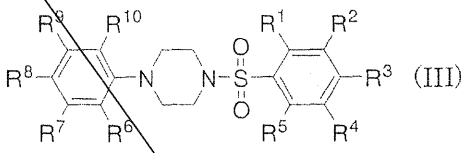
Claims

[Claim 1] A method of producing a compound represented by Formula (III):

[Chemical formula 1]

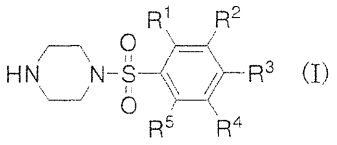


wherein R^1, R^2, R^3, R^4, and R^5 each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;

R^6, R^7, R^8, R^9, and R^{10} each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, hydroxy, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;

comprising reacting a compound represented by Formula (I):

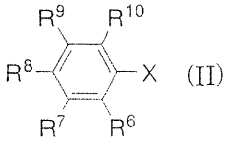
[Chemical formula 2]



wherein R^1, R^2, R^3, R^4, and R^5 are as defined above;

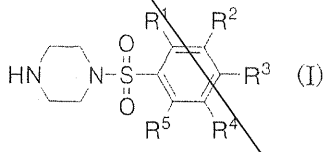
with a compound represented by Formula (II):

[Chemical formula 3]



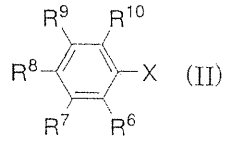
wherein R^6, R^7, R^8, R^9, and R^{10} are as defined above;
X represents a halogen atom, optionally substituted alkylsulfonyloxy, or optionally substituted arylsulfonyloxy;
in the presence of a palladium compound, an organic phosphorus compound, and a base in a solvent.

[Claim 2] The method according to claim 1, comprising
Step A of reacting the compound represented by Formula (I):
[Chemical formula 4]



(I)

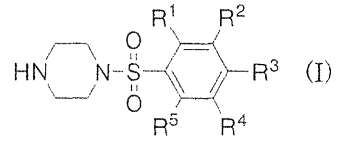
wherein R^1, R^2, R^3, R^4, and R^5 are as defined in claim 1;
with the palladium compound, the organic phosphorus compound, and the base; and
Step B of adding the compound represented by Formula (II):
[Chemical formula 5]



(II)

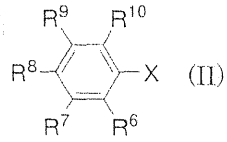
wherein R^6, R^7, R^8, R^9, R^{10}, and X are as defined in claim 1.

[Claim 3] The method according to claim 1, comprising:
Step C of mixing the palladium compound and the organic phosphorus compound;
Step D of adding the compound represented by Formula (I):
[Chemical formula 6]



(I)

wherein R^1, R^2, R^3, R^4, and R^5 are as defined in claim 1; and the base to the mixture obtained in Step C; and
Step E of adding the compound represented by Formula (II):
[Chemical formula 7]



(II)

wherein R^6, R^7, R^8, R^9, R^{10}, and X are as defined in claim 1; to the mixture obtained in Step D.

[Claim 4] The method according to claim 1, wherein the palladium compound is palladium acetate.

[Claim 5] The method according to claim 1, wherein the organic phosphorus compound is diadamantylbutyl phosphine.

[Claim 6] The method according to claim 1, which is conducted in the presence of sulfinate.

[Claim 7] The method according to claim 2, wherein Step A is conducted in the presence of sulfinate.

[Claim 8] The method according to claim 3, wherein Step D is conducted in the presence of sulfinate.

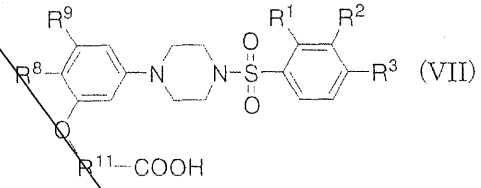
[Claim 9] The method according to any one of claims 6 to 8, wherein the sulfinate is sodium para-toluene sulfinate.

[Claim 10] The method according to claim 1, wherein R^4, R^5, R^6, and R^{10} are hydrogen atoms, R^1, R^2, and R^9 each independently are a hydrogen atom, a halogen atom, or alkyl, R^3 is alkyloxy or alkylthio, R^7 is hydroxy or optionally substituted alkyloxy, R^8 is a halogen atom, optionally substituted alkyl, optionally substituted alkyloxy, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted an non-aromatic heterocyclic group, and X is halogen atom.

[Claim 11] The method according to claim 1, wherein R^1, R^2, R^4, R^5, R^6, and R^{10} are hydrogen atoms, R^9 is a hydrogen atom or a halogen atom, R^3 is alkyloxy, R^7 is hydroxy, R^8 is a halogen atom, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group, and X is a halogen atom.

[Claim 12] A method of producing a compound represented by Formula (VII):

[Chemical formula 8]

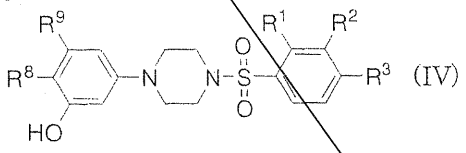


(VII)

wherein R^1, R^2, R^3, R^8, and R^9 are as defined in claim 1; R^{11} is alkylene or alkenylene; comprising:

Step F of obtaining a compound represented by Formula (IV):

[Chemical formula 9]

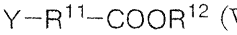


(IV)

wherein R^1, R^2, R^3, R^8, and R^9 are as defined in claim 1; by the method according to claim 1;

Step G of reacting the compound represented by Formula (IV) with a compound represented by Formula (V):

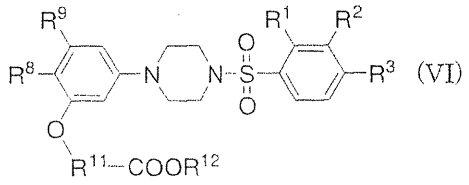
[Chemical formula 10]



(V)

wherein R^{11} is defined above; R^{12} is a hydrogen atom or alkyl; Y is a halogen atom, optionally substituted alkylsulfonyl, or optionally substituted arylsulfonyl; in the presence of a base to obtain a compound represented by Formula (VI):

[Chemical formula 11]



(VI)

wherein R^1, R^2, R^3, R^8, and R^9 are as defined in claim 1; R^{11} and R^{12} are as defined above; and

additional Step H of subjecting the compound represented by Formula (VI) to hydrolysis when R^{12} is alkyl.

[Claim 13] The method according to claim 12, wherein Y is halogen atom.

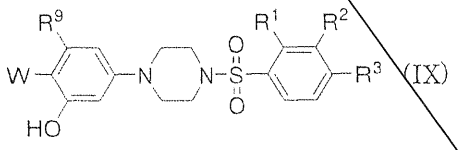
[Claim 14] The method according to claim 12, wherein R^1, R^2,

and R^9 each independently are a hydrogen atom, a halogen atom, or alkyl, R^3 is alkyloxy or alkylthio, R^8 is a halogen atom, optionally substituted alkyl, optionally substituted alkyloxy, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group, and R^{11} is alkylene.

[Claim 15] The method according to claim 12, wherein R^1, R^2, and R^9 each independently are a hydrogen atom, a halogen atom, or alkyl, R^3 is alkyloxy or alkylthio, R^8 is a halogen atom, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group, and R^{11} is methylene.

[Claim 16] A method of producing a compound represented by Formula (IX):

[Chemical formula 12]

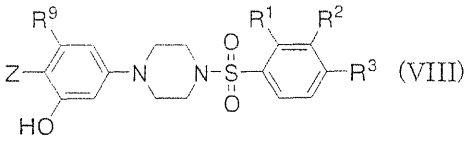


(IX)

wherein R^1, R^2, R^3, and R^9 are as defined in claim 1; W is optionally substituted aryl or optionally substituted heteroaryl; comprising:

Step I of obtaining a compound represented by Formula (VIII):

[Chemical formula 13]



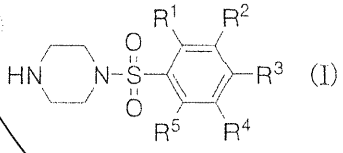
(VIII)

wherein R^1, R^2, R^3, and R^9 are as defined in claim 1; Z is a halogen atom; by the method according to claim 1; and

Step J of reacting the compound represented by Formula (VIII) with an organic boronic acid.

[Claim 17] A method of producing a compound represented by Formula (I):

[Chemical formula 14]

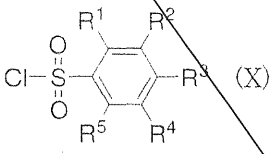


(I)

wherein R^1, R^2, R^3, R^4, and R^5 are as defined in claim 1; comprising:

Step K of adding a compound represented by Formula (X):

[Chemical formula 15]



(X)

wherein R^1, R^2, R^3, R^4, and R^5 are as defined in claim 1; to a solution of piperazine;

Step L of adding water to the reaction mixture and extracting it with an organic solvent; and

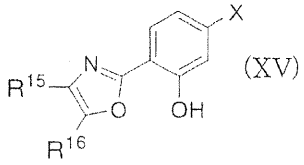
Step M of making the organic phase obtained in Step L acidic by adding an acid, and extracting it with water; and

Step N of making the aqueous phase obtained in Step M alkaline by adding a base to cause precipitation of crystals.

[Claim 18] The method according to claim 17, wherein R^1, R^2, R^4, and R^5 are a hydrogen atom, and R^5 is alkoxy.

[Claim 19] A method of producing a compound represented by Formula (XV):

[Chemical formula 16]

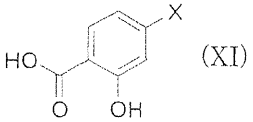


(XV)

wherein X is as defined in claim 1; R^{15} and R^{16} each independently represent hydrogen atom or alkyl; comprising:

Step P of reacting a compound represented by Formula (XI):

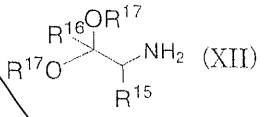
[Chemical formula 17]



(XI)

wherein X is as defined in claim 1; with a compound represented by Formula (XII):

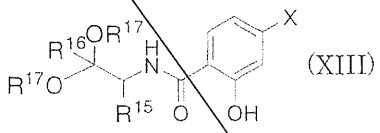
[Chemical formula 18]



(XII)

wherein R^{15} and R^{16} are as defined above; R^{17} is alkyl; to obtain a compound represented by Formula (XIII):

[Chemical formula 19]

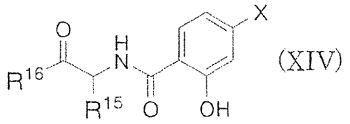


(XIII)

wherein X is as defined in claim 1; R^{15}, R^{16}, and R^{17} are as defined above;

Step Q of reacting the compound represented by Formula (XIII) with an acid to obtain a compound represented by Formula (XIV):

[Chemical formula 20]



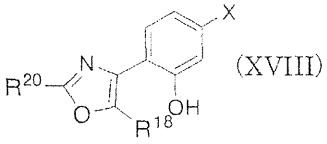
(XIV)

wherein X is as defined in claim 1; R^{15} and R^{16} are as defined above; and

Step R of closing the ring of the compound represented by Formula (XIV).

[Claim 20] A method of producing a compound represented by Formula (XVIII):

[Chemical formula 21]

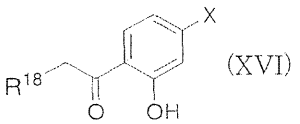


(XVIII)

wherein X is as defined in claim 1; R^{18} is a hydrogen atom or alkyl; and R^{20} is a hydrogen atom or alkyl; comprising:

Step S of halogenating a compound represented by Formula (XVI):

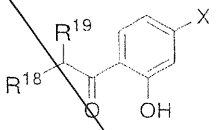
[Chemical formula 22]



(XVI)

wherein X is as defined in claim 1; R^{18} is a hydrogen atom or alkyl; to obtain a compound represented by Formula (XVII):

[Chemical formula 23]



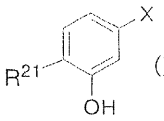
(XVII)

wherein X is as defined in claim 1; R^{18} is as defined above; R^{19} is a halogen atom; and

Step T of reacting the compound represented by Formula (XVII) with a compound represented by the formula: $R^{20}COONH_4$ wherein R^{20} is as defined above.

[Claim 21] A compound represented by Formula (XIX):

[Chemical formula 24]

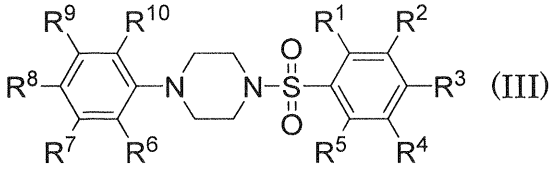


(XIX)

wherein X is as defined in claim 1; R^{21} is optionally substituted 5-membered heteroaryl; a pharmaceutically acceptable salt thereof, or a solvate thereof.

Claims

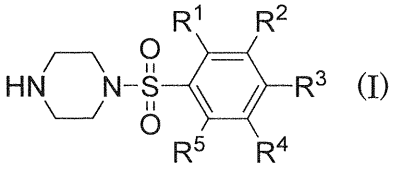
[Claim 1] A method of producing a compound represented by Formula (III):



(III)

wherein R^1, R^2, R^3, R^4, and R^5 each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;
R^6, R^7, R^8, R^9, and R^{10} each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, hydroxy, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;
the method comprising

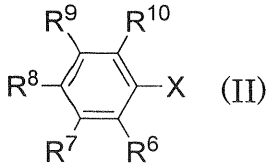
Step A of reacting a compound represented by Formula (I):



(I)

wherein R^1, R^2, R^3, R^4, and R^5 are as defined above;
with a palladium compound, an organic phosphorus compound, and a base in a solvent; and

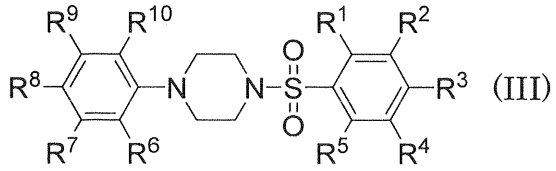
Step B of adding a compound represented by Formula (II):



(II)

wherein R^6, R^7, R^8, R^9, R^{10}, are as definedabove and X represents a halogen atom, optionally substituted alkylsulfonyloxy, or optionally substituted arylsulfonyloxy.

[Claim 2] A method of producing a compound represented by Formula (III):

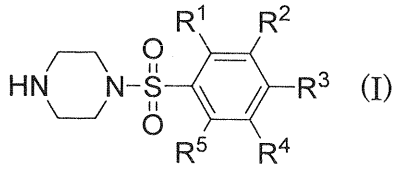


(III)

wherein R^1, R^2, R^3, R^4, and R^5 each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;
R^6, R^7, R^8, R^9, and R^{10} each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, hydroxy, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;
the method comprising:

Step C of mixing a palladium compound and an organic phosphorus compound in a solvent;

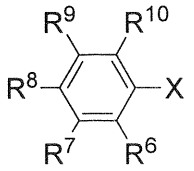
Step D of adding the compound represented by Formula (I):



(I)

wherein R^1, R^2, R^3, R^4, and R^5 are as defined above; and a base to the mixture obtained in Step C; and

Step E of adding the compound represented by Formula (II):



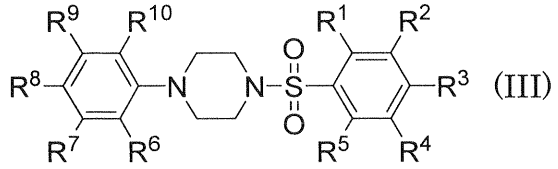
(II)

wherein R^6, R^7, R^8, R^9, R^{10} are as definedabove and X represents a halogen atom, optionally substituted alkylsulfonyloxy, or optionally substituted arylsulfonyloxy; to the mixture obtained in Step D.

[Claim 3] The method according to claim 1 or 2, wherein the palladium compound is palladium acetate.

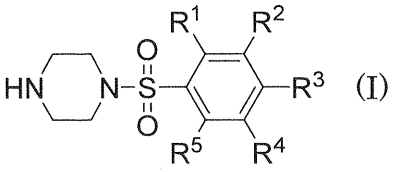
[Claim 4] The method according to claim 1 or 2, wherein the organic phosphorus compound is diadamantylbutyl phosphine.

[Claim 5] A method of producing a compound represented by Formula (III):



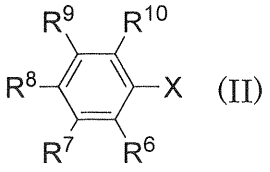
(III)

wherein R^1, R^2, R^3, R^4, and R^5 each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;
R^6, R^7, R^8, R^9, and R^{10} each independently represent a hydrogen atom, a halogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, hydroxy, optionally substituted alkyloxy, optionally substituted alkylthio, acyl, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group;
the method comprising reacting a compound represented by Formula (I):



(I)

wherein R^1, R^2, R^3, R^4, and R^5 are as defined above;
with a compound represented by Formula (II):



(II)

wherein R^6, R^7, R^8, R^9, and R^{10} are as defined above;
X represents a halogen atom, optionally substituted alkylsulfonyloxy, or optionally substituted arylsulfonyloxy;
in the presence of a palladium compound, an organic phosphorus compound, and a base in a solvent and the method is conducted in the presence of sulfinate.

[Claim 6] The method according to claim 1, wherein Step A is conducted in the presence of sulfinate.

[Claim 7] The method according to claim 2, wherein Step D is conducted in the presence of sulfinate.

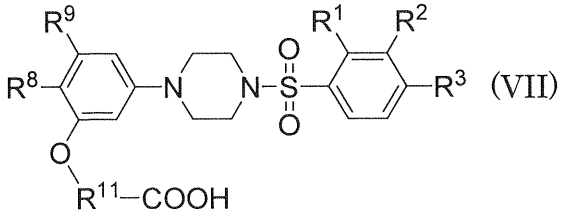
[Claim 8] The method according to any one of claims 5 to 7, wherein the sulfinate is sodium para-toluene sulfinate.

[Claim 9] The method according to claim 1 or 2, wherein R^4, R^5, R^6, and R^{10} are hydrogen atoms, R^1, R^2, and R^9 each independently are a hydrogen atom, a halogen atom, or alkyl, R^3 is alkyloxy or alkylthio, R^7 is hydroxy or optionally substituted alkyloxy, R^8 is a halogen atom, optionally substituted alkyl, optionally substituted alkyloxy, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted non-aromatic heterocyclic group, and X is halogen atom.

[Claim 10] The method according to claim 1 or 2, wherein R^1, R^2, R^4, R^5, R^6, and R^{10} are hydrogen atoms, R^9 is a hydrogen atom or a halogen atom, R^3 is alkyloxy, R^7 is hydroxy, R^8 is a halogen atom, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted

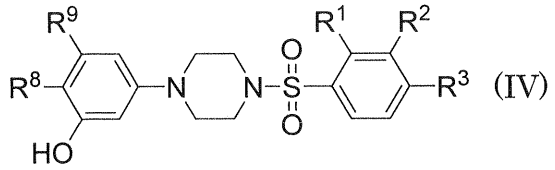
non-aromatic heterocyclic group, and X is a halogen atom.

[Claim 11] The method according to claim 1 or 2 comprising the step of producing a compound represented by Formula (VII):
[Chemical formula 8]



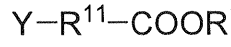
wherein R^1, R^2, R^3, R^8, and R^9 are as defined in claim 1; R^{11} is alkylene or alkenylene; comprising:

Step F of obtaining a compound represented by Formula (IV):

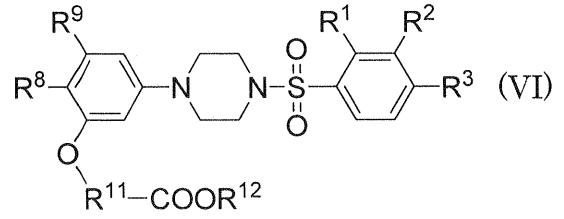


wherein R^1, R^2, R^3, R^8, and R^9 are as defined in claim 1; by the method according to claim 1 or 2;

Step G of reacting the compound represented by Formula (IV) with a compound represented by Formula (V):



wherein R^{11} is defined above; R^{12} is a hydrogen atom or alkyl; Y is a halogen atom, optionally substituted alkylsulfonyl, or optionally substituted arylsulfonyl; in the presence of a base to obtain a compound represented by Formula (VI):



wherein R^1, R^2, R^3, R^8, and R^9 are as defined in claim 1; R^{11} and R^{12} are as defined above; and

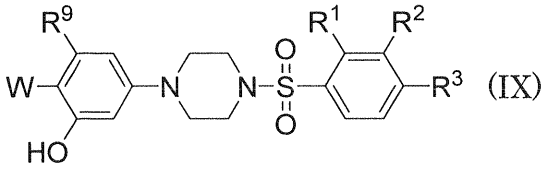
additional Step H of subjecting the compound represented by Formula (VI) to hydrolysis when R^{12} is alkyl.

[Claim 12] The method according to claim11, wherein Y is halogen atom.

[Claim 13] The method according to claim 11, wherein R^1, R^2, and R^9 each independently are a hydrogen atom, a halogen atom, or alkyl, R^3 is alkyloxy or alkylthio, R^8 is a halogen atom, optionally substituted alkyl, optionally substituted alkyloxy, optionally substituted alkyloxycarbonyl, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group, and R^{11} is alkylene.

[Claim 14] The method according to claim 11, wherein R^1, R^2, and R^9 each independently are a hydrogen atom, a halogen atom, or alkyl, R^3 is alkyloxy or alkylthio, R^8 is a halogen atom, optionally substituted carbamoyl, optionally substituted amino, optionally substituted aryl, optionally substituted heteroaryl, or an optionally substituted non-aromatic heterocyclic group, and R^{11} is methylene.

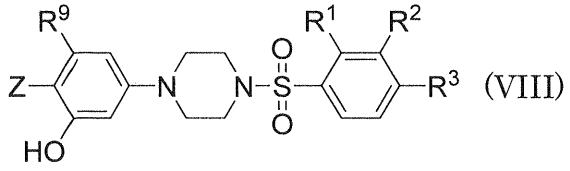
[Claim 15] The method according to claim 1 or 2 comprising the step of producing a compound represented by Formula (IX):



(IX)

wherein R^1, R^2, R^3, and R^9 are as defined in claim 1; W is optionally substituted aryl or optionally substituted heteroaryl; comprising:

Step I of obtaining a compound represented by Formula (VIII):



(VIII)

wherein R^1, R^2, R^3, and R^9 are as defined in claim 1; Z is a halogen atom; by the method according to claim 1 or 2; and

Step J of reacting the compound represented by Formula (VIII) with an organic boronic acid.