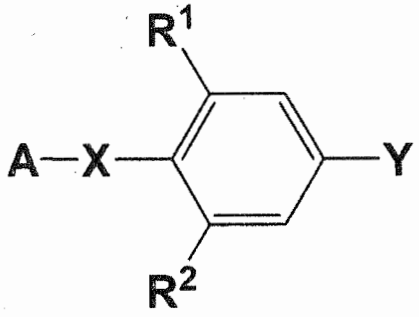
CLAIMS

1 A production method comprising reacting a compound represented by the following formula (1)

~~Compound 1~~



(1)

(wherein in formula (1),

R^1 represents a hydrogen atom or halogen atom;

R^2 represents a hydrogen atom, a cyano group, a nitro group, a halogen atom, a formyl group or a halomethyl group;

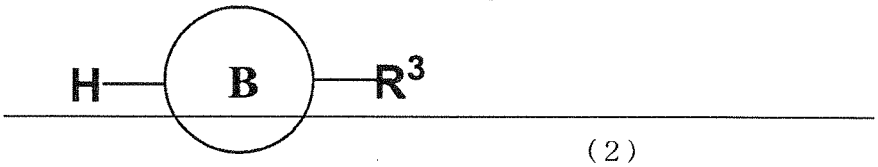
A represents a hydrogen atom, a C_1 to C_8 alkyl group, a C_3 to C_6 cycloalkyl group, a phenyl group, a fluorine atom (only when X is bond), or protecting group for a hydroxyl group (only when X is an oxygen atom),

A may be substituted with 1 to 3 substituents, such substituents include a group selected from the group consisting of a halogen atom, a C_1 to C_4 alkyl group, a C_1 to C_4 alkoxy group, a C_1 to C_4 alkylthio group, a C_3 to C_6 cycloalkyl group, a phenyl group, a phenoxy group, and a pyridyl group;

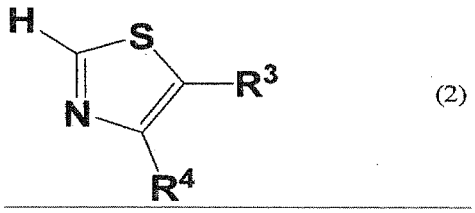
X represents a bond (only when A is a phenyl group or a fluorine atom), or an oxygen atom; and Y represents a leaving group),

and a compound represented by the following formula (2)

~~Compound 2~~



(2)



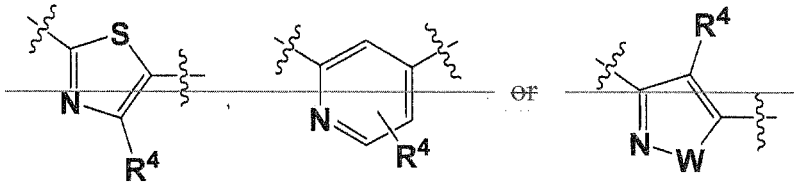
(2)

(wherein in formula (2),

H represents a hydrogen atom;

~~B represents a group selected from the following formulae;~~

~~Compound 3~~



R^3 represents a -$COOR^{3a}$ or -COR^{3b};

R^{3a} represents a hydrogen atom, a C_1 to C_4 alkyl group, or an ester-type protecting group of a carboxyl group;

R^{3b} represents an amide-type protecting group for ~~of~~ a carboxyl group, the protecting group forming ~~formed~~ an amide with a neighboring ~~an adjacent~~ carbonyl group;

R^4 represents a hydrogen atom, a halogen atom, or C_1 to C_4 alkyl~~; and~~

~~W represents an oxygen atom, or a sulfur atom)~~,

in the presence of

(i) a palladium compound,

(ii) a ligand capable of coordinating to the palladium compound or a salt thereof,

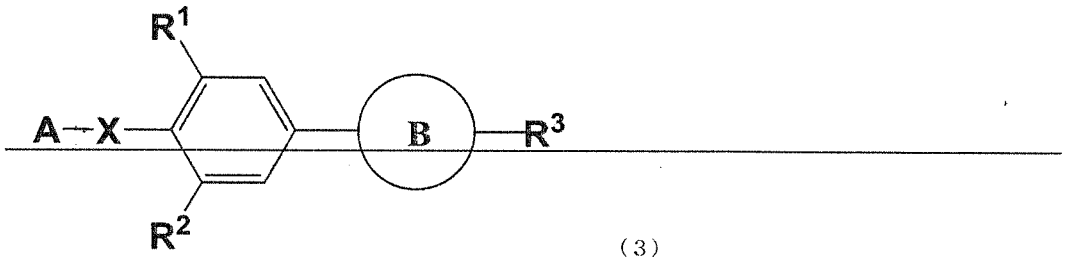
(iii) a base,

(iv) a C_1 to C_{40} carboxylic acid or a salt thereof

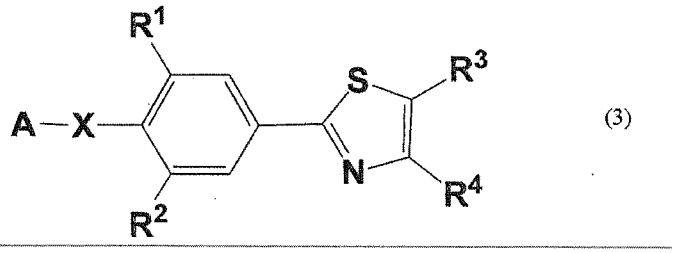
(v) at least one additive selected from the group of consisting of copper, silver, and salts thereof, and complexes thereof;

to produce a phenyl-substituted heterocyclic derivative represented by the following formula (3)

~~Compound 4~~



(3)



(3)

~~(~~Wherein in formula (3),

the definition of A, X, R^1 and R^2 is the same as defined in formula (1), and that of ~~B~~ ~~and~~ R^3 and R^4 is the same as in formula (2)~~)~~.

2. The method of production according to claim 1, wherein A is a C_1 to C_5 alkyl group.

3. The method of production according to claim 1, wherein A is an isobutyl group.

4. The method of production according to any one of claims 1 to 3, wherein X is an oxygen atom.

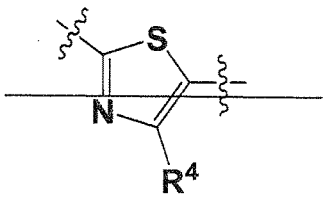
5. The method of production according to any one of claims 1 to 4, wherein R^1 is a hydrogen atom.

6. The method of production according to any one of claims 1 to 5, wherein R^2 is a cyano group.

7. The method of production according to any one of claims 1 to 6, wherein Y represents a halogen atom, -OCO_2-(C_1 to C_4 alkyl group), -OCO_2-(phenyl group), -OSO_2-(C_1 to C_4 alkyl group), -OSO_2-(phenyl group), or a diazonium group, and ,in Y, the C_1 to C_4 alkyl group can be substituted with 1 to 3 halogen atoms, and the phenyl group can be substituted with 1 to 5 optional substituents selected from halogen atoms and C_1 to C_4 alkyl groups.

~~8. The method of production according to any one of claims 1 to 7, wherein B is a group represents by the following group.~~

~~Compound 5~~



~~9~~8. The method of production according to any one of claims 1 to ~~8~~7, wherein R^3 is $COOR^{3a}$ and R^{3a} is a C_1 to C_4 alkyl group.

~~10~~9. The method of production according to any one of claims 1 to 8, wherein R^4 is a methyl group.

~~11~~10. The method of production according to any one of claims 1 to ~~10~~9, wherein the palladium compound is zerovalent palladium, or a salt of monovalent or divalent palladium.

~~12~~11. The method of production according to any one of claims 1 to ~~10~~9, wherein the palladium compound is palladium(II) acetate ($Pd(OAc)_2$), palladium(II) propionate ($Pd(O(C{=}O)CH_2CH_3)_2$), palladium(II) 2-methylpropanoate ($Pd(O(C{=}O)CH(CH_3)_2)_2$),

palladium(II) pivalate ($Pd(OPiv)_2$), palladium(II) chloride ($PdCl_2$), palladium(II) bromide ($PdBr_2$), or palladium(0).

~~13~~12. The method of production according to any one of claims 1 to ~~09~~, wherein the palladium compound is palladium(II) 2-methylpropanoate ($Pd(O(C=O)CH(CH_3)_2)_2$), palladium(II) pivalate ($Pd(OPiv)_2$), palladium(II) chloride ($PdCl_2$), palladium(II) bromide ($PdBr_2$), or palladium(0).

~~14~~13. The method of production according to any one of claims 1 to ~~13~~12, wherein the ligand is a phosphine-type ligand.

~~15~~14. The method of production according to claim ~~14~~13, wherein the phosphine-type ligand is a phosphine-type ligand represented by $R^5P(R^6)R^7$ (R^5 and R^6 are each independently a C_3 to C_8 alkyl group or an alicyclic hydrocarbon group wherein the number of hydrogen atoms bonded to each carbon atom of R^5 and R^6 which bind to a phosphorus atom is 0 or 1, R^7 is a C_1 to C_8 alkyl group, an alicyclic hydrocarbon group, a C_6 to C_{12} aryl group, or a heteroaryl group).

~~16~~15. The method of production according to claim ~~15~~14, wherein the phosphine-type ligand is tri(*tert*-butyl)phosphine, di(*tert*-butyl)methylphosphine, *tert*-butyldicyclohexylphosphine, di(*tert*-butyl)cyclohexylphosphine, or tri(cyclohexyl)phosphine.

~~17~~16. The method of production according to any one of claims 1 to ~~16~~15, wherein the base is a hydroxide of an alkali metal or a Group 2 element, a fluoride of an alkali metal, a phosphate of an alkali metal, or a carbonate or a hydrogen carbonate of an alkali metal or a Group 2 element.

~~18~~17. The method of production according to claim ~~17~~16, wherein the base is potassium carbonate, potassium hydrogen carbonate, sodium carbonate, or sodium hydrogen

carbonate.

~~19~~18. The method of production according to any one of claims 1 to ~~18~~17, wherein the carbon atom of the carboxyl group at the α-position in the C_1 to C_{40} carboxylic acid is not the carbon atom on the aromatic ring and the number of hydrogen atoms bonded to the carbon atom of the carboxyl group at the α-position is 0 or 1.

~~20~~19. The method of production according to claim ~~19~~18, wherein the C_1 to C_{40} carboxylic acid contains one carboxyl group and consists of only carbon atoms and hydrogen atoms as constituent atoms except for the carboxyl group.

~~21~~20. The method of production according to claim ~~20~~19, wherein the C_1 to C_{40} carboxylic acid is 2-methylpropanoic acid or pivalic acid.

~~22~~21. The method of production according to any one of claims 1 to ~~21~~20, wherein a divalent palladium salt of the C_1 to C_{40} carboxylic acid is used instead of using (i) the palladium compound and (iv) the C_1 to C_{40} carboxylic acid and a salt thereof independently.

~~23~~22. The method of production according to any one of claims 1 to ~~21~~20, wherein a monovalent copper salt or a monovalent silver salt of the C_1 to C_{40} carboxylic acid is used instead of using (iv) the C_1 to C_{40} carboxylic acid or a salt thereof and (v) the additive independently.

~~24~~23. The method of production according to any one of claims 1 to 22, wherein the additive is zerovalent copper or a salt of monovalent copper.

~~25~~24. The method of production according to any one of claims 1 to ~~23~~22, wherein the additive is at least one additive selected from the group consisting of copper(I) oxide, copper(I) fluoride, copper(I) chloride, copper(I) bromide, copper(I) iodide, copper(I) formate, copper(I) acetate, copper(I)propionate, copper(I) 2-methylpropanoate, copper(I)

2-ethylbutanoate, copper(I) 2-methylbutanoate, copper(I) 2-methylpentanoate, copper(I) 2-methylhexanoate, copper(I) 2-methylheptanoate, copper(I) 2,2-dimethylbutanoate, copper(I) 2,3-dimethylbutanoate, copper(I) 2,2-dimethylpentanoate, copper(I) 2,3,3-trimethylbutanoate, copper(I) 2-ethylhexanoate, copper(I) 2,2-diethylbutanoate, copper(I) 2,2,4-trimethylpentanoate, copper(I) 2-methyloctanoate, copper(I) 2-methylundecanoate, copper(I) 2-methylnonanoate, copper(I) pivalate, copper(I) cyclopropanoate, copper(I) 2,2,3,3-tetramethylcyclopropanoate, copper(I) cyclopentanoate, and copper(I) 1-adamantanecarboxylate.

~~26~~25. The method of production according to any one of claims 1 to ~~23~~22, wherein the additive is zerovalent silver or a salt of monovalent silver.

~~27~~26. The method of production according to any one of claims 1 to ~~23~~22, wherein the additive is at least one additive selected from the group consisting of silver(I) oxide, silver(I) fluoride, silver(I) chloride, silver(I) bromide, silver(I) iodide, silver(I) formate, silver (I) acetate, silver(I) propionate, silver(I) 2-methylpropanoate, silver(I) 2-ethylbutanoate, silver(I) 2-methylbutanoate, silver(I) 2-methylpentanoate, silver(I) 2-methylhexanoate, silver(I) 2-methylheptanoate, silver(I) 2,2-dimethylbutanoate, silver(I) 2,3-dimethylbutanoate, silver(I) 2,2-dimethylpentanoate, silver(I) 2,3,3-trimethylbutanoate, silver(I) 2-ethylhexanoate, silver(I) 2,2-diethylbutanoate, silver(I) 2,2,4-trimethylpentanoate, silver(I) 2-methyloctanoate, silver(I) 2-methylundecanoate, silver(I) 2-methylnonanoate, silver(I) pivalate, silver(I) cyclopropanoate, silver(I) 2,2,3,3-tetramethylcyclopropanoate, silver(I) cyclopentanoate, and silver(I) 1-adamantanecarboxylate.