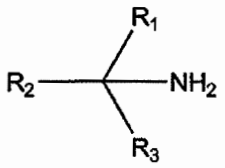
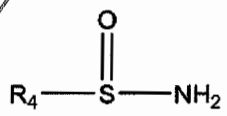
What is claimed is:

1. A method for resolution of a mixture of pinocembrin optical isomers, in particular a pinocembrin racemate, said method comprising performing the resolution by using a chiral primary amine or a chiral sulfinamide as a resolving agent.

2. The method according to claim 1, wherein said chiral primary amine and said chiral sulfinamide are respectively represented by the following general formulas:





chiral primary amine chiral sulfinamide

wherein,

R_1 is selected from -H, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$ or $-CH_2OH$;

R_2 is selected from phenyl, benzyl, or phenyl or benzyl with a substituent on aromatic ring thereof, $-CH_2OH$, $-CH(OH)CH_3$, $-CH(OH)C_2H_5$, phCH(OH)- , wherein the substituent is selected from $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH(CH_3)_2$, $-NO_2$, $-CF_3$, -F, -Cl, -I, -OH, $-OCH_3$, $-OC_2H_5$, $-COOCH_3$, $-COOC_2H_5$, $-CONH_2$, $-CONHCH_3$, $-CONHC_2H_5$, $-CON(CH_3)_2$ or $-CONHCH(CH_3)_2$;

R_3 has the same definition as those of R_1 and R_2 with proviso that R_3 does not have the same structure as R_1 or R_2 dose at the same time;

R_4 is selected from an alkyl having 1-6 carbon atoms, an aryl or aralkyl having 6-9 carbon atoms, a substituted alkyl having 1-6 carbon atoms, a substituted aryl or aralkyl having 6-9 carbon atoms, wherein the substituent is selected from $-NO_2$, $-CF_3$, -F, -Cl, -I, -OH, $-OCH_3$, $-OC_2H_5$, $-COOCH_3$, $-COOC_2H_5$, $-CONH_2$, $-CONHCH_3$, $-CONHC_2H_5$, $-CON(CH_3)_2$, $-CONHCH(CH_3)_2$.

3. The method according to claim 1, comprising the following steps:

(1) performing a derivation reaction of a mixture of pinocembrin optical isomers, which is optionally subjected to a phenolic hydroxyl group protection, with a chiral primary amine or a chiral sulfinamide to provide a mixture of diastereoisomers, and performing a separation of the mixture of diastereoisomers and optionally performing a purification; and

(2) dederivatizing the separated diastereoisomers, and performing a deprotection if the mixture of pinocembrin optical isomers is subjected to the phenolic hydroxyl group protection, and optionally performing a purification, to obtain (R)-(+)-pinocembrin and/or (S)-(-)-pinocembrin.

4. The method according to claim 3, wherein the phenolic hydroxyl group protection is performed by using a protective group before the derivation reaction in the step (1), and the protective group is removed after the derivation.

5. The method according to claim 4, wherein the protective group is benzyl, methyl, acetyl, methoxymethyl, in particular, the phenolic hydroxyl group protection is performed by using benzyl chloride or benzyl bromide.

6. The method according to any one of claims 3-5, wherein the derivation reaction is performed under the catalysis of a Lewis acid.

7. The method according to any one of claims 3-6, wherein the molar ratio of the chiral primary amine or chiral sulfinamide to the mixture of pinocembrin optical isomers is in the range of 10:1 to 1:1, preferably 1:1.

8. The method according to any one of claims 3-7, wherein the chiral primary amine is D- or L-α-phenethylamine; the chiral sulfonamide is a sulfonamide selected from phenylsulfinamide, p-tolylsulfinamide or tert-butylsulfinamide in R- or S-form.

9. The method according to any one of claims 3-8, wherein the separation or purification of the step (1) is crystallization, extraction or chromatography, especially column chromatography.

10. The method according to any one of claims 3-9, wherein the step (2) is performed through hydrolization of the diastereoisomers, especially in the presence of an acid, wherein the acid is preferably an inorganic acid such as HCl, HNO_3, H_2SO_4, H_3PO_4, HOAc or a combination thereof, especially preferably a HCl aqueous solution having a concentration of 10% in the hydrolization system.

11. The method according to any one of claims 3-10, wherein the deprotection of the dederivatized diastereoisomers is performed through a reduction reaction, preferably through a hydrogenation reaction using Pd/C as catalyst.

12. The method according to claim 6, wherein the Lewis acid is selected from $TiCl_4$ or $Ti(OEt)_4$ or a mixture thereof, and the molar ratio of the Lewis acid to the mixture of pinocembrin optical isomers is preferably in the range of 5:1 to 0.1:1, more preferably 0.5:1.

13. The method according to claim 11, wherein the molar ratio of the Pd/C to the mixture of pinocembrin diastereoisomers is in the range of

0.1:1 to 5:1, preferably 0.8:1.

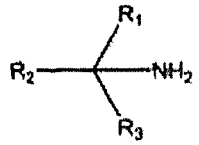
14. A (R)-(+)-pinocembrin obtained by the method for resolution according to any one of claims 1-13.

What is claimed is:

1. A method for resolution of a mixture of pinocembrin optical isomers, said method comprising performing the resolution by using a chiral primary amine or a chiral sulfinamide as a resolving agent.

2. The method according to claim 1, wherein the method is used for resolution of a pinocembrin racemate.

3. The method according to claim 1 or 2, wherein said chiral primary amine and said chiral sulfinamide are respectively represented by the following general formulas:



chiral primary amine



chiral sulfinamide

wherein,

R_1 is selected from -H, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$ or $-CH_2OH$;

R_2 is selected from phenyl, benzyl, or phenyl or benzyl with a substituent on aromatic ring thereof, $-CH_2OH$, $-CH(OH)CH_3$, $-CH(OH)C_2H_5$, phCH(OH)-, wherein the substituent is selected from $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH(CH_3)_2$, $-NO_2$, $-CF_3$, -F, -Cl, -I, -OH, $-OCH_3$, $-OC_2H_5$, $-COOCH_3$, $-COOC_2H_5$, $-CONH_2$, $-CONHCH_3$, $-CONHC_2H_5$, $-CON(CH_3)_2$ or $-CONHCH(CH_3)_2$;

R_3 has the same definition as those of R_1 and R_2 with proviso that R_3 does not have the same structure as R_1 or R_2 does at the same time;

R_4 is selected from an alkyl having 1-6 carbon atoms, an aryl or aralkyl having 6-9 carbon atoms, a substituted alkyl having 1-6 carbon atoms, a substituted aryl or aralkyl having 6-9 carbon atoms, wherein the substituent is selected from $-NO_2$, $-CF_3$, -F, -Cl, -I, -OH, $-OCH_3$, $-OC_2H_5$, $-COOCH_3$, $-COOC_2H_5$, $-CONH_2$, $-CONHCH_3$, $-CONHC_2H_5$, or $-CON(CH_3)_2$, $-CONHCH(CH_3)_2$.

4. The method according to claim 1 or 2, comprising the following steps:

(1) performing a derivation reaction of a mixture of pinocembrin optical isomers, which is optionally subjected to a phenolic hydroxyl group protection, with a chiral primary amine or a chiral sulfinamide to provide a mixture of diastereoisomers, and performing a separation of the mixture of diastereoisomers and optionally performing a purification; and

(2) dederivatizing the separated diastereoisomers, and performing a deprotection if the mixture of pinocembrin optical isomers is subjected to the phenolic hydroxyl group protection, and optionally performing a purification, to obtain (R)-(+)-pinocembrin and/or (S)-(-)-pinocembrin.

5. The method according to claim 4, wherein the phenolic hydroxyl group protection is performed by using a protective group before the derivation reaction in the step (1), and the protective group is removed after the derivation.

6. The method according to claim 5, wherein the protective group is benzyl, methyl, acetyl, or methoxymethyl.

7. The method according to claim 5, wherein the phenolic hydroxyl group protection is performed by using benzyl chloride or benzyl bromide.

8. The method according to any one of claims 4-7, wherein the derivation reaction is performed under the catalysis of a Lewis acid.

9. The method according to any one of claims 4-8, wherein the molar ratio of the chiral primary amine or chiral sulfinamide to the mixture of pinocembrin optical isomers is in the range of 10:1 to 1:1.

10. The method according to claim 9, wherein the molar ratio of the chiral primary amine or chiral sulfinamide to the mixture of pinocembrin optical isomers is 1:1.

11. The method according to any one of claims 4-10, wherein the chiral primary amine is D- or L-α-phenethylamine; the chiral sulfonamide is a sulfonamide selected from phenylsulfinamide, p-tolylsulfinamide or tert-butylsulfinamide in R- or S-form.

12. The method according to any one of claims 4-11, wherein the separation or purification of the step (1) is crystallization, extraction or chromatography.

13. The method according to claim 12, wherein the separation or purification of the step (1) is column chromatography.

14. The method according to any one of claims 4-13, wherein the step (2) is performed through hydrolization of the diastereoisomers.

15. The method according to claim 14, wherein the step (2) is performed through hydrolization of the diastereoisomers in the presence of an acid.

16. The method according to claim 15, wherein the acid is an inorganic acid.

17. The method according to claim 15, wherein the acid is HCl, HNO_3, H_2SO_4, H_3PO_4, HOAc or a combination thereof.

18. The method according to claim 17, wherein the acid is a HCl aqueous solution having a concentration of 10% in the hydrolization system.

19. The method according to any one of claims 4-18, wherein the deprotection of the dederivatized diastereoisomers is performed through a reduction reaction.

20. The method according to claim 19, wherein the deprotection of the dederivatized diastereoisomers is performed through a hydrogenation reaction using Pd/C as catalyst.

21. The method according to claim 8, wherein the Lewis acid is selected from $TiCl_4$ or $Ti(OEt)_4$ or a mixture thereof.

22. The method according to claim 21, wherein the molar ratio of the Lewis acid to the mixture of pinocembrin optical isomers is in the range of 5:1 to 0.1:1.

23. The method according to claim 21, wherein the molar ratio of the Lewis acid to the mixture of pinocembrin optical isomers is 0.5:1.

24. The method according to claim 19 or 20, wherein the molar ratio of the Pd/C to the mixture of pinocembrin diastereoisomers is in the range of 0.1:1 to 5:1.

25. The method according to claim 24, wherein the molar ratio of the Pd/C to the mixture of pinocembrin diastereoisomers is 0.8:1.