

by R³ is preferably a substituent as defined above. More preferred is a halogen atom, a cyano group or a 5- to 7-membered monocyclic unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, more preferred is a cyano group or a 5- to 7-membered monocyclic unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and more preferred is a cyano group or a pyridinyl group.

[0053] The “optionally substituted C1-C6 alkyl group” represented by R³ is preferably a C1-C6 alkyl group which may have, as a substituent, a cyano group or a 5- to 7-membered monocyclic unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom. More preferred is a methyl group, a cyanomethyl group or a pyridinylmethyl group.

[0054] The “optionally substituted C3-C7 cycloalkyl group” represented by R³ is preferably a C3-C7 cycloalkyl group, and is more preferably a cyclopropyl group or a cyclobutyl group.

[0055] R³ is preferably C(=O)R⁵, C(=S)R⁶ or an optionally substituted C1-C6 alkyl group. More preferred is C(=O)R⁵; C(=S)R⁶; or a C1-C6 alkyl group which may have, as a substituent, a cyano group or a 5- to 7-membered monocyclic unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, more preferred is C(=O)R⁵ or C(=S)R⁶, and most preferred is C(=O)R⁵.

[0056] In the compound of the present invention represented by general formula (I), R⁴ is a hydrogen atom, an optionally substituted C1-C6 alkyl group, an optionally substituted C3-C7 cycloalkyl group, or an optionally substituted carbonylamino group.

[0057] The “optionally substituted C1-C6 alkyl group” represented by R⁴ is preferably a C1-C6 alkyl group, and is more preferably a methyl group.

[0058] The “optionally substituted C3-C7 cycloalkyl group” represented by R⁴ is preferably a C3-C7 cycloalkyl group, and is more preferably a cyclopropyl group or a cyclobutyl group.

[0059] The “optionally substituted carbonylamino group” represented by R⁴ is preferably a carbonylamino group which may have a C1-C6 alkyl group, and is more preferably a methylcarbonylamino group or a dimethylcarbonylamino group.

[0060] R⁴ is preferably a hydrogen atom or a C1-C6 alkyl group, and is more preferably a hydrogen atom.

[0061] In the compound of the present invention represented by general formula (I), R⁵ is an optionally substituted C1-C6 alkyl group, an optionally substituted C3-C7 cycloalkyl group, an optionally substituted C1-C6 alkoxy group, an optionally substituted amino group, an optionally substituted 4- to 10-membered monocyclic or polycyclic saturated heterocyclic group, an optionally substituted 5- to 10-membered monocyclic or polycyclic unsaturated heterocyclic group, or an optionally substituted 6- to 10-membered monocyclic or polycyclic aromatic hydrocarbon group.

[0062] A “C1-C6 alkyl group” in the “optionally substituted C1-C6 alkyl group”

represented by R⁵ is preferably a methyl group.

[0063] A “substituent” on the “optionally substituted C1-C6 alkyl group” represented by R⁵ is preferably a substituent as defined above. More preferred is a halogen atom, a C1-C6 alkoxy group or a C1-C6 mono- or di-alkylamino group, more preferred is a fluorine atom, a methoxy group, an ethoxy group, a monomethylamino group or a dimethylamino group, and most preferred is a fluorine atom.

[0064] The “optionally substituted C1-C6 alkyl group” represented by R⁵ is preferably a C1-C6 alkyl group which may have, as a substituent, a halogen atom, a C1-C6 alkoxy group or a C1-C6 mono- or di-alkylamino group. More preferred is a C1-C6 alkyl group which may have, as a substituent, a fluorine atom, a methoxy group, an ethoxy group, a monomethylamino group or a dimethylamino group, more preferred is a C1-C6 alkyl group which may have a fluorine atom, and most preferred is a difluoromethyl group.

[0065] The “optionally substituted C3-C7 cycloalkyl group” represented by R⁵ is preferably a C3-C7 cycloalkyl group, and is more preferably a cyclopropyl group or a cyclobutyl group.

[0066] The “optionally substituted C1-C6 alkoxy group” represented by R⁵ is preferably a C1-C6 alkoxy group, and is more preferably a methoxy group, an ethoxy group or a pyrazin-2-ylmethoxy group, more preferably an ethoxy group or a pyrazin-2-ylmethoxy group.

[0067] The “optionally substituted amino group” represented by R⁵ is preferably a C1-C6 mono- or di-alkylamino group, and is more preferably a C1-C6 monoalkylamino group, more preferably an ethylamino group.

[0068] The “optionally substituted 4- to 10-membered monocyclic or polycyclic saturated heterocyclic group” represented by R⁵ is preferably a 4- to 10-membered monocyclic or polycyclic fully saturated heterocyclic group having 1 to 4 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom. More preferred is an azetidiny group, a pyrrolidinyl group or a morpholino group.

[0069] A “5- to 10-membered monocyclic or polycyclic unsaturated heterocyclic group” in the “optionally substituted 5- to 10-membered monocyclic or polycyclic unsaturated heterocyclic group” represented by R⁵ is preferably a 5- to 10-membered monocyclic or polycyclic fully unsaturated or partially saturated heterocyclic group having 1 to 4 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom. Preferred is a pyridazinyl group, a pyrimidinyl group, an oxazolyl group, an oxadiazolyl group, a pyrazinyl group, a pyridinyl group, an imidazolyl group, a furanyl group, an isoxazolyl group, a triazolopyridinyl group, a triazolyl group, a triazinyl group, a thiazolyl group, a thiadiazolyl group, an imidazopyrazinyl group or a pyrazolyl group, more preferred is an isoxazolyl group, a pyrazolyl group, an oxazolyl group, an oxadiazolyl group, a pyrazinyl group or a pyridazinyl group, and more preferred is a pyrazolyl group, an oxazolyl group, an oxadiazolyl group, a pyrazinyl group or a pyridazinyl group.

In general formula (XIII), the leaving group represented by L_4 is a hydrogen atom or an acetyl group.

This step may be carried out according to generally known procedures (e.g., Synthetic Communications, Vol. 19, p. 561, 1989), for example, may be carried out in the presence of a base in a solvent not adversely affecting the reaction.

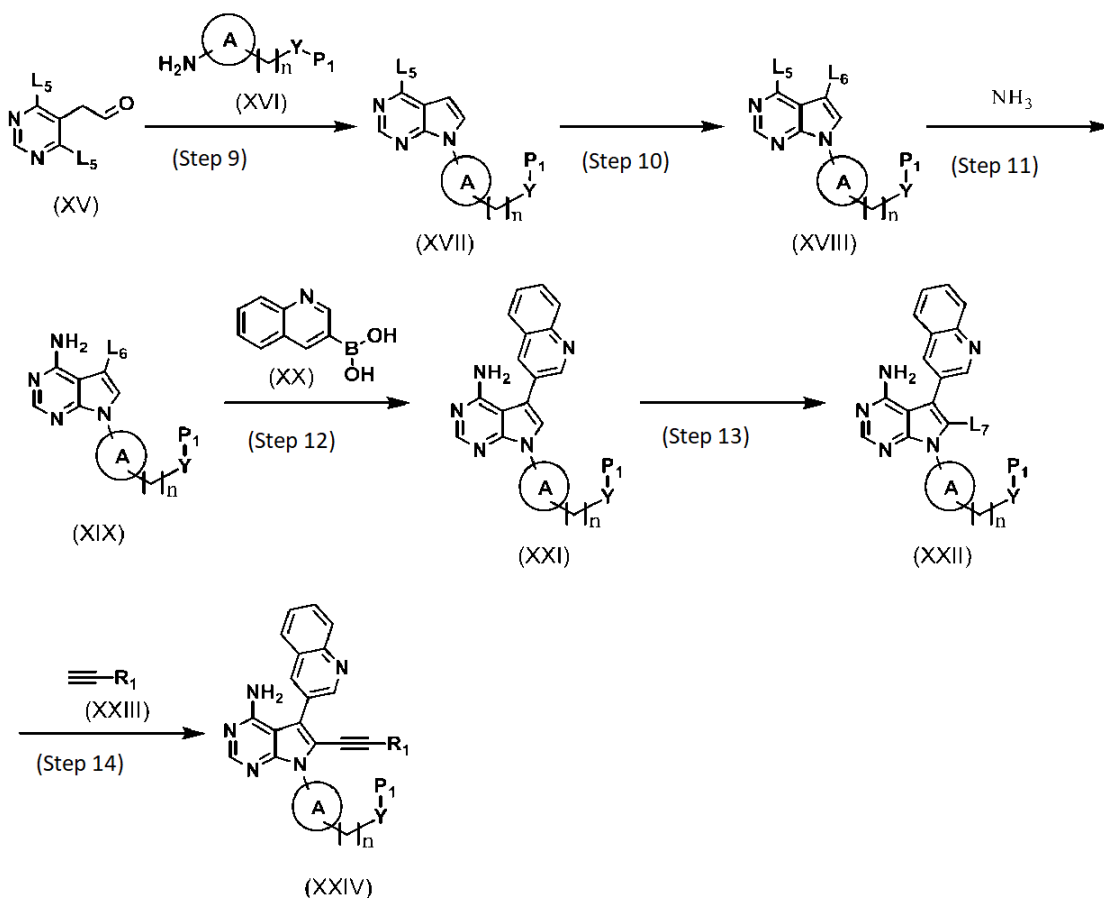
Examples of a base include alkali metal salts (e.g., sodium bicarbonate, sodium carbonate, potassium carbonate, cesium carbonate, potassium phosphate, sodium hydroxide), metal hydrides (e.g., potassium hydride, sodium hydride), alkali metal alkoxides (e.g., sodium methoxide, sodium ethoxide, potassium tert-butoxide), etc.

Any solvent may be used as long as it does not adversely affect the reaction, and examples include hydrocarbon-based solvents (e.g., benzene, toluene, xylene), nitrile-based solvents (e.g., acetonitrile), ether-based solvents (e.g., 1,2-dimethoxyethane, tetrahydrofuran, 1,4-dioxane), alcohol-based solvents (e.g., methanol, ethanol), aprotic polar solvents (e.g., dimethylformamide, dimethyl sulfoxide), water, or mixtures thereof.

The reaction temperature is usually -100°C to 100°C , and preferably -78°C to 50°C .

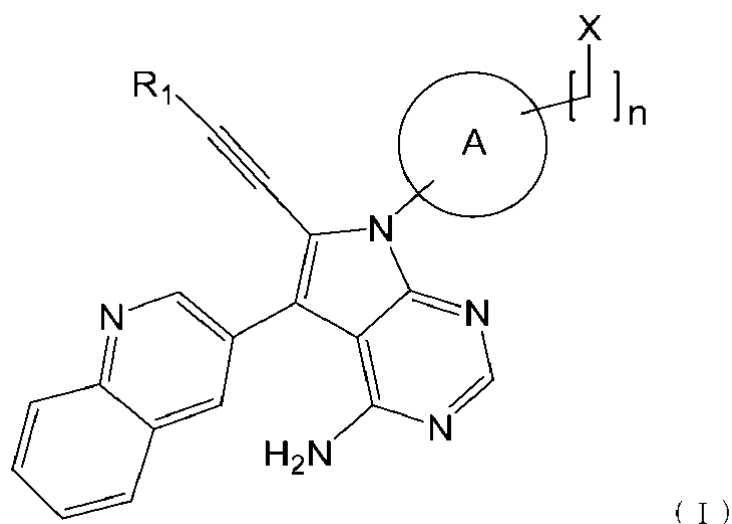
The reaction time is usually 5 minutes to 7 days, and preferably 1 hour to 24 hours.

[0107] [Preparation process 2]



CLAIMS

1. A compound represented by the following general formula (I):



wherein

R^1 is a hydrogen atom or an optionally substituted C1-C3 alkyl group;

X is NR^2R^3 , OR^4 or an optionally substituted monocyclic or polycyclic saturated or unsaturated heterocyclic group;

R^2 is a hydrogen atom or an optionally substituted C1-C6 alkyl group;

R^3 is a hydrogen atom, $C(=O)R^5$, $C(=S)R^6$, $S(=O)_2R^7$, an optionally substituted C1-C6 alkyl group, or an optionally substituted C3-C7 cycloalkyl group;

R^4 is a hydrogen atom, an optionally substituted C1-C6 alkyl group, an optionally substituted C3-C7 cycloalkyl group, or an optionally substituted carbonylamino group;

R^5 is an optionally substituted C1-C6 alkyl group, an optionally substituted C3-C7 cycloalkyl group, an optionally substituted C1-C6 alkoxy group, an optionally substituted amino group, an optionally substituted 4- to 10-membered monocyclic or polycyclic saturated heterocyclic group, an optionally substituted 5- to 10-membered monocyclic or polycyclic unsaturated heterocyclic group, or an optionally substituted 6- to 10-membered monocyclic or polycyclic aromatic hydrocarbon group;

R^6 is a hydrogen atom, an optionally substituted C1-C6 alkyl group, an optionally substituted C1-C6 mono- or di-alkylamino group, an optionally substituted C3-C7 cycloalkyl group, or an optionally substituted 4- to 10-membered monocyclic or polycyclic saturated heterocyclic group having 1 to 4 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom;

R^7 is an optionally substituted C1-C6 alkyl group, an optionally substituted C3-C7 cycloalkyl group, an optionally substituted 5- to 10-membered saturated or unsaturated heterocyclic group, or an optionally substituted 6- to 10-membered aromatic

hydrocarbon group;

the ring A is bicyclo[2.2.1]heptane or bicyclo[2.2.2]octane; and

n represents an integer of 0 to 3;

or a pharmaceutically acceptable salt thereof.

2. The compound or pharmaceutically acceptable salt thereof according to claim 1, wherein R¹ is a hydrogen atom or a C1-C3 alkyl group.

3. The compound or pharmaceutically acceptable salt thereof according to claim 1 or 2, wherein X is NR²R³, OR⁴ or a 5- to 7-membered monocyclic saturated or unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom;

R² is a hydrogen atom or a C1-C6 alkyl group;

R³ is C(=O)R⁵, C(=S)R⁶ or a C1-C6 alkyl group (which may have, as a substituent, a cyano group, a halogen atom or a 5- to 7-membered monocyclic unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom);

R⁴ is a hydrogen atom;

R⁵ is an optionally substituted C1-C6 alkyl group, a C1-C6 alkoxy group, a C1-C6 mono- or di-alkylamino group, an optionally substituted 5- to 10-membered monocyclic or polycyclic unsaturated heterocyclic group, or a 6- to 10-membered monocyclic or polycyclic aromatic hydrocarbon group; and

R⁶ is a C1-C6 mono- or di-alkylamino group, or a 4- to 10-membered monocyclic or polycyclic saturated heterocyclic group having 1 to 4 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, which may have a C1-C6 alkyl group.

4. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein n is 0 or 1.

5. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 4, wherein R¹ is a hydrogen atom.

6. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 5, wherein X is NR²R³ or a 5- to 7-membered monocyclic saturated or unsaturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom;

R² is a hydrogen atom;

R³ is C(=O)R⁵; and

R⁵ is an optionally substituted C1-C6 alkyl group, a C1-C6 alkoxy group, a C1-C6 mono- or di-alkylamino group, an optionally substituted 5- to 10-membered

monocyclic or polycyclic unsaturated heterocyclic group, or a 6- to 10-membered monocyclic or polycyclic aromatic hydrocarbon group.

7. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 6, wherein X is NR^2R^3 or a 5- to 7-membered monocyclic saturated heterocyclic group having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom;

R^2 is a hydrogen atom;

R^3 is $\text{C}(=\text{O})\text{R}^5$; and

R^5 is a C1-C6 alkyl group which may have a halogen atom, or a 5- to 10-membered monocyclic or polycyclic fully unsaturated or partially saturated heterocyclic group having 1 to 4 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, which may have a C1-C6 alkyl group.

8. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein the ring A is bicyclo[2.2.1]heptane.

9. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 8, wherein n is 0.

10. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 9, wherein the substituents are each selected from a halogen atom, a cyano group, a nitro group, an amino group, a hydroxyl group, an alkyl group, a haloalkyl group, a cycloalkyl group, an aralkyl group, an alkoxy group, a methylsulfonyl group, an alkoxyalkyl group, a hydroxyalkyl group, a fluoromethoxy group, a mono- or di-alkylamino group, a mono- or di-alkylaminoalkyl group, a carbonylamino group, an oxo group, an oxide group, a carboxyl group, an alkoxycarbonyl group, a phosphine oxide group, a saturated or unsaturated heterocyclic group, a heterocyclic alkyl group and an aromatic hydrocarbon group.

11. A compound selected from the following group of compounds:

(1) 6-ethynyl-7-(4-morpholinobicyclo[2.2.1]heptan-1-yl)-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine-4-amine,

(2) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)-1-methyl-1H-pyrazole-5-carboxamide,

(3) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)-2,2-difluoroacetamide,

(4) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)-5-methyl-1,2,4-oxadiazole-3-carboxamide,

(5) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)-5-methylpyrazine-2-carboxamide,

(6) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)oxazole-2-carboxamide,
(7) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)pyrazine-2-carboxamide,
(8) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)pyridazine-3-carboxamide,
(9) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)pyrimidine-5-carboxamide,
(10) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)-1-cyclopropyl-1H-pyrazole-5-carboxamide, and
(11) N-(4-(4-amino-6-ethynyl-5-(quinolin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[2.2.1]heptan-1-yl)isoxazole-5-carboxamide;
or a pharmaceutically acceptable salt thereof.

12. An antitumor agent comprising the compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, as an active ingredient.

13. A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, and a pharmaceutically acceptable carrier.

14. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, for use in the treatment of a tumor.

15. The use of the compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, in the manufacture of a medicament for the treatment of a tumor.