(m, 3H), 1.92 (dd, *J* = 9.6, 3.4 Hz, 4H), 1.69 (d, *J* = 14.5 Hz, 2H), 1.28 - 1.20 (m, 2H), 1.17 - 1.08 (m, 2H). MS(ESI,m/z): 517[M+H]$^+$.

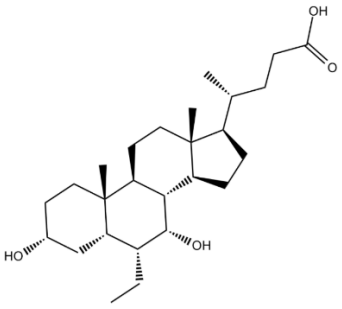
Examples of pharmacological experiments

Test method for FXR activity at the molecular level

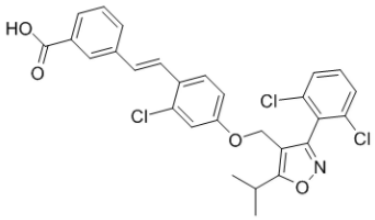
FXR activity was determined using recombinant GST-FXR fusion protein by Perkin Elmer's AlphaScreen detection reagent. The reaction in this method was carried out in a 384-well plate, and the total reaction volume was 15 μL. The mixture of protein, agonist, co-regulatory factor, AlphaScreen® acceptor beads and AlphaScreen® donor beads was reacted in a buffer containing Tris-HCl 50 mM (pH7.4), 50 mM NaCl, BSA 0.1%, and 1mM DTT. The FXR activity was reflected by the fluorescence signal intensity at 570nm wavelength detected by the Envision fluorescence detector. The value of EC50 was calculated by the software Graphpad Prism 5.

Test method for FXR activity at the cell level

The FXR expression plasmid and FXRE luciferase reporter plasmid at a ratio of 1:9 was co-transfected into 293T cells, and then the transfected cells were seeded on a 96-well flat-bottom microplate (ViewPlate-96, White 96- well Microplate with Clear Bottom, PerkinElmer) at 5×10^5/well. The cells were cultured for 24 hours to ensure plasmid expression. Then the FXR receptor agonist to be tested was added and acted for 18 hours. The fluorescence intensity was detected using luciferase kit (steady-Glo Luciferase Assay system) to reflect the compound's activation efficiency on the FXR receptor.



OCA



GW4064

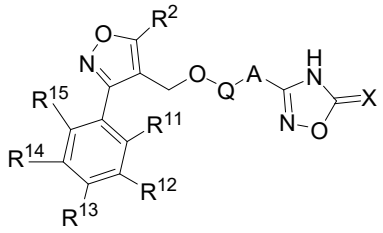
In the preliminary screening, the test compound and the two positive compounds OCA, GW4064 acted on the cells at 10 μM, and the relative activities of the test compound to the two positive compounds were determined respectively (relative activity = (signal intensity of test compound -blank)/(signal intensity of positive compound -blank)×100%). The compound whose relative activity is higher than 50% of the positive compound enters the re-screening. The appropriate concentration interval was selected, and the dose-dependent relationship, that is, the EC50 value, was calculated.

Table 1 Activity test results

Test sample	FXR activity at the molecular level	FXR activity at the ~~molecular~~ cell level	
	EC_{50} (μM)	Activity relative to OCA (%) 10μM	EC_{50} (μM)
OCA	0.374	100	1.16

Claims

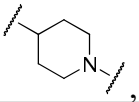
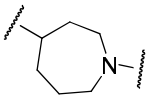
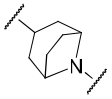
1. A compound represented by general formula I, or enantiomer, diastereomer, tautomer, racemate, solvate, ~~prodrug~~ or pharmaceutically acceptable salt thereof,



(I)

wherein, R^{11}, R^{12}, R^{13}, R^{14} and R^{15} are each independently hydrogen, halogen, halogenated $C_{1\text{-}6}$ alkyl, halogenated C_1-C_6 alkoxy, C_1-C_6 alkyl, or $C_{1\text{-}6}$ alkoxy~~, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkoxy, cyano or nitro~~;

R^2 is C_6-~~C_{12}~~ aryl, C_1-C_6 alkyl or C_3-C_6 cycloalkyl;

Q is ~~a 4-8 membered heterocyclyl~~ , , or , wherein N is attached to A;

A is ~~the following~~ substituted or unsubstituted ~~group:~~ phenyl, or ~~–~~substituted or unsubstituted pyridyl, ~~thienyl, furyl, indazolyl, indolyl, benzothienyl, benzofuranyl,~~ and the "substituted" means that there is one, two or three substituents selected from the group consisting of halogen, C_1-C_6 alkyl, halogenated $C_{1\text{-}6}$ alkyl~~, halogenated C_1-C_6 alkoxy, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and C_3-C_6 cycloalkoxy~~;

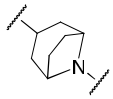
X is O~~ or S~~.

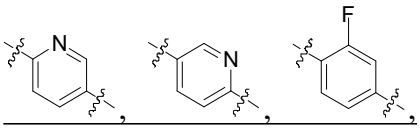
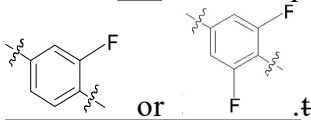
2. The compound of claim 1, wherein R^{11}, R^{12}, R^{13}, R^{14} and R^{15} are each independently hydrogen, fluorine, chlorine, bromine, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, trifluoromethyl, or trifluoromethoxy.

3. The compound of claim 1, wherein R^{11}, and R^{15} are each independently hydrogen, chlorine, bromine, trifluoromethyl, or trifluoromethoxy;

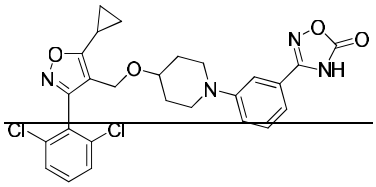
R^{12}, R^{13}, and R^{14} are hydrogen.

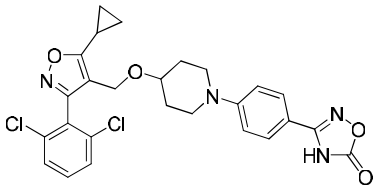
~~3~~4. The compound of claim 1, wherein R^2 is phenyl, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, cyclopropyl, cyclobutyl or cyclopentyl.

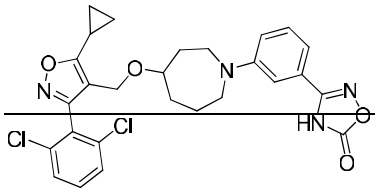
4~~5~~. The compound of claim 1, wherein Q is  ~~a 4-7 membered nitrogen-containing heterocyclyl~~.

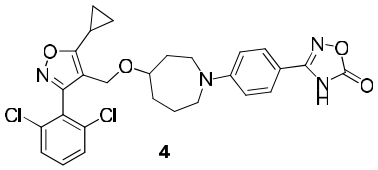
~~5.~~ 6. The compound of claim 1, wherein A is ,  or . ~~the following substituted or unsubstituted group: phenyl, pyridyl, thienyl, furyl, indazolyl, indolyl, benzothienyl, benzofuranyl; and the "substituted" means that there is one or two substituents selected from the group consisting of fluorine, chlorine, bromine, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, C_1-C_4 alkoxy, and C_3-C_6 cycloalkoxy.~~

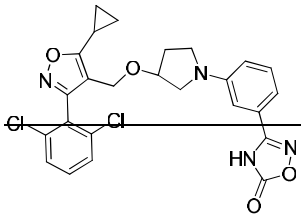
~~6~~7. The compound of claim 1, wherein the compound is:

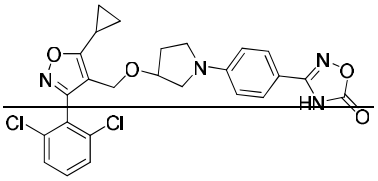

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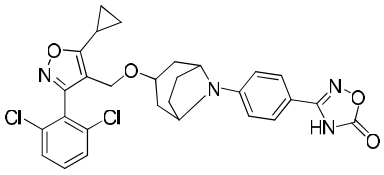

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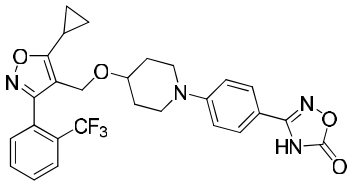

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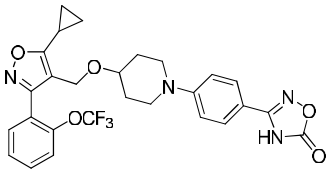

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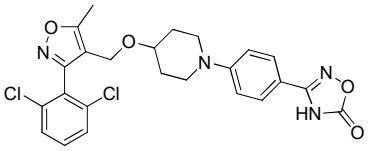

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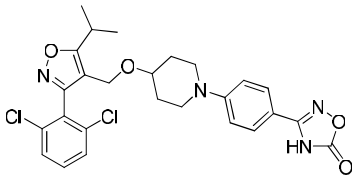

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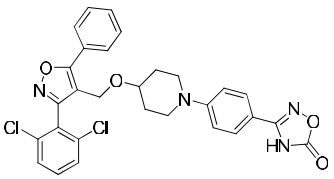

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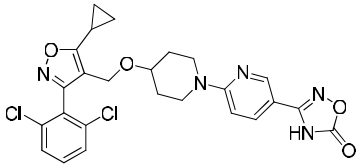

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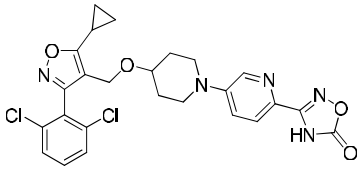

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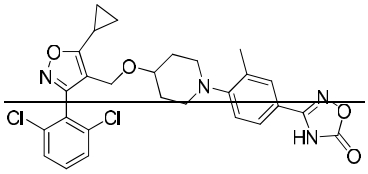

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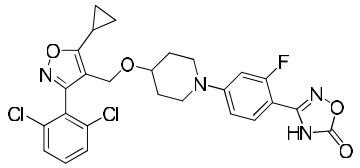

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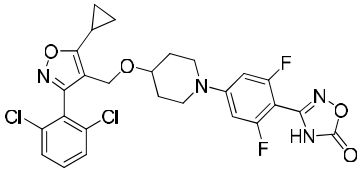

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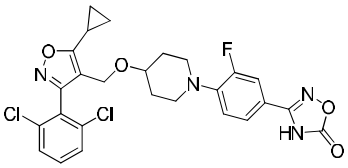

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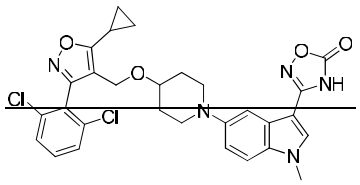

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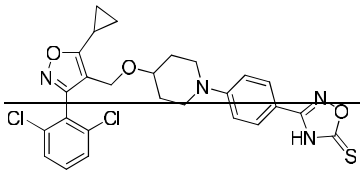

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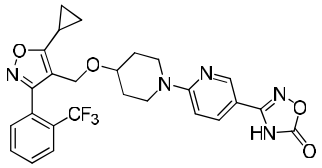

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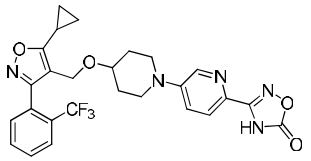
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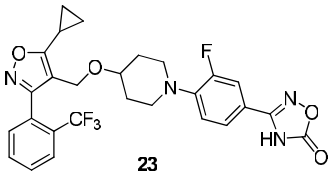
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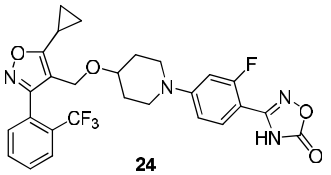
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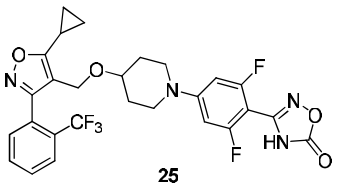
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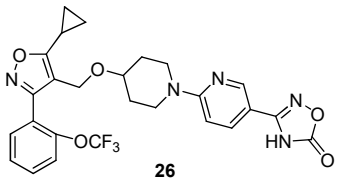
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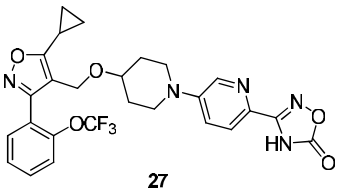
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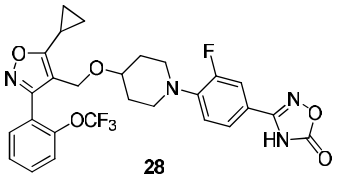
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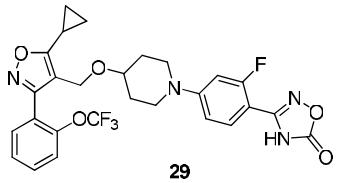
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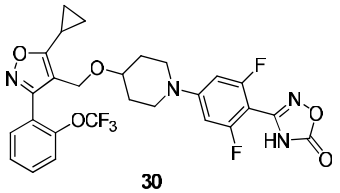
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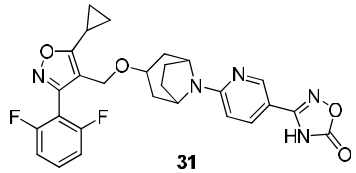
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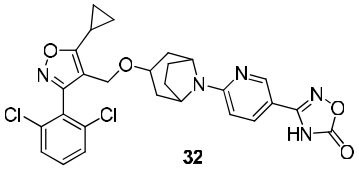
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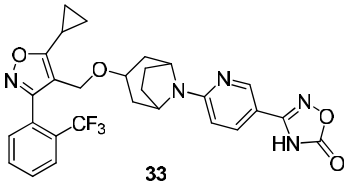
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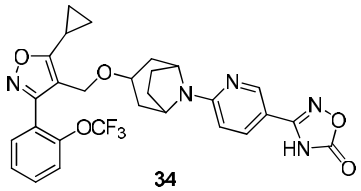
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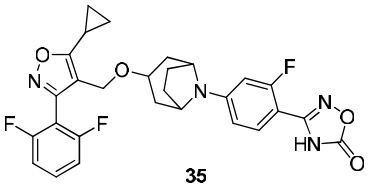
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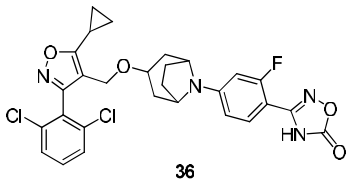
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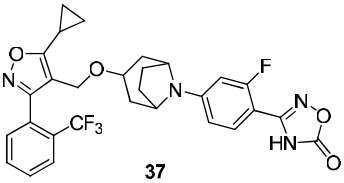
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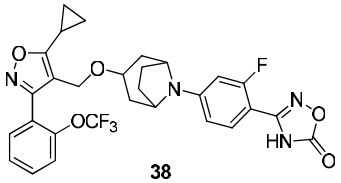
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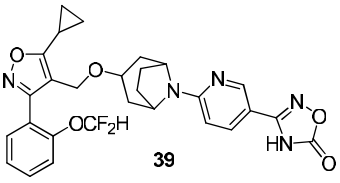
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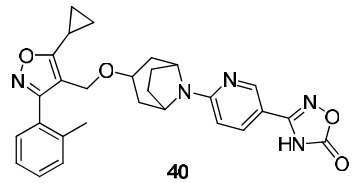


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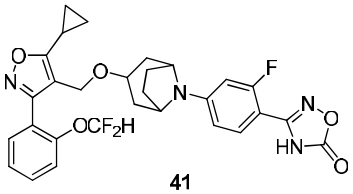


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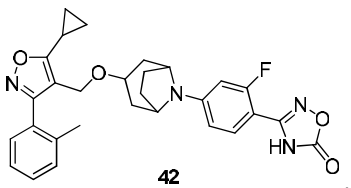
or



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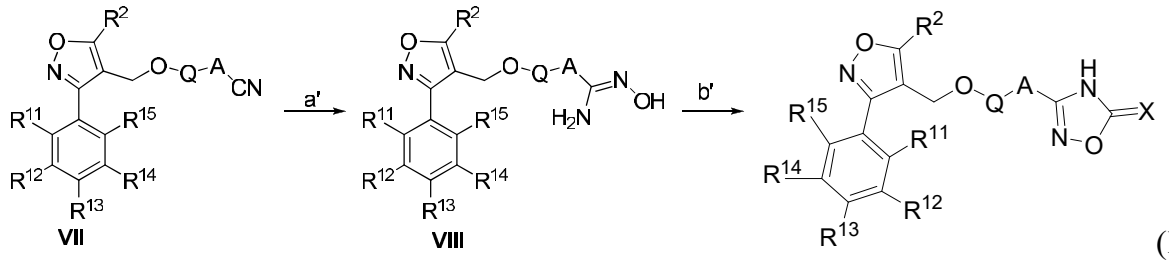
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~~7~~8. A method for preparing the compound according to claim 1, wherein the method comprises the following steps:



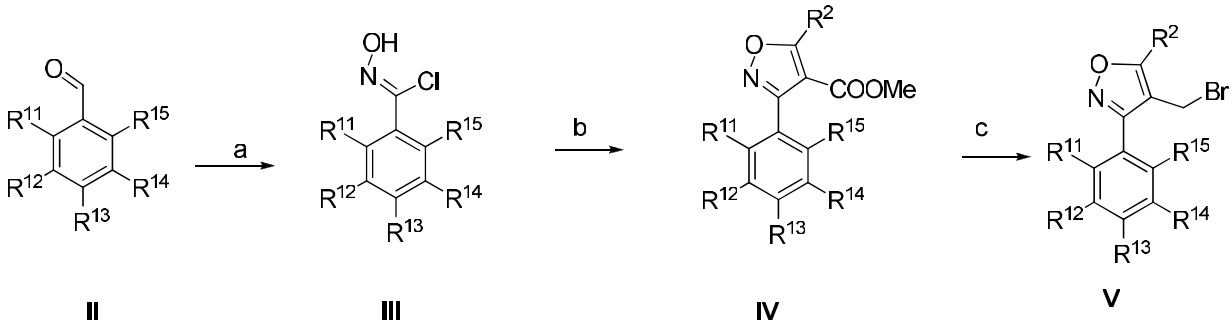
(I)

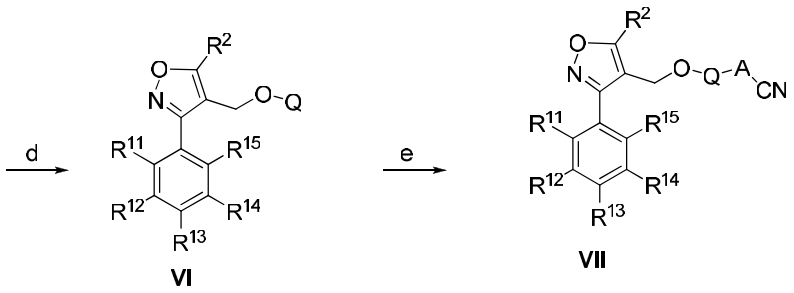
(a') reacting a compound represented by general formula VII with hydroxylamine hydrochloride to produce a compound represented by general formula VIII;

(b') reacting the compound represented by the general formula VIII under the action of phosgene, triphosgene, carbonyldiimidazole or thiocarbonyldiimidazole to produce the compound represented by the general formula I,

wherein, X, R^2, Q, A, R^{11}, R^{12}, R^{13}, R^{14} and R^{15} are defined as in claim 1.

9~~8~~. The method of claim 8~~7~~, wherein the compound represented by the general formula VII is prepared by the following steps:





a) reacting substituted benzaldehyde compound represented by general formula II as starting materials with hydroxylamine hydrochloride to obtain an intermediate and then chlorinating the intermediate with N-chlorosuccinimide (NCS) to produce a compound represented by general formula III;

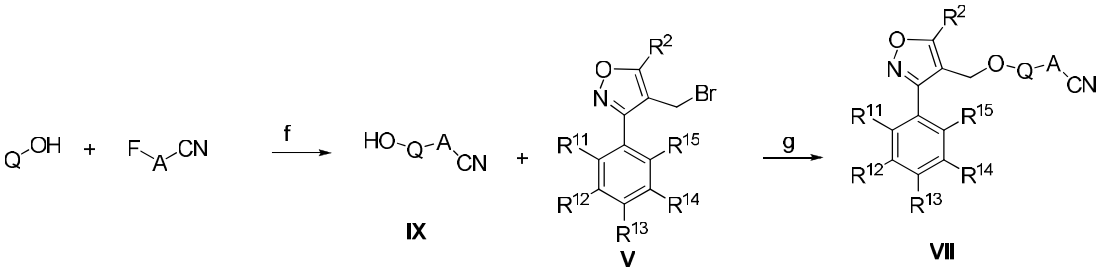
b) reacting the compound represented by the general formula III with 3-oxopropionate to obtain a compound represented by the general formula IV;

c) reducing the ester in the compound represented by formula IV to produce alcohol, and then brominating to produce a compound represented by V;

d) reacting the compound represented by general formula V with Q-OH to produce a compound represented by general formula VI;

e) coupling the compound represented by general formula VI with Br-A-CN under the catalysis of copper or palladium to obtain the compound represented by general formula VII,

or prepared by the following steps:



IX V VII

f) reacting Q-OH with F-A-CN to generate a compound represented by general formula IX;

g) reacting a compound represented by the general formula V with the compound represented by the general formula IX to produce the compound represented by the general formula VII,

in each formula, R^2, Q, A, R^{11}, R^{12}, R^{13}, R^{14} and R^{15} are defined as in claim 1.

~~9~~10. A pharmaceutical composition comprising the compound represented by the general formula I ~~of claim 1~~, ~~or~~ the enantiomer, diastereomer, tautomer, racemate, solvate, ~~prodrug,~~ or pharmaceutically acceptable salt thereof of claim 1; and

a pharmaceutically acceptable carrier.

~~10~~11. Use of the compound represented by the general formula I ~~of claim 1~~, or the enantiomer, diastereomer, tautomer, racemate, solvate, ~~prodrug,~~ or pharmaceutically acceptable salt thereof of claim 1 ~~:~~

~~(a) as an FXR agonist;~~

~~(b)~~ for the manufacture of a medicament for the treatment of FXR-related diseases;

~~(c) to reduce the levels of ALP, ALT, AST and TBA in serum;~~

~~(d) to reduce the amount of hydroxyproline in liver tissue;~~

~~(e) to down-regulate the expression of α-SMA and Col1α1 mRNA in liver tissue; or~~

~~(f) to reduce the content of collagen in the liver.~~

wherein the FXR-related disease is non-alcoholic fatty liver, primary biliary cirrhosis, primary sclerosing cholangitis, gallstone, non-alcoholic liver cirrhosis, liver fibrosis, cholestatic liver disease, hyperlipidemia, hypercholesterolemia, or diabetes.