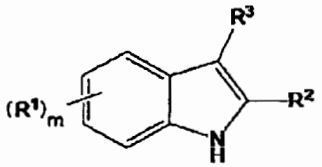
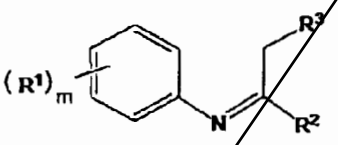
CLAIMS

1. A method for the synthesis of an indole of Formula (I) or a salt thereof,



Formula (I)

the method comprising oxidizing a N-aryl imine of Formula (II)



Formula (II)

in the presence of a palladium-based catalyst, an oxidant selected from the group consisting of copper (II) acetate, benzoquinone, tert-butylhydroperoxide, di-tert-butyl peroxide (tBuOOtBu), tert-butyl benzoyl peroxide (BzOOtBu), molecular oxygen (O_2), air, or combinations thereof and a solvent comprising or consisting essentially of dimethylsulfoxide,

wherein

R^1 at each occurrence is independently selected from the group consisting of hydrogen, optionally substituted C_1-C_{20} alkyl, optionally substituted C_3-C_{20} mono-, or poly-cycloalkyl, optionally substituted 2-20-membered heteroalkyl, optionally substituted 3-20-membered mono-, or poly-heterocycloalkyl; halogen, -OR, wherein R is optionally substituted C_1-C_{20} alkyl; wherein R^2 is selected from the group consisting of optionally substituted C_2-C_{20} alkenyl, optionally substituted 2-20-membered heteroalkenyl, optionally substituted monocyclic, condensed polycyclic or bridged polycyclic C_5-C_{20} aryl, and optionally substituted 5-20-membered monocyclic, condensed polycyclic or bridged polycyclic heteroaryl; wherein R^3 is selected from the group consisting of hydrogen, C_1-C_{20} alkyl, C_2-C_{20} alkenyl; monocyclic,

condensed polycyclic or bridged polycyclic C_5-C_{20} aryl; C_3-C_{20} mono-, or poly-cycloalkyl; and C_3-C_{20} mono-, or poly-cycloalkenyl;

m is 0, 1, 2, 3, or 4;

wherein

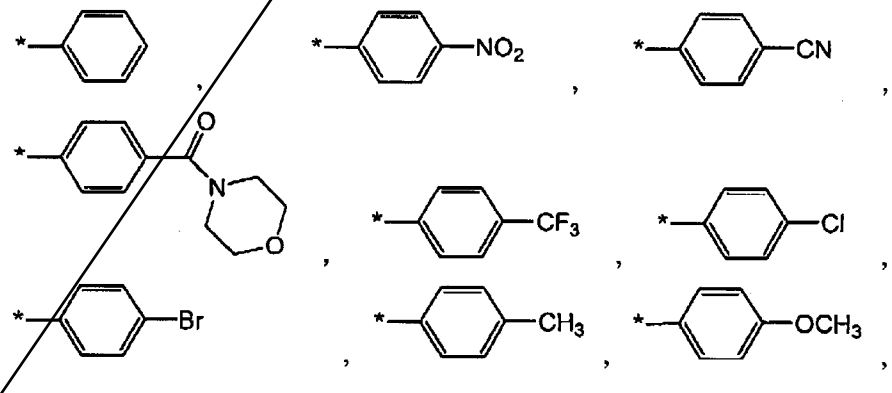
R^1 at each occurrence is positioned on the phenyl ring in 3-, 4-, 5-, or 6-position with respect to the bond linking the phenyl to the –N-H group according to Formula (I) or the –N=C group according to Formula (II).

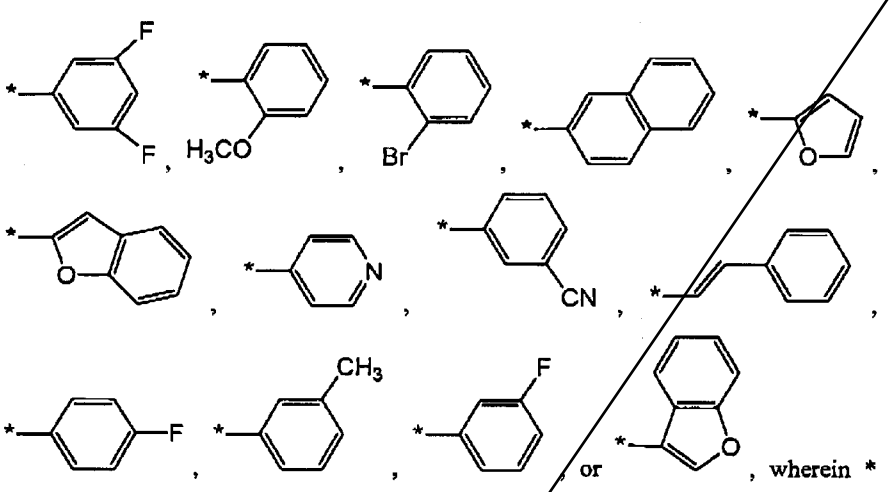
2. The method according to claim 1, wherein R^1 at each occurrence is independently selected from the group consisting of hydrogen, alkyl, -(O)alkyl, and halogen.

3. The method according to claim 1 or 2, wherein R^1 at each occurrence is independently selected from the group consisting of -H, $-OCH_3$, and -Cl.

4. The method according to any one of claims 1 to 3, wherein R^1 is positioned on the phenyl ring in 4-position with respect to the bond linking the phenyl to the –N-H group according to Formula (I) or the –N=C group according to Formula (II).

5. The method according to claim 1, wherein R^2 is



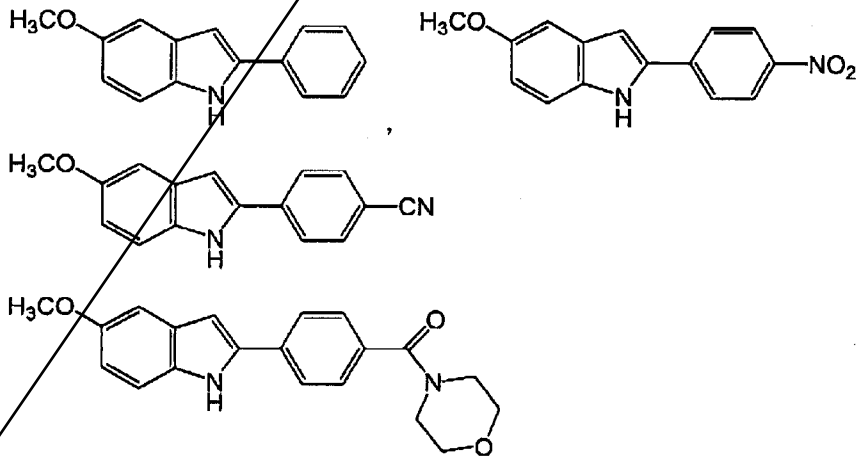


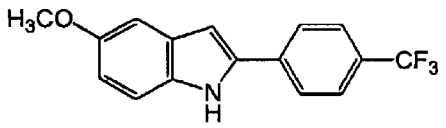
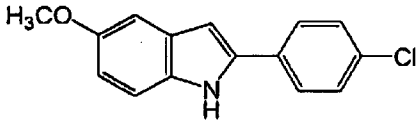
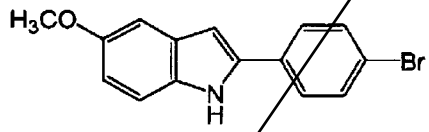
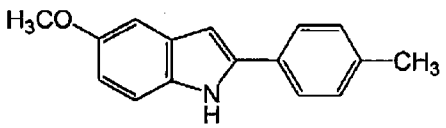
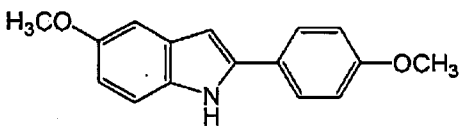
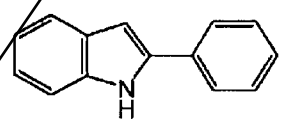
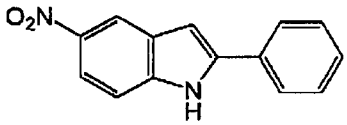
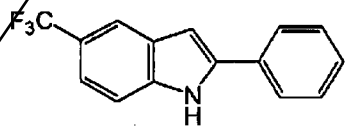
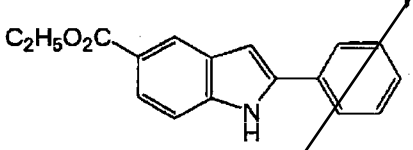
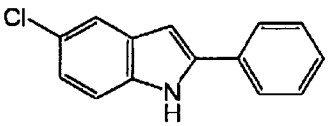
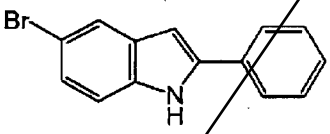
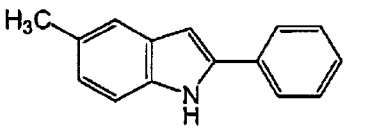
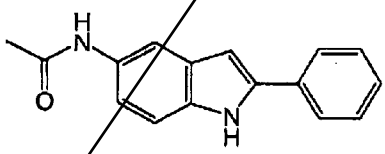
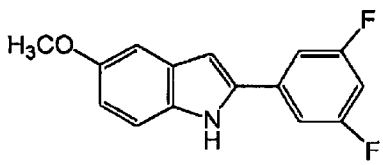
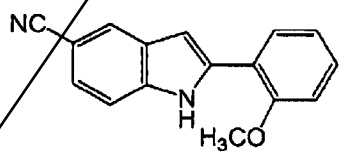
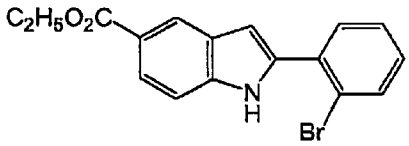
denotes the point in which R^2 is connected to the parent molecular moiety.

6. The method according to any one of claims 1 to 5, wherein R^3 is hydrogen or phenyl.

7. The method according to any one of claims 1 to 6, wherein the indole is 2-aryl indole, 2-alkenyl indole, 2,3-diaryl indole, 2-aryl-3-alkenyl indole, 2-alkenyl-3-aryl indole, 2,3-dialkenyl indole, 2-aryl-3-alkyl indole, or 2-alkenyl-3-alkyl indole.

8. The method according to any one of claims 1 to 7, wherein the indole is



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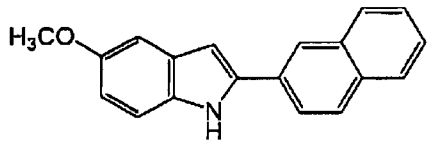
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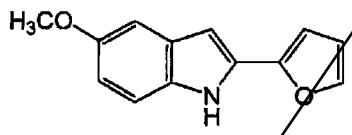
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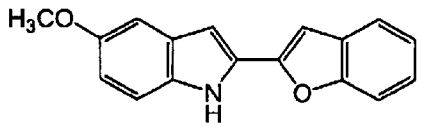
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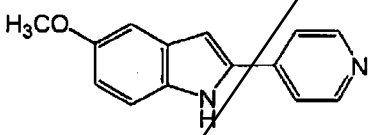
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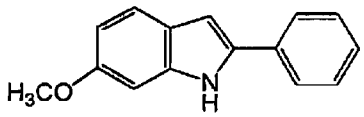
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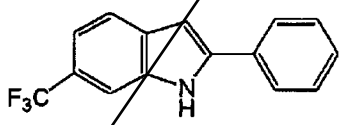
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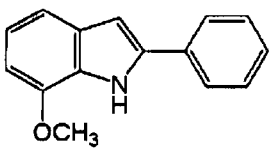
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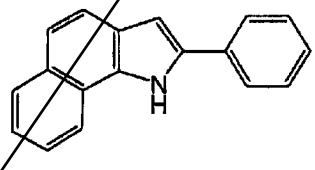
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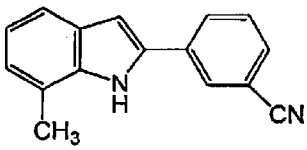
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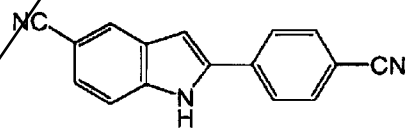
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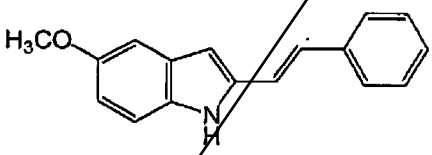
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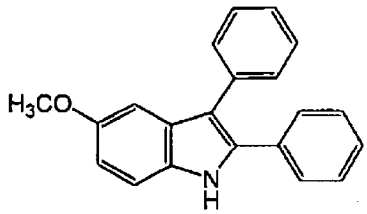
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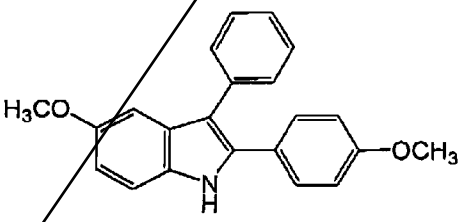
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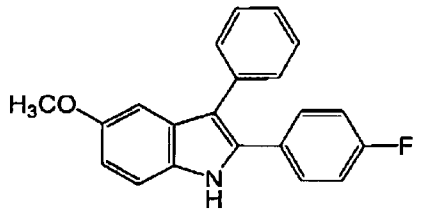
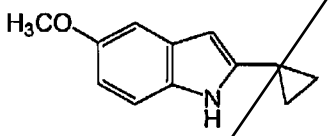
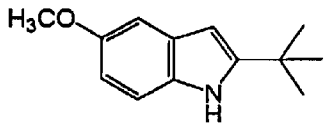
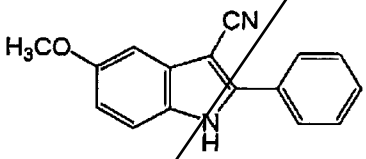
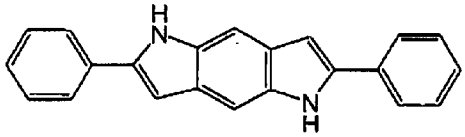
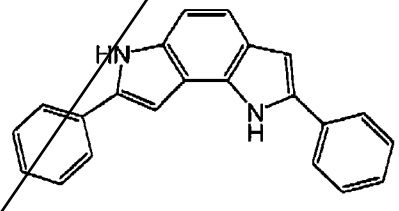
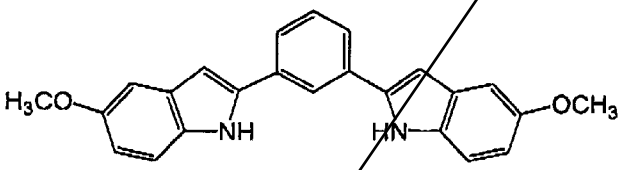
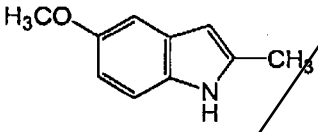
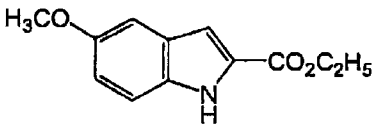
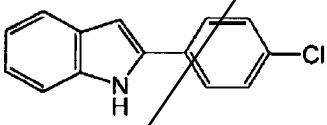
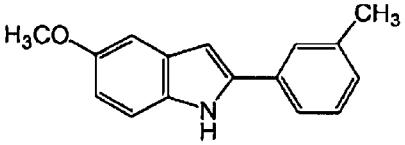
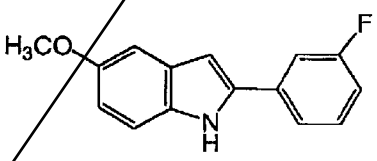
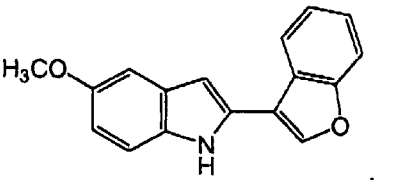

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9. The method according to any one of claims 1 to 8, wherein the palladium-based catalyst is selected from the group consisting of palladium metal, palladium (II) acetate, sodium palladium (II) chloride, palladium (II) acetylacetonate, palladium(II) trifluoroacetate, palladium hydroxide, palladium(II) bromide, palladium (II) chloride, palladium(II) cyanide, palladium(II) hexafluoroacetylacetonate, palladium(II) iodide, palladium(II) nitrate dehydrate, palladium(II) nitrate hydrate, palladium(II) oxide, palladium (II) propionate, palladium (II) sulfate, palladium (II) sulfide, or mixtures thereof.

10. The method according to claim 9, wherein the palladium-based catalyst comprises or consists essentially of palladium (II) acetate.

11. The method according to any one of claims 1 to 10, wherein the amount of palladium-based catalyst is in the range of about 0.1 mol% to about 20 mol% with respect to the amount of N-aryl imine.

12. The method according to any one of claims 1 to 11, wherein the amount of palladium-based catalyst is in the range of about 5 mol% to about 10 mol% with respect to the amount of N-aryl imine.

13. The method according to any one of claims 1 to 12, wherein the oxidant comprises or consists essentially of copper (II) acetate.

14. The method according to any one of claims 1 to 12, wherein the oxidant comprises or consists essentially of molecular oxygen (O_2)

15. The method according to any one of claims 1 to 14, wherein the amount of oxidant is about 0.5 equivalence to about 5 equivalence of the amount of of N-aryl imine.

16. The method according to any one of claims 1 to 15, wherein the amount of oxidant is about 2 equivalence to about 3 equivalence of the amount of of N-aryl imine.

17. The method according to any one of claims 1 to 16, further comprising reacting in the presence of an additive.

18. The method according to claim 17, wherein the additive comprises a quaternary ammonium salt of Formula (III)

$(R_4)_nN\text{-}X$ Formula (III)

wherein

R_4 at each occurrence is independently selected from C_1-C_{20} alkyl;
n is 1, 2, 3 or 4; and
X is selected from the group consisting of a halogen and -$OCOCH_3$.

19. The method according to claim 17 or 18, wherein the additive is selected from the group consisting of Bu_4NBr, Bu_4NCl, Bu_4NI, and $Bu_4NOCOCH_3$.

20. The method according to claim 19, wherein the additive comprises or consists essentially of Bu_4NBr.

21. The method according to any one of claims 17 to 20, wherein the amount of additive is about 1 equivalence to about 3 equivalence of the amount of of N-aryl imine.

22. The method according to any one of claims 17 to 21, wherein the additive comprises a ligand for the palladium-based catalyst.

23. The method according to claim 22, wherein the ligand is selected from the group consisting of pyridine, 2,2'-bipyridine, 1,10-phenanthroline, PPh_3, dppm, dppe, dppp, dcpe, $P(c\text{-hex})_3$, $P(tBu)_3$, $P(C_6F_5)_3$, P(2, 4, 6-$Me_3C_6H_2)_3$, and mixtures thereof.

24. The method according to claim 22 or 23, wherein the amount of ligand is about 1 equivalence to about 2 equivalence of the amount of of palladium present in the palladium-based catalyst.

25. The method according to any one of claims 1 to 24, wherein the method is carried out at a temperature in the range of about 0 °C to about 150 °C.

26. The method according to claim 25, wherein the method is carried out at about 40 °C.

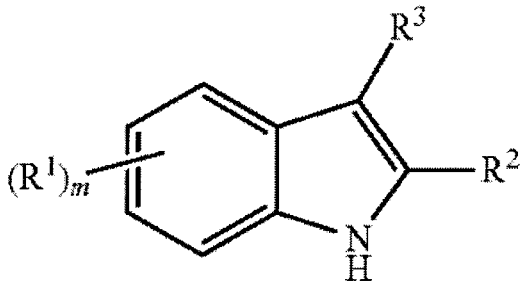
27. The method according to claim 25, wherein the method is carried out at ambient temperature.

28. The method according to any one of claims 1 to 27, wherein the method is carried out at atmospheric pressure.

CLAIMS

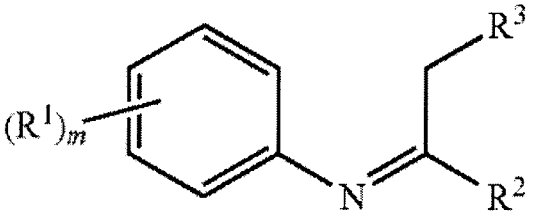
1. A method for the synthesis of an indole of Formula (I) or a salt thereof,

Formula (I)



the method comprising oxidizing a N-aryl imine of Formula (II)

Formula (II)



in the presence of a palladium-based catalyst, an oxidant selected from the group consisting of copper (II) acetate, benzoquinone, tert-butylhydroperoxide, di-tert-butyl peroxide (tBuOOtBu), tert-butyl benzoyl peroxide (BzOOtBu), molecular oxygen (O_2), and air, or combinations thereof and a solvent comprising of dimethylsulfoxide, wherein the amount of oxidant is about 0.5 equivalence to about 5 equivalence of N-aryl amine;

wherein

R^1 at each occurrence is independently selected from the group consisting of hydrogen, optionally substituted C_1-C_{20} alkyl, optionally substituted C_3-C_{20} mono-, or poly-cycloalkyl, optionally substituted 2-20-membered heteroalkyl, optionally substituted 3-20-membered mono-, or poly-heterocycloalkyl, halogen, and —OR; wherein R is optionally substituted C_1-C_{20} alkyl; wherein R^2 is selected from the group consisting of optionally substituted C_2-C_{20} alkenyl, optionally substituted 2-20-membered heteroalkenyl, optionally substituted monocyclic, condensed polycyclic or bridged polycyclic C_5-C_{20} aryl, and optionally substituted 5-20-membered monocyclic, condensed polycyclic or bridged polycyclic heteroaryl; wherein R^3 is selected from the group consisting of hydrogen, C_1-C_{20} alkyl, C_2-C_{20} alkenyl; monocyclic, condensed polycyclic or bridged polycyclic C_5-C_{20} aryl; C_3-C_{20} mono-, or poly-cycloalkyl; and C_3-C_{20} mono-, or poly-cycloalkenyl;

m is 0, 1, 2, 3, or 4;

wherein

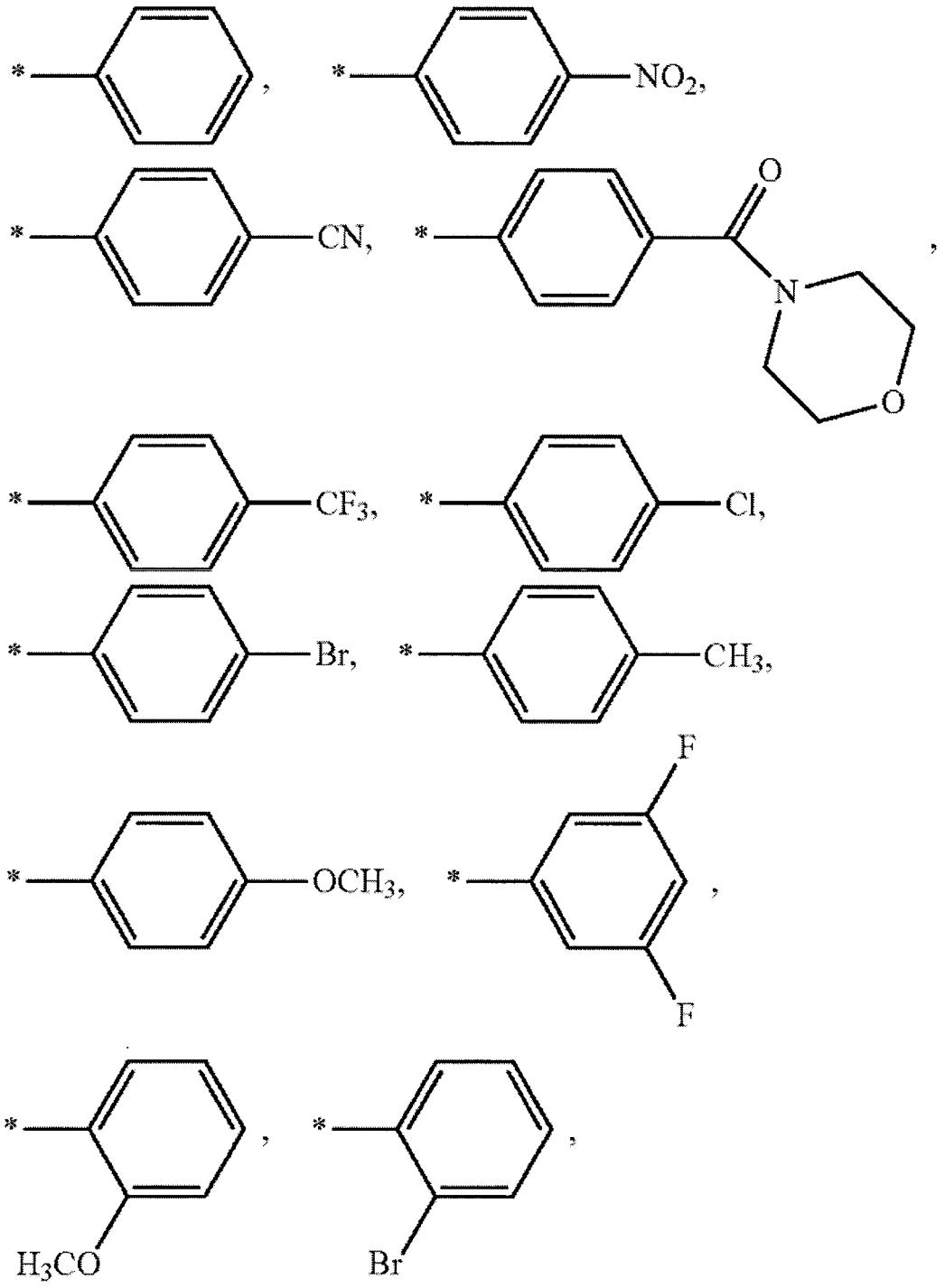
R^1 at each occurrence is positioned on the phenyl ring in 3-, 4-, 5-, or 6-position with respect to the bond linking the phenyl to the —N—H group according to Formula (I) or the —N=C group according to Formula (II).

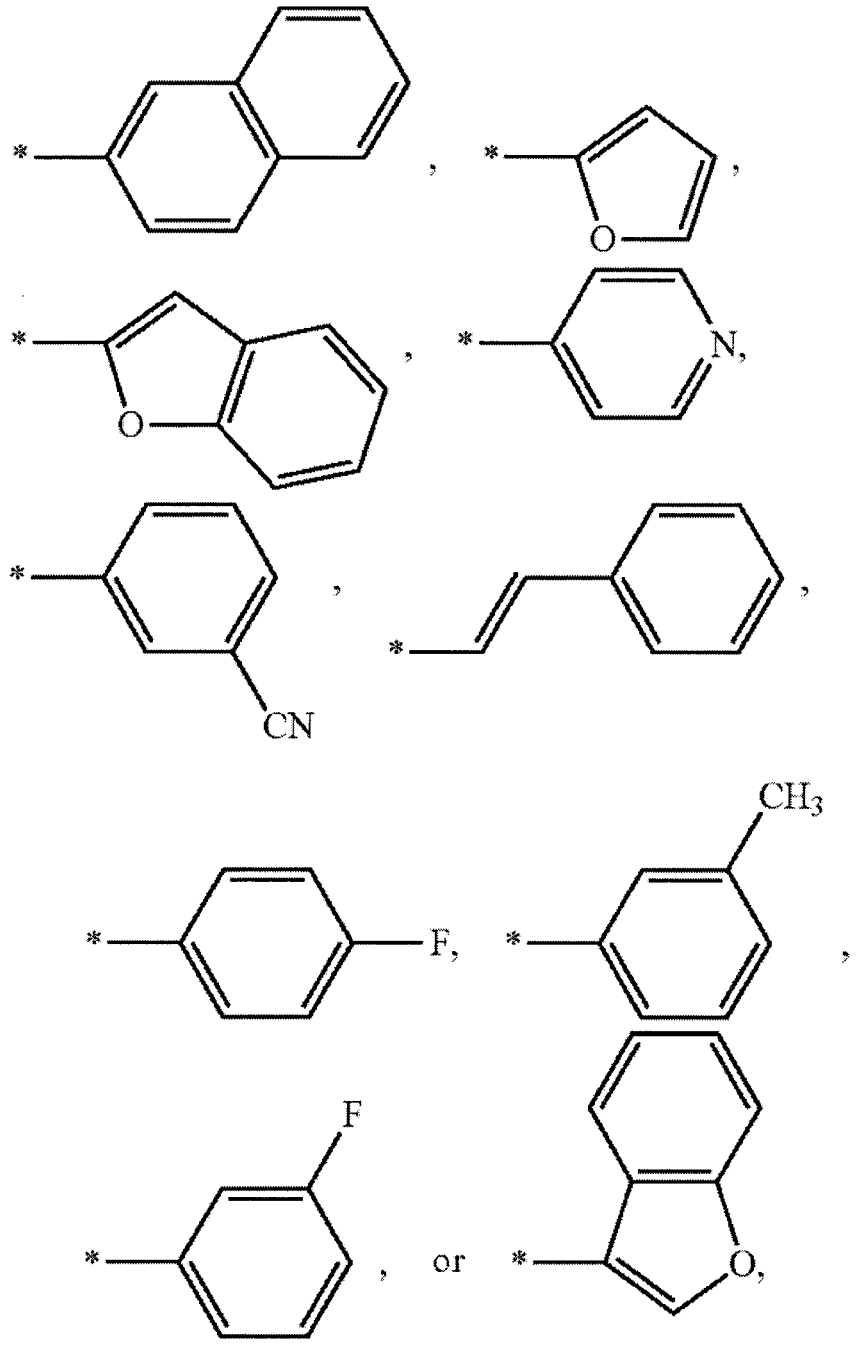
2. The method according to claim **1**, wherein R^1 at each occurrence is independently selected from the group consisting of hydrogen, alkyl, —O-alkyl, and halogen.

3. The method according to claim **1**, wherein R^1 at each occurrence is independently selected from the group consisting of —H, —OCH_3, and —Cl.

4. The method according to claim **1**, wherein R^1 is positioned on the phenyl ring in 4-position with respect to the bond linking the phenyl to the —N—H group according to Formula (I) or the —N═C group according to Formula (II).

5. The method according to claim **1**, wherein R^2 is



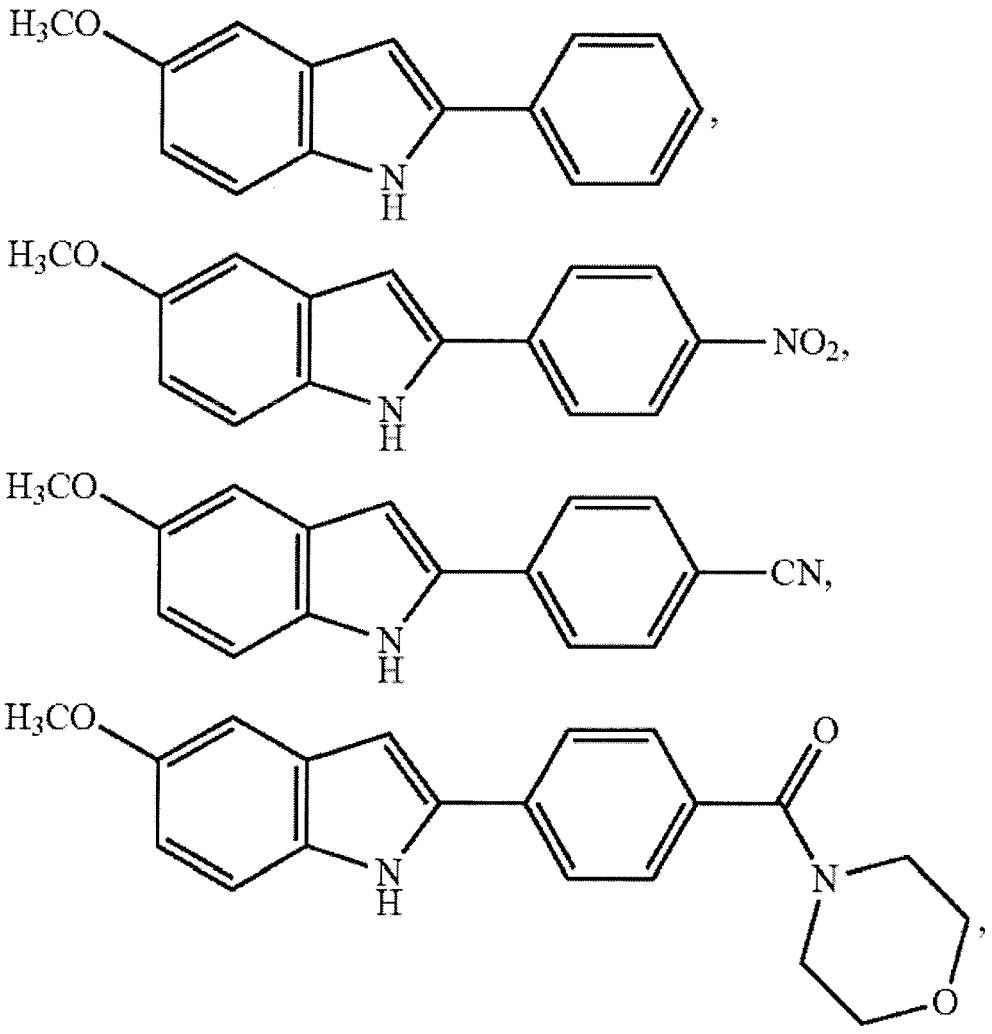


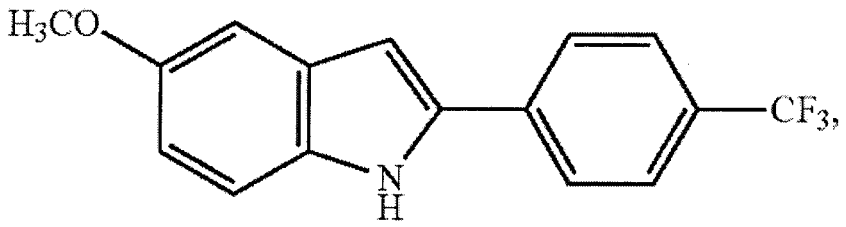
wherein * denotes the point in which R^2 is connected to the parent molecular moiety.

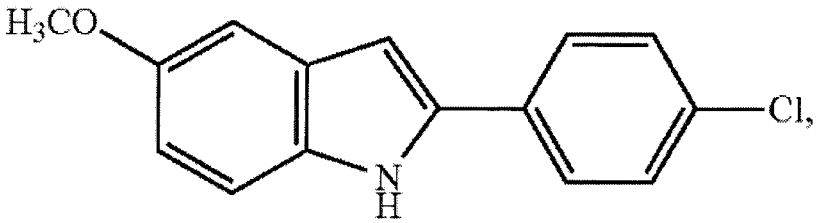
6. The method according to claim **1**, wherein R^3 is hydrogen or phenyl.

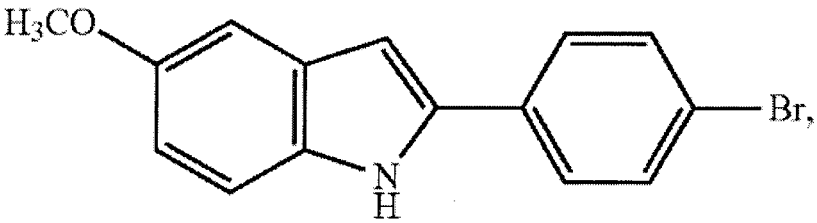
7. The method according to claim **1**, wherein the indole is 2-aryl indole, 2-alkenyl indole, 2,3-diaryl indole, 2-aryl-3-alkenyl indole, 2-alkenyl-3-aryl indole, 2,3-dialkenyl indole, 2-aryl-3-alkyl indole, or 2-alkenyl-3-alkyl indole.

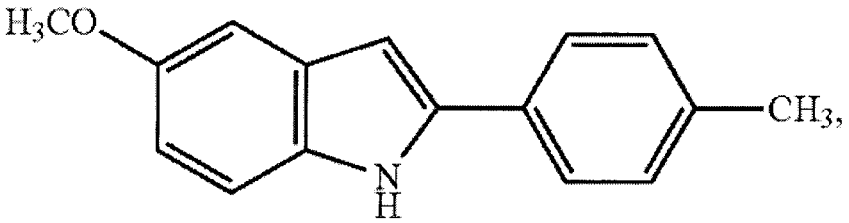
8. The method according to claim **1**, wherein the indole is

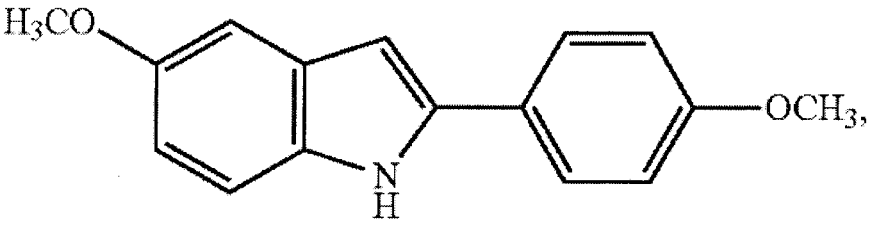


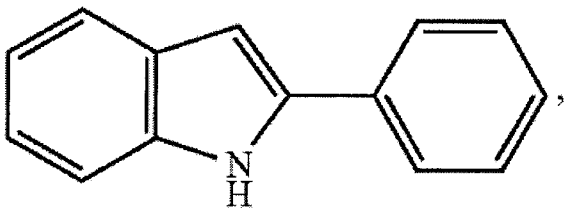


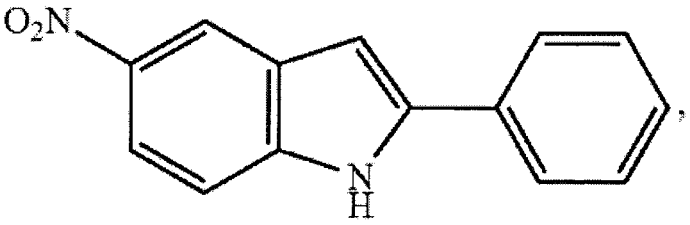


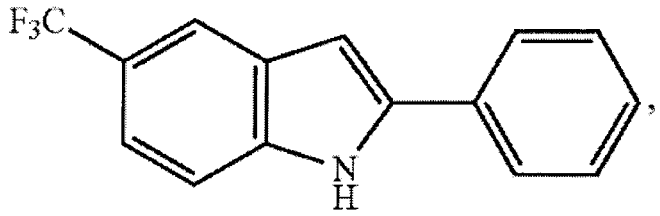


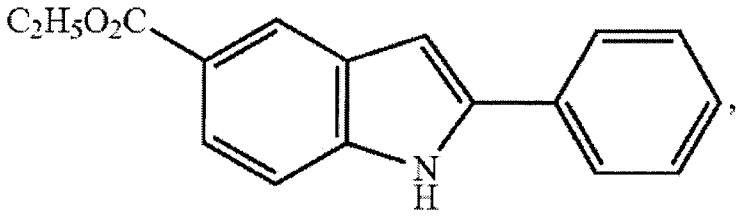


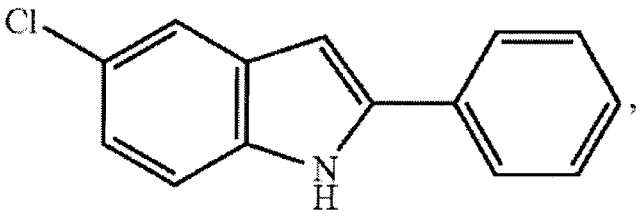


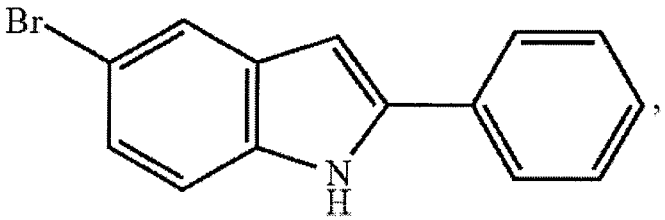


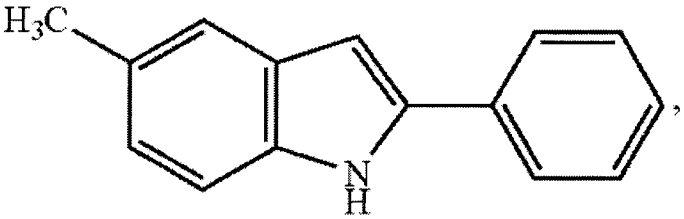


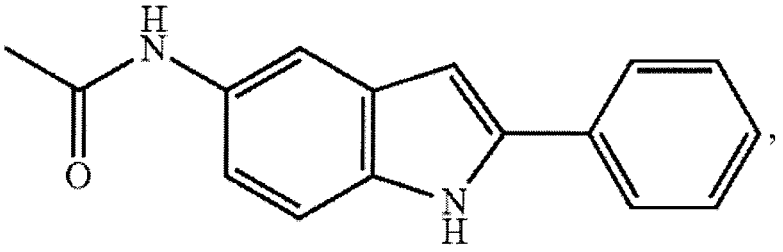


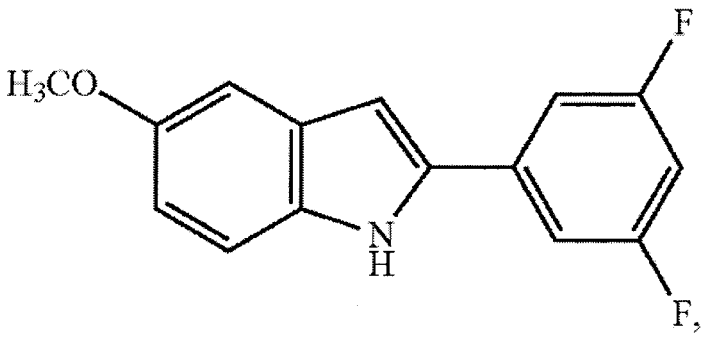


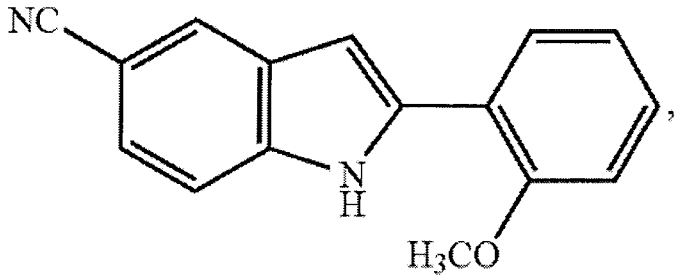








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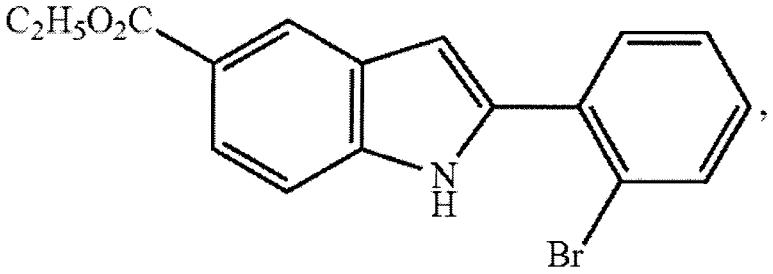
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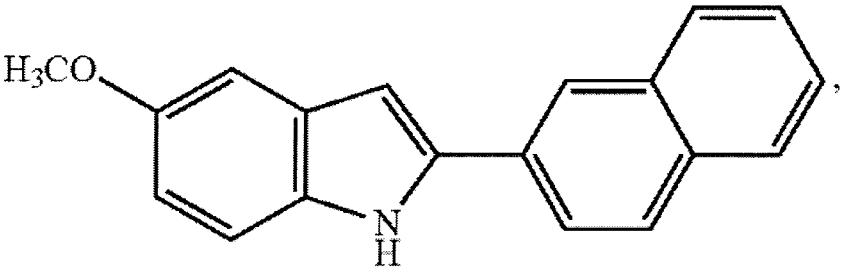
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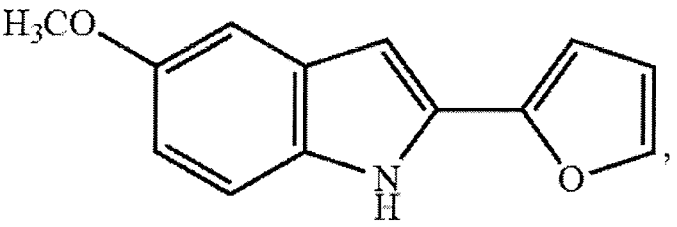
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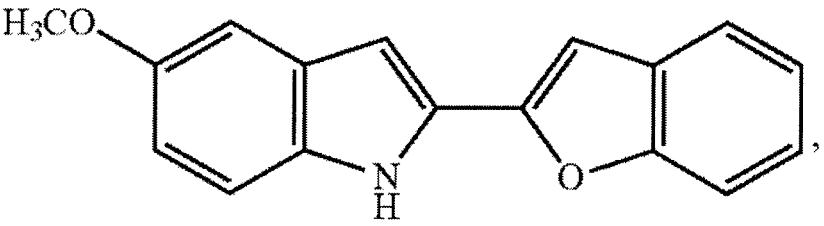
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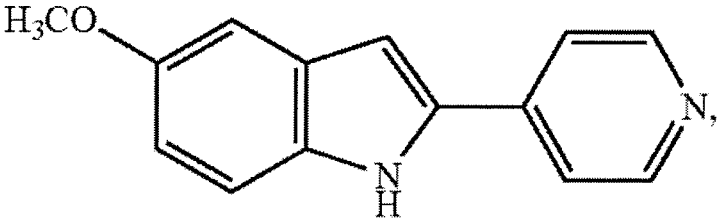
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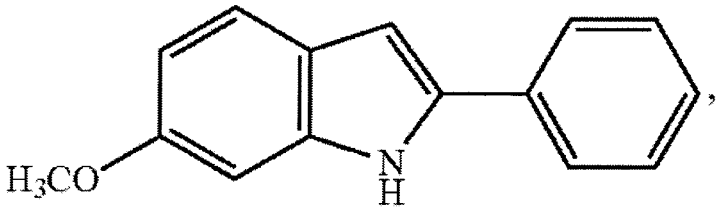
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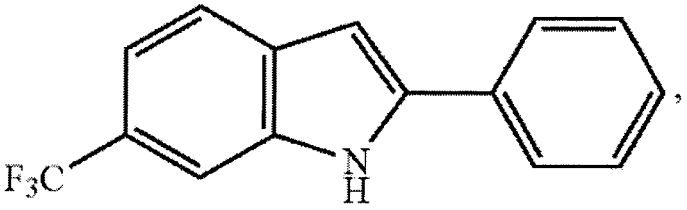
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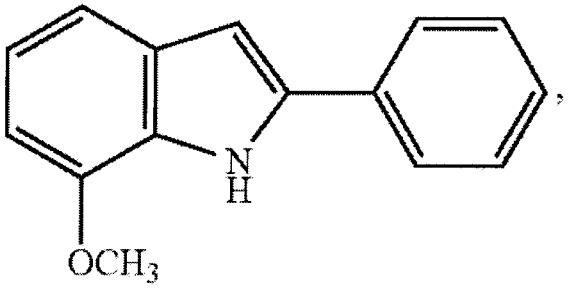
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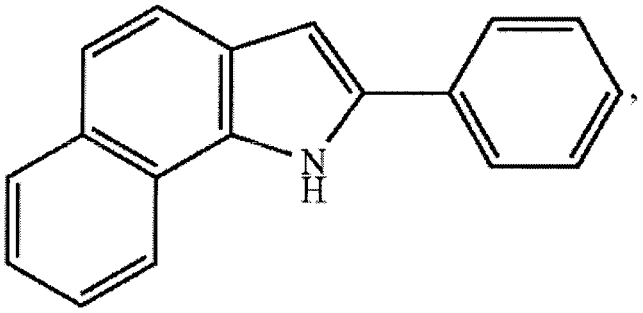
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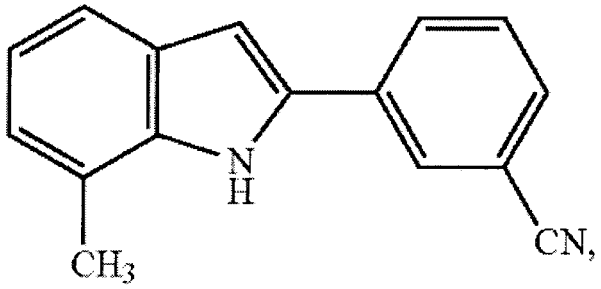
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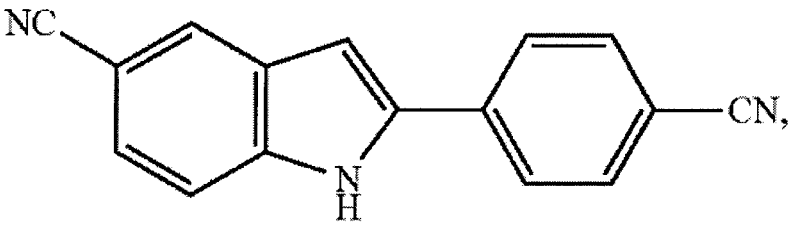
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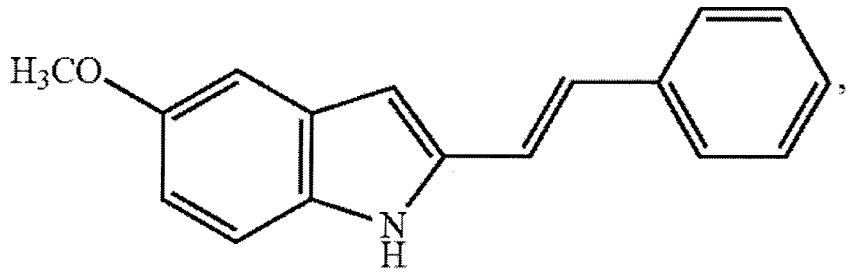
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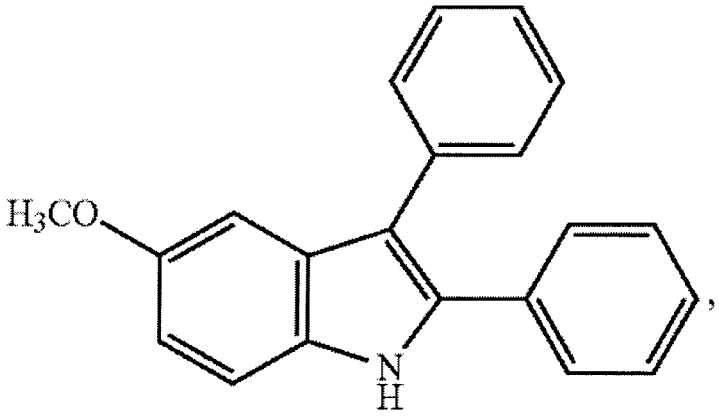
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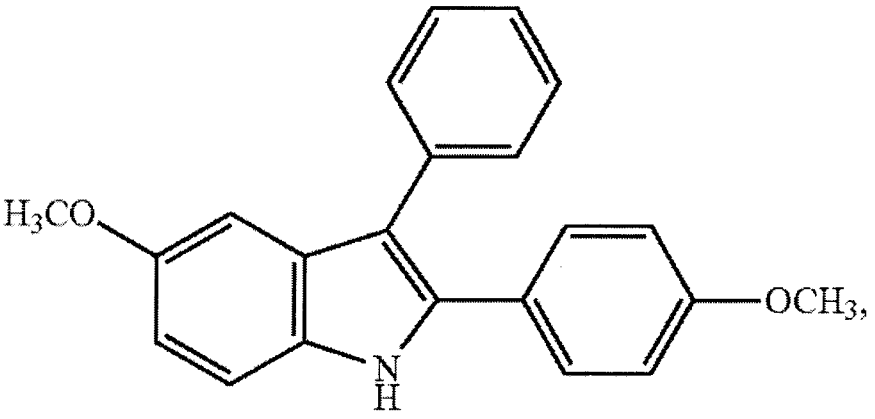
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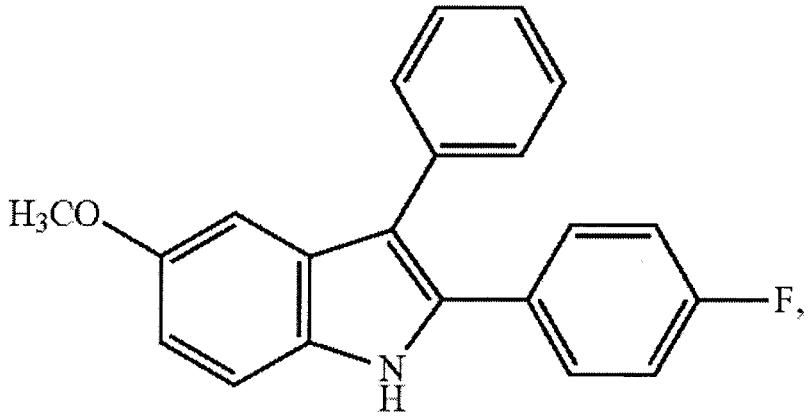
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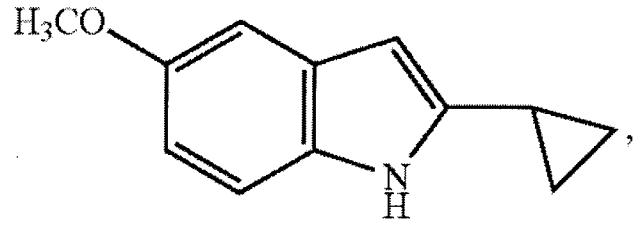

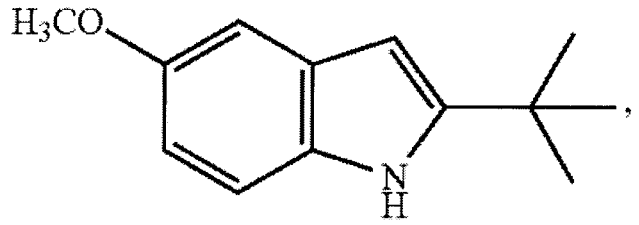

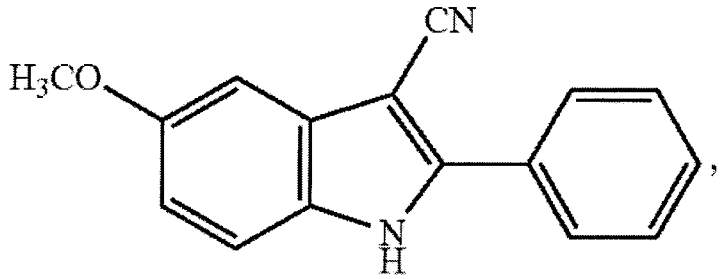

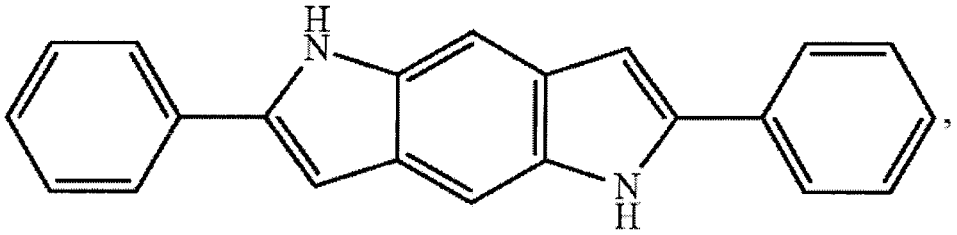

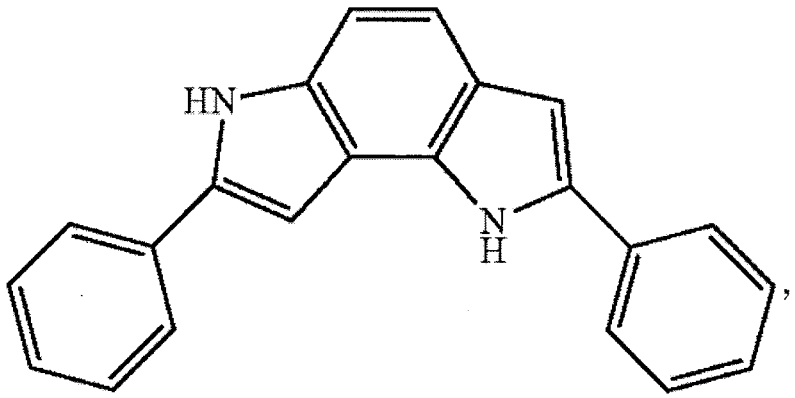

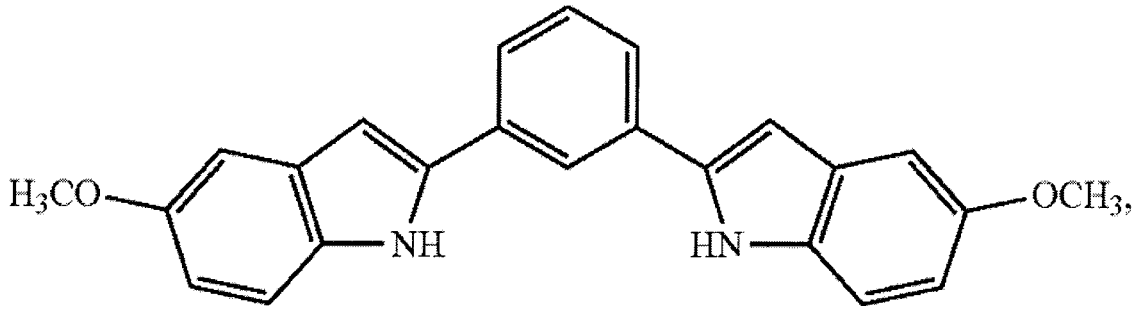

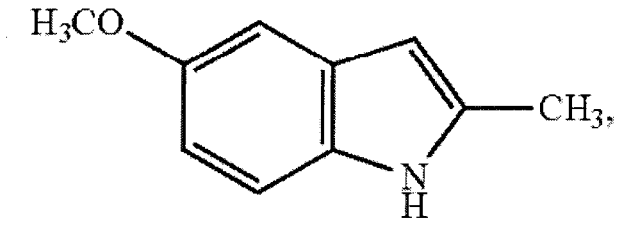

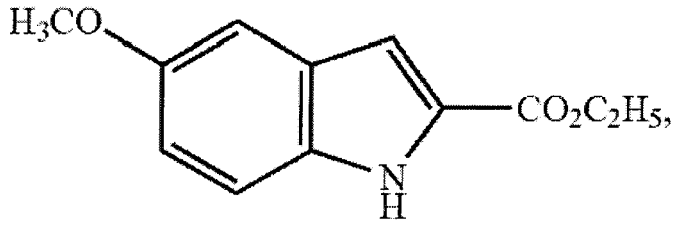

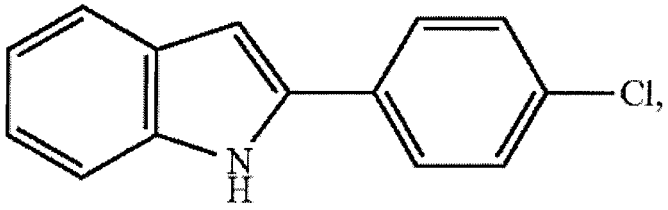

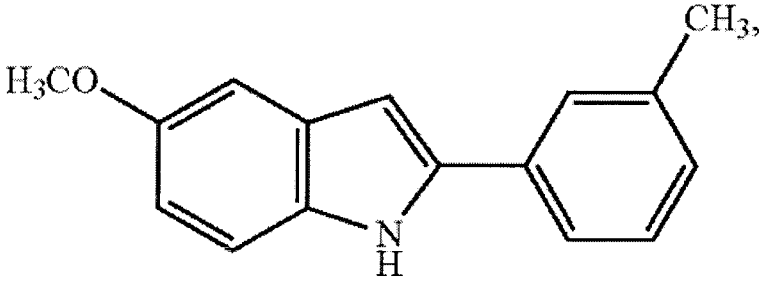

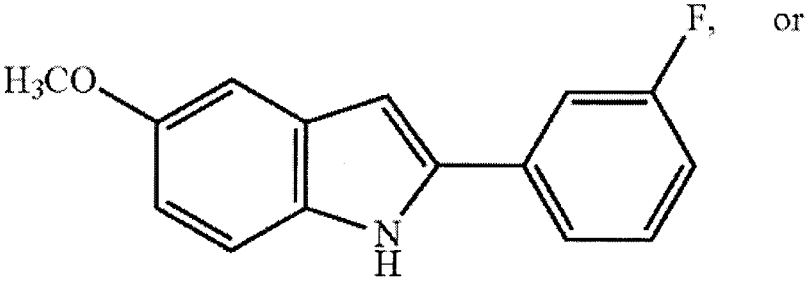

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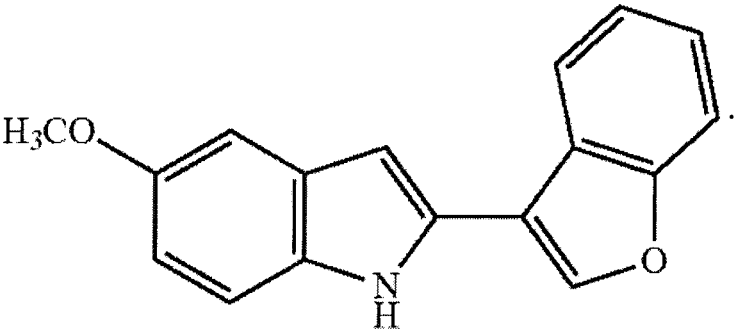

9. The method according to claim **1**, wherein the palladium-based catalyst is selected from the group consisting of palladium metal, palladium (II) acetate, sodium palladium (II) chloride, palladium (II) acetylacetonate, palladium(II) trifluoroacetate, palladium hydroxide, palladium(II) bromide, palladium (II) chloride, palladium(II) cyanide, palladium(II) hexafluoroacetylacetonate, palladium(II) iodide, palladium(II) nitrate dehydrate, palladium(II) nitrate hydrate, palladium(II) oxide, palladium (II) propionate, palladium (II) sulfate, and palladium (II) sulfide, or mixtures thereof.

10. The method according to claim **9**, wherein the palladium-based catalyst comprises of palladium (II) acetate.

11. The method according to claim **1**, wherein the amount of palladium-based catalyst is in the range of about 0.1 mol % to about 20 mol %, with respect to the amount of N-aryl imine.

12. The method according to claim **1**, wherein the oxidant comprises of copper (II) acetate.

13. The method according to claim **1**, wherein the oxidant comprises of molecular oxygen (O_2).

14. The method according to claim **1**, wherein the amount of oxidant is about 2 equivalence to about 3 equivalence, of the amount of N-aryl imine.

15. The method according to claim **1**, further comprising reacting in the presence of an additive, wherein the additive comprises a quaternary ammonium salt of Formula (III)

$(R_4)_nN—X$ Formula (III)

wherein

R_4 at each occurrence is independently selected from C_1-C_{20} alkyl;

n is 1, 2, 3 or 4; and

X is selected from the group consisting of a halogen and —$OCOCH_3$.

16. The method according to claim **15**, wherein the additive is selected from the group consisting of Bu_4NBr, Bu_4NCl, Bu_4NI, and $Bu_4NOCOCH_3$.

17. The method according to claim **15**, wherein the amount of additive is about 1 equivalence to about 3 equivalence of the amount of N-aryl imine.

18. The method according to claim **15**, wherein the additive comprises a ligand for the palladium-based catalyst, wherein the ligand is selected from the group consisting of pyridine, 2,2'-bipyridine, 1,10-phenanthroline, PPh_3, dppm, dppe, dppp, dcpe, P(c-hex)$_3$, P(tBu)$_3$, $P(C_6F_5)_3$, and P(2,4,6-$Me_3C_6H_2)_3$, or mixtures thereof.

19. The method according to claim **18**, wherein the amount of ligand is about 1 equivalence to about 2 equivalence of the amount of palladium present in the palladium-based catalyst.

20. The method according to claim **1**, wherein the method is carried out at a temperature in the range of about 0° C. to about 150° C.