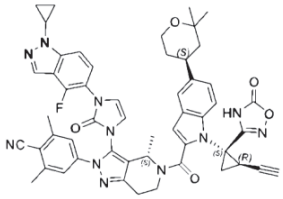
Example 329



tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2R)-2-ethynyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 947.3 [M+1].

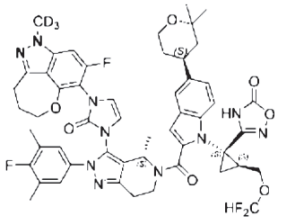
Example 330



tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S, 2R)-2-ethynyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 926.3 [M+1].

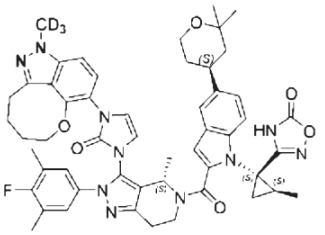
Example 331



2-bromo-3,5-difluorophenol was used as a raw material, and a product was obtained following the synthesis method in Example 282.

MS m/z (ESI): 1008.4 [M+1].

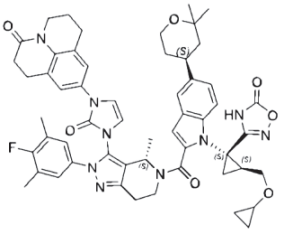
Example 332



Ethyl 5-bromopentanoate was used as a raw material, and a product was obtained following the synthesis method in Example 282.

MS m/z (ESI): 938.4 [M+1].

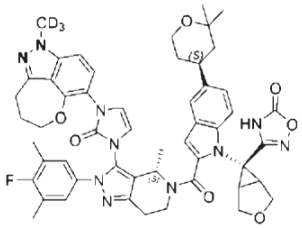
Example 333



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-3-(3-carbonyl-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 1-((1S, 2S)-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 were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

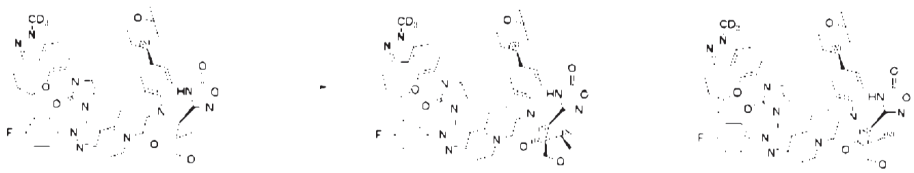
MS m/z (ESI): 976.4 [M+1].

Example 334



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-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-(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 a product was obtained following steps 3 and 4 of Example 25.

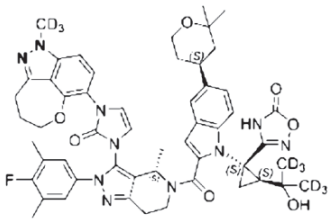
MS m/z (ESI): 952.4 [M+1].



Example 334 was resolved to obtain 334-1 and 334-2.

MS m/z (ESI): 952.4 [M+1].

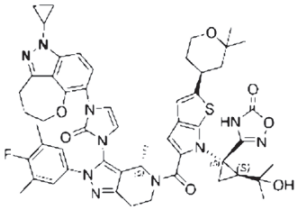
Example 335



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-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-((1S, 2S)-2-(2-hydroxylpropan-2-yl-1,1,1,3,3,3-d6)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 974.4 [M+1].

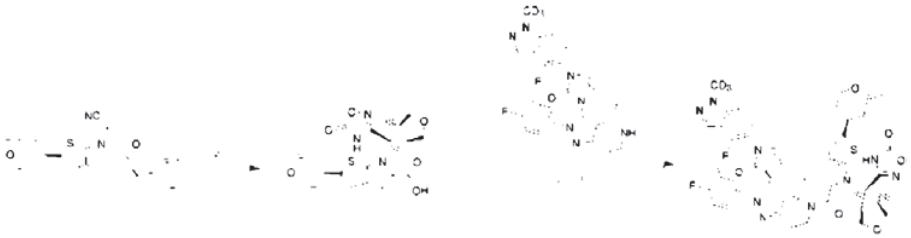
Example 336



tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S, 2S)-2-(2-hydroxylpropan-2-yl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid were used as raw materials, and a product was obtained following steps 3 and 4 of Example 25.

MS m/z (ESI): 997.4 [M+1].

Example 337



Step 1: (3aR, 6aS)-tetrahydrofuro[3,4-d][1,3,2]dioxothiazole 2,2-dioxide and (S)-6-(cyanomethyl)-2-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-N-methyl-N-phenyl-6H-thieno[2,3-b]pyrrole-5-carboxamide were used as raw materials, and the target compound was synthesized following steps 3 to 6 of Example 65.

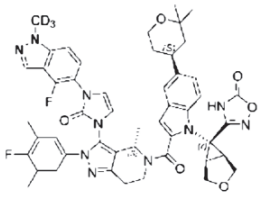
MS m/z (ESI): 446.1 [M+1].

Step 2: 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1R, 5S, 6r)-6-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-3-oxabicyclo[3.1.0]hexan-6-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid and (S)-1-(4-fluoro-1-(methyl-d3)-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 compound was synthesized following step 7 of Example 65.

MS m/z (ESI): 920.4 [M+1].

Example 338

3-((3R, 4r, 5S)-4-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-((S)-3-(3-(4-fluoro-1-(methyl-d3)-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)-1H-indol-1-yl)tetrahydro-2H-pyran-4-yl)-1,2,4-oxadiazole-5(4H)-one

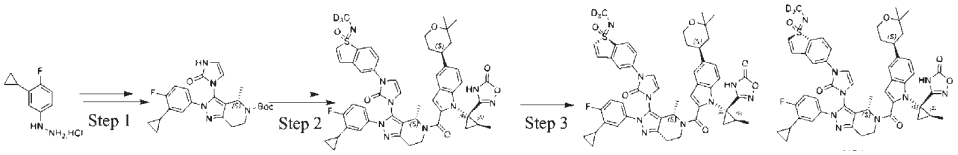


Following the synthesis method in Example 65-1, a product was obtained.

^{1}H NMR (400MHz, DMSO) δ [12.25(s) and 11.59(s), total 1H], 8.32 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.50-7.44 (m, 2H), 7.29 (d, *J* = 8.6 Hz, 1H), 7.19 (d, *J* = 6.2 Hz, 2H), 7.09 (s, 1H), 6.97-6.87 (m, 2H), 5.68 (s, 1H), 4.27 -4.07 (m, 3H), 3.83-3.63 (m, 5H), 3.13-2.80 (m, 4H), 2.26 (s, 6H), 1.68-1.42 (m, 8H), 1.28 (s, 3H), 1.19 (s, 3H).

MS m/z (ESI): 914.3 [M+1].

Example 515



Step 1: (3-cyclopropyl-4-fluorophenyl)hydrazine hydrochloride was used as a raw material, and the target product was obtained following the synthesis method for intermediate G.

MS m/z (ESI): 454.2 [M+1].

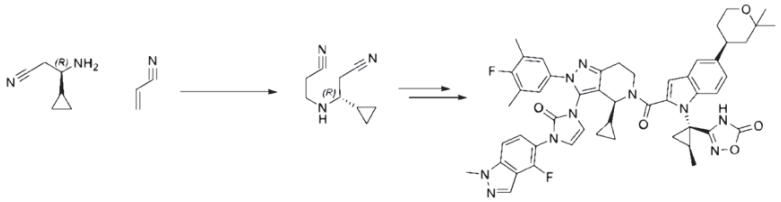
Step 2: 5-bromo-1-((methyl-d3)imino)-1H-1l4-benzo[b]thiophene 1-oxide and tert-butyl (S)-2-(3-cyclopropyl-4-fluorophenyl)-4-methyl-3-(2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate were used as raw materials, and the target product was obtained following the synthesis method in steps 2 to 4 of Example 175.

MS m/z (ESI): 927.3 [M+1].

Step 3: The resulting product was chirally resolved to obtain 515-1 and 515-2.

MS m/z (ESI): 927.3 [M+1].

Example 516



Step 1: In a 250 mL reaction bottle, (R)-3-amino-3-cyclopropylpropanenitrile (10.0 g, 90.78 mmol) was dissolved in ethanol (50.0 mL), and then triethylamine (11.02 g, 108.93 mmol) and acrylonitrile (5.78 g, 108.93 mmol) were added, and the reaction solution was stirred at 70°C for 3 hours. The reaction was stopped, cooled to room temperature, and concentrated to obtain the title product (R)-3-((2-cyanoethyl)amino)-3-cyclopropylpropanenitrile (21.0 g), yield: 87.8%.

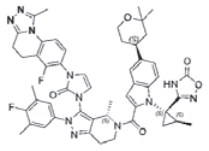
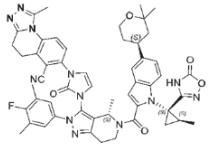
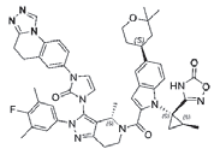
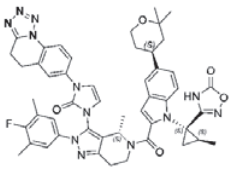
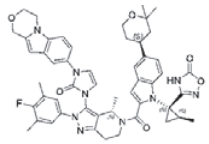
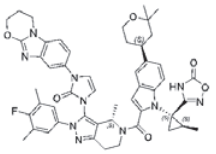
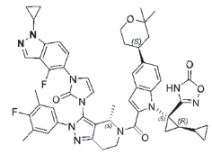
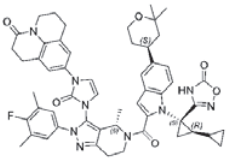
MS m/z (ESI): 164.1 [M+1].

Step 2: (R)-3-((2-cyanoethyl)amino)-3-cyclopropyl propanenitrile was used as a raw material, and a product was obtained following Example 1.

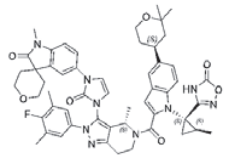
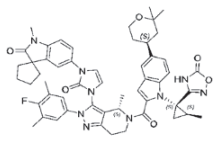
MS m/z (ESI): 909.3 [M+1].

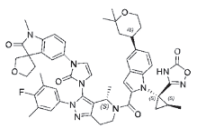
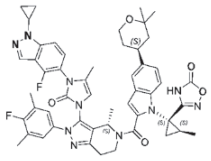
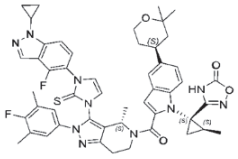
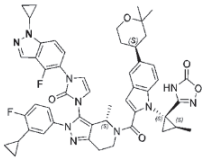
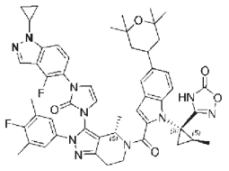
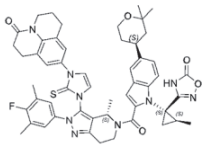
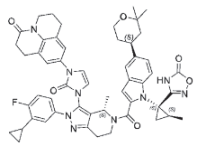
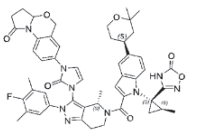
The following examples can be prepared following Example 1.

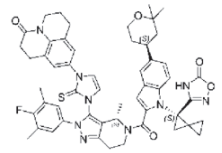
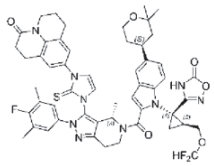
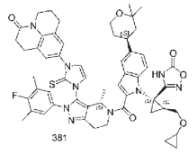
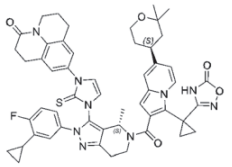
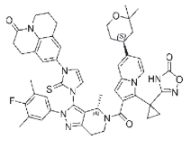
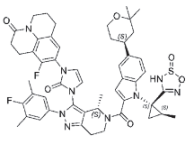
Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)

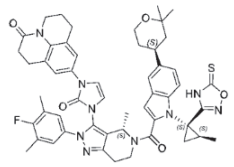
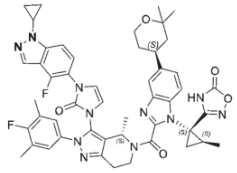
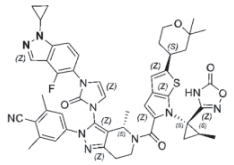
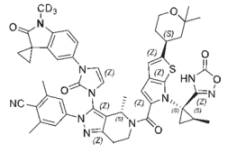
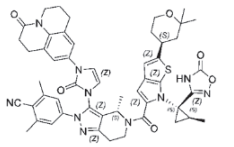
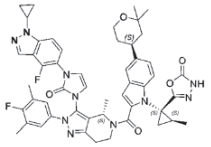
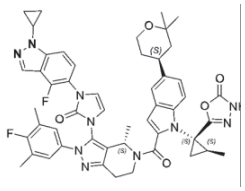
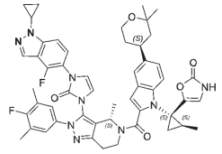
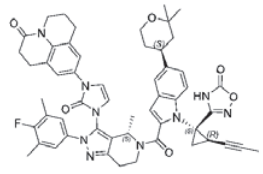
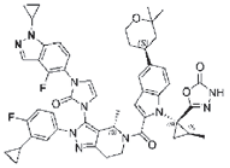
339	 7-Bromo-6-fluoro-1-methyl-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinoline as raw material	936.4[M+1]	340	 Refer to Example 339 for raw material	943.4[M+1]
341	 Refer to Example 339 for raw material	904.4[M+1]	342	 7-Bromo-4,5-dihydrotetrazolo[1,5-a]quinoline as raw material	905.4[M+1]
343	 8-Bromo-3,4-dihydro-1H-[1,4]oxaazino[4,3-a]indole as raw material	906.4[M+1]	344	 8-Bromo-3,4-dihydro-2H-benzo[4,5]imidazo[2,1-b][1,3]oxazine as raw material	907.4[M+1]
345	 5-Bromo-4-fluoro-1-cyclopropyl-1H-indazole and intermediate E1 as raw materials	935.4[M+1]	346	 9-Bromo-2,3,6,7-tetrahydro-1H,5Hpyrido[3,2,1-ij]quinoline-5-one and intermediate E1	946.4[M+1]

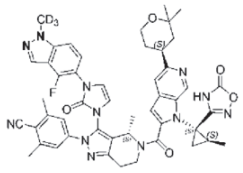
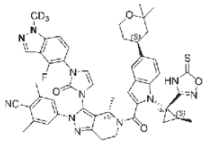
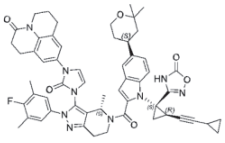
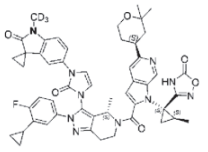
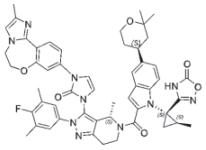
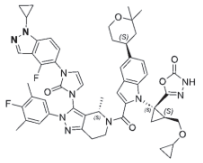
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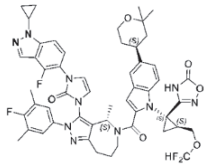
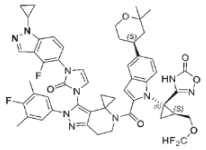
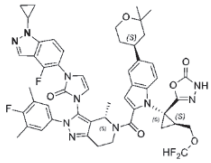
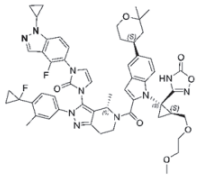
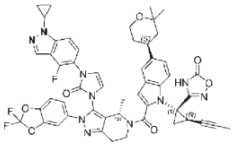
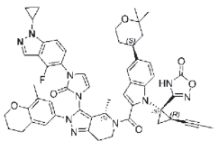
Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
347	 5-Bromo-1-methyl-2,3,5,6-tetrahydrospiroindoline-3,4-pyran-2-one as raw material	950.4 [M+1]	348	 5-Bromo-1-methylspirocyclopentane-1,3-indoline-2-one as raw material	934.4 [M+1]

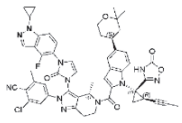
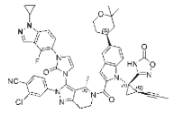
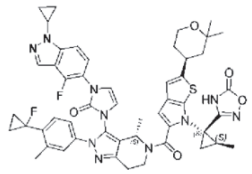
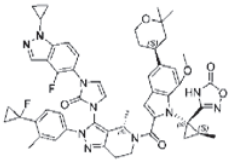
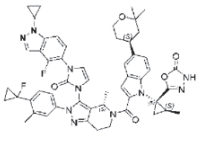
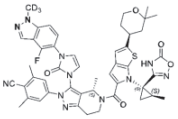
349	 5-Bromo-1-methyl-4,5-dihydro-2H-spirofuran-3,3-indoline-2-one as raw material	936.4 [M+1]	351		923.4 [M+1]
350	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole and tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-thio-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate as raw materials	925.3 [M+1]	352	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole and tert-butyl (S)-2-(3-cyclopropyl-4-fluorophenyl)-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 as raw materials	921.3 [M+1]
353	 1-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid and 175c as raw materials	937.4 [M+1]	354	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one and tert-butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-thio-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate as raw materials	936.4 [M+1]
355	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one and tert-butyl (S)-2-(3-cyclopropyl-4-fluorophenyl)-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 as raw materials	932.4 [M+1]	356	 7-Bromo-3,3a-dihydro-5H-benzo[d]pyrrolo[2,1-b][1,3]oxazine-1(2H)-one and (S)-1-(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 as raw materials	

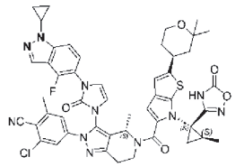
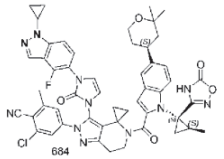
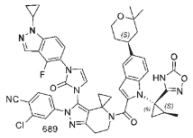
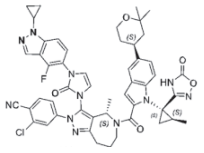
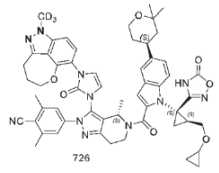
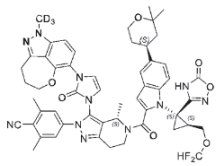
357	 (S)-9-(3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-thioxy-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H, 5H-pyrido[3,2,1-ij]quinoline-5-one and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((S)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)spiro[2.2]pentan-1-yl)-1H-indole-2-carboxylic acid as raw materials	948.4 [M+1]	358	 (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 1-((1S,2S)-2-((difluoromethoxy)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 as raw materials	1002.3 [M+1]
359	 (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-thioxy2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H, 5H-pyrido[3,2,1-ij]quinoline-5-one and 1-((1S,2S)-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 as raw materials	992.4 [M+1]	360	 (S)-9-(3-(2-(3-cyclopropyl-4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-thio-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H, 5H-pyrido[3,2,1-ij]quinoline-5-one and (S)-7-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-3-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)indolizine-2-carboxylic acid as raw materials	934.3 [M+1]
361	 (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)	922.3 [M+1]	363	 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-indazole-2-carboxylic acid and (S)-8-fluoro-9-	958.3 [M+1]

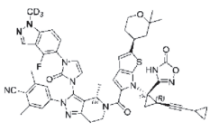
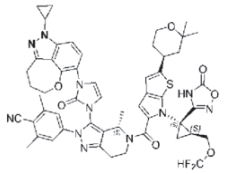
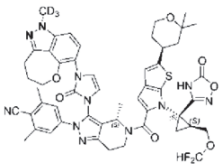
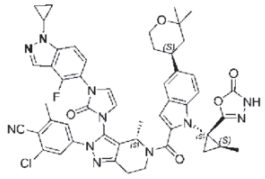
	-2,3,6,7-tetrahydro-1H, 5H-pyrido [3,2,1-ij]quinoline-5-one and (S)-7-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-3-(1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)indolizine-2-carboxylic acid as raw materials			(3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one as raw materials	
362	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one as raw material	936.4 [M+H]+	364	 Methyl 5-bromo-1H-benzo[d]imidazole-2-carboxylate as raw material, following Example intermediate F	910.4 [M+H]+
365	 Intermediate G as raw material	922.4 [M+1]	366	 Intermediate G as raw material	922.4 [M+1]
367	 Intermediate G as raw material	933.4 [M+1]	368		909.4 [M+1]
369		909.4 [M+1]	370		908.4 [M+1]
371	 tert-Butyl (S)-2-(4-fluoro-3,5-dimethylphenyl)	944.4 [M+1]	375	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole,	921.4 [M+1]

	-4-methyl-3-(2-carbonyl-3-(3-carbonyl-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)-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-((1S,2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indole-2-carboxylic acid as raw materials			tert-butyl (S)-2-(3-cyclopropyl-4-fluorophenyl)-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-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)cyclopropyl)-1H-indole-2-carboxylic acid as raw materials	
373	 5-Bromo-4fluoro-1-(methyl-d3)-1H-indazole, intermediate G and intermediate F as raw materials	894.4 [M+1]	374	 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 as raw material, following Example 373	909.4 [M+1]
372	 1-((1S,2R)-2-(cyclopropylethynyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indazole-2-carboxylic acid as raw material	970.4 [M+1]	376	 Intermediate F as raw material, following synthesis method in Example 375	922.4 [M+1]
377	 9-Bromo-2-methyl-5,6-dihydrobenzo[f]imidazo[1,2-d][1,4]oxaazepine as raw material	933.4 [M+1]	378		965.4 [M+1]

379	 (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-2,4,5,6,7,8-hexahydropyrazolo[4,3-c]azepin-3-yl)-1,3-dihydro-2H-imidazole-2-one and 1-((1S,2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran4yl)-1H-indole-2-carboxylic acid as raw materials	989.4 [M+1]	380	 1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2'-(4-fluoro-3,5-dimethylphenyl)-2',5',6',7'-tetrahydrospiro[cyclopropane-1,4'-pyrazolo[4,3-c]pyridin]-3'-yl)-1,3-dihydro-2H-imidazole-2-one and 1-((1S,2S)-2-((difluoromethoxy)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 as raw materials	987.4 [M+1]
381	 (S)-1-(1-cyclopropyl4fluoro-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 and 1-((1S,2S)-2-((difluoromethoxy)methyl-carbonyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran4yl)-1H-indole-2-carboxylic acid as raw materials	975.4 [M+1]	382	 (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-((2-methoxyethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indole-2-carboxylic acid as raw materials	1009.4 [M+H]+
383	 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indole-2-carboxylic acid and (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-	967.3 [M+H]+	384	 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indole-2-carboxylic acid and 1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(8-methylchroman-6-yl)-4,5,6,7-tetrahydro	957.4 [M+H]+

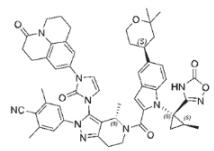
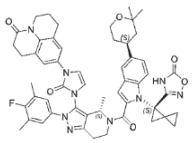
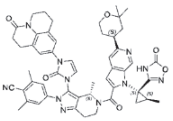
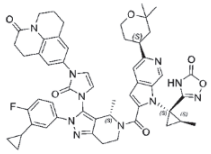
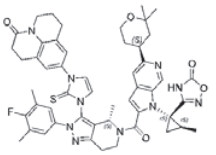
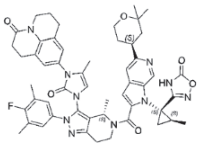
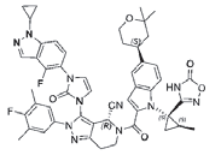
	(2,2-difluorobenzo[d][1,3]dioxazol-5-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one as raw materials			-2H-pyrido[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one as raw materials	
385	 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indole-2-carboxylic acid and (S)-2-chloro-4-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)-6-methylbenzonitrile as raw materials	960.3 [M+H]+	386	 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2R)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)-2-(prop-1-yn-1-yl)cyclopropyl)-1H-indazole2-carboxylic acid and (S)-2-chloro-4-(3-(3-(1-cyclopropyl4fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile as raw materials	946.3 [M+H]+
387	 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid and (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one as raw materials	941.3 [M+H]+	388	 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-7-methoxy-1-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-1H-indazole-2-carboxylic acid and (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one as raw materials	965.4 [M+H]+
389	 (S)-1-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-3-(2-(4-(1-fluorocyclopropyl)-3-methylphenyl)-4-methyl-4,5,6,7-tetrahydro	935.4 [M+H]+	395	 (S)-4-(3-(3-(4-fluoro-1-(methyl-d3)-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-	899.3 [M+1]

	-2H-pyrazolo[4,3-c]pyridin-3-yl)-1,3-dihydro-2H-imidazole-2-one and 5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)cyclopropyl)-1H-indole-2-carboxylic acid as raw materials			1H-imidazol-1-yl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)-2,6-dimethylbenzonitrile and 2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid as raw materials	
390		942.3 [M+1]	391		948.3 [M+1]
394	 tert-Butyl 8-cyano-7-carbonyl-4-azaspiro[2.5]octane-4-carboxylate and 4-bromo-2-chlorobenzonitrile as raw materials, following intermediate G and Example 25	934.3 [M+1]	393	 tert-Butyl (2S)-3-cyano-2-methyl-4-carbonylazepane-1-carboxylate and 4-bromo-2-chlorobenzonitrile as raw materials, following intermediate G and Example 25	936.3 [M+1]
396	 (S)-2,6-dimethyl-4-(4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile and 1-((1S,2S)-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 as raw materials	987.4 [M+1]	397	 (S)-2,6-dimethyl-4-(4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-2-yl)benzonitrile and 1-((1S,2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran 4yl)-1H-indole-2-carboxylic acid as raw materials	997.4 [M+1]

398	 tert-Butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-3-(3-(4-fluoro-1-(methyl-d3)-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 6-((1S,2R)-2-(cyclopropylethyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid as raw materials	949.3 [M+1]	399	 tert-Butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-3-(3-(2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4-methyl-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 6-((1S,2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid as raw materials	1026.3 [M+1]
400	 tert-Butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate and 6-((1S,2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-6H-thieno[2,3-b]pyrrole-5-carboxylic acid as raw materials	1003.3 [M+1]	392		936.3 [M+1]

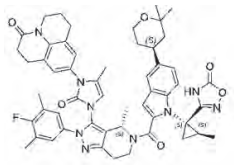
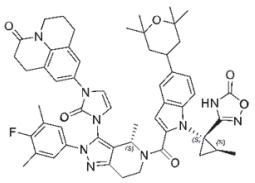
The following examples can be prepared following Example 29.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)

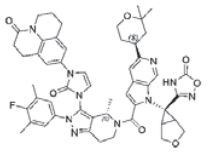
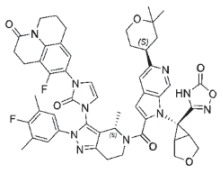
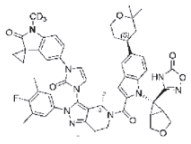
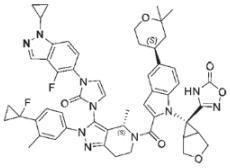
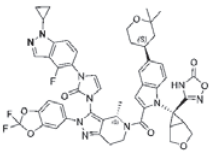
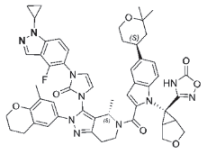
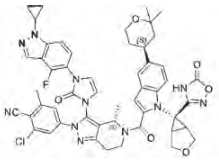
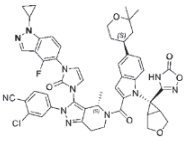
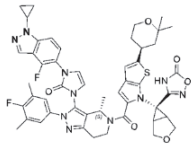
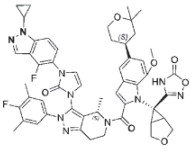
401	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one as raw material	927.4 [M+1]	402	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one as raw material	932.4[M+1]
403	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one and tert-butyl (S)-2-(4-cyano-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate as raw materials	928.3[M+H]+	404	 The same raw material as Example 403	933.3[M+H]+
405	 The same raw material as Example 403	937.3[M+H]+	406	 The same raw material as Example 403	935.3[M+H]+
407	 (R)-2-(4-fluoro-3,5-dimethylphenyl)-3-(2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-4-carbonitrile as raw material	920.4[M+1]			

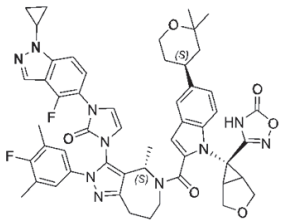
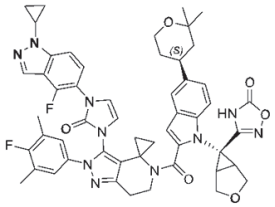
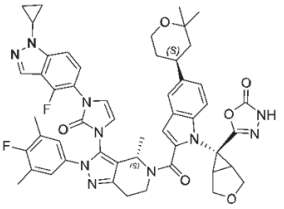
The following examples can be prepared following Example 34.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)

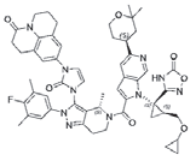
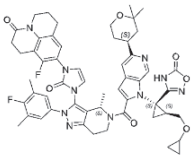
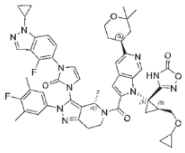
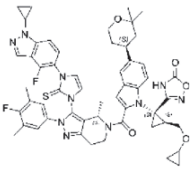
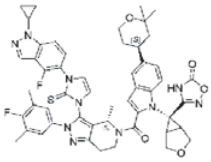
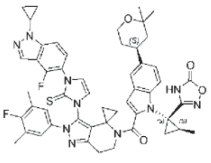
408		934.4 [M+1]	409	 1-((1S,2S)-2-methyl-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxylic acid as raw material	948.4 [M+1]

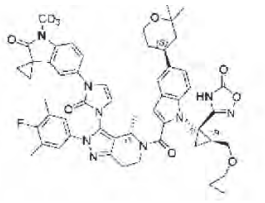
The following examples can be prepared following Example 62.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
410	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one as raw material	949.4 [M+H]+	411		967.4 [M+1]
412	 5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one as raw material	937.4 [M+1]	413		963.4 [M+1]
414		971.3 [M+1]	415		961.4 [M+1]
416		964.3 [M+1]	417		950.3 [M+1]
418		943.3 [M+1]	419		967.4 [M+1]

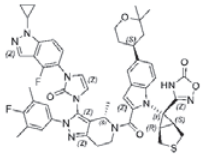
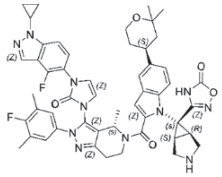
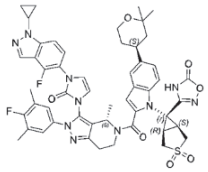
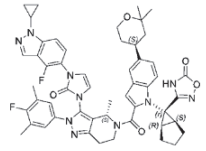
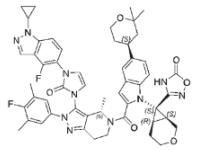
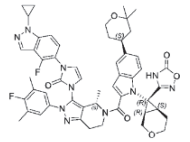
420		951.4 [M+1]	421		949.4 [M+1]
422		937.4 [M+1]			

The following examples can be prepared following Example 63.

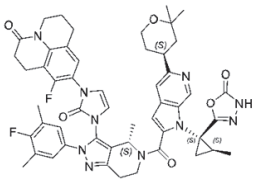
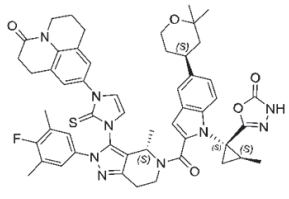
Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
423	 9-Bromo-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinoline-5-one as raw material	977.4[M+H]+	424		995.4[M+1]
425	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	966.4[M+1]	426	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	981.4[M+1]
427	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	953.4[M+1]	428	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	937.4[M+1]

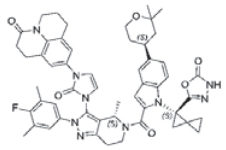
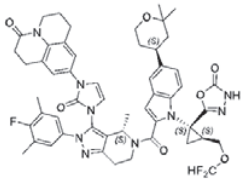
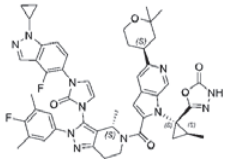
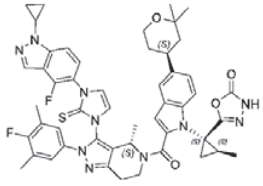
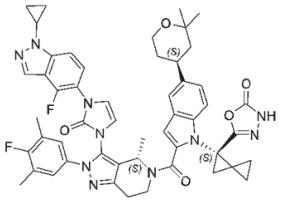
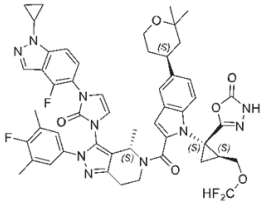
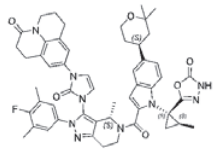
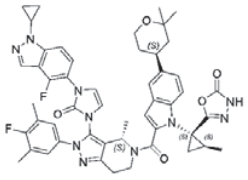
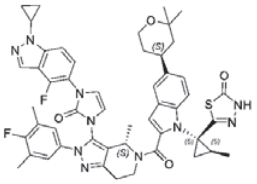
429	 5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one as raw material	965.4[M+1]			

The following examples can be prepared following Example 65 or 65-1.

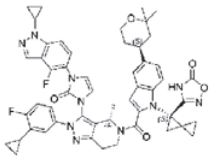
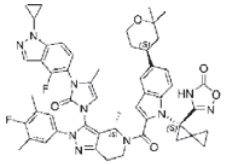
Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
430	 (3R,4S)-tetrahydrothiophene-3,4-diol as raw material	953.4 [M+1]	431	 (3R,4R)-1-(tertbutoxycarbonyl)-3,4-dihydroxylpyrrolidine as raw material	936.4 [M+1]
432		985.4 [M+1]	433		935.4 [M+1]
434		951.4 [M+1]	435		951.4 [M+1]

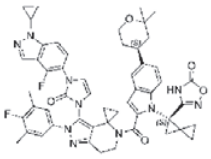
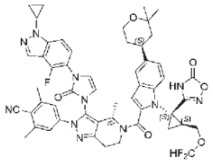
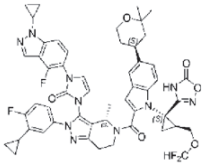
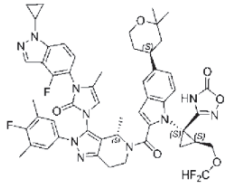
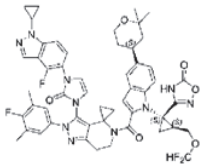
The following examples can be prepared following Example 82.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
436		939.4 [M+1]	437		936.4[M+1]

438		932.4 [M+1]	439		986.4[M+1]
440		910.4 [M+1]	441		925.4[M+1]
442		921.4 [M+1]	443		975.4[M+1]
444		920.4 [M+1]	445		909.4[M+1]
446		925.4 [M+1]			

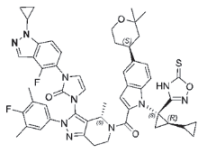
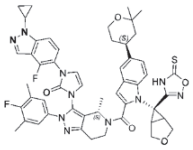
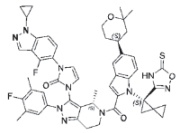
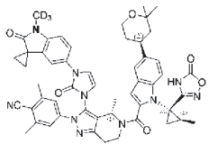
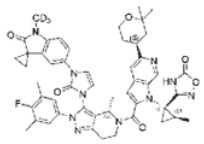
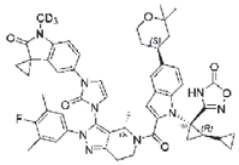
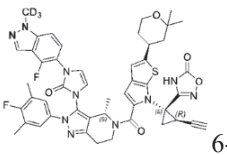
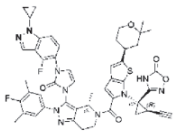
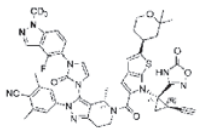
The following examples can be prepared following Example 126.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
447	 tert-Butyl 2-(3-cyclopropyl-4-fluorophenyl)-3-(2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2,4,6,7-tetrahydro-5H-pyrazolo[4,3-c]pyridine-5-carboxylate as raw material	933.4 [M+1]	448	 (S)-1-(2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridin-3-yl)-4-methyl-1,3-dihydro-2H-imidazole-2-one as raw material	935.4 [M+1]

449	 1-(2'-(4-fluoro-3,5-dimethylphenyl)-2',5',6',7-tetrahydrospiro[cyclopropane-1,4'-pyrazolo[4,3-c]pyridin]-3'-yl)-1,3-dihydro-2H-imidazole-2-one as raw material	933.4 [M+1]	450	 1-((1S,2S)-2-((difluoromethoxy)methyl)-1-(5-carbonyl-4,5-dihydro-1,2,4-oxadiazol-3-yl)cyclopropyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-indazole-2-carboxylic acid as raw material	982.4 [M+1]
451	 1-((1S,2S)-2-((difluoromethoxy)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 as raw material	987.4 [M+1]	452	 1-((1S,2S)-2-((difluoromethoxy)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 as raw material	989.4 [M+1]
453	 1-((1S,2S)-2-((difluoromethoxy)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 as raw material	987.4 [M+1]			

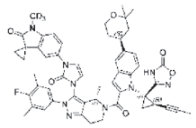
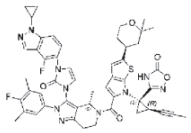
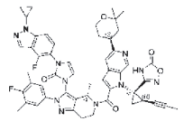
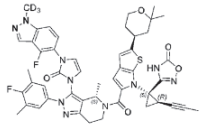
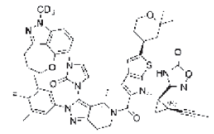
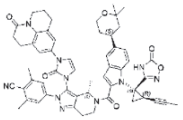
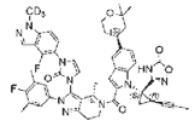
The following examples can be prepared following Example 135.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)

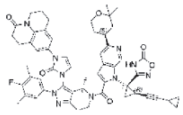
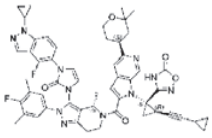
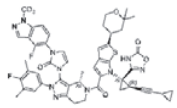
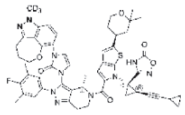
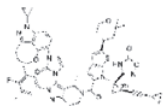
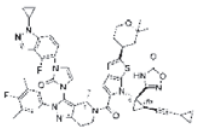
454		951.4 [M+H]+	455	 3,4-Dihydroxyltetrahydrofuran as raw material	953.4 [M+H]+
458	 1-(Hydroxymethyl)cyclopropane-1-ol as raw material	937.4 [M+H]+	457	 5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one and intermediate G as raw materials	916.4 [M+1]
458	 5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one and intermediate F as raw materials	910.4 [M+1]	459	 5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one as raw material	935.4 [M+1]
460	 6-(Cyanomethyl)-2-[2,2-dimethyltetrahydropyran-4-yl]-*N*-methyl-*N*-phenylthieno[2,3-*b*]pyrrole-5-carboxamide as raw material	902.3 [M+1]	461	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	925.3 [M+1]
462	 5-Bromo-4-fluoro-1-(methyl-d3)-1H-indazole as raw material	909.3 [M+1]			

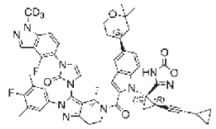
The following examples can be prepared following Example 144.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)

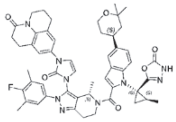
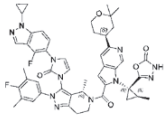
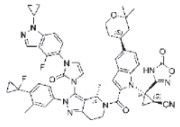
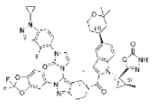
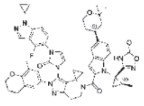
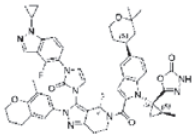
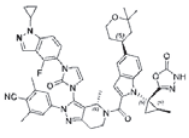
463	 5'-Bromo-1'-(methyl-d3)spiro[cycloprop-1,3'-dihydroindole]-2'-one as raw material	933.4[M + 1]	468	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	939.3[M +1]
465	 3-((1S,2R)-1-(2-((S)-3-(3-(1-cyclopropyl-4-fluoro-1H-indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one as raw material	934.4[M + 1]	466	 3-((1S,2R)-1-(2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-5-((S)-3-(3-(4-fluoro-1-(methyl-d3)-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-b]pyridine-5-carbonyl)-6H-thieno[2,3-b]pyrrole-6-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one as raw material	916.3[M +1]
467	 3-((1S,2R)-1-(2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-5-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-6H-thieno[2,3-b]pyrrol-6-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one as raw material	954.4 [M+H]	464	 3-((1S,2R)-1-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-((S)2(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-3-(3-carbonyl-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-1H-pyrrolo[2,3-c]pyridin-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazol-5(4H)-one as raw material	951.4[M +1]
469		910.4 [M+1]			

The following examples can be prepared following Example 145.

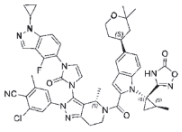
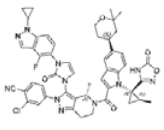
Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
470	 3-((1S,2R)-1-(5-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(2-carbonyl-3-(3-carbonyl-2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-1H-pyrrolo[2,3-c]pyridin-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazol-5(4H)-one as raw material	971.4[M+1]	471	 3-((1S,2R)-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-pyrrolo[2,3-c]pyridin-1-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one as raw material	960.4[M+1]
472	 3-((1S,2R)-1-(2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-5-((S)-3-(3-(4-fluoro-1-(methyl-d3)-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)-6H-thieno[2,3-b]pyrrol-6-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one as raw material	942.3[M+1]	473	 3-((1S,2R)-1-(2-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)-5-((S)-2-(4-fluoro-3,5-dimethylphenyl)-4-methyl-3-(3-(2-(methyl-d3)-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazol-5-yl)-2-carbonyl-2,3-dihydro-1H-imidazol-1-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-5-carbonyl)-6H-thieno[2,3-b]pyrrol-6-yl)-2-ethynylcyclopropyl)-1,2,4-oxadiazole-5(4H)-one as raw material	980.4[M+H]
474	 5-Bromo-2-cyclopropyl-2,7,8,9-tetrahydrooxepino[4,3,2-cd]indazole as raw material	1003.4[M+1]	475	 5-Bromo-1-cyclopropyl-4-fluoro-1H-indazole as raw material	965.3[M+1]

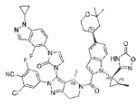
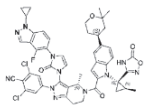
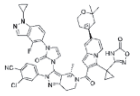
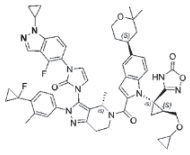
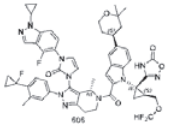
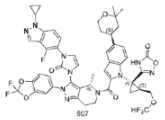
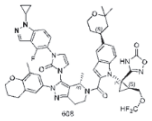
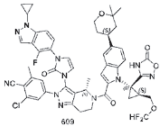
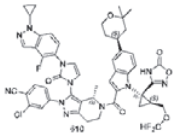
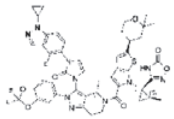
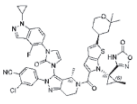
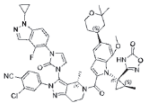
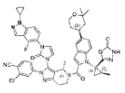
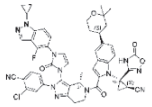
476		936.4 [M+1]			

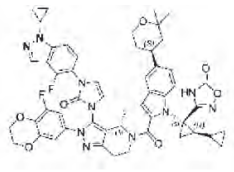
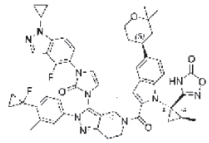
The following examples can be prepared following Example 368.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
477		920.4[M+1]	478		910.4 [M+1]
483	 (4-(1-Fluorocyclopropyl)-3-methylphenyl)hydrazine as raw material	946.4[M+1]	480	 (2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine as raw material	943.3 [M+1]
481		945.4[M+1]	482		933.4 [M+1]
479		916.4[M+1]			

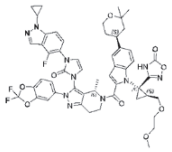
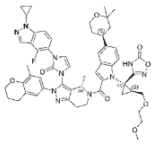
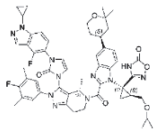
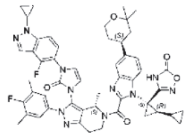
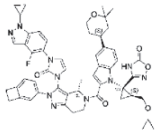
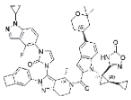
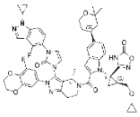
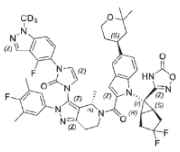
The following examples can be prepared following Example 182.

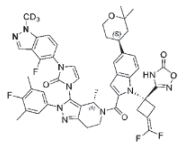
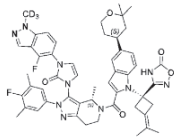
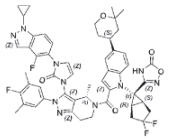
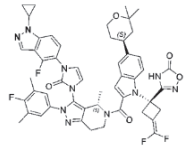
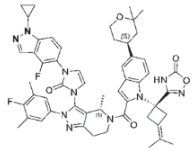
Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
484	 4-Bromo-2-chloro-6-methylbenzonitrile as raw material	936.3 [M+1]	485	 4-Bromo-2-chlorobenzonitrile as raw material	922.3[M+1]

486	 4-Bromo-2-chloro-6-fluorobenzonitrile as raw material	940.3 [M+1]	487	 4-Bromo-2,6-dichlorobenzonitrile as raw material	956.3[M+1]
488	 4-Bromo-2-chlorobenzonitrile as raw material	908.3 [M+1]	489		991.4[M+1]
490	 5-Bromo-2-(1-fluorocyclopropyl)-1,3-dimethylbenzene as raw material	1001.4 [M+1]	491	 5-Bromo-2,2-difluorobenzo[d][1,3]dioxazole as raw material	1009.3 [M+1]
492	 6-Bromo--8-methylchromane as raw material	999.4 [M+1]	493	 4-Bromo-2-chloro6methylbenzonitrile as raw material	1002.3 [M+1]
494	 4-Bromo-2-chlorobenzonitrile as raw material	988.3 [M+1]	495	 (2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine as raw material	949.3[M+1]
496	 4-Bromo-2-chlorobenzonitrile as raw material	928.2 [M+1]	497	 4-Bromo-2-chlorobenzonitrile as raw material	952.3[M+1]
498	 4-Bromo-2-chlorobenzonitrile as raw material	922.3 [M+1]	499		933.3[M+1]

500	 (8-Fluoro-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)hydrazine as raw material	965.4 [M+1]	501	 (4-(1-Fluorocyclopropyl)-3-methylphenyl)hydrazine as raw material	

The following examples can be prepared following Example 189.

Example	Structural formula of compound	MS m/z (ESI)	Example	Structural formula of compound	MS m/z (ESI)
502	 (2,2-Difluorobenzo[d][1,3]dioxazol-5-yl)hydrazine as raw material, following intermediate G	1017.3 [M+H]+	503	 (8-Methylchroman-6-yl)hydrazine as raw material, following intermediate G	1007.4 [M+H] +
504	 (4-Fluoro-3,5-dimethylphenyl)hydrazine as raw material	966.4 [M+1]	505	 (4-Fluoro-3,5-dimethylphenyl)hydrazine as raw material	936.4 [M+1]
506	 Bicyclo[4.2.0]oct-1,3,5-trien-3-yl hydrazine as raw material	945.4[M + 1]	507	 Bicyclo[4.2.0]oct-1,3,5-trien-3-yl hydrazine as raw material	915.4 [M+1]
508	 (8-Fluoro-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)hydrazine as raw material	995.4[M + 1]	509	 cis-4,4-difluorocyclopentane-1,2-diol as raw material	948.4 [M+1]

510	 5-(Difluoromethylene)-2,2-dimethyl-1,3-dioxane as raw material	934.4[M + 1]	511	 2-isopropylidenepropane-1,3-diol as raw material	926.4 [M+1]
512	 cis-4,4-difluorocyclopentane-1,2-diol as raw material	971.4[M + 1]	513	 5-(Difluoromethylene)-2,2-dimethyl-1,3-dioxane as raw material	957.4 [M+1]
514	 2-isopropylidenepropane-1,3-diol as raw material	949.4[M + 1]			

Biological test and evaluation

The present disclosure will be further described and explained below in conjunction with test examples, but these examples are not meant to limit the scope of the present disclosure.

I. Determination of ability of compounds of the present disclosure to stimulate cAMP production in cell lines stably transfected with human GLP1 receptors

1. Experimental objective:

The objective of the test example was to test the ability of compounds to activate human GLP-1 receptor on the cell surface. The ability of the compounds to activate human GLP-1 receptors was characterized by the EC_{50} for the agonist-stimulated cAMP production.

In this experiment, compounds and cells were co-incubated for 30 minutes.

2. Experimental reagents and instruments

2.1 Experimental instruments:

Microplate reader (BioTek Synergy H1)

Pipettor (Eppendorf & Rainin)

2.2 Experimental reagents

DMEM/F12, casein, 384-well plate, IBMX, Cisbio cAMP-Gs Dynamic kit

3. Experimental method:

The cryopreserved cell line CHO-K1/GLP-1R/CRE-luc stably transfected with human GLP1 receptors was taken from a liquid nitrogen tank, quickly thawed in a water bath at 37°C, and resuspended in a DMEM/F12 medium. After centrifugation, the cells were washed once and resuspended in a DMEM/F12 medium containing 0.1% casein as a test buffer. The cell density was adjusted with the test buffer after centrifugation, and the cells were plated in a 384-well plate at a density of 1500 cells/5 μL/well, and 2.5 μL of an IBMX working solution prepared with the buffer (with the final concentration of IBMX being 0.5 mM) and 2.5 μL of the compound sample diluted in gradients (starting from 1000 to 333.33 nM, 3-fold dilution and 12 concentrations) were then added to each well.

Centrifugation was performed at 1000 rpm for 1 minute, and the plate was left to stand and incubated at 37°C for 0.5 hour, Detection was performed using the Cisbio cAMP-Gs Dynamic kit, that is, cAMP-d2 and Anti-cAMP-Eu3+-Cryptate were diluted 18-fold and 20-fold respectively with cAMP Lysis & Detection Buffer, and separately mixed uniformly, 5 μL of diluted cAMP-d2 solution was added to each well, centrifugation was performed at 1000 rpm for 1 minute, shaking was performed for 30 seconds for uniform mixing, 5 μL of diluted Anti-cAMP-Eu3+-Cryptate solution was then added, centrifugation was performed at 1000 rpm for 1 minute, and incubation was performed at room temperature in the dark for 1 hour. The HTRF signal was read by using Biotek Synergy H1 microplate reader with an excitation wavelength of 320 nm and emission wavelengths of 620 nm and 665 nm.

4. Experimental data processing method:

The signal ratio (665 nm/620 nm*10,000) was calculated, and the nonlinear fitting of the signal ratio and sample concentration was performed using a four-parameter equation in GraphPad Prism 10 to obtain the EC_{50} value.

5. Experimental conclusion:

According to the above scheme, the compounds of the present disclosure exhibited EC_{50} values for cAMP production as shown in Table 1 in the experiment where they stimulated cAMP production in cell lines stably transfected with hGLP1R for 0.5 hour.

Table 1 EC_{50} values for cAMP production in cell lines stably transfected with human GLP1 receptors stimulated by the example compounds of the present disclosure

Example	EC_{50} (nM)	Example	EC_{50} (nM)
1	0.37	67	1.4
7	0.30	144	1.0
8	0.51	162	0.25
15	0.32	285	0.71
19	0.88	287	0.9
23	0.14	339	0.51
41	0.9	342	1.5
61	1.39		

The experimental results showed that the example compounds of the present disclosure showed good biological activity in the experiment where they stimulated cAMP production in cell lines stably transfected with human GLP1 receptors.

II. Determination of ability of compounds of the present disclosure to stimulate cAMP production in cell lines stably transfected with human GLP1 receptors

1. Experimental objective: The objective of the test example was to test the ability of compounds to activate human GLP-1 receptor on the cell surface. The ability of the compounds to activate human GLP-1 receptors was characterized by the EC_{50} for the agonist-stimulated cAMP production.

In this experiment, compounds and cells were co-incubated for 2 hours.

2. Experimental reagents and instruments

2.1 Experimental instruments:

microplate reader and pipettor

2.2 Experimental reagents

DMEM/F12 medium, casein, 384-well plate, IBMX, Cisbio cAMP-Gs Dynamic kit

3. Experimental method:

The cryopreserved cell line CHO-K1/GLP-1R/CRE-luc stably transfected with human GLP1 receptors was taken from a liquid nitrogen tank, quickly thawed in a water bath at 37°C, and resuspended in a DMEM/F12 medium. After centrifugation, the cells were washed once and resuspended in a DMEM/F12 medium containing 0.1% casein as a test buffer. The cell density was adjusted with the test buffer after centrifugation, and the cells were plated in a 384-well plate at a density of 1500 cells/5 μL/well, and 2.5 μL of an IBMX working solution prepared with the buffer (with the final concentration of IBMX being 0.5 mM) and 2.5 μL of the compound sample diluted in gradients (starting from 1000 to 333.33 nM, 3-fold dilution and 12 concentrations) were then added to each well. Centrifugation was performed at 1000 rpm for 1 minute, and the plate was left to stand and incubated at 37°C for 2 hours. Detection was performed using the Cisbio cAMP-Gs Dynamic kit, that is,

cAMP-d2 and Anti-cAMP-Eu^{3+}-Cryptate were diluted 18-fold and 20-fold respectively with cAMP Lysis&Detection Buffer, and separately mixed uniformly, 5 μL of diluted cAMP-d2 solution was added to each well, centrifugation was performed at 1000 rpm for 1 minute, shaking was performed for 30 seconds for uniform mixing, 5 μL of diluted Anti-cAMP-Eu3 $^{+}$-Cryptate solution was then added, centrifugation was performed at 1000 rpm for 1 minute, and incubation was performed at room temperature in the dark for 1 hour. The HTRF signal was read by using Biotek Synergy H1 microplate reader with an excitation wavelength of 320 nm and emission wavelengths of 620 nm and 665 nm.

4. Experimental data processing method:

The signal ratio (665 nm/620 nm*10,000) was calculated, and the nonlinear fitting of the signal ratio and sample concentration was performed using a four-parameter equation in GraphPad Prism 10 to obtain the EC_{50} value.

5. Experimental conclusion:

According to the above scheme, the compounds of the present disclosure exhibited EC_{50} values for cAMP production as shown in Table 2 in the experiment where they stimulated cAMP production in cell lines stably transfected with hGLP1R for 2 hour.

Table 2 EC_{50} values for cAMP production in cell lines stably transfected with human GLP1 receptors stimulated by the example compounds of the present disclosure

Example	EC_{50} (nM)	Example	EC_{50} (nM)
34	0.11	174	0.15
43	0.06	187	0.08
49	0.032	190	0.04
50	0.053	194	0.009
65-1	0.06	195	0.035
67	0.024	200	0.09
68	0.016	282	0.074
143	0.013	285	0.09
144	0.05	338	0.023
162	0.10		

III. Effect of single administration of compounds of the present disclosure on intraperitoneal glucose tolerance in GLP-1R humanized mice

1. Experimental objective:

The objective was to evaluate the effect of a single administration of the compounds of the present disclosure on blood glucose changes in an intraperitoneal glucose tolerance test (*ip*GTT) in GLP-1R humanized C57BL/6 mice.

2. Experimental materials:

C57BL/6_*hGLP-1R*, male, 5-8 weeks; Ultra-clean workbench; Electronic balance; Active blood glucose monitoring meter; Glucose.

3. Experimental operations and data processing:

3.1. One day before the experiment, the animals were randomly divided into groups according to their body weights, with 5 animals per group. All animals underwent overnight fasting with food withdrawn for at least 16 h before administration.

3.2. A 0.2 g/mL glucose solution was prepared with pure water and filtered through a 0.22 μm filter membrane for later use.

3.3 On the day of the test, before administration, blood glucose levels of each animal were sequentially measured by the tail-clipping method and recorded as baseline values.

The method for testing blood glucose involved: placing the mice in a restrainer, disinfecting the tail tip with alcohol cotton balls, cutting a small portion from the tail tip with scissors, discarding the first drop of blood, and taking the second drop of blood to a prepared blood glucose test strip to detect the blood glucose level.

3.4. The animals were administered according to their body weights, and the administration time for each animal was recorded. Blood glucose levels of each animal were sequentially measured 1 h after administration and recorded as 0 min blood glucose levels.

3.5. Subsequently, depending on the body weight on that day, either pure water or glucose solution (volume: 10 mL/kg; glucose dose: 2 g/kg) was immediately administered via intraperitoneal injection.

3.6. Blood glucose levels of each mouse were measured at 15, 30, 60, 90, and 120 min after the injection of pure water or glucose solution, and the time points and the corresponding data were recorded.

3.7. After the test was completed, all animals were allowed to resume feeding.

3.8. Data processing:

The blood glucose (BG)-time curve was plotted and the area under the blood glucose-time curve was calculated according to the formula:

AUC (mmol/L.hr) = (BG0 + BG15) × 0.25/2 + (BG15 + BG30) × 0.25/2 + (BG30 + BG60) × 0.5/2 + (BG60 + BG90) × 0.5/2 + (BG90 + BG120) × 0.5/2.

Note: BG0, BG15, BG30, BG60, BG90 and BG120 represent the blood glucose levels before glucose administration (0 min) and at15, 30, 60, 90 and 120 min after glucose administration, respectively.

The blood glucose decline rate at each time point and AUC was calculated on the basis of the mean blood glucose level and blood glucose AUC at each time point according to the formula: blood glucose decline rate = (blood glucose of model control group/AUC - blood glucose of administration group/AUC)/blood glucose of model control group/AUC × 100%.

The example compounds of the present disclosure could effectively reduce blood glucose levels in mice with a blood glucose decline rate of greater than 20%, preferably, the compounds achieved a blood glucose decline rate of greater than 40%, and more preferably, the compounds achieved a blood glucose decline rate of greater than 60%.

IV. Effect of long-term administration of compounds of the present disclosure on body weight and food intake in GLP-1R humanized mice fed with CDAHFD high-fat diet

1. Experimental objective:

The test objective was to evaluate the effect of the long-term administration of the compounds of the present disclosure on the body weight and food intake in GLP-1R humanized C57BL/6 mice fed with CDAHFD high-fat diet.

2. Experimental reagents and instruments

C57BL/6_*hGLP-1R*, male, 5-8 weeks, purchased from Biocytogen Pharmaceuticals (Beijing) Co., Ltd.

Choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD), purchased from Shanghai Bopai Biotechnology Co., Ltd. (Research diet-A06071302)

Ultra-clean workbench (CJ-2F, Suzhou Fengshi Experimental Animal Equipment Co., Ltd.)

Electronic balance (BSA2202S-CW, Sartorius)

3. Experimental method

3.1 On the starting day of high-fat diet feeding, C57BL/6 mice were randomly divided into two groups according to their body weights, wherein the first group was used as a Blank group (7 mice) and received normal control diet, and the remaining animals were fed with the high-fat diet until the end of the experiment to establish a model group.

3.2 On week 4 of CDAHFD feeding, the animals in the model group were randomly divided into groups (7 mice per group) according to their body weights, wherein the first group was used as Vehicle group administered with a vehicle (Vehicle: 10% PEG400/10% PG/80% glycine buffer (100 mM glycine, 26 mM NaOH, pH 9) buffer); and the remaining groups were used as administration groups. The administration scheme involved: orally administering the corresponding compounds once daily for an administration period of 21 days (administration dose: 0.3 mg/kg, 1mg/kg, 3 mg/kg and 10 mg/kg; administration volume: 10 mL/kg). The blank group continued to be fed with normal diet and was orally administered with the vehicle once daily.

3.3 The day of the administration was defined as Day 0.

3.4 At each administration, the animals were weighed and the data were recorded. Oral administration was performed at an administration volume of 10 mL/kg according to their body weights.

3.5 Commencing on day 0 of the experiment, food intake measurement was conducted every three days for the mice in all groups. Specifically, after each weighing and administration, the feed was changed, and the addition amount and the remaining amount were recorded.

3.6 On Day 21 (last day), all mice were euthanized in turn according to the grouping order. Plasma and tissues (liver, kidney, ileum, pancreas and brain) were taken for PK detection, and serum was taken for blood biochemical detection (ALT, AST, TG, TC, LDL-C).

4. Experimental data processing and statistical analysis

The body weight and body weight change rate of mice after administration were summarized and statistically analyzed. The body weight change rate was calculated according to the formula: (BWt-BW0)/BW0 × 100%. BWt denotes the body weight of mice on day t of the experiment, and BW0 denotes the body weight of mice on day 0 of the experiment.

The food intake was calculated according to the formula: (addition amount (g) - remaining amount (g)) /animal number in each cage, and the cumulative food intake was the aggregated daily food intake per animal during administration.

Experimental data was analyzed and plotted with GraphPad Prism software. The comparison between the two groups was performed using a t-test method. The comparison among three or more groups was performed using a one-way ANOVA method. $p < 0.05$ was defined as a statistically significant difference.

The experimental results were as shown in Table 3 below.

Table 3 Experiment of long-term administration of the compounds of the present disclosure on the body weight and food intake in GLP-1R humanized mice fed with CDAHFD high-fat diet

Example	Dose	Weight change (%)-D21
Example 67	3 mg/kg	-20.34%
Example 143	3 mg/kg	-19.43%
Example 144	0.3 mg/kg	-10.40%
	1 mg/kg	-14.70%

V. Pharmacokinetic evaluation test in mice

1. Study objective:

The objective was to study the pharmacokinetic behavior of the compounds of the present disclosure in Balb/c mice (plasma) as test animals after oral administration at a dose of 5 mg/kg and intravenous administration at a dose of 1 mg/kg.

2. Experimental scheme:

2.1 Experimental drugs:

The example compounds of the present disclosure, made in house.

2.2 Experimental animals:

3 Balb/c mice per group, male.

2.3 Formulation prescription:

Preparation of a drug for oral administration: 10% PEG400/10% PG/80% glycine buffer (100 mM glycine, 64 Mm NaOH, pH 10) buffer.

10 ml of PEG400, 10 ml of PG and 80 ml of glycine buffer (100 mM glycine, 64 Mm NaOH, pH = 9) were measured into a 100 ml volumetric flask, and the resulting mixture was vortexed, uniformly mixed, and sonicated to obtain a clear solution.

Single PK: The example compound was weighed and added into a 4 mL glass bottle, the solution was added, and the resulting mixture was sonicated for 10 min to obtain a colorless clear solution with a concentration of 0.5 mg/mL.

Cassette PK: 5 example compounds with similar weights were weighed and added into a 4 mL glass bottle, the solution was added, and the resulting mixture was sonicated for 10 min to obtain a colorless clear solution with a concentration of 0.5 mg/mL.

Preparation of a drug for intravenous administration: 5% DMSO + 10% Solutol HS15 + 85% PBS

The example compound was weighed; on the basis of the total administration volume, 5% of DMSO was added, and vortexed and sonicated for 2 min to achieve complete dissolution, 10% of Solutol HS15 was then added, and vortexed and sonicated for 2 min to achieve complete dissolution, and finally 85% of PBS was added, and vortexed and sonicated for 5 min; and the resulting mixture was filtered through a 0.22 μm filter membrane to obtain a colorless and transparent clear solution with a concentration of 0.2 mg/mL.

2.4 Administration:

After overnight fasting, 3 male Balb/c mice were orally administered (p.o.) with the solution, respectively, at a dose of 5 mg/kg and an administration volume of 10 mL/kg.

After overnight fasting, 3 male Balb/C mice were intravenously administered (I.V.) with the solution, respectively, at a dose of 1 mg/kg and an administration volume of 5 mL/kg.

2.5 Sample collection:

Blood collection: 0.04 mL of blood was collected from the orbit of mice before administration and at 0.083 (IV), 0.25, 0.5, 1, 2, 4, 6, 8 and 24 h after administration, placed in an EDTA-K_2 anticoagulation tube, and centrifuged at 6000 rpm at 4°C for 6 min to separate plasma which was stored at -80°C. The animals were fed 4 h after administration.

2.6 Sample treatment:

1) 160 μL of acetonitrile was added to 40 μL of the plasma sample for precipitation, and the resulting mixture was mixed and then centrifuged at 3500 × g for 5 to 20 minutes.

2) The treated supernatant solution was taken and subjected to LC/MS/MS to analyze the concentrations of the test compounds. LC/MS/MS analysis instrument: AB Sciex API 4000 Qtrap.

2.7 Liquid phase analysis:

- Liquid phase conditions: Shimadzu LC-20AD pump
- Chromatographic column: Agilent ZORBAX XDB-C18 (50 × 2.1 mm, 3.5 μm), mobile phase: liquid A: 0.1%

aqueous formic acid solution, liquid B: acetonitrile

- Flow rate: 0.4 mL/min
- Elution time: 0-4.0 min, the eluent was as follows:

Time/min	Liquid A	Liquid B
0.01	90%	10%
0.5	90%	10%
0.8	5%	95%
2.4	5%	95%
2.5	90%	10%
4.0	Stop	

3. Experimental results and analysis

The main pharmacokinetic parameters were calculated using WinNonlin 6.1. The results of pharmacokinetic experiments in mice were as shown in Table 4 below:

Table 4: Pharmacokinetic parameters of oral administration of compounds of the present disclosure in mice

Parameters	tmax (h)	Cmax (ng/mL)	AUC 0-t (ng/mL*h)	AUC 0-∞ (ng/mL*h)	t1/2 (h)	MRT 0-∞ (h)
Example 7	0.5	2970	10324	10768	1.6	2.8
Example 25	2.0	2057	30498	39006	10.7	15.2
Example 32	1.0	1044	8986	9322	5.3	6.7
Example 34*	1.0	1510	12052	13316	7.8	9.0
Example 35*	1.2	3073	32868	40998	10.3	13.9
Example 49*	1.0	2430	15698	16631	6.5	7.1
Example 65-1*	2.7	1220	10636	10946	4.8	6.5
Example 67*	4.0	1430	11219	12121	7.6	8.2
Example 143*	2.0	1204	12212	13260	6.9	9.0
Example 144*	3.0	2237	23506	35060	15.7	20.8
Example 194	2.7	1843	19136	32185	19.9	26.6
Example 282*	2.0	1510	15026	18163	9.7	13.0
Example 287*	1.0	5323	27885	27973	3.0	4.2

Note: * represents “single PK”

3.4 Experimental conclusion:

The experimental results showed that the example compounds of the present disclosure exhibited good metabolic properties, with good exposure (AUC) and maximum plasma concentration C_{max}.

VI. Pharmacokinetic determination in SD rats

1. Study objective:

The objective was to study the pharmacokinetic behavior of the following example compounds in SD rat (plasma) as test animals after oral administration at a dose of 5 mg/kg.

2. Experimental scheme

2.1 Experimental drugs:

The example compounds of the present disclosure, made in house.

2.2 Experimental animals:

3 SD rats per group, male.

2.3 Formulation prescription:

Preparation of a drug for oral administration: 10% PEG400/10% PG/80% glycine buffer (100 mM glycine, 64 Mm NaOH, pH 10) buffer.

10 ml of PEG400, 10 ml of PG and 80 ml of glycine buffer (100 mM glycine, 64 Mm NaOH, pH = 9) were measured into a 100 ml volumetric flask, and the resulting mixture was vortexed, uniformly mixed, and sonicated to obtain a clear solution.

The example compound was weighed and added into a 4 mL glass bottle, the solution was added, the PH was adjusted with 1 M NaOH until complete dissolution, the PH was then adjusted to 9.0-9.5 with 1 M HCl, the resulting mixture was sonicated for 10 min to obtain a colorless clear solution with a concentration of 0.5 mg/mL.

Preparation of a drug for intravenous administration: 5% DMSO + 10% Solutol HS15 + 85% PBS

The example compound was weighed; on the basis of the total administration volume, 5% of DMSO was added, and vortexed and sonicated for 2 min to achieve complete dissolution, 10% of Solutol HS15 was then added, and vortexed and sonicated for 2 min to achieve complete dissolution, and finally 85% of PBS was added, and vortexed and sonicated for 5 min; and the resulting mixture was filtered through a 0.22 μm filter membrane to obtain a colorless and transparent clear solution with a concentration of 0.2 mg/mL.

2.4 Administration:

After overnight fasting, 3 male rats were orally administered (p.o.) with the solution, respectively, at a dose of 5 mg/kg and an administration volume of 10 mL/kg.

After overnight fasting, 3 male rats were intravenously administered (I.V.) with the solution, respectively, at a dose of 1 mg/kg and an administration volume of 5 mL/kg.

2.5 Sample collection:

0.2 mL of blood was collected from the jugular vein of rats before administration and at 0.083 (IV), 0.25, 0.5, 1, 2, 4, 6, 8 and 24 h after administration, placed in an EDTA-K_2 test tube, and centrifuged at 6000 rpm at 4°C for 6 min to separate plasma which was stored at -80°C. The animals were fed 4 h after administration.

2.6 Sample treatment:

1) 160 μL of acetonitrile was added to 40 μL of the plasma sample for precipitation, and the resulting mixture was mixed and then centrifuged at 3500 × g for 5 to 20 minutes.

2) 100 μL of the treated supernatant solution was taken and subjected to LC/MS/MS to analyze the concentrations of the test compounds.

2.6 Liquid phase analysis

- Liquid phase conditions: Shimadzu LC-20AD pump
- Mass spectrometry conditions: AB Sciex API 4000 mass spectrometer
- Chromatographic column: phenomenex Gemiu 5 μm C18 50 × 4.6 mm
- Mobile phase: liquid A: 0.1% aqueous formic acid solution, liquid B: methanol
- Flow rate: 1.0 mL/min
- Elution time: 0-4.0 min, the eluent was as follows:

Time/min	Liquid A	Liquid B
0.01	90%	10%
0.5	90%	10%
0.8	5%	95%
2.4	5%	95%
2.5	90%	10%
4.0	Stop	

3. Experimental results and analysis

The main pharmacokinetic parameters were calculated using WinNonlin 8.2. The results of pharmacokinetic experiments in rats were as shown in Table below:

Table 5: Pharmacokinetic parameters of oral administration of compounds of the present disclosure in rats

Parameters	tmax (h)	Cmax (ng/mL)	AUC 0-t (ng/mL*h)	AUC 0-∞ (ng/mL*h)	t1/2 (h)	MRT 0-∞ (h)
Example 25	6.0	1963	28488	37268	10.5	16.4
Example 35	4.7	1111	12387	14093	7.2	11.5
Example 282	6.0	971	12151	13888	7.3	12.0

The example compounds of the present disclosure exhibited good metabolic properties, with good exposure (AUC) and maximum plasma concentration C_{max}.

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VII. Pharmacokinetic evaluation test in beagle dogs

1. Study objective:

The object was to study the pharmacokinetic behavior of the compounds of the present disclosure in beagle dogs (plasma) as test animals after oral administration at a dose of 2 mg/kg.

2. Experimental scheme:

2.1 Experimental drugs:

The example compounds of the present disclosure, made in house.

2.2 Experimental animals:

3 beagle dogs per group, male.

2.3 Formulation prescription:

Preparation of a drug for oral administration: 10% PEG400/10% PG/80% glycine buffer (100 mM glycine, 64 Mm NaOH, pH 10) buffer.

10 ml of PEG400, 10 ml of PG and 80 ml of glycine buffer (100 mM glycine, 64 mM NaOH, pH = 9) were measured into a 100 ml volumetric flask, and the resulting mixture was vortexed, uniformly mixed, and sonicated to obtain a clear solution.

Single PK: The compound of the present disclosure was weighed and added into a 100 mL glass bottle, the solution was added, the PH was adjusted with 1 M NaOH until complete dissolution, the PH was then adjusted to 9.0-9.5 with 1 M HCl, the resulting mixture was sonicated for 10 min to obtain a colorless clear solution with a concentration of 0.4 mg/mL.

2.4 Administration:

After overnight fasting, 3 male beagle dogs were orally administered (p.o.) with the solution, respectively, at a dose of 2 mg/kg and an administration volume of 5 mL/kg.

2.5 Sample collection:

Blood collection: 0.3 mL of blood was collected from the forelimb vein of beagle dogs before administration and at 0.25, 0.5, 1, 2, 4, 6, 8 and 24 h after administration, placed in an EDTA-K_2 anticoagulation tube, and centrifuged at 6000 rpm at 4°C for 6 min to separate plasma which was stored at -80°C. The animals were fed 4 h after administration.

2.6 Sample treatment:

1) 160 μL of acetonitrile was added to 40 μL of the plasma sample for precipitation, and the resulting mixture was mixed and then centrifuged at 3500 × g for 5 to 20 minutes.

2) The treated supernatant solution was taken and subjected to LC/MS/MS to analyze the concentrations of the test compounds. LC/MS/MS analysis instrument: AB Sciex API 4000 Qtrap.

2.7 Liquid phase analysis:

- Liquid phase conditions: Shimadzu LC-20AD pump
- Chromatographic column: Agilent ZORBAX XDB-C18 (50 × 2.1 mm, 3.5 μm), mobile phase: liquid A: 0.1% aqueous formic acid solution, liquid B: acetonitrile
- Flow rate: 0.4 mL/min
- Elution time: 0-4.0 min, the eluent was as follows:

Time/min	Liquid A	Liquid B
0.01	90%	10%
0.5	90%	10%
0.8	5%	95%
2.4	5%	95%
2.5	90%	10%
4.0	Stop	

3. Experimental results and analysis

The results of pharmacokinetic experiments in beagle dogs were as shown in Table 6 below:

Table 6: Pharmacokinetic parameters of oral administration of compounds of the present disclosure in dogs

Parameters	tmax (h)	Cmax (ng/mL)	AUC 0-t (ng/mL*h)	AUC 0-∞ (ng/mL*h)	t1/2 (h)	MRT 0-∞ (h)

Example 34	1.7	1330	9088	9387	5.1	5.7
Example 65-1	2.8	4362	40996	43882	5.9	8.1
Example 67	1.5	2111	11497	11782	4.2	5.7
Example 143	2.7	2044	13798	17797	3.3	4.8
Example 144	1.7	2473	15894	16614	5.8	6.5
Example 194	1.0	5830	40130	43742	7.6	8.3
Example 282	2.0	858	9131	10795	8.5	12.1
Example 285	1.5	3597	19167	19417	4.1	5.3
Example 287	2.3	1880	17008	17250	3.7	6.1
Example 338	1.3	3915	20922	21417	4.4	5.3

VIII. Pharmacokinetic evaluation test in cynomolgus monkeys

Oral administration

1. Study objective:

The objective was to study the pharmacokinetic behavior of the compounds of the present disclosure in cynomolgus monkeys (plasma) as test animals after oral administration at a dose of 5 mg/kg.

2. Experimental scheme:

2.1 Experimental drugs:

The example compounds of the present disclosure, made in house.

2.2 Experimental animals:

3 cynomolgus monkeys per group, male.

2.3 Formulation prescription:

Preparation of a drug for oral administration: 10% PEG400/10% PG/80% glycine buffer (100 mM glycine, 64 Mm NaOH, pH 10) buffer.

10 ml of PEG400, 10 ml of PG and 80 ml of glycine buffer (100 mM glycine, 64 mM NaOH, pH = 9) were measured into a 100 ml volumetric flask, and the resulting mixture was vortexed, uniformly mixed, and sonicated to obtain a clear solution.

Single PK: The compound of the present disclosure was weighed and added into a 100 mL glass bottle, the solution was added, the PH was adjusted with 1 M NaOH until complete dissolution, the PH was then adjusted to 9.0-9.5 with 1 M HCl, the resulting mixture was sonicated for 10 min to obtain a colorless clear solution with a concentration of 1 mg/mL.

2.4 Administration:

After overnight fasting, 3 male cynomolgus monkeys were orally administered (p.o.) with the solution, respectively, at a dose of 5 mg/kg and an administration volume of 5 mL/kg.

2.5 Sample collection:

Blood collection: 0.3 mL of blood was collected from the forelimb vein of cynomolgus monkeys before administration and at 0.25, 0.5, 1, 2, 4, 6, 8 and 24 h after administration, placed in an EDTA-K_2 anticoagulation tube, and centrifuged at 6000 rpm at 4°C for 6 min to separate plasma which was stored at -80°C. The animals were fed 4 h after administration.

2.6 Sample treatment:

1) 160 μL of acetonitrile was added to 40 μL of the plasma sample for precipitation, and the resulting mixture was mixed and then centrifuged at 3500 × g for 5 to 20 minutes.

2) The treated supernatant solution was taken and subjected to LC/MS/MS to analyze the concentrations of the test compounds. LC/MS/MS analysis instrument: AB Sciex API 4000 Qtrap.

2.7 Liquid phase analysis:

- Liquid phase conditions: Shimadzu LC-20AD pump
- Chromatographic column: Agilent ZORBAX XDB-C18 (50 × 2.1 mm, 3.5 μm), mobile phase: liquid A: 0.1% aqueous formic acid solution, liquid B: acetonitrile
- Flow rate: 0.4 mL/min

- Elution time: 0-4.0 min, the eluent was as follows:

Time/min	Liquid A	Liquid B
0.01	90%	10%
0.5	90%	10%
0.8	5%	95%
2.4	5%	95%
2.5	90%	10%
4.0	Stop	

3. Experimental results and analysis

The results of pharmacokinetic experiments in cynomolgus monkeys were as shown in Table 7 below:

Table 7: Pharmacokinetic parameters of oral administration of compounds of the present disclosure in monkeys

Parameters	tmax (h)	Cmax (ng/mL)	AUC 0-t (ng/mL*h)	AUC 0-∞ (ng/mL*h)	t1/2 (h)	MRT 0-∞ (h)
Example 65-1	2.0	4458	29678	30783	5.6	7.5
Example 143	2.7	4044	26020	26180	3.2	5.1
Example 282	4.0	570	7557	17047	47.6	68.9

Intravenous administration

1. Study objective:

The objective was to study the pharmacokinetic behavior of the compounds of the present disclosure in cynomolgus monkeys (plasma) as test animals after intravenous administration at a dose of 0.2 mg/kg.

2. Experimental scheme

2.1 Experimental drugs:

The example compounds of the present disclosure, made in house.

2.2 Experimental animals:

3 cynomolgus monkeys per group, male, purchased from Guangxi Xiongsen Primate Experimental Animal Breeding and Development Co., Ltd., with animal production license number: SCXK (Guangxi) 2021-0004).

2.3 Formulation prescription:

Preparation of a drug for intravenous administration: 5% DMSO + 10% Solutol HS15 + 85% PBS

The compound of the present disclosure was weighed; on the basis of the total volume, 5% of DMSO was added, and vortexed and sonicated for 2 min to achieve complete dissolution, 10% of Solutol HS15 was then added, and vortexed and sonicated for 2 min to achieve complete dissolution, and finally 85% of PBS was added, and vortexed and sonicated for 5 min; and the resulting mixture was filtered through a 0.22 μm filter membrane to obtain a colorless and transparent clear solution with a concentration of 0.1 mg/mL.

2.4 Administration:

After overnight fasting, 3 male cynomolgus monkeys were intravenously administered (I.V.) with the solution, respectively, at a dose of 0.2 mg/kg and an administration volume of 2 mL/kg. 2.5 Sample collection:

0.5 mL of blood was collected from the forelimb vein of cynomolgus monkeys before administration and at 0.083, 0.25, 0.5, 1, 2, 4, 8 and 24 h after administration, placed in an EDTA-K_2 tube, and centrifuged at 6000 rpm at 4°C for 6 min to separate plasma which was stored at -80°C.

2.6 Sample treatment:

160 μL of acetonitrile was added to 40 μL of the plasma sample for precipitation, and the resulting mixture was mixed and then centrifuged at 3500 × g for 5 to 20 minutes.

100 μL of the treated supernatant solution was taken and subjected to LC/MS/MS to analyze the concentrations of the test compounds.

2.7 Liquid phase analysis

Liquid phase conditions: Shimadzu LC-20AD pump

Mass spectrometry conditions: AB Sciex API 4000 mass spectrometer

Chromatographic column: phenomenex Gemiu 5 μm C18 50 × 4.6 mm

Mobile phase: liquid A: 0.1% aqueous formic acid solution, liquid B: acetonitrile
Flow rate: 0.8 mL/min
Elution time: 0-4.0 min, the eluent was as follows:

Time/min	Liquid A	Liquid B
0.01	90%	10%
0.5	90%	10%
0.8	5%	95%
2.4	5%	95%
2.5	90%	10%
4.0	Stop	

3. Experimental results and analysis

The main pharmacokinetic parameters were calculated using WinNonlin 8.2. The results of pharmacokinetic experiments in cynomolgus monkeys were as shown in Table 8 below:

Table 8: Pharmacokinetic parameters of injection administration of compounds of the present disclosure in monkeys

Parameters	C0 (ng/mL)	AUC 0-t (ng/mL*h)	AUC 0-∞ (ng/mL*h)	t1/2 (h)	MRT 0-∞ (h)
Example 282	1076	1676	1929	9.8	10.3

IX. Effect of long-term administration of compounds of the present disclosure on the body weight and food intake in GLP-1R humanized mice fed with HFD high-fat diet

1. Experimental objective:

The test objective was to evaluate the effect of the long-term administration of the compounds on the body weight and food intake in GLP-1R humanized C57BL/6 mice fed with a high-fat diet.

2. Experimental reagents and instruments

C57BL/6_*hGLP-1R*, male, 60% high-fat diet (HFD), ultra-clean workbench, electronic balance.

3. Experimental method

3.1 On the starting day of high-fat diet feeding, C57BL/6 mice were randomly divided into two groups according to their body weights, wherein the first group was used as a Blank group (7 mice) and received normal control diet, and the remaining animals were fed with the high-fat diet until the end of the experiment to establish a model group.

3.2 On week 8 of HFD feeding, the animals in the model group were randomly divided into groups (7 mice per group) according to their body weights, wherein the first group was used as Vehicle group administered with a vehicle (Vehicle: 10% PEG400/10% PG/80% glycine buffer (100 mM glycine, 26 mM NaOH, pH 9) buffer); and the remaining groups were used as administration groups. The administration scheme involved: orally administering the corresponding compounds once daily for an administration period of 21 days (administration dose: 10 mg/kg; administration volume: 10 mL/kg). The blank group continued to be fed with normal diet and was orally administered with the vehicle once daily.

3.3 The day of the administration was defined as Day 0.

3.4 At each administration, the animals were weighed and the data were recorded. Oral administration was performed at an administration volume of 10 mL/kg according to their body weights.

3.5 Commencing on day 0 of the experiment, food intake measurement was conducted every three days for the mice in all groups. Specifically, after each weighing and administration, the feed was changed, and the addition amount and the remaining amount were recorded.

3.7 On Day 21 (last day), all mice were euthanized in turn according to the grouping order. Plasma and tissues (liver, kidney, ileum, pancreas and brain) were taken for PK detection, and serum was taken for blood biochemical detection (ALT, AST, TG, TC, LDL-C).

4. Experimental data processing and statistical analysis

The body weight and body weight change rate of mice after administration were summarized and statistically analyzed. The body weight change rate was calculated according to the formula: (BWt-BW0)/BW0 × 100%. BWt denotes the body weight of mice on day t of the experiment, and BW0 denotes the body weight of mice on day 0 of the experiment.

The food intake was calculated according to the formula: (addition amount (g) - remaining amount (g)) /animal number in each cage, and the cumulative food intake was the aggregated daily food intake per animal during administration.

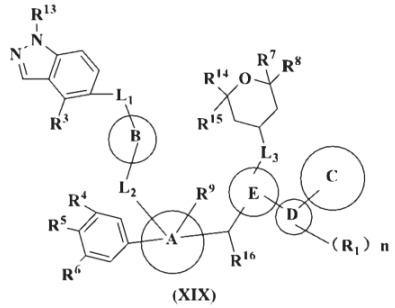
Experimental data was analyzed and plotted with GraphPad Prism software. The comparison between the two groups was performed using a t-test method. The comparison among three or more groups was performed using a one-way ANOVA method. $p < 0.05$ was defined as a statistically significant difference.

The example compounds of the present disclosure exhibited a good body weight loss effect in GLP-1R humanized C57BL/6 mice fed with a high-fat diet over a long-term administration, with a body weight decline rate of greater than 5%, further preferably greater than 10%.

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Claims:

1. 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 C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, 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 or C_{2-6}alkynyl, wherein the C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, 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 or C_{2-6}alkynyl 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;

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;

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,

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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, 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^9 or 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;

preferably, R^9or 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;

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

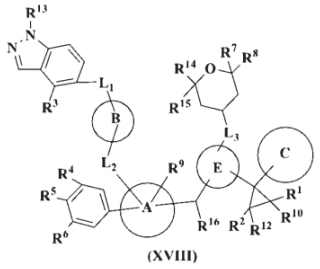
or when n is not 1,

R^1 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;

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

2. The compound according to claim 1, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the general formula (XIX) is further shown as general formula (XVIII):



(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_{1-3}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;

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 $-(CH_2)_{m4}C(O)OR_{a2}$ 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;

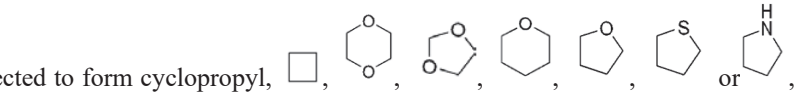
R_{a1}, R_{a2}, R_{b1} or R_{c2} is each independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, thio, C_{1-3}alkyl, C_{1-3}deuterated alkyl, C_{1-3}haloalkyl, C_{1-3}deuterated haloalkyl, C_{1-3}hydroxyalkyl, C_{1-3}deuterated hydroxyalkyl, C_{1-3}sulfanyl, C_{1-3}deuterated 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,

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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;

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_{3-6}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;

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;

R^{13}, L_1, L_2, L_3, ring A, ring B, ring C, and ring E are as defined in claim 1; and

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

3. The compound according to claim 2, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein

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

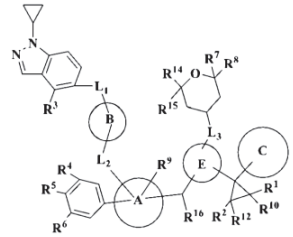
more preferably, R^{13} is selected from cyclopropyl or $-CD_3$, wherein the cyclopropyl or $-CD_3$ is optionally further substituted by one or more substituents of deuterium, halogen or C_{1-3}alkyl; and

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

4. The compound according to claim 2, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein

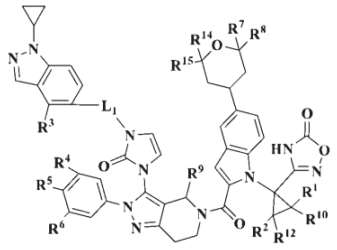
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the general formula (XVIII) is further shown as general formula (XVIII-A):



(XVIII-A)

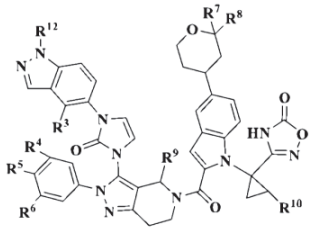
or the general formula (XVIII) is further shown as general formula (XVIII-B):



(XVIII-B)

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^{14}, R^{15}, R^{16}, L_1, L_2 and L_3 are defined as in claim 2.

5. The compound according to claim 1, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the general formula (XIX) is further shown as general formula (V):



(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 and 5- to 10-membered heteroaryl are 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 and 5- to 10-membered heteroaryl;

preferably, R^4, R^5or 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 and C_{1-3}alkoxy;

more preferably, R^4, R^5or R^6 each is independently selected from fluoro, methyl, cyano, ethynyl, methylthio, amino, cyclopropyl,

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or oxetane; optionally further substituted by halogen, methoxy, or deuterated methyl;

or $R^5$and R^6 are linked 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 are 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 and 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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, and $-NR_{a5}S(O)NR_{a4}R_{b4}$, 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 and 5- to 10-membered heteroaryl are 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 and 5- to 10-membered heteroaryl;

R_{a1}, R_{b1}, R_{a2}, R_{b2}, R_{a3}, R_{b3}, R_{a4}, R_{b4} or R_{a5} 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, and 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} are linked 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 are 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 and 5- to 10-membered heteroaryl;

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

R^{12} is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, 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 or C_{2-6}alkynyl, 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 and 5- to 10-membered heteroaryl;

n1 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;

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;

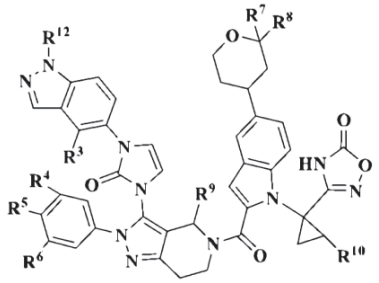
when R^7, R^8, R^9, R^{10}, and R^{12} are methyl, R^3 is fluoro, R^5 is halogen, and R^4 is methyl, R^6 is not methyl;

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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.

6. The compound according to claim 1, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the general formula (XIX) is further shown as general formula (V):



(V)

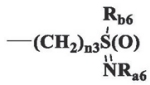
wherein

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}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^4, R^5or 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 or 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;

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

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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n2}R_{a5}R_{b5}$ 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,

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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;

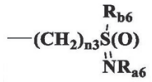
R^7, R^8, R^9 or R^{10} each is independently selected from hydrogen, deuterium, halogen, amino, nitro, hydroxyl, cyano, oxo, C_{1-6}alkyl, C_{1-6}deuterated alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered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

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;

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^{12} is selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl, 5- to 10-membered heteroaryl, 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, $-(CH_2)_{n2}R_{a5}R_{b5}$ 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;

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or

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;

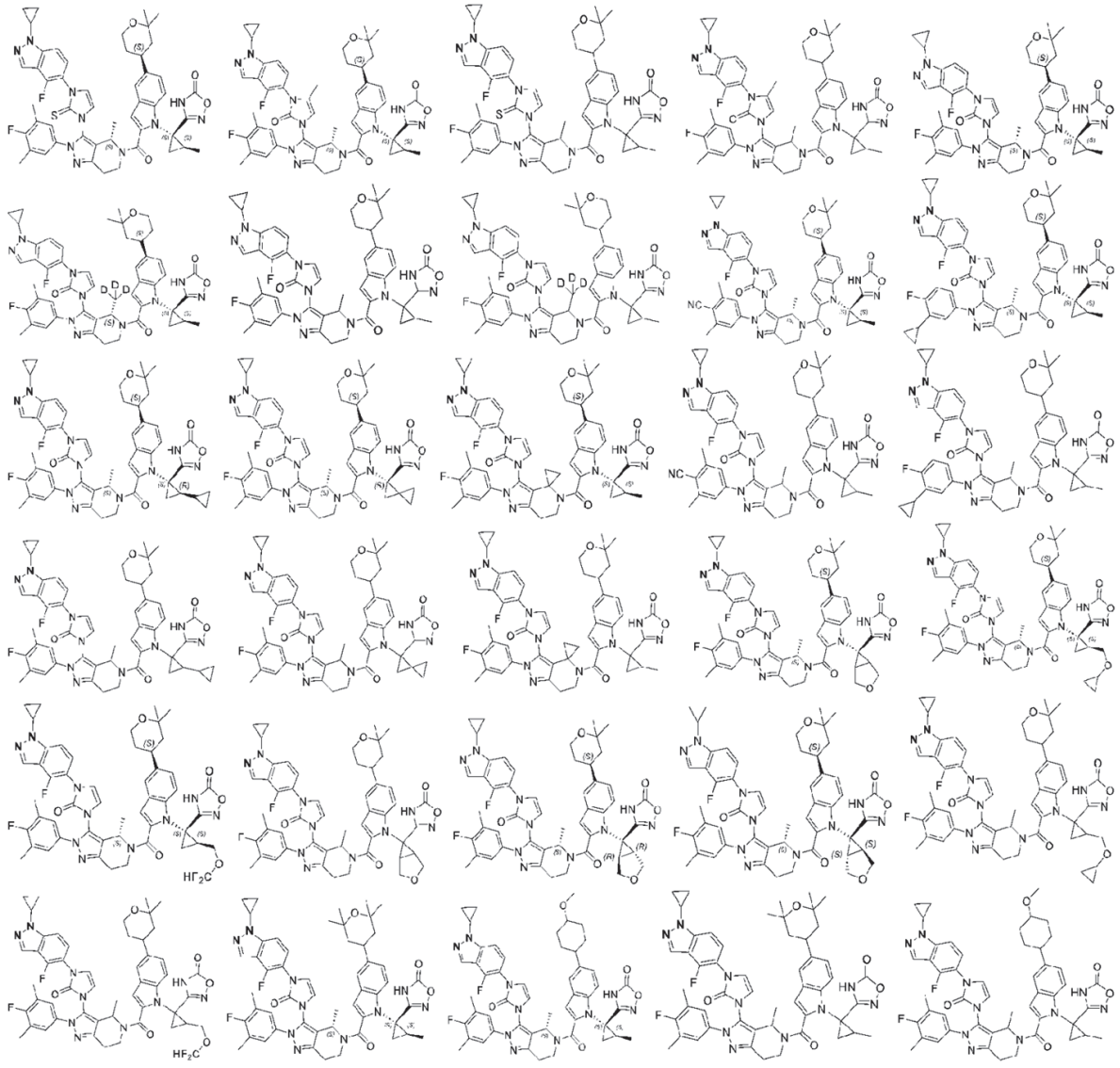
preferably, R^{10} is linked with the atoms to which it is connected and adjacent atoms to form C_{3-6}cycloalkyl, 3- to 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

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

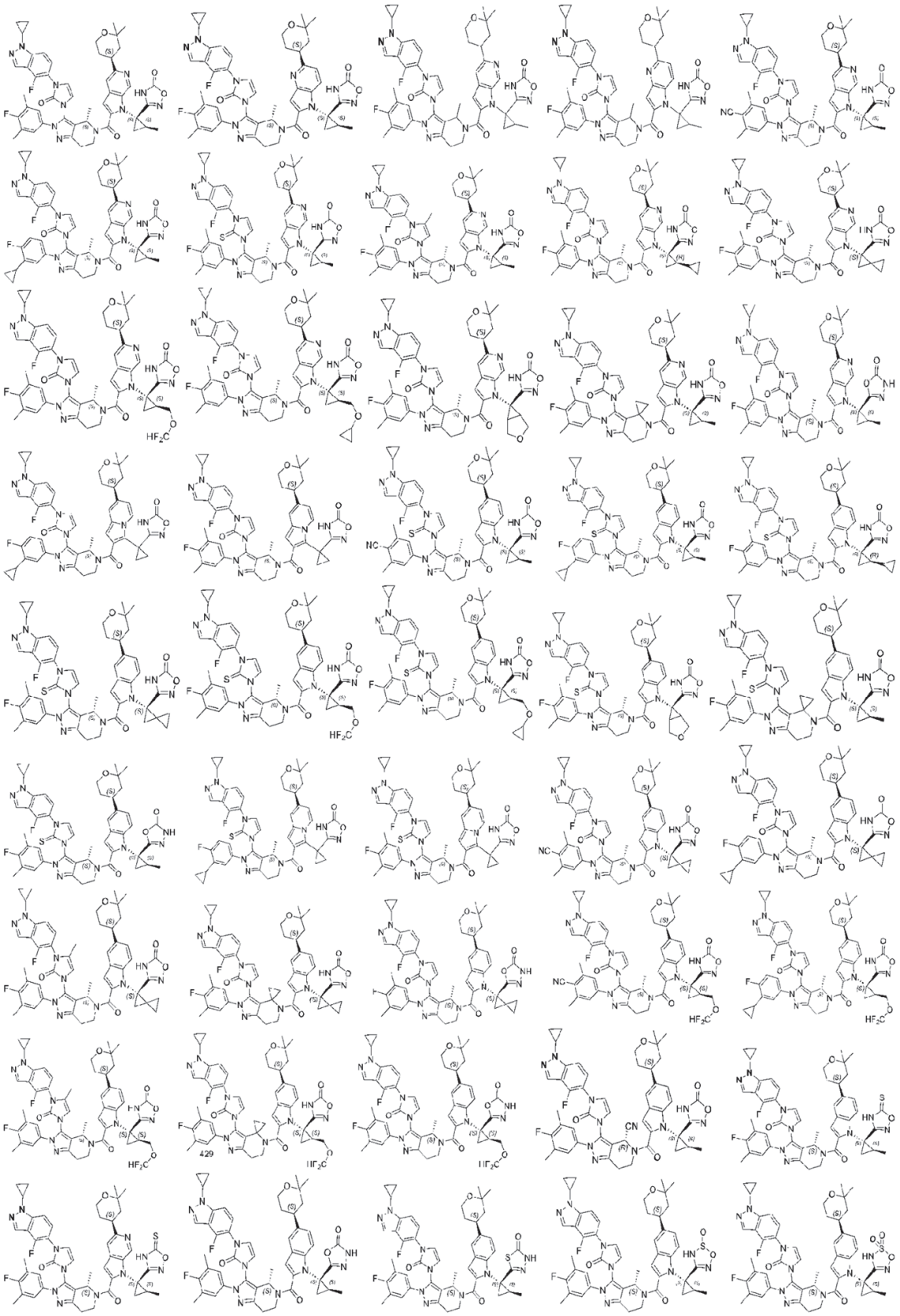
n1-n3 are an integer of 0-5; and

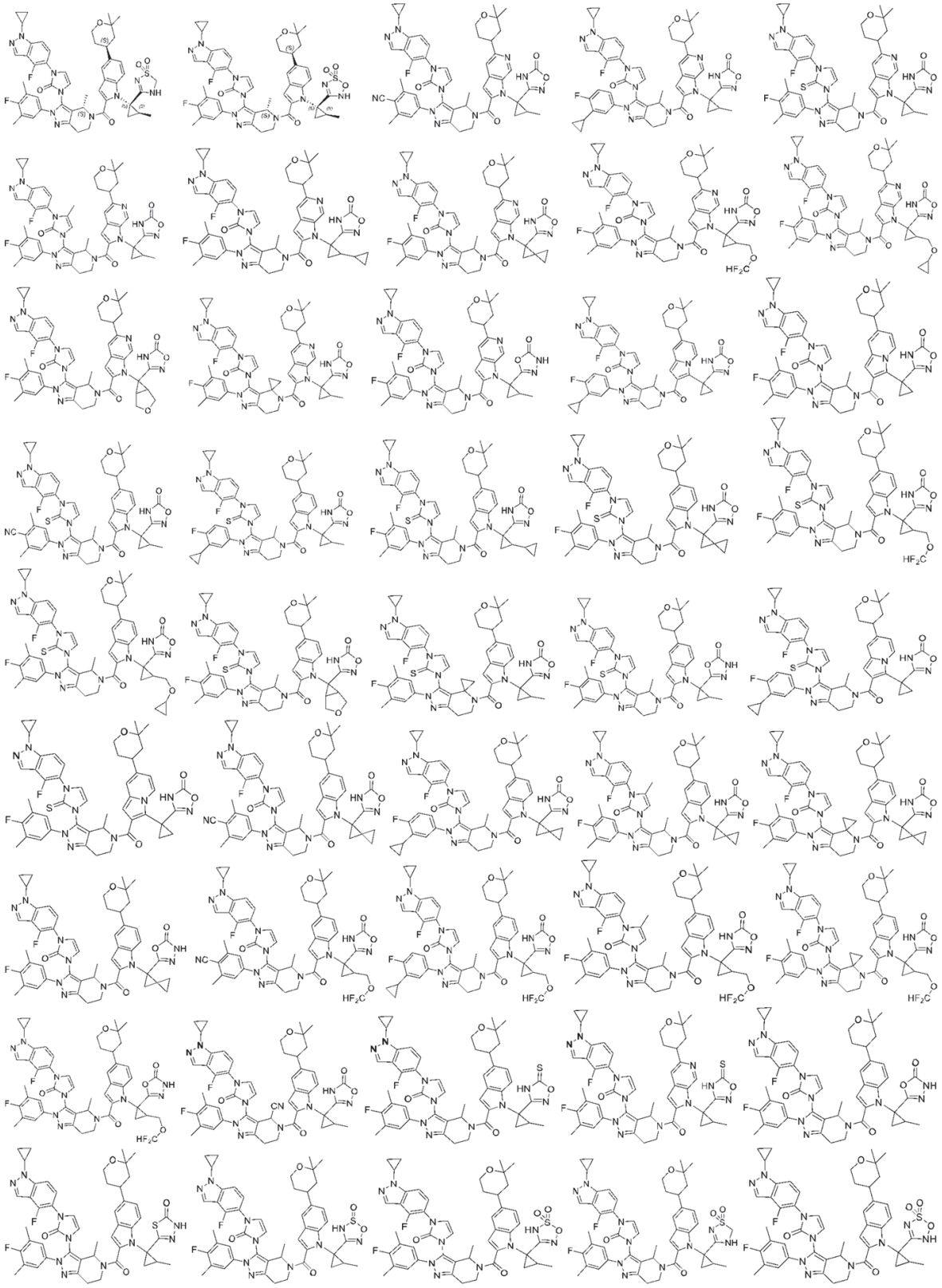
m1 is an integer of 0-5.

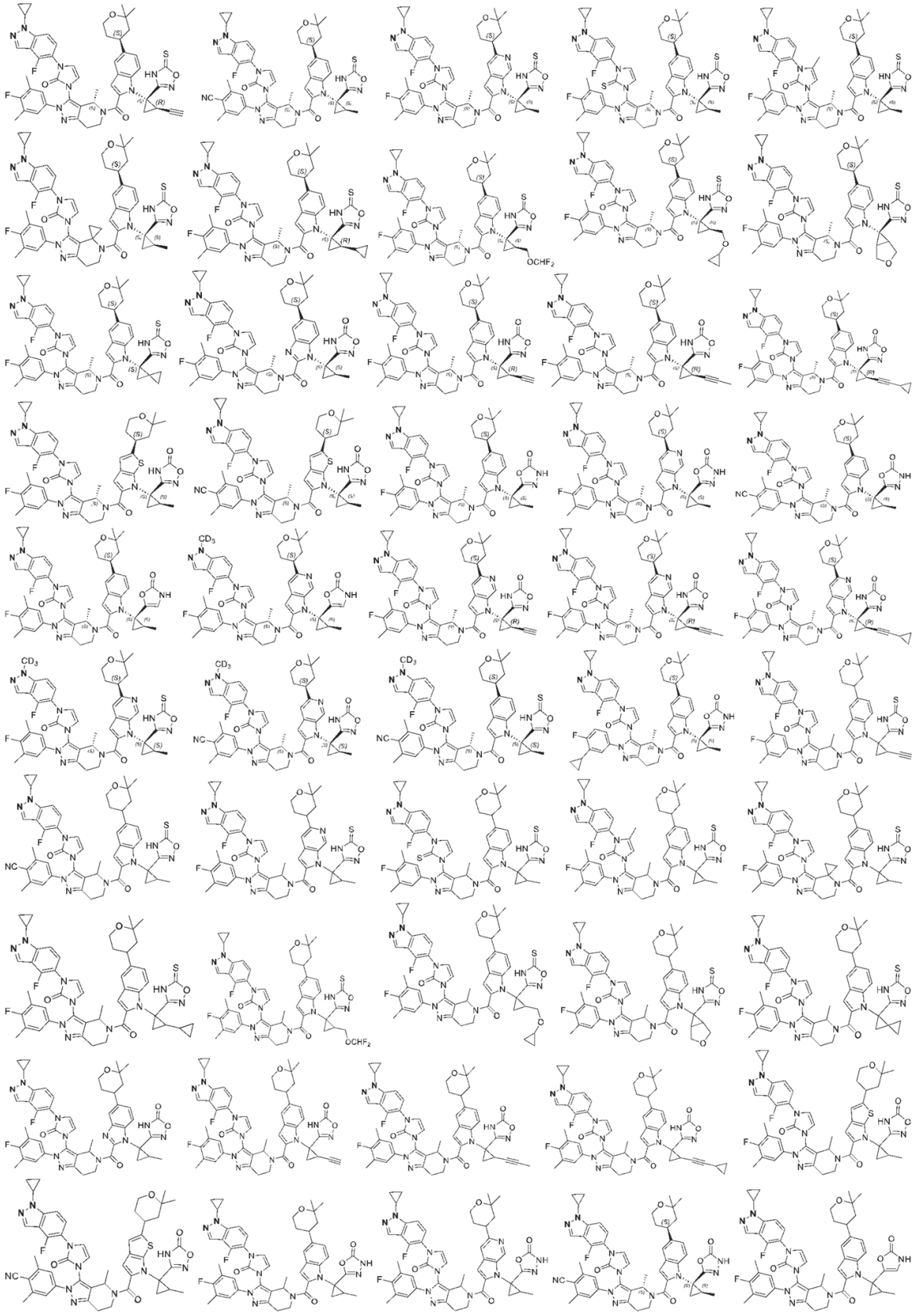
7. The compound according to claim 1, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:

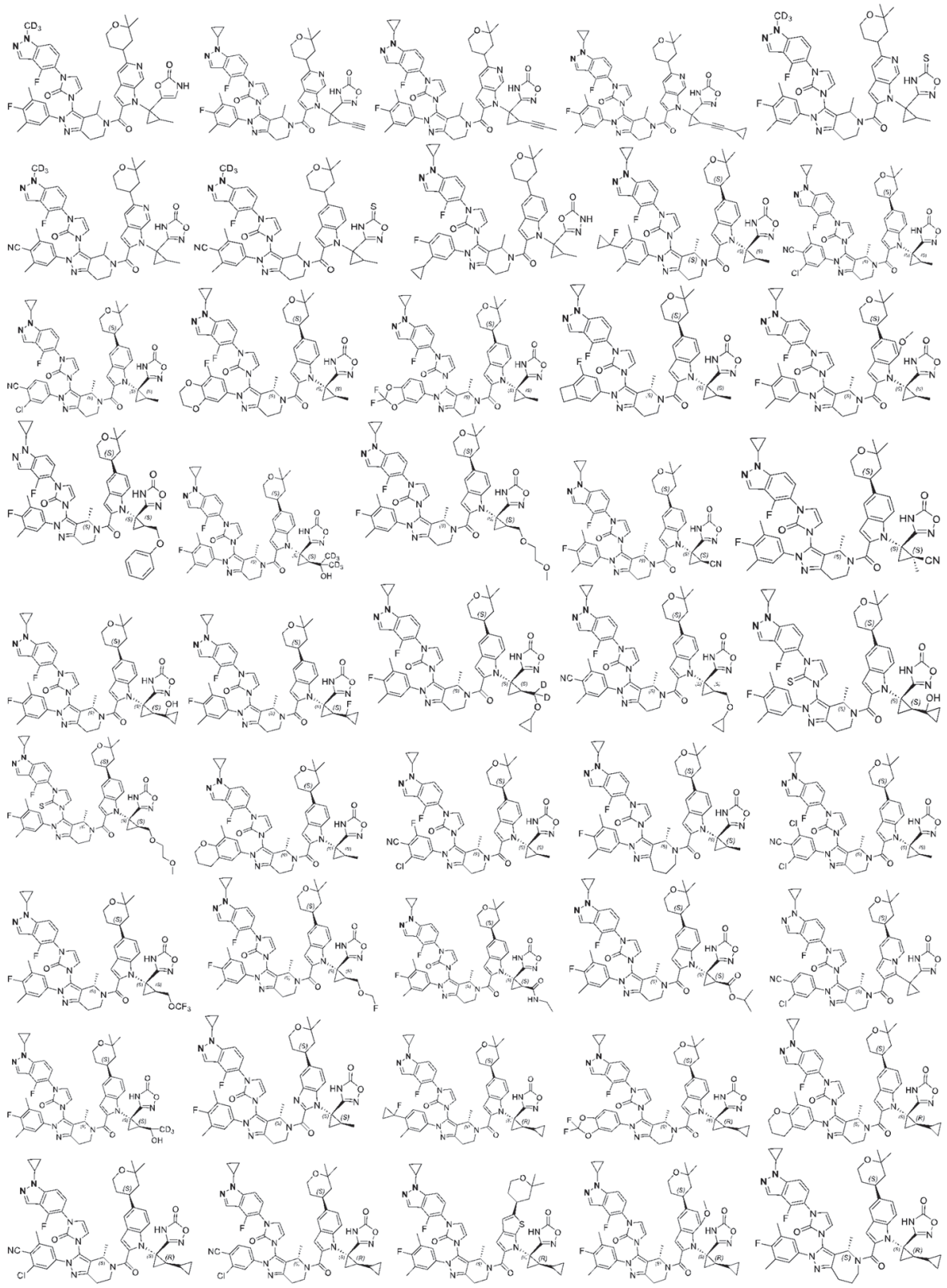


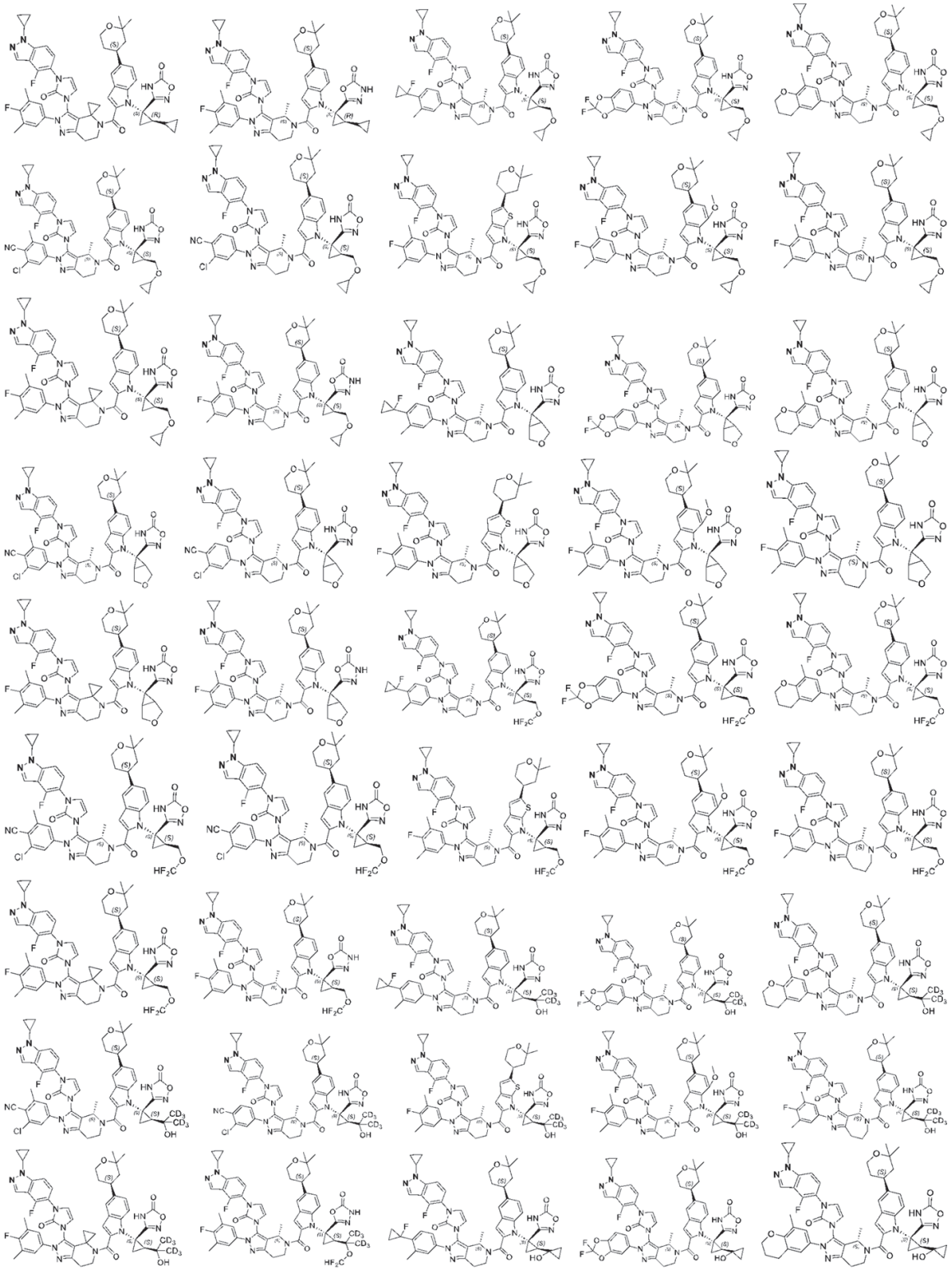
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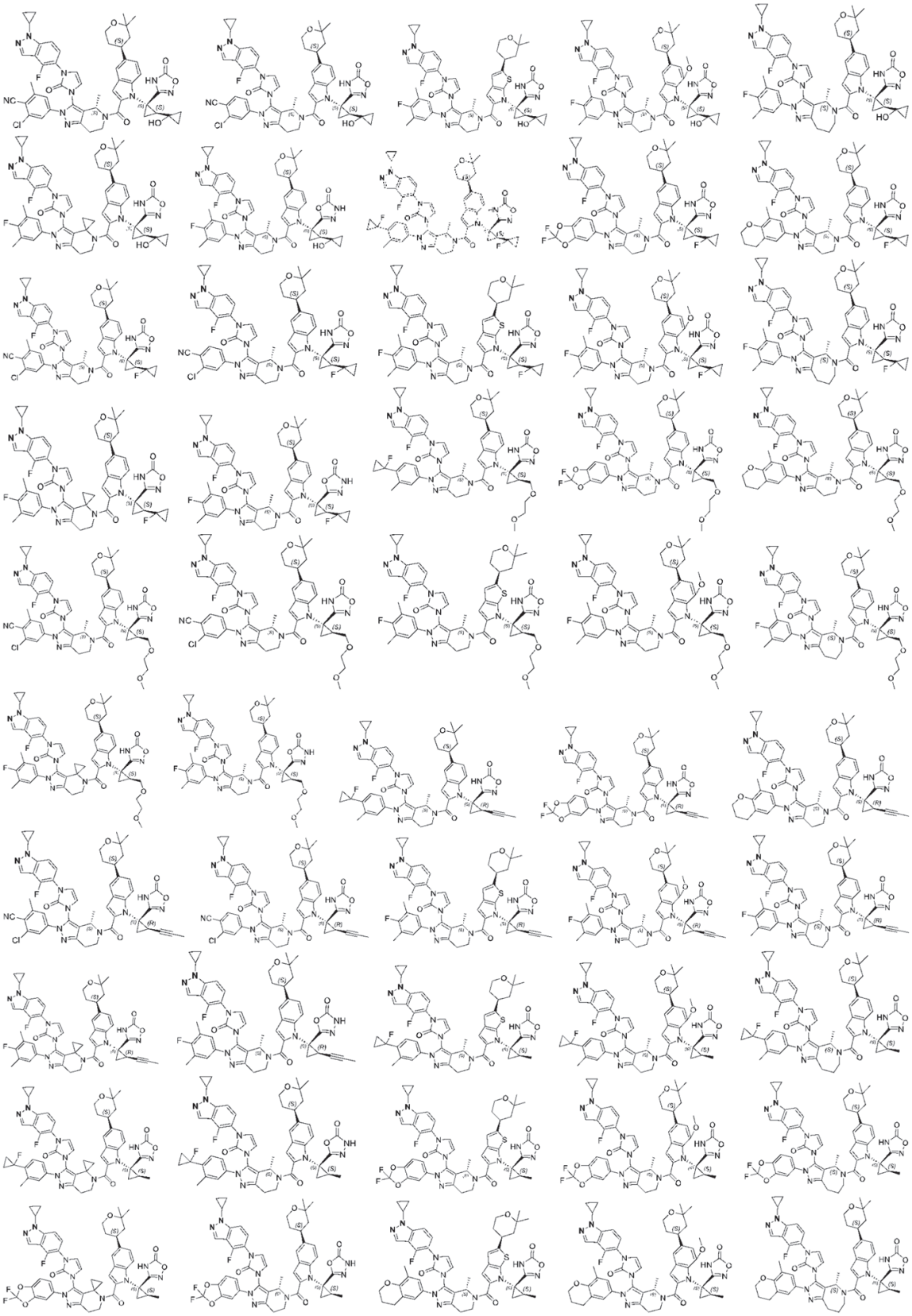

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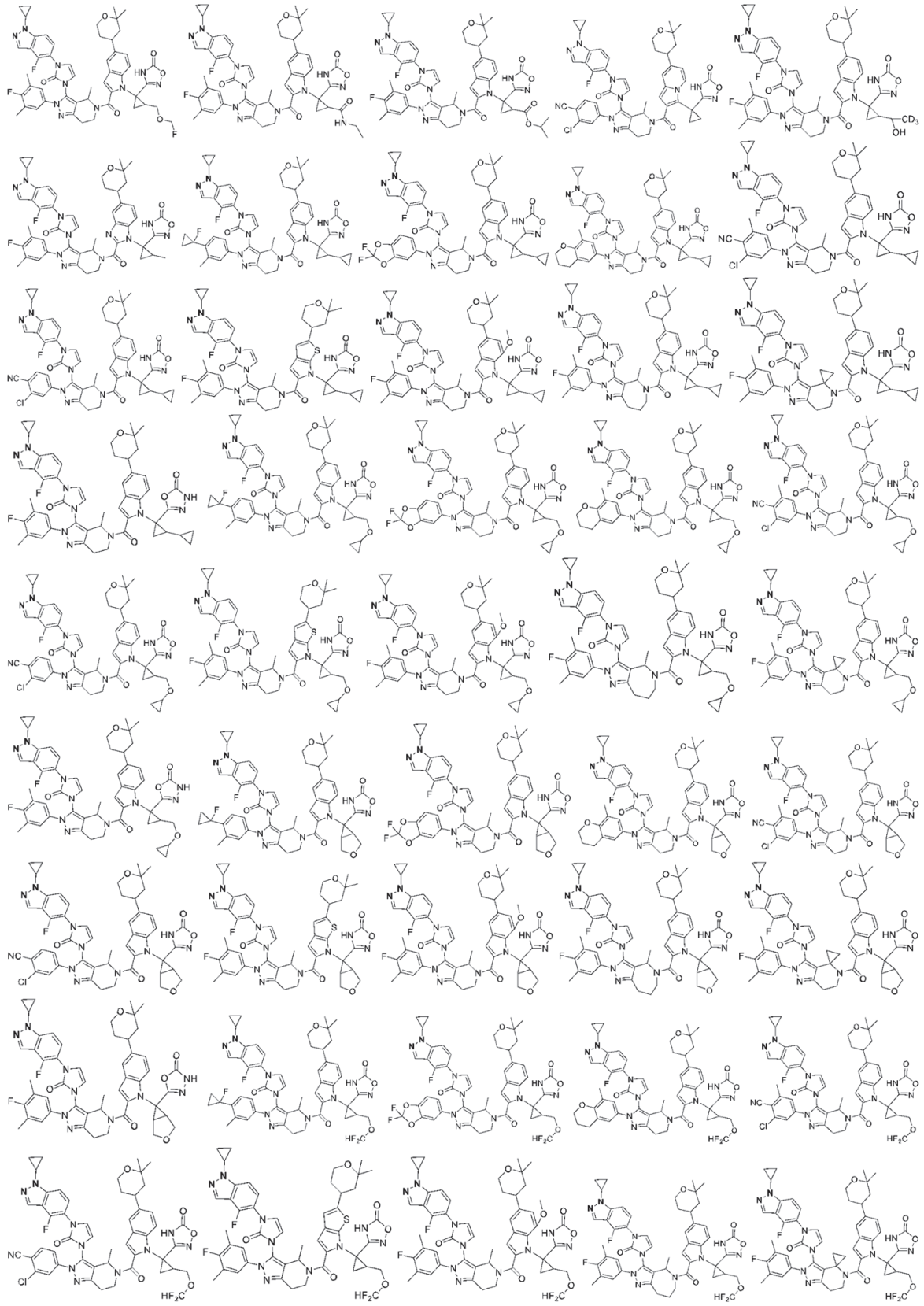




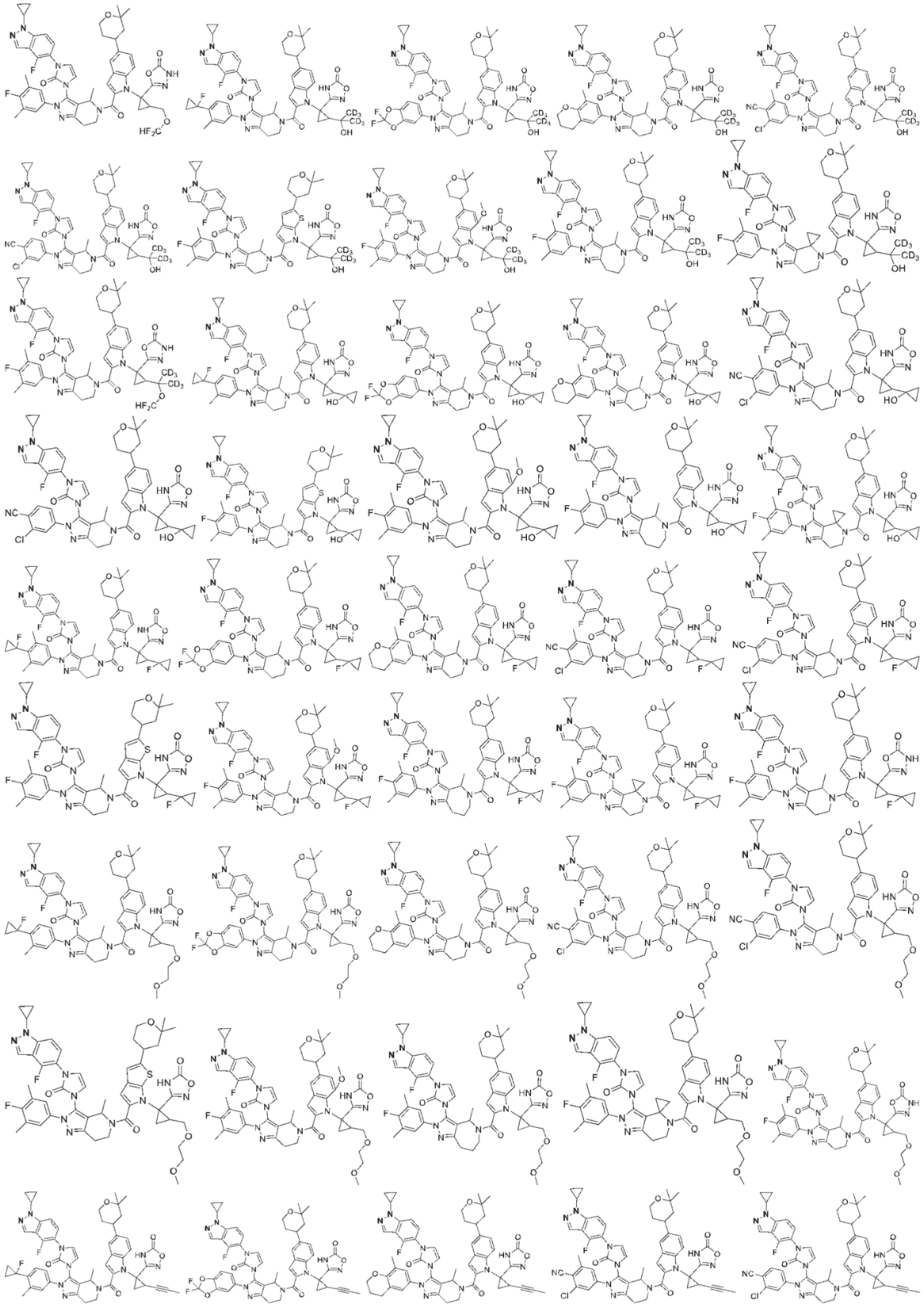


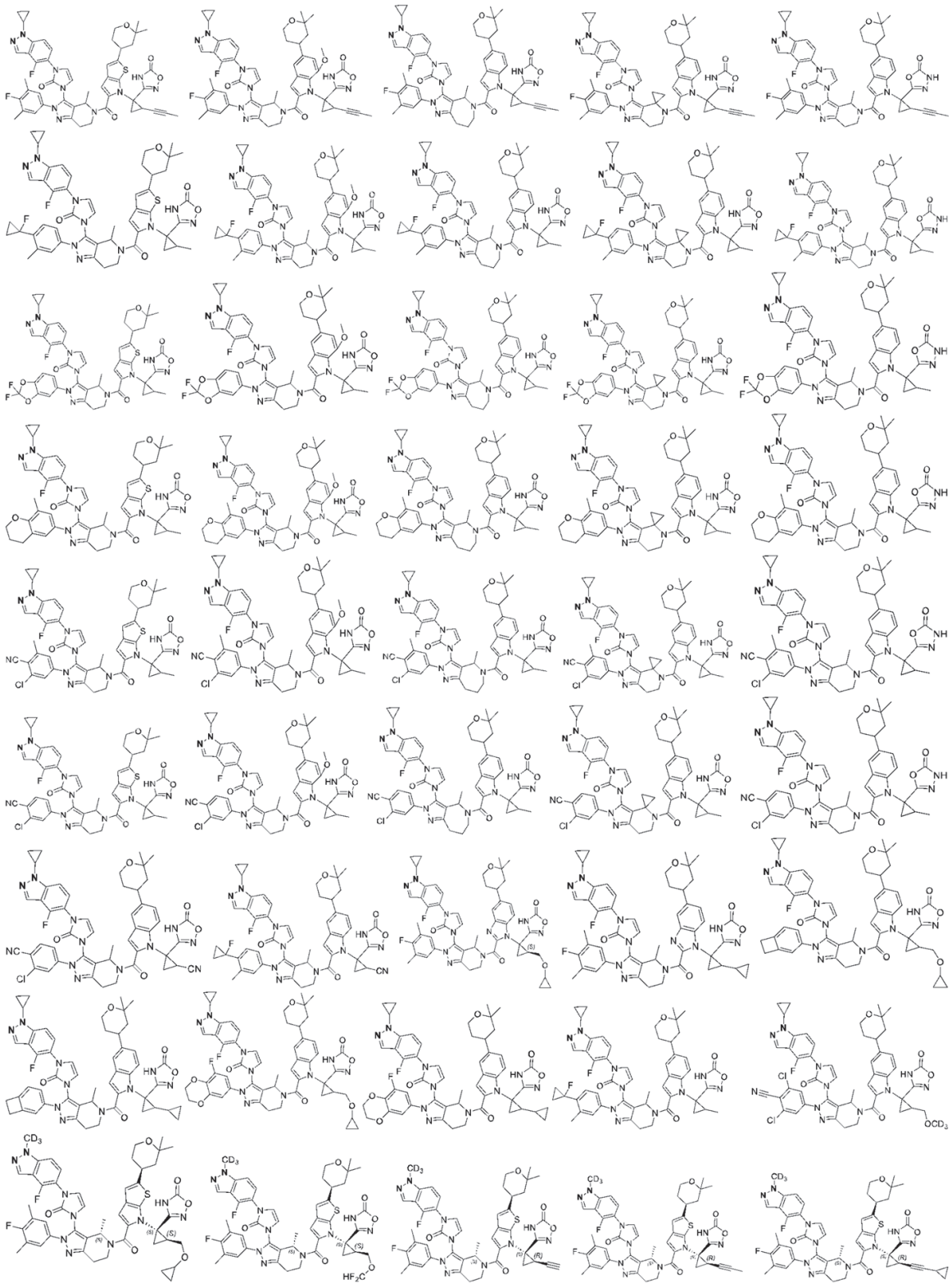
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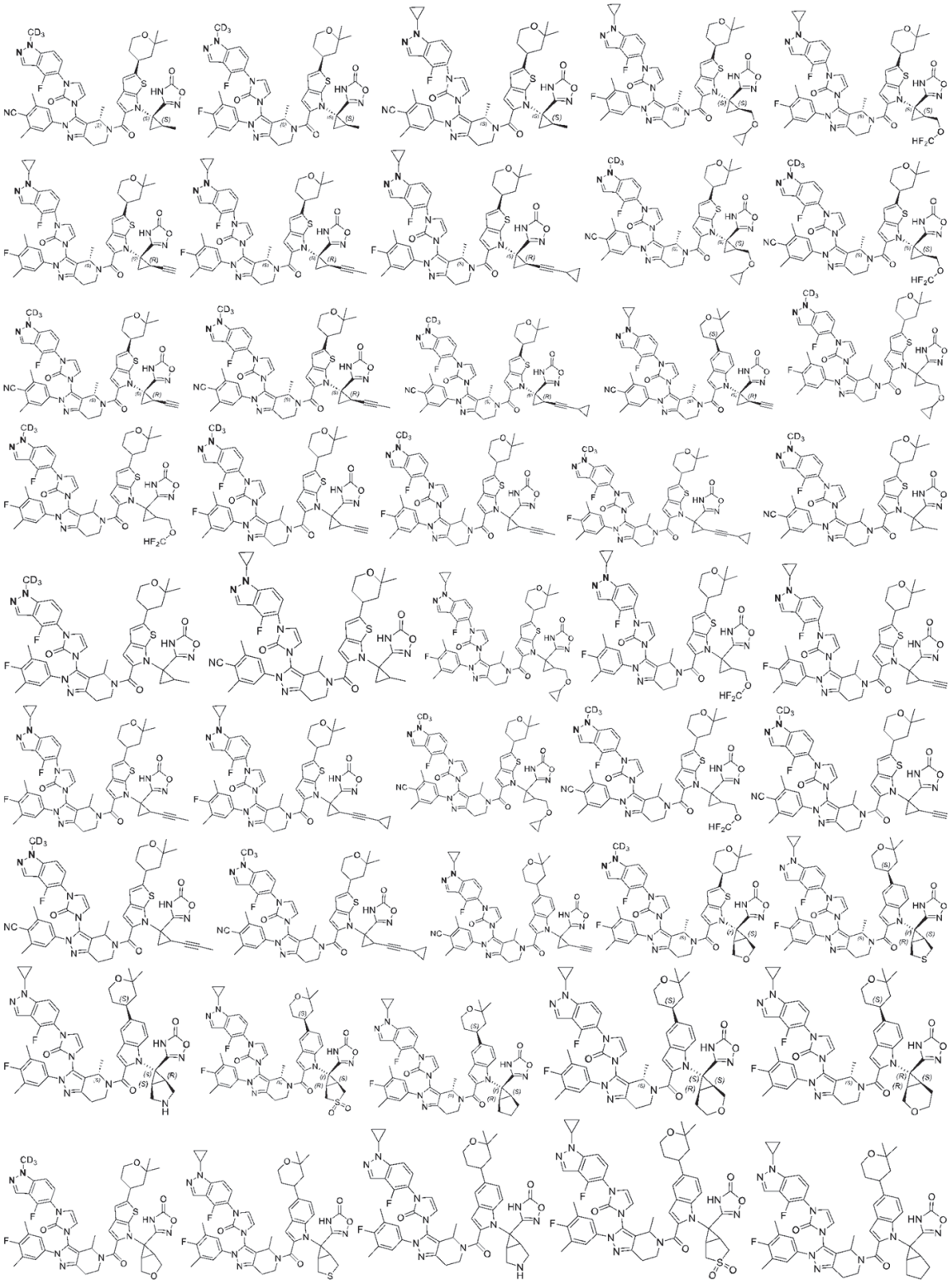


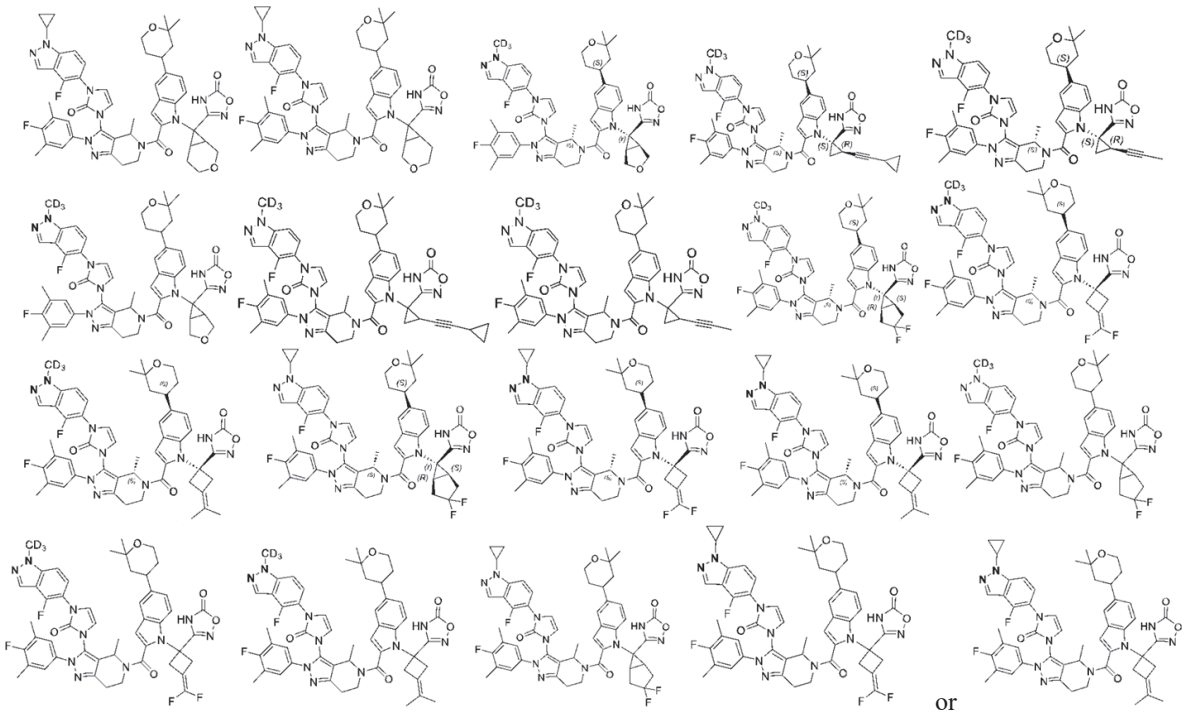


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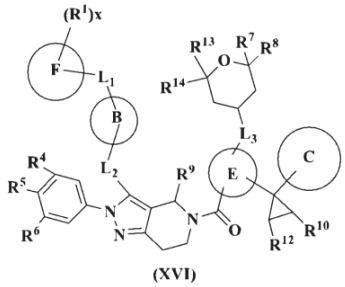






or .

8. A compound of general formula (XVI), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



(XVI)

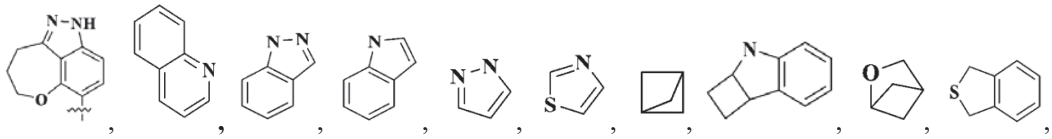
wherein

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

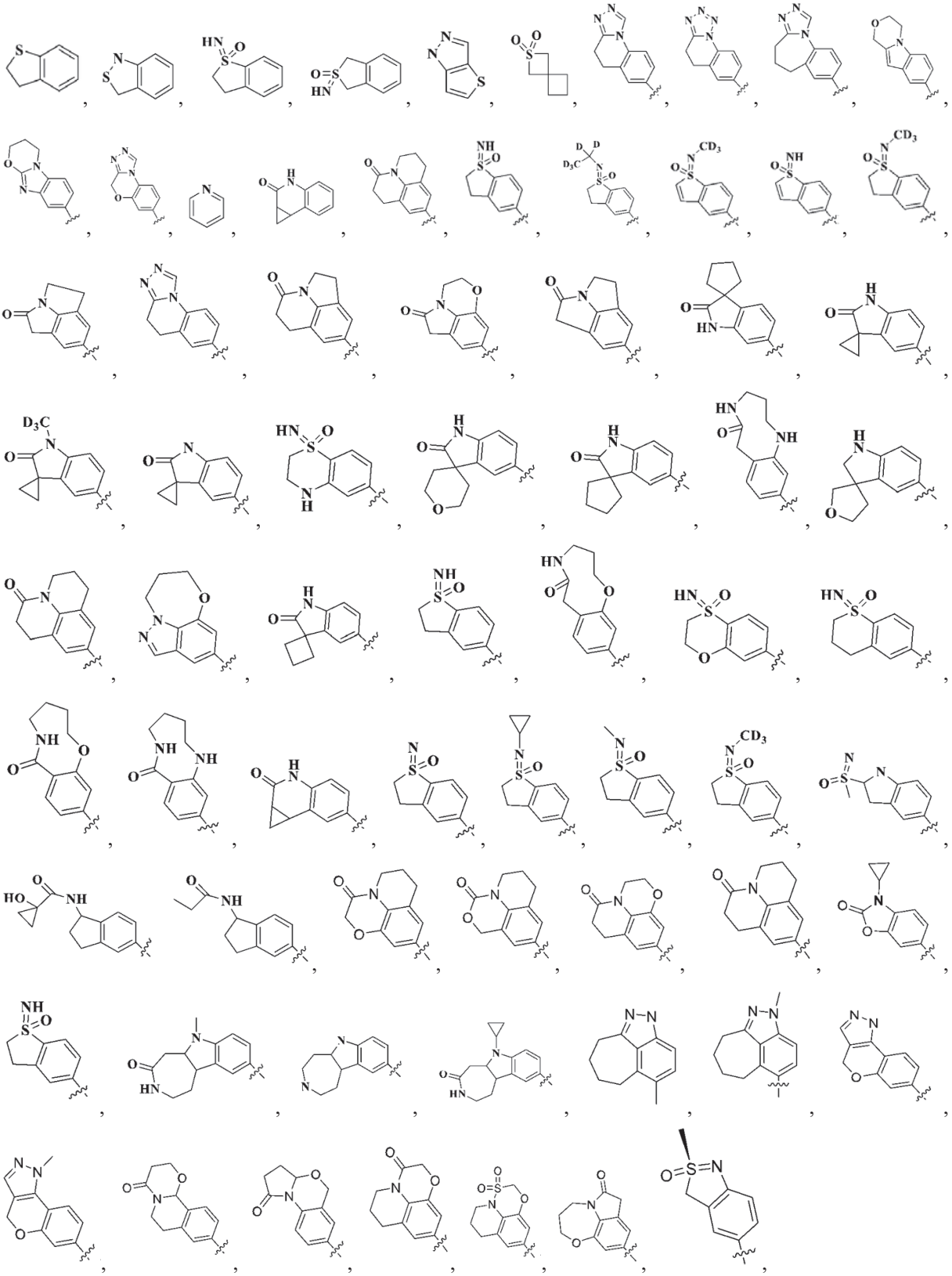
preferably, ring F is selected from 3- to 14-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{3-12}cycloalkyl, C_{6-14}aryl or 5- to 14-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S ;

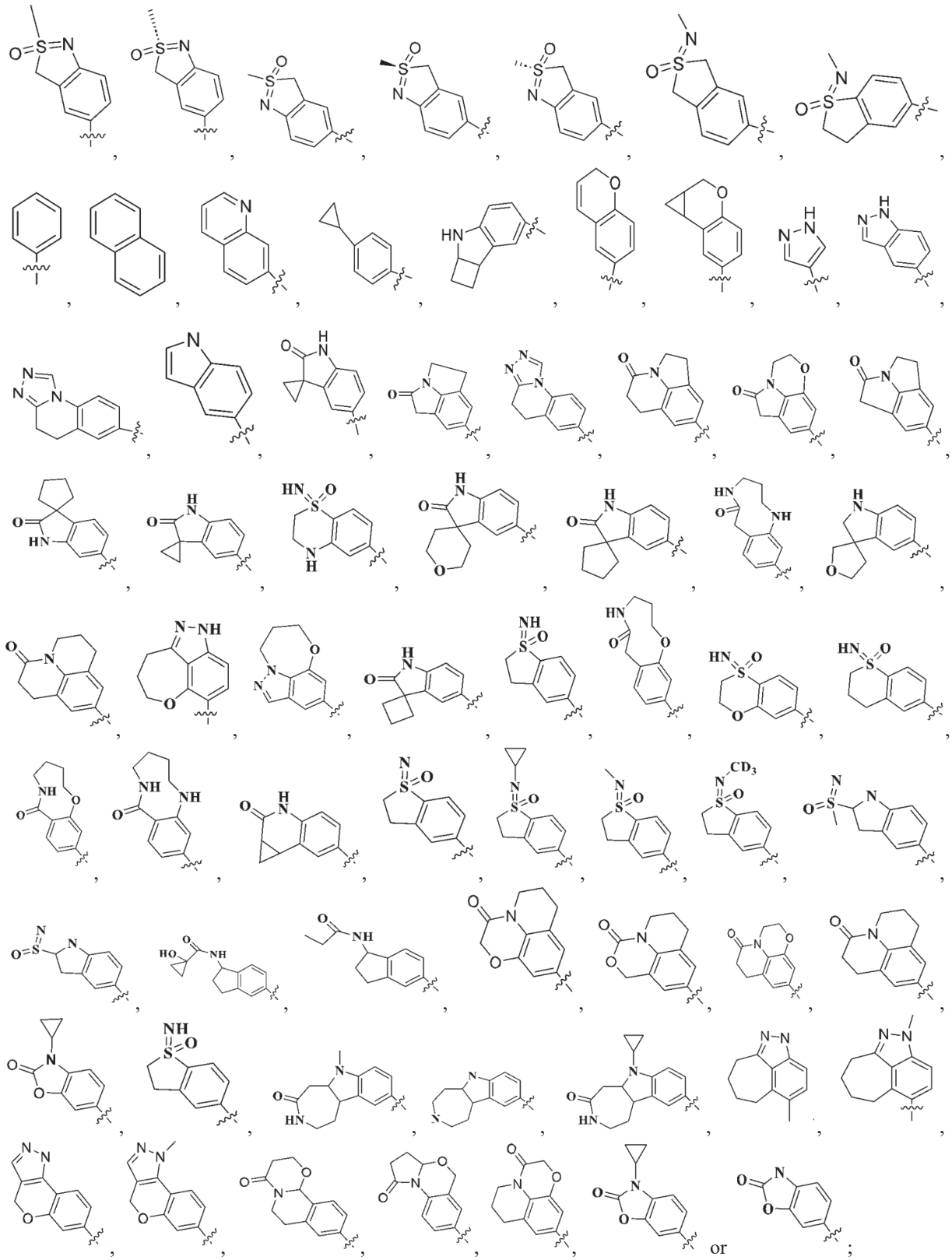
more preferably, ring F is selected from 5- to 14-membered heterocyclyl containing 1-3 heteroatoms selected from N, O or S, C_{3-10}cycloalkyl, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 heteroatoms selected from N, O or S;

further preferably, ring F is selected from 8- to 14-membered tricyclic fused heterocyclyl containing 1-5 heteroatoms, 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;

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

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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;

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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, 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 substituted by one or more substituents;

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 $-(CH_2)_{n5}NR_{b5}$, 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 $\{=NR_{15}$, 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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{a5}$, $-(CH_2)_{n1}C(O)NR_{a6}R_{b6}$, $-(CH_2)_{n1}P(O)R_{a3}R_{b3}$, $-(CH_2)_{n3}\overset{R_{b7}}{\underset{NR_{a7}}{S(O)}}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$, optionally further substituted by one or more substituents of $\{=NR_{15}$, halogen, amino, nitro, hydroxyl, cyano, oxo, $-NS(O)R_{a1}R_{b1}$, C_{1-6}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 $\{=NR_{15}$, 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, $-NS(O)R_{a1}R_{b1}$, $-(CH_2)_{n1}S(O)NR_{a2}R_{b2}$, $-P(O)R_{a3}R_{b3}$, $-NR_{a5}S(O)NR_{a4}R_{b4}$, $-(CH_2)_{n3}\overset{R_{b6}}{\underset{NR_{a6}}{S(O)}}$, $-(CH_2)_{n1}S(O)_2R_{a5}$, $-(CH_2)_{n1}O(CH_2)_{n2}R_{b5}$, $-(CH_2)_{n1}NR_{a8}C(O)R_{b8}$, $-(CR_{a8}R_{b8})_{n4}C(O)NR_{a9}R_{b9}$, $-(CH_2)_{n1}S(O)_2R_{b5}$ or $-(CH_2)_{n5}C(O)NR_{a10}R_{b10}$;

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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, 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^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}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, 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 -$(CH_2)_{m1}OR_{c1}$, 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 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;

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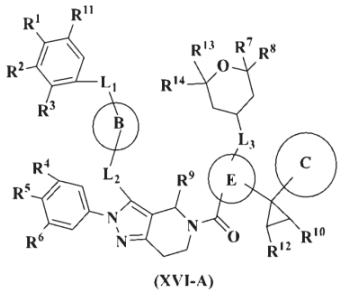
or

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;

preferably, 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; and

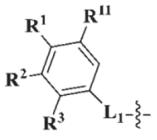
n1-n5, m1 or x each is independently selected from 0, 1, 2, 3, 4 or 5.

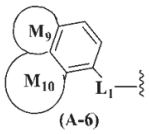
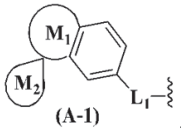
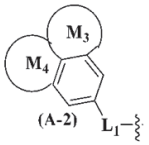
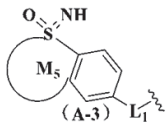
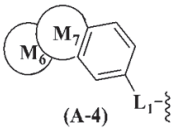
9. The compound according to claim 8, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the general formula (XVI) is further shown as general formula (XVI-A):

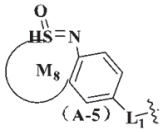


(XVI-A)

wherein



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_{3-12}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;

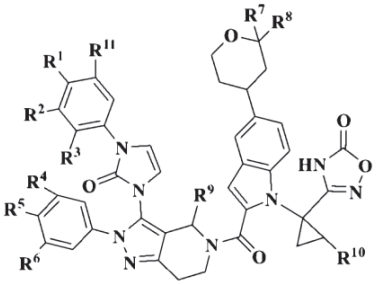
preferably, ring M_1, ring M_2, ring M_3, ring M_4, ring M_5, ring M_6, ring M_7, ring M_8, M_9 or M_{10} each is independently selected from C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl containing 1-3 N, O or S atoms, C_{6-10}aryl or 5- to 10-membered heteroaryl containing 1-3 N, O or S atoms, optionally 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;

further 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; and

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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}, and R^{14} are defined as in claim 9.

10. The compound according to claim 8, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the general formula (XVI) is further shown as general formula (II):



(II)

wherein

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;

preferably, 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, C_{6-10}aryl or 5- to 8-membered heteroaryl, optionally further substituted by one or more substituents of halogen, amino or oxo;

more 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;

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;

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 6-membered heterocyclyl, C_{6-10}aryl or 5- to 8-membered heteroaryl;

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}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,

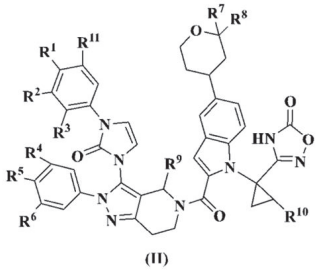
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C_{1-6}haloalkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, 3- to 8-membered heterocyclyl, C_{6-10}aryl or 5- to 10-membered heteroaryl is optionally further substituted by one or more 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; and

n1 is an integer of 0-5.

11. The compound according to claim 8, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the general formula (XVI) is further shown as general formula (II):



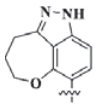
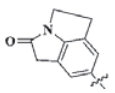
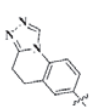
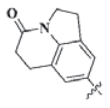
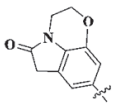
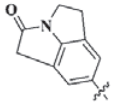
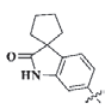
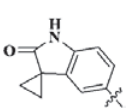
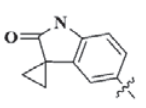
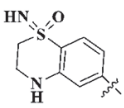
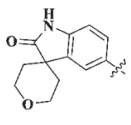
(II)

wherein

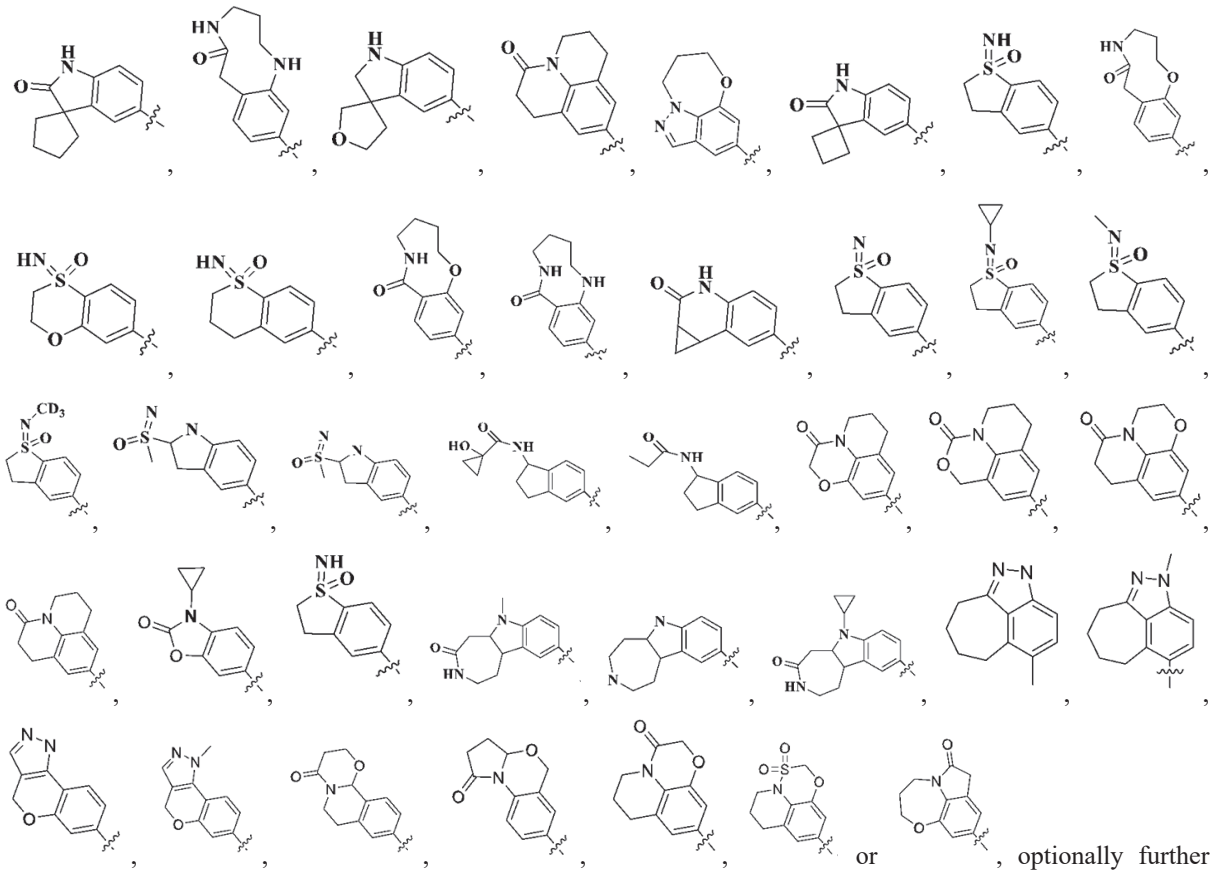
R^1 and R^2, and R^1 and R^{11}, respectively, are linked with adjacent atoms to form C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl, wherein the C_{3-12}cycloalkyl, 3- to 12-membered heterocyclyl, C_{6-14}aryl or 5- to 14-membered heteroaryl is optionally 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;

preferably, 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, C_{3-6}cycloalkyl, amino or oxo;

more 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 C_{3-6}cycloalkyl, or oxo;

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

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

R^1, R^2, R^3or 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,

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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, 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;

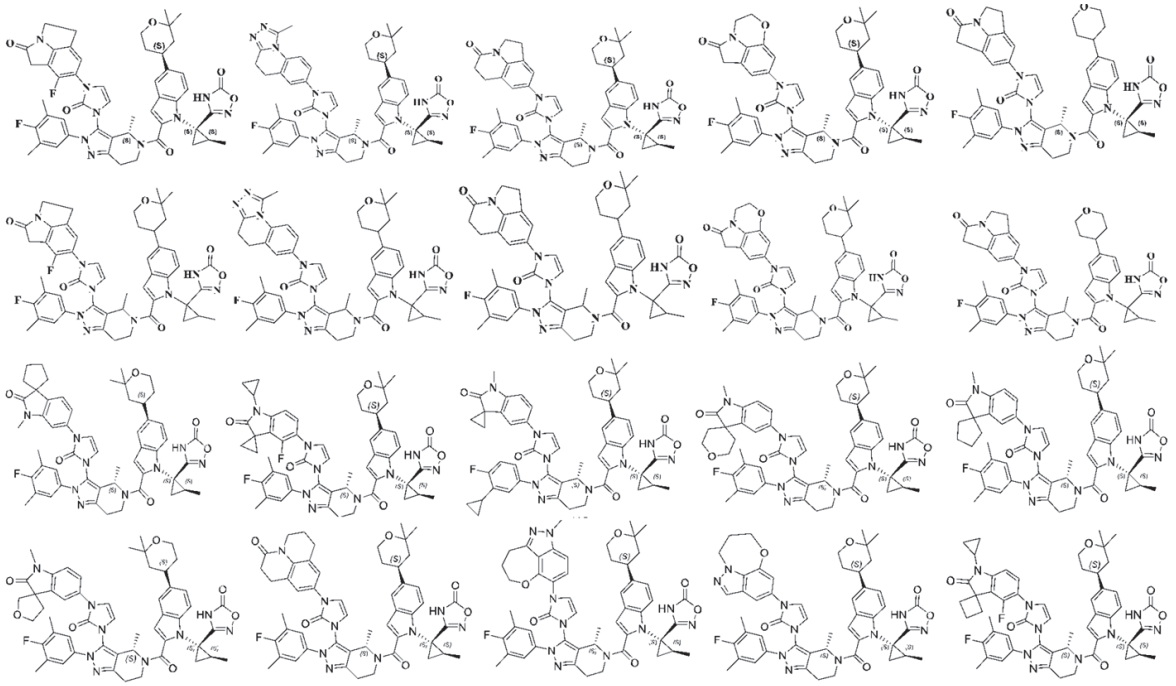
or

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;

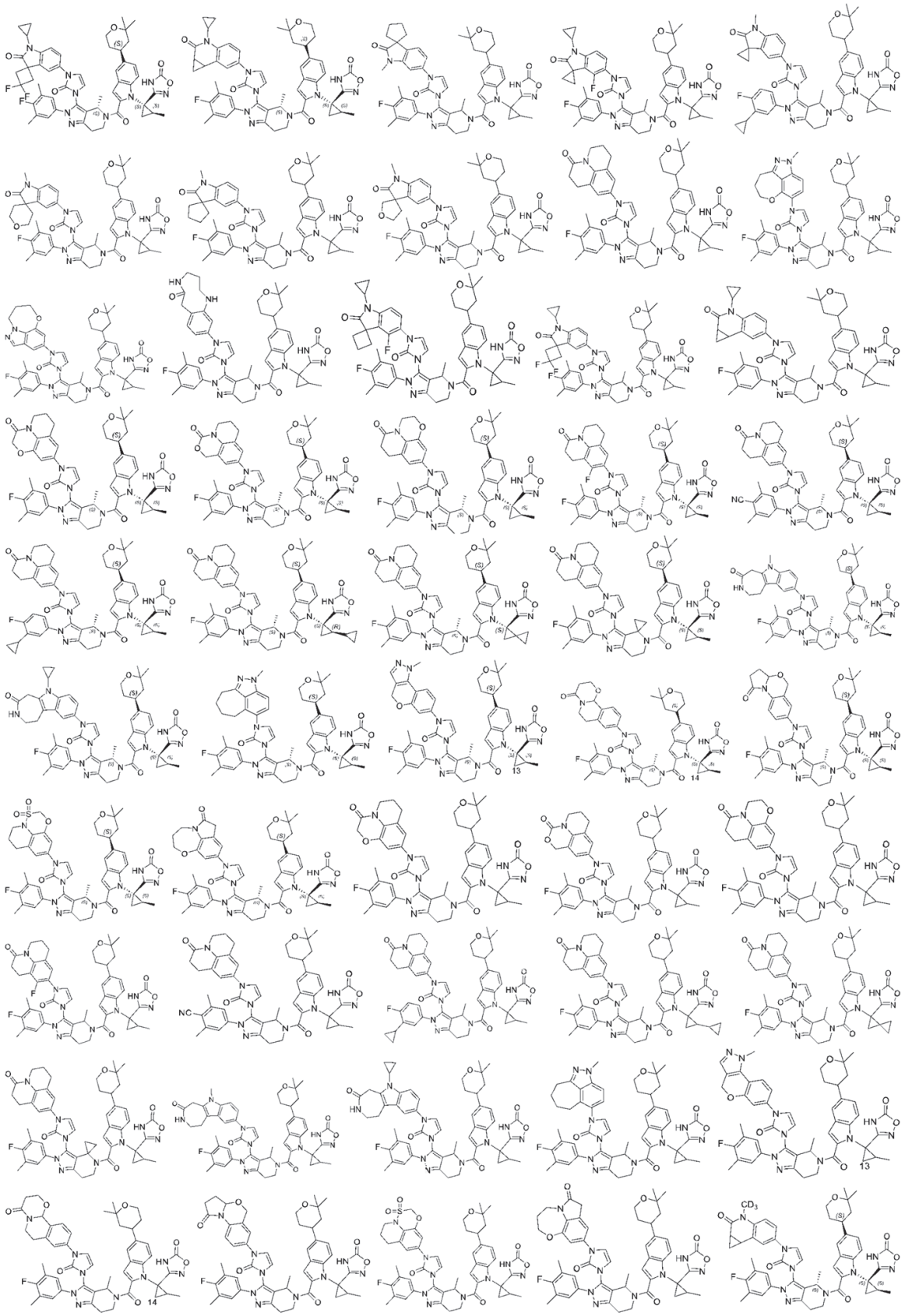
n1 is an integer of 0-5; and

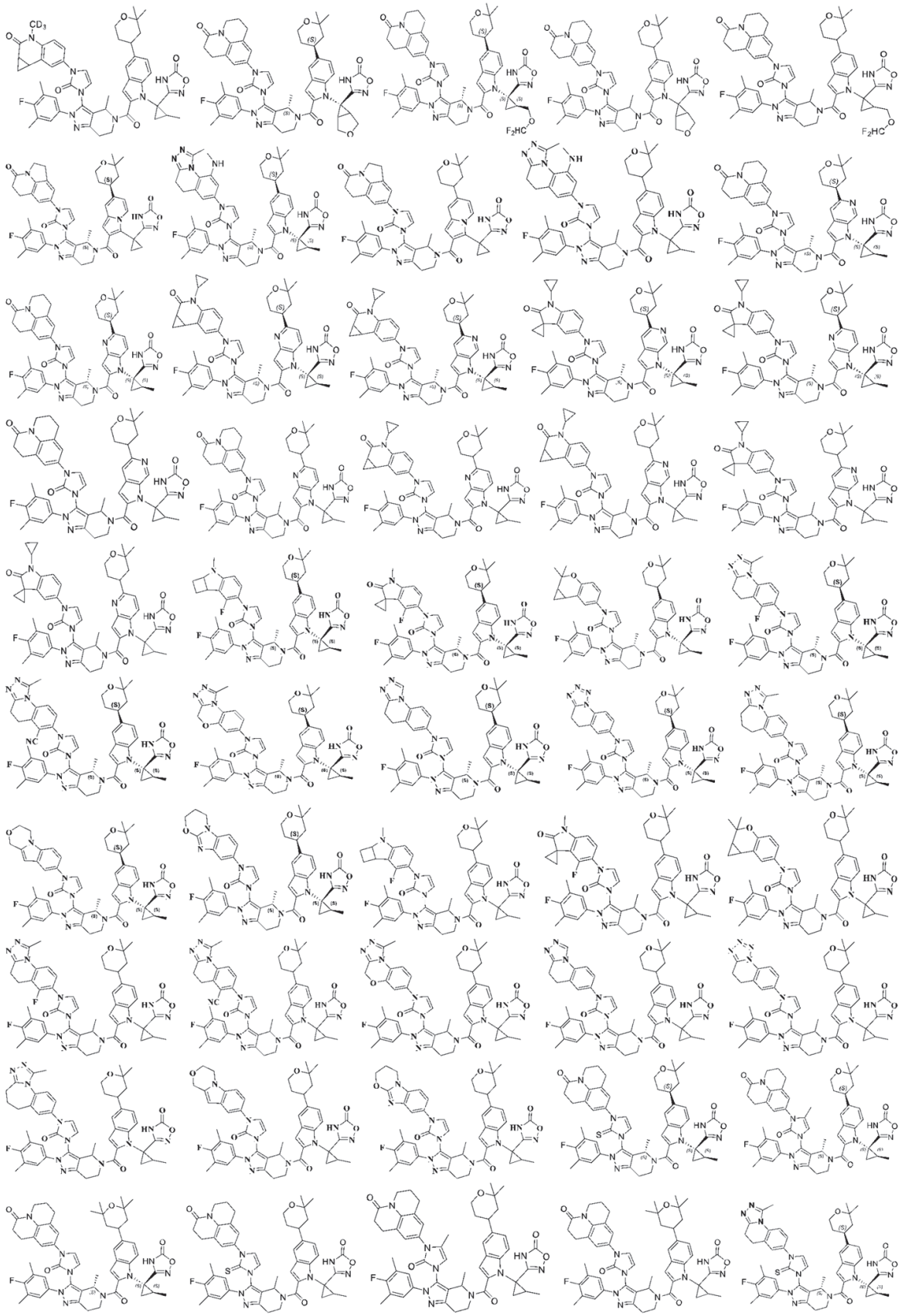
m1 is an integer of 0-5.

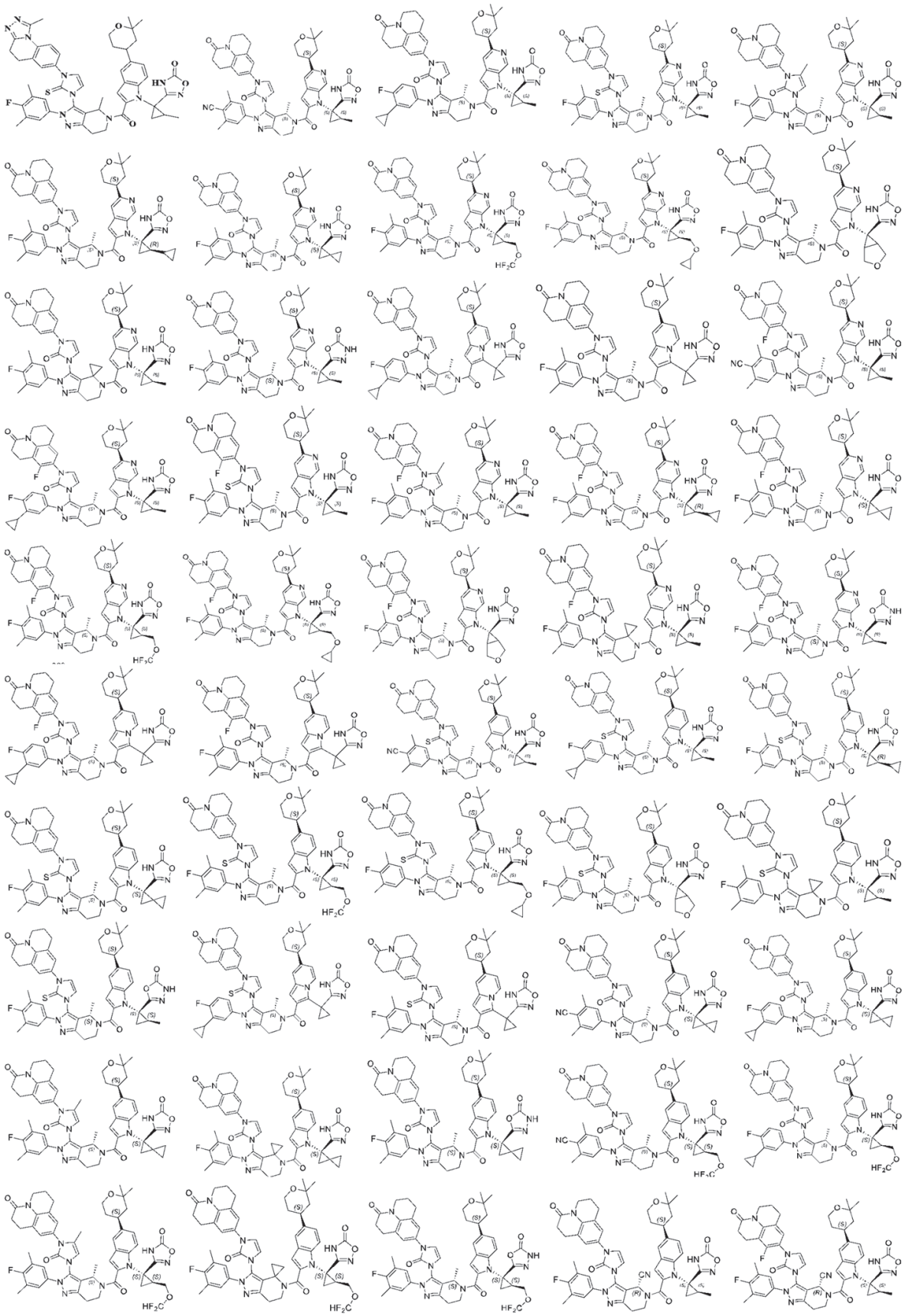
12. The compound according to any one of claims 8-11, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:

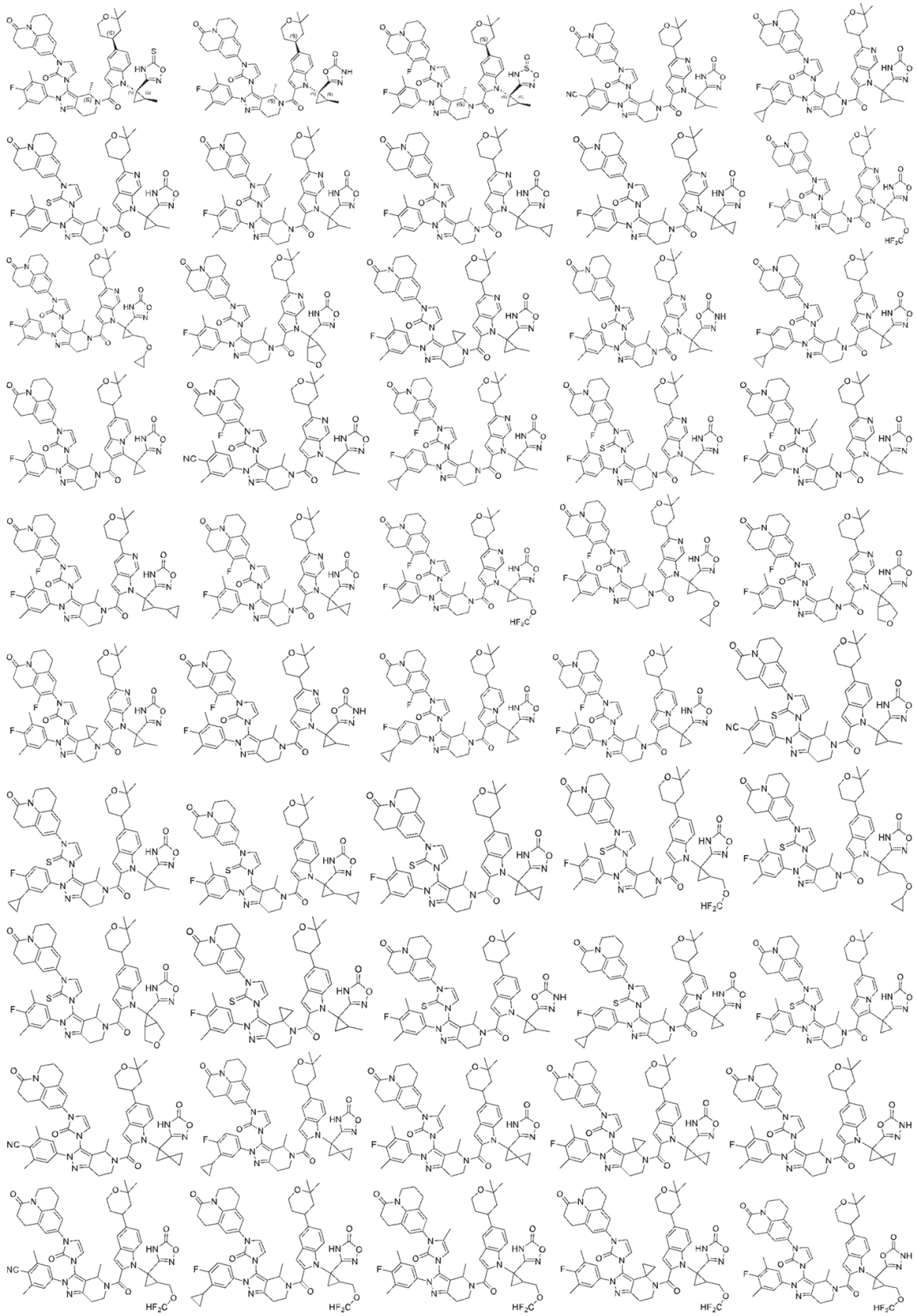


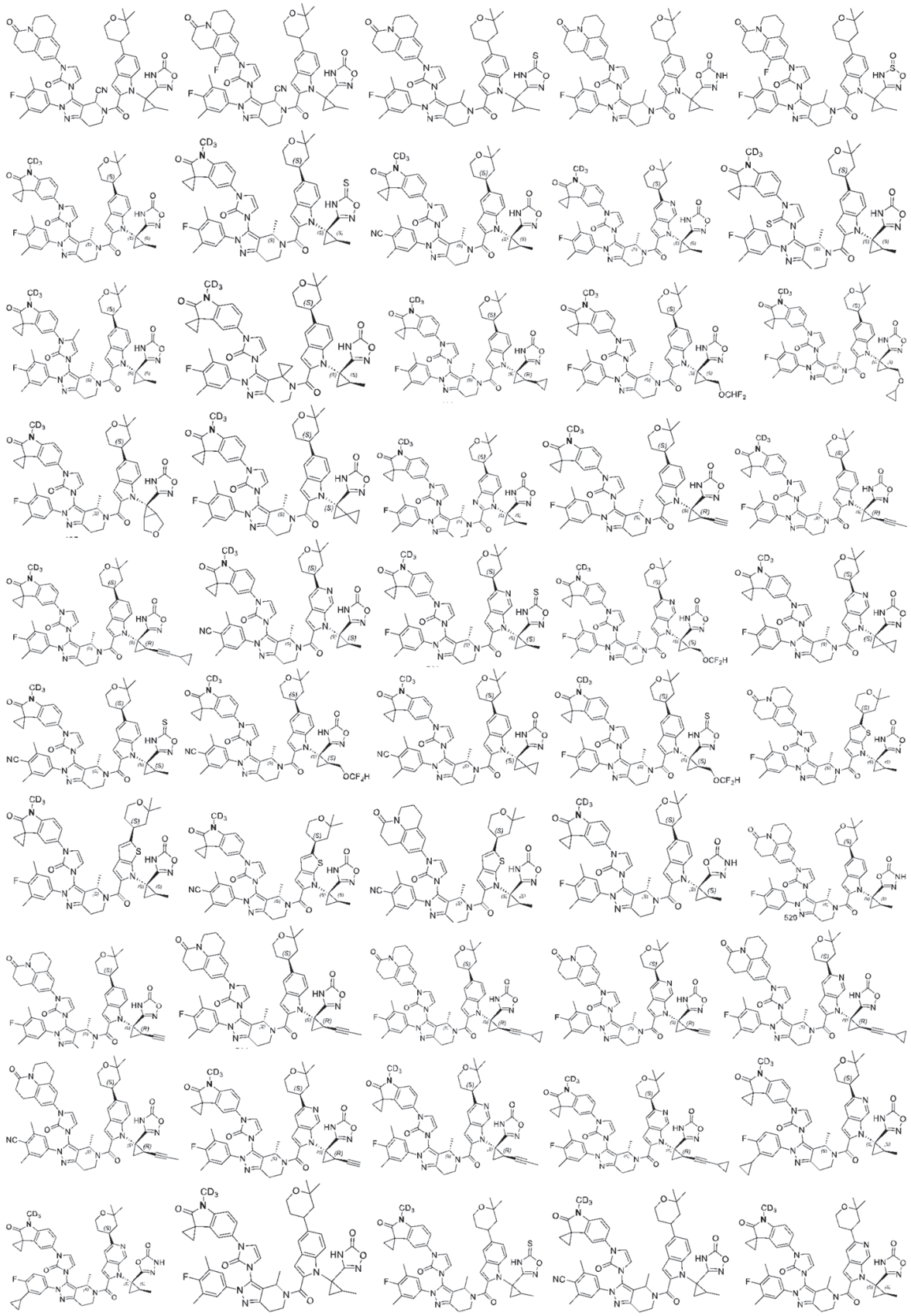
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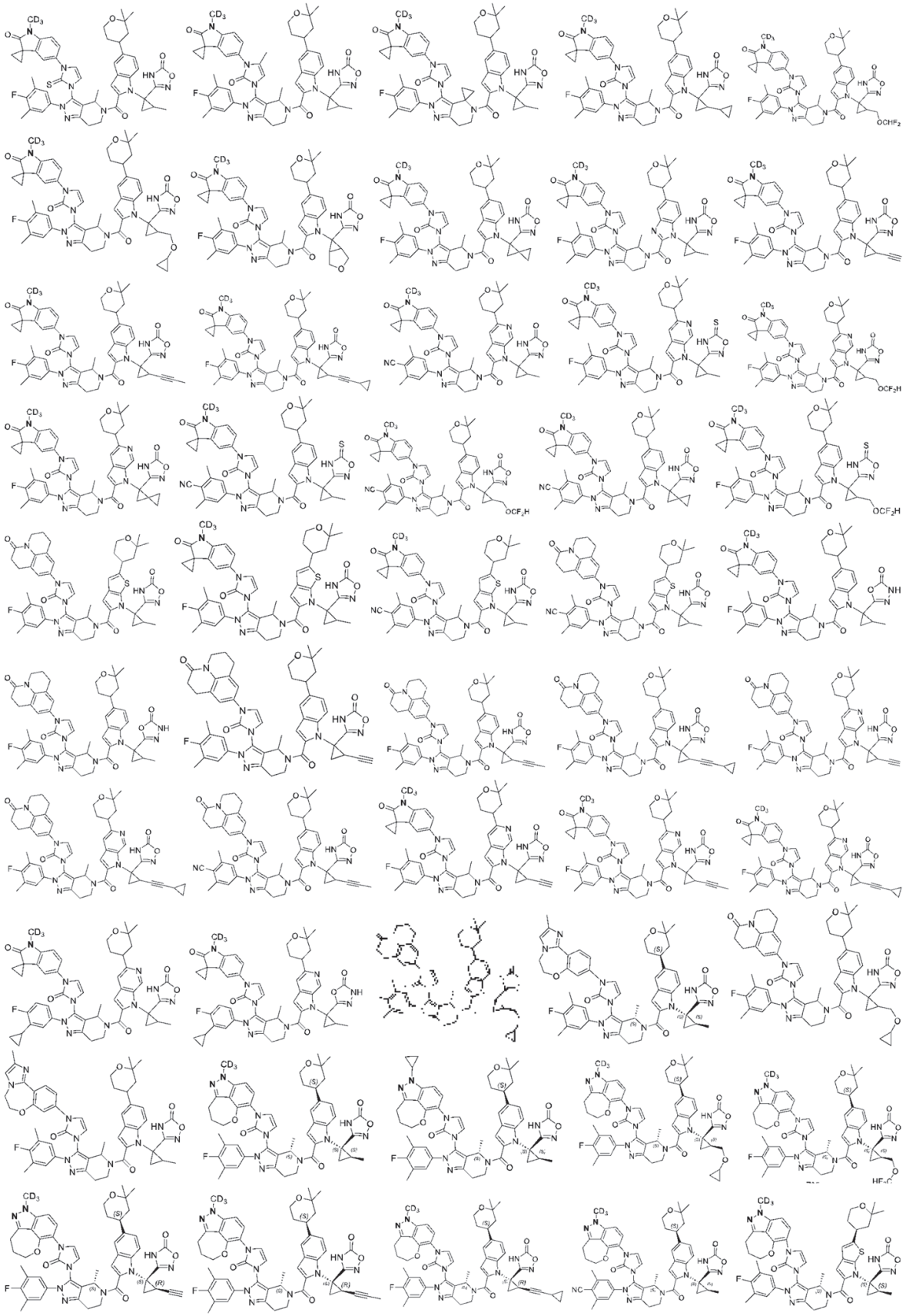


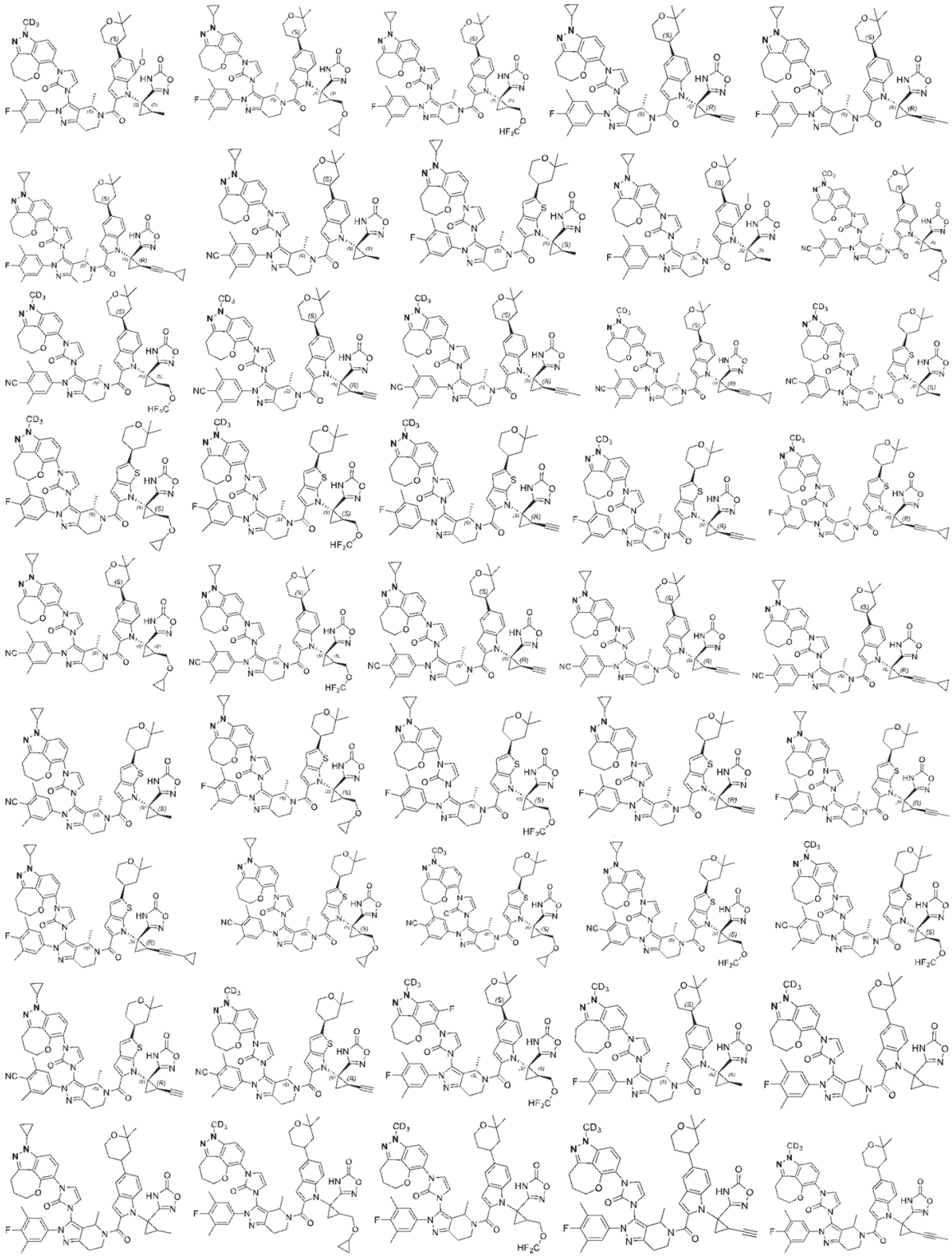


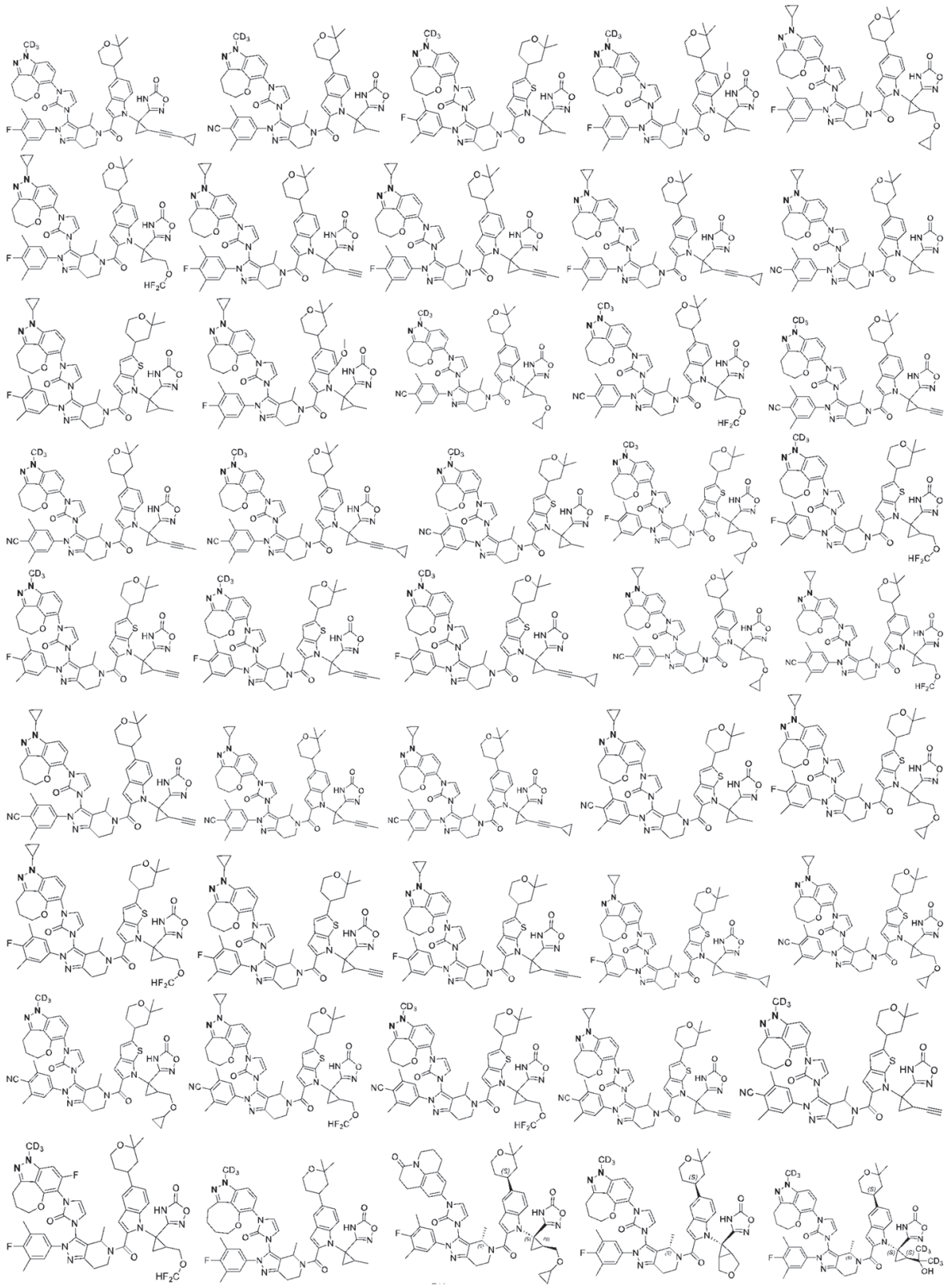


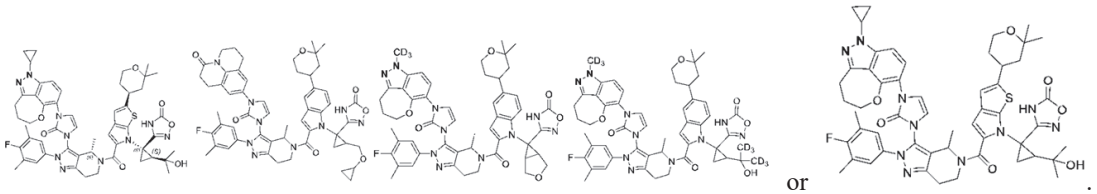




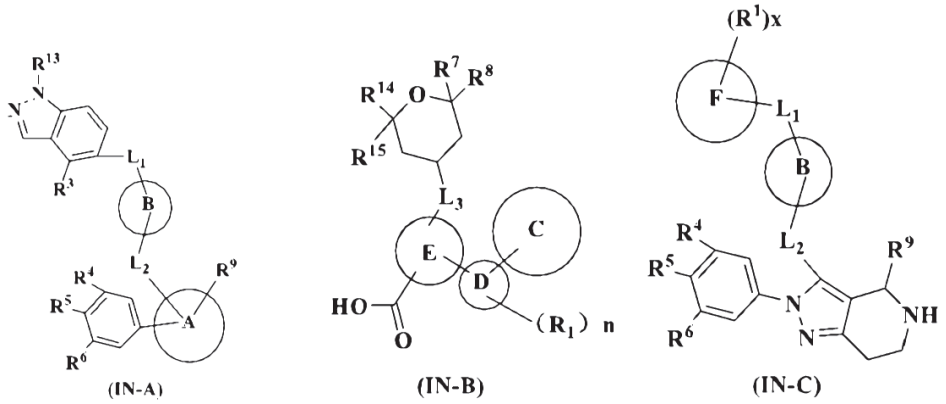








13. A compound of general formula (IN-A), (IN-B) or (IN-C), a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof:



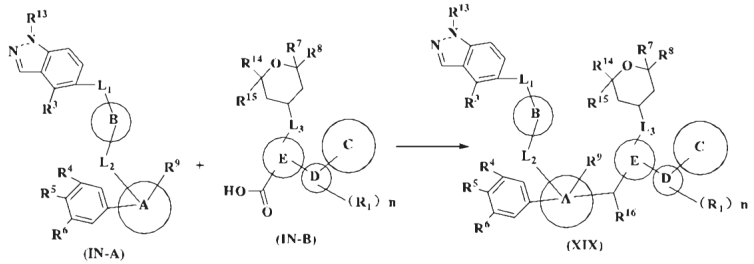
(IN-A) (IN-B) (IN-C)

wherein in general formula (IN-A), R^{13} 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; and ring A, ring B, L_1, L_2, R^3, R^4, R^5, R^6, and R^9 are defined as in claim 1;

in 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; and ring C, ring E, L_3, R^1, R^7, R^8, R^{14}, R^{15}, and n are defined as in claim 1; and

in general formula (IN-C), ring F is selected from 8- to 14-membered tricyclic fused heterocyclyl containing 1-5 heteroatoms; and ring B, L_1, L_2, R^1, R^4, R^5, R^6, R^9, and x are defined as in claim 8.

14. A method for preparing a general formula compound according to claims 1-12, wherein the method comprises the following step:



(IN-A) (IN-B) (XIX)

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 claim 1;

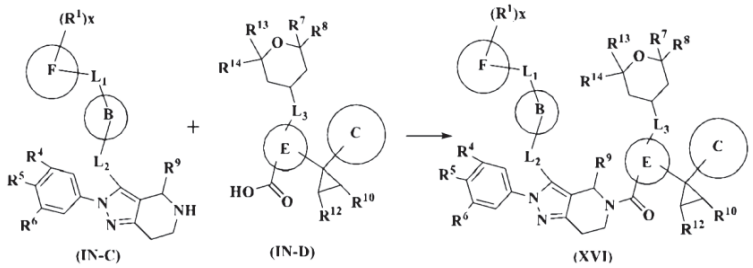
reacting general formula (IN-A) with general formula (IN-B) under the action of a condensation agent and a base to obtain general formula (XIX);

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

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

or comprises the following steps:

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(IN-C) (IN-D) (XVI)

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 claim 8;

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, preferably DIEA.

15. A pharmaceutical composition, comprising a therapeutically effective dose of a compound according to any one of claims 1-12, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers or excipients.

16. Use of a compound according to any one of claims 1-12, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 15 in the preparation of a GLP-1 receptor agonist drug.

17. Use of a compound according to any one of claims 1-12, a prodrug thereof, a stereoisomer thereof or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 15 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.

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TRANSLATION CERTIFICATION

Date: May 20, 2025

To whom it may concern:

This is to certify that the attached translation is an accurate representation of the documents PCT/CN2024/108192 filed on July 29, 2024, received by this office. The translation was completed from:

- Simplified Chinese

To:

- English

Wenli ZHANG, Senior Reviser in RWS, attests to the following:

"To the best of my knowledge, the aforementioned documents are a true, full and accurate translation of the specified documents."

Wenli Zhang

Signature of Wenli ZHANG