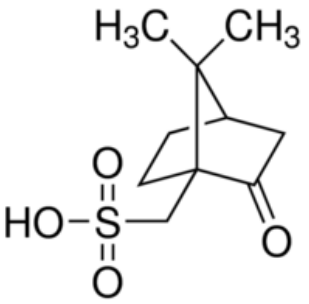


,

to provide a compound of Formula (Ic),

wherein

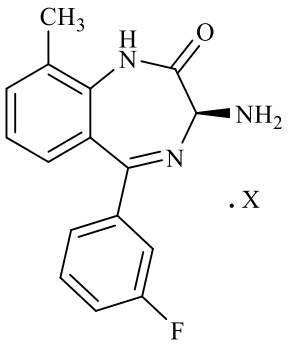
R^1 each is independently Cl, F, Br, I, OCH_3, CN or NO_2;

R^2 each is independently identical or different C_1-C_5 alkyl;

n^1 is an integer between 1 and 5; and

n^2 is an integer between 1 and 4.

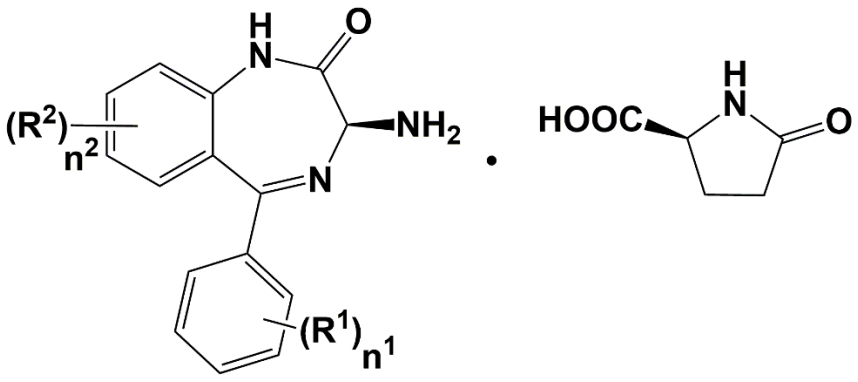
[006d] In a further aspect of the present disclosure, there is provided a compound represented by the following structure:



Compound (2),

wherein X comprises: chloride, acetate, adipate, alginate, ascorbate, aspartate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, hydroiodide, maleate, 2-hydroxyethanesulfonate, lactate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oxalate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, salicylate, succinate, sulfate, sulfonate, tartrate, thiocyanate, toluenesulfonate, or undecanoate salt, or any combination thereof.

[007] In one example, the present disclosure provides a method of preparing the compound of Formula (Ib),

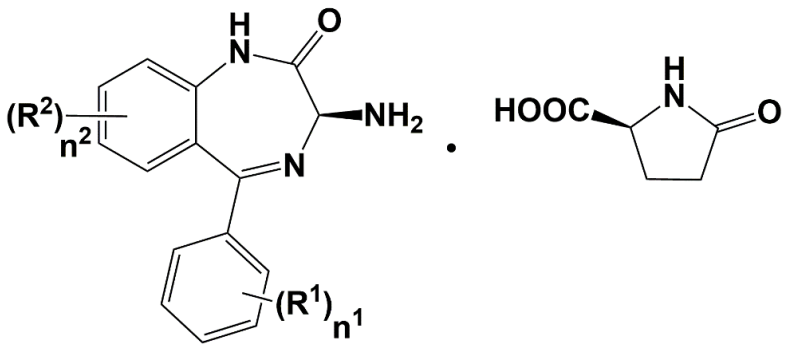


Formula (Ib)

CLAIMS

What is claimed is:

1. A method of preparing the compound of Formula (Ib),



Formula (Ib)

wherein

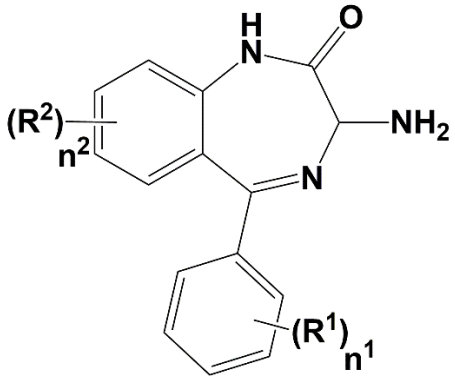
R^1 each is independently Cl, F, Br, I, OCH_3, CN or NO_2;

R^2 each is independently identical or different C_1-C_5 alkyl;

n^1 is an integer between 1 and 5; and

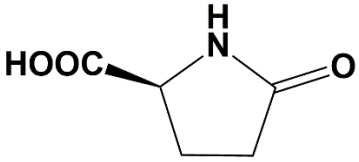
n^2 is an integer between 1 and 4;

comprising the step of: reacting the compound of Formula (Ia)



Formula (Ia)

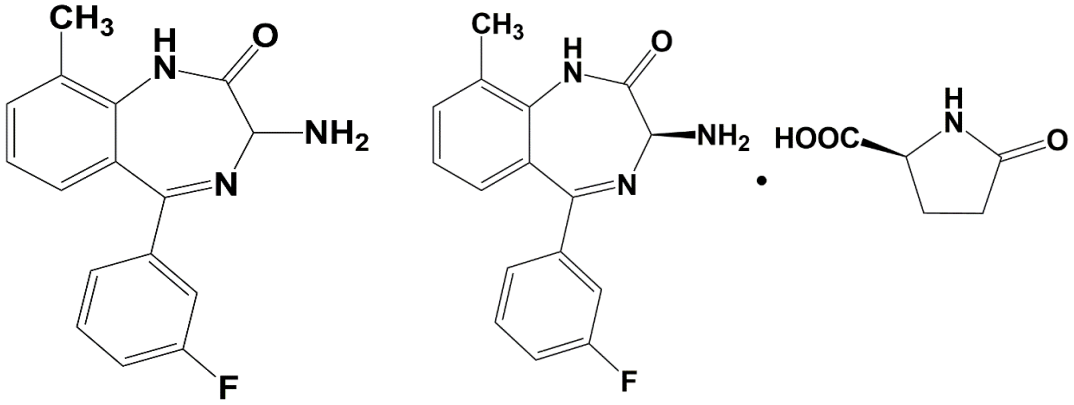
with L-pyroglutamic acid (L-PGA),



L-pyroglutamic acid (L-PGA),

in the presence of solvent and with or without catalyst to obtain a compound of Formula (Ib).

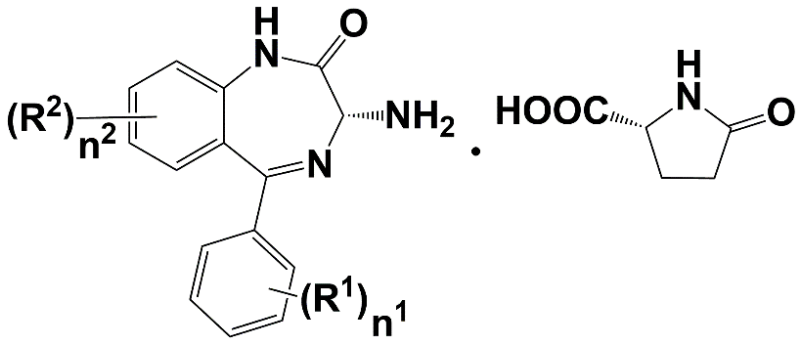
2. The method according to claim 1, wherein the compound of Formula (Ia) is represented by Compound (1a) and the compound of Formula (Ib) is represented by Compound (1b):



Compound (1a) and Compound (1b).

3. The method of claim 1, wherein the yield of the compound of Formula (Ib) is greater than 50%.

4. A method of preparing the compound of Formula (Id),



Formula (Id)

wherein

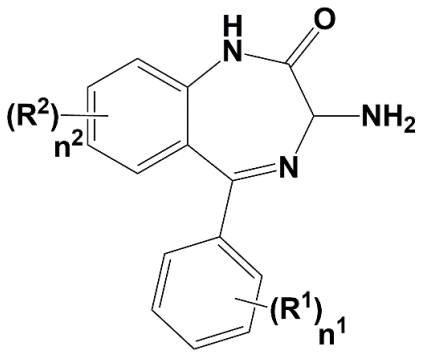
R^1 each is independently Cl, F, Br, I, OCH_3, CN or NO_2;

R^2 each is independently identical or different C_1-C_5 alkyl;

n^1 is an integer between 1 and 5; and

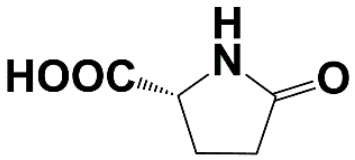
n^2 is an integer between 1 and 4;

comprising the steps of: reacting the compound of Formula (Ia)



Formula (Ia)

with D-pyroglutamic acid (D-PGA),



D-pyroglutamic acid (D-PGA)

in the presence of solvent and with or without catalyst to obtain a compound of Formula (Id).

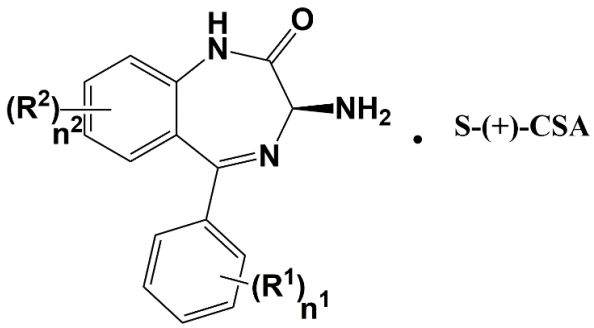
5. The method of claim 4, wherein the yield of the compound of Formula (Id) is greater than 50%.
6. The method according to any one of claims 1-5, wherein the catalyst comprises benzaldehyde, salicylaldehyde, 3,5-dichlorosalicylaldehyde, p-nitrobenzaldehyde or any combination thereof.
7. The method according to claim 6, wherein the catalyst comprises 3,5-dichlorosalicylaldehyde.
8. The method according to any one of claims 1-7, wherein 0.001 to 1.0 mole equivalents of the catalyst compared to the compound of Formula (Ia) are used.
9. The method according to claim 8, wherein 0.03 mole equivalents of the catalyst compared to the compound of Formula (Ia) are used.
10. The method according to any one of claims 1-9, wherein the solvent comprises an alcoholic solvent; an ester solvent; an ether solvent; an hydrocarbon solvent; a polar aprotic solvent; a ketone solvent; a chloro solvent; a nitrile solvent; a polar solvent; or any combination thereof.

11. The method according to claim 10, wherein the alcoholic solvent is ethanol.

12. The method according to any one of claims 1-11, wherein the reaction is conducted at a temperature between 0-100 ºC.

13. The method according to claim 12, wherein the temperature is between 60-65 ºC.

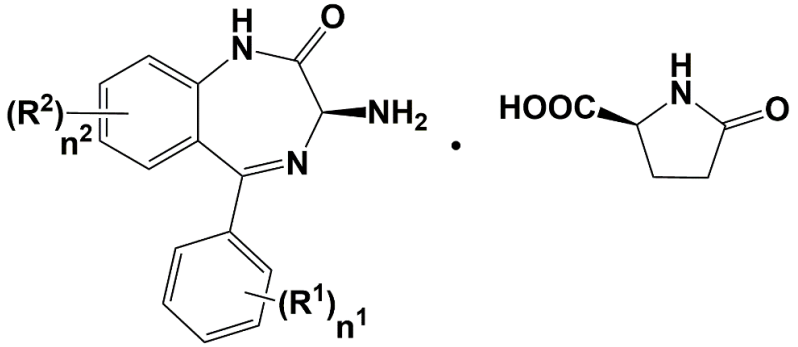
14. A method of preparing the compound of Formula (Ic),



Formula (Ic)

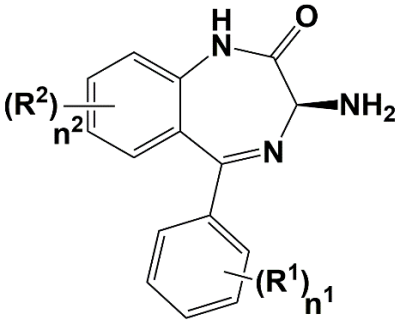
comprising the steps of:

a) reacting the compound of Formula (Ib):



Formula (Ib)

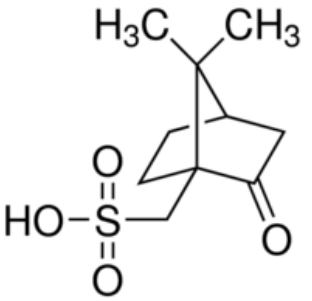
with a base and solvent to provide a compound of Formula (I); and



Formula (I)

b) reacting the compound of Formula (I) with

S (+) camphor sulfonic acid (CSA):



,

to provide a compound of Formula (Ic),

wherein

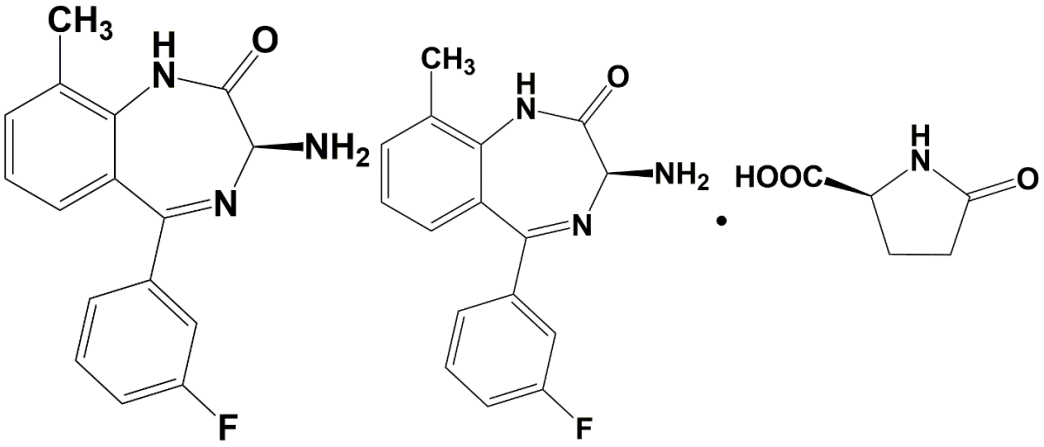
R^1 each is independently Cl, F, Br, I, OCH_3, CN or NO_2;

R^2 each is independently identical or different C_1-C_5 alkyl;

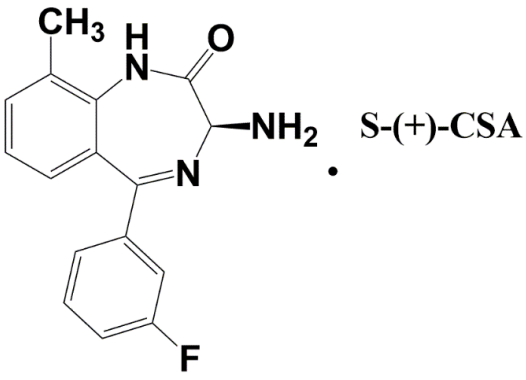
n^1 is an integer between 1 and 5; and

n^2 is an integer between 1 and 4.

15. The method according to claim 14, wherein the compound of Formula (I) is represented by Compound (1); the compound of Formula (Ib) is represented by Compound (1b); and the compound of Formula (Ic) is represented by Compound (1c):

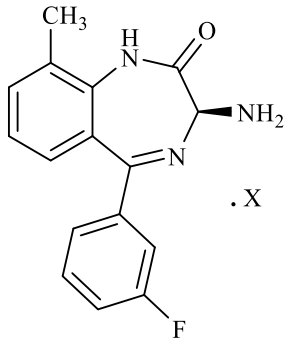


Compound (1); Compound (1b); and



Compound (1c).

16. The method according to claim 14 or 15, wherein the base comprises an inorganic base, an organic base, or any combination thereof.
17. The method according to claim 16, wherein the inorganic base comprises: an alkali metal hydroxide; an alkali metal hydride; an alkali metal alkoxide; an alkali metal carboxylate; an alkali metal carbonate, bicarbonate, or any combination thereof.
18. The method according to claim 17, wherein the alkali metal carbonate is sodium bicarbonate.
19. The method according to any one of claims 16-18, wherein the organic base comprises: a primary amine, a secondary amine, an aromatic amine, a tertiary amine, or any combination thereof.
20. The method according to any one of claims 14-19, wherein the solvent comprises an alcoholic solvent; an ester solvent; an ether solvent; an hydrocarbon solvent; a polar aprotic solvent; a ketone solvent; a chloro solvent; a nitrile solvent; a polar solvent; or any combination thereof.
21. The method according to claim 20, wherein the ester solvent is isopropyl acetate.
22. The method according to any one of claims 14-21, wherein the reaction of step (a) is conducted at a temperature between 0-45 ºC.
23. The method according to claim 22, wherein the temperature is between 5-10 ºC.
24. The method according to any one of claims 1-23, wherein the chiral purity of the compound of Formula (I), (Ib), (Ic) or (Id) is greater than 99%.
25. The method according to claim 24, wherein the chiral purity is greater than 99.5%.
26. A compound represented by the following structure:



Compound (2),

wherein X comprises: chloride, acetate, adipate, alginate, ascorbate, aspartate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate,

ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, hydroiodide, maleate, 2-hydroxyethanesulfonate, lactate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oxalate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, salicylate, succinate, sulfate, sulfonate, tartrate, thiocyanate, toluenesulfonate, or undecanoate salt, or any combination thereof.