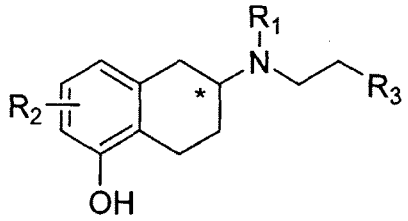
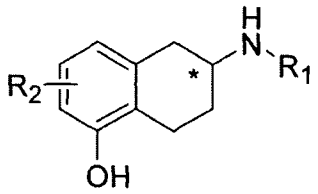
WHAT IS CLAIMED IS:

1. A method for preparing a compound of formula (I), comprising:

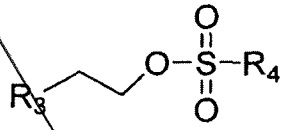


(I)

reacting a compound of formula (II) with a compound of formula (III) under an alkaline condition and in the presence of a sulfite,



(II)



(III)

wherein,

(*) represents a chiral center; the compound of formula (I) and the compound of formula (II) is a R or S configuration or a racemic mixture;

R_1 is a straight or branched alkyl containing 1-4 carbon atoms;

R_2 is hydrogen, a straight or branched alkyl containing 1-4 carbon atoms;

R_3 is a straight or branched alkyl containing 1-6 carbon atoms, alkoxy, cycloalkoxy, an optionally substituted phenyl, or a heterocyclyl; and

R_4 is alkyl, haloalkyl, optionally substituted aryl.

2. The method according to claim 1, wherein the chiral center (*) of the compound of formula (I) and formula (II) is S configuration.

3. The method according to claim 1 or claim 2 wherein R_3 is thienyl or pyridyl.

4. The method according to any one of claims 1-3 wherein R_4 is methyl, trifluoromethyl, methylphenyl or nitrophenyl.

5. The method according to any one of claims 1-4, wherein R_1 is methyl, ethyl or n-propyl; R_2 is methyl or hydrogen; R_3 is 3-pyridyl or 2-thienyl; and R_4 is 4-methylphenyl or 4-nitrophenyl.

6. The method according to claim 5, wherein R_1 is n-propyl, R_2 is hydrogen, R_3 is 2-thienyl, and R_4 is 4-methylphenyl.

7. The method according to any one of claims 1-6, wherein the sulfite is alkaline metal sulfites including sodium sulfite and potassium sulfite; alkaline earth metal sulfites including magnesium sulfite and calcium sulfite; or other sulfites including ammonium sulfite and zinc sulfite.

8. The method according to claim 7 wherein the sulfite is sodium sulfite or potassium sulfite.

9. The method according to any of claims 1-8, wherein the molar ratio of the sulfite to the compound of formula (II) is (0.8-2.5):1.

10. The method according to claim 9, wherein the molar ratio of the sulfite to the compound of formula (II) is 1.3:1.

11. The method according to any one of claims 1-10, wherein the molar ratio of the compound of formula (III) to the compound of formula (II) is (1.1-5.0):1.

12. The method according to claim 11, wherein the molar ratio of the compound of formula (III) to the compound of formula (II) is 1.5:1.

13. The method according any one of claims 1-12 wherein the compound of formula (I) is

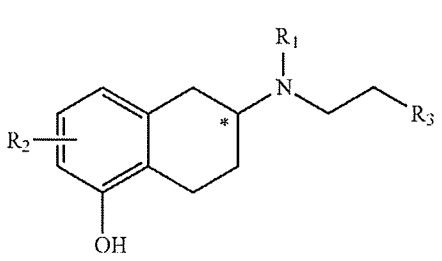
rotigotine.

14. The method according any one of claims 1-12, further comprising converting the compound of formula (I) to a salt form.

15. The method according to claim 14 wherein the salt form is hydrochlorate salt.

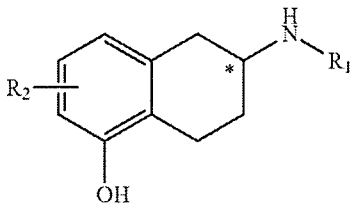
What is claimed is:

1. A method for preparing a compound of formula (I), comprising:

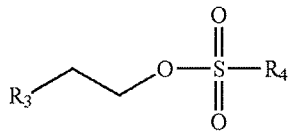


(I)

reacting a compound of formula (II) with a compound of formula (III) under an alkaline condition and in the presence of a sulfite,



(II)



(III)

wherein,
(*) represents a chiral center; the compound of formula (I) and the compound of formula (II) is an R or S configuration or a racemic mixture;
R_1 is a straight or branched alkyl containing 1-4 carbon atoms;
R_2 is hydrogen, a straight or branched alkyl containing 1-4 carbon atoms;
R_3 is a straight or branched alkyl containing 1-6 carbon atoms, alkoxy, cycloalkoxy, an phenyl or substituted phenyl or a heterocyclyl; and
R_4 is alkyl, haloalkyl, aryl or substituted aryl wherein the sulfite is an alkaline metal sulfite, an alkaline earth metal sulfite, ammonium sulfite, or zinc sulfite wherein the substituted phenyl or the substituted aryl is substituted with a substituent selected from the group consisting of oxo, halogen, hydroxy, cyano, nitro, amino, alkylamino, dialkylamino, alkyl, alkoxy, haloalkyl, unsubstituted aryl, heterocyclyl, $-NR_aR_b$, $-NR_aC(=O)R_b$, $-NR_aC(=O)NR_aR_b$, $-NR_aC(=O)OR_b$, $-NR_aS(=O)_2R_b$, $-OR_a$, $-C(=O)R_a$ $-C(=O)OR_a$, $-C(=O)NR_aR_b$, $-OCH_2C(=O)NR_aR_b$, $-OC(=O)NR_aR_b$, $-SH$, $-SR_a$, $-SOR_a$, $-S(=O)_2NR_aR_b$, $-S(=O)_2R_a$, $-SR_aC(=O)NR_aR_b$, $-OS(=O)_2R_a$ and $-S(=O)_2OR_a$, wherein R_a and R_b are independently hydrogen, alkyl, haloalkyl, alkoxy, or unsubstituted aryl.

2. The method according to claim 1, wherein the chiral center (*) of the compound of formula (I) and formula (II) is S configuration.

3. The method according to claim 1, wherein R_3 is thienyl or pyridyl.

4. The method according to claim 1, wherein R_4 is methyl, trifluoromethyl, methylphenyl or nitrophenyl.

5. The method according to claim 1, wherein R_1 is methyl, ethyl or n-propyl; R_2 is methyl or hydrogen; R_3 is 3-pyridyl or 2-thienyl; and R_4 is 4-methylphenyl or 4-nitrophenyl.

6. The method according to claim 5, wherein R_1 is n-propyl, R_2 is hydrogen, R_3 is 2-thienyl, and R_4 is 4-methylphenyl.

7. The method according to claim 1, wherein the alkaline metal sulfite is sodium sulfite or potassium sulfite and the alkaline earth metal sulfite is magnesium sulfite or calcium sulfite.

8. The method according to claim 7 wherein the alkaline metal sulfite is sodium sulfite or potassium sulfite.

9. The method according to claim 1, wherein the molar ratio of the sulfite to the compound of formula (II) is (0.8-2.5):1.

10. The method according to claim 9, wherein the molar ratio of the sulfite to the compound of formula (II) is 1.3:1.

11. The method according to claim 1, wherein the molar ratio of the compound of formula (III) to the compound of formula (II) is (1.1-5.0):1.

12. The method according to claim 11, wherein the molar ratio of the compound of formula (III) to the compound of formula (II) is 1.5:1.

13. The method according to claim 1, wherein the compound of formula (I) is rotigotine.

14. The method according to claim 1, further comprising converting the compound of formula (I) to a salt form.

15. The method according to claim 14, wherein the salt form is hydrochlorate salt.

16. The method according to claim 2, wherein R_3 is thienyl or pyridyl.

17. The method according to claim 2, wherein R_4 is methyl, trifluoromethyl, methylphenyl or nitrophenyl.

18. The method according to claim 3, wherein R_4 is methyl, trifluoromethyl, methylphenyl or nitrophenyl.

19. The method according to claim 2, wherein R_1 is methyl, ethyl or n-propyl; R_2 is methyl or hydrogen; R_3 is 3-pyridyl or 2-thienyl; and R_4 is 4-methylphenyl or 4-nitrophenyl.

20. The method according to claim 3, wherein R_1 is methyl, ethyl or n-propyl; R_2 is methyl or hydrogen; R_3 is 3-pyridyl or 2-thienyl; and R_4 is 4-methylphenyl or 4-nitrophenyl.