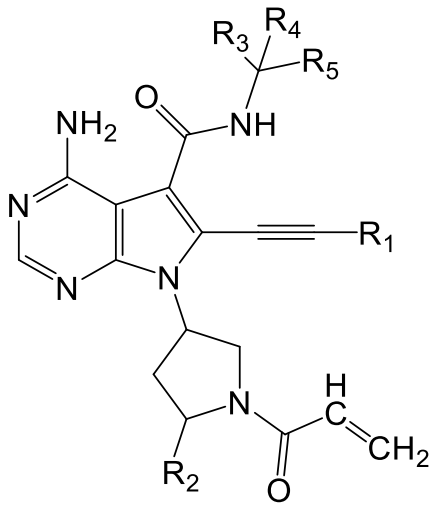
CLAIMS

[Claim 1]

A therapeutic agent for a disease associated with EGFR, comprising a pyrimidine compound represented by the following formula (I), or a pharmaceutically acceptable salt thereof as an active ingredient:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

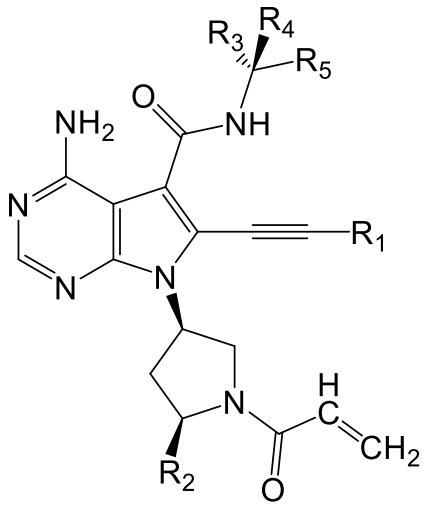
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim 2]

The therapeutic agent according to claim 1, wherein the pyrimidine compound is a compound represented by the following formula (II):



(II)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim 3]

The therapeutic agent according to claim 1 or 2, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_2 is a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups as a substituent(s).

[Claim 4]

The therapeutic agent according to any one of claims 1 to 3, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_3 is a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s).

[Claim 5]

The therapeutic agent according to any one of claims 1 to 4, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_5 is a phenyl group optionally having 1 or 2 substituents selected from the group consisting of fluorine atoms and chlorine atoms.

[Claim 6]

The therapeutic agent according to any one of claims 1 to 5, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_1 is a methyl group, a tert-butyl group, or a cyclopropyl group.

[Claim 7]

The therapeutic agent according to any one of claims 1 to 6, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_2 is a methyl group, an ethyl group, a methoxymethyl group, or an ethoxymethyl group.

[Claim 8]

The therapeutic agent according to any one of claims 1 to 7, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_3 is a methyl group.

[Claim 9]

The therapeutic agent according to any one of claims 1 to 8, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_4 is a hydrogen atom.

[Claim 10]

The therapeutic agent according to any one of claims 1 to 9, wherein the pyrimidine compound is a compound represented by the formula (I) or (II) wherein

R_5 is a phenyl group.

[Claim 11]

The therapeutic agent according to any one of claims 1 to 10, wherein the pyrimidine compound is a compound selected from the following (1) to (3):

(1) 7-((3R,5S)-1-acryloyl-5-methylpyrrolidin-3-yl)-4-amino-N-((R)-1-phenylethyl)-6-(prop-1-yn-1-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(2) 7-((3R,5S)-1-acryloyl-5-methylpyrrolidin-3-yl)-4-amino-6-(cyclopropylethynyl)-N-((R)-1-phenylethyl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide, and

(3) 7-((3R,5S)-1-acryloyl-5-methylpyrrolidin-3-yl)-4-amino-6-(3,3-dimethylbut-1-yn-1-yl)-N-((R)-1-phenylethyl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide.

[Claim 12]

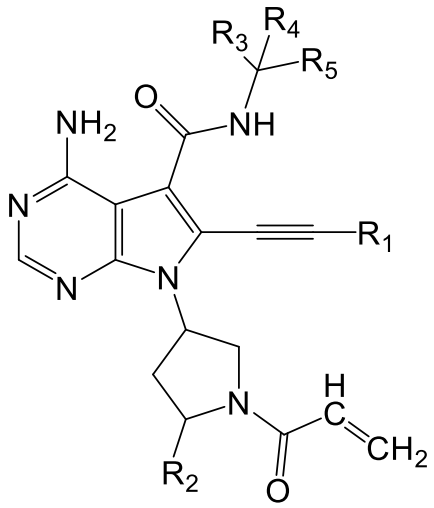
The therapeutic agent according to any one of claims 1 to 11, wherein the pyrimidine compound is 7-((3R,5S)-1-acryloyl-5-methylpyrrolidin-3-yl)-4-amino-6-(cyclopropylethynyl)-N-((R)-1-phenylethyl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide.

[Claim 13]

The therapeutic agent according to any one of claims 1 to 12, wherein the disease associated with EGFR is malignant tumor having EGFR overexpression, EGFR gene amplification, or an EGFR mutation.

[Claim 14]

An EGFR inhibitor comprising a pyrimidine compound represented by the following formula (I), or a pharmaceutically acceptable salt thereof as an active ingredient:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

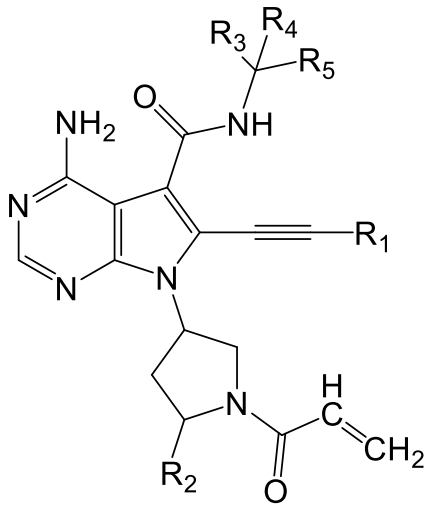
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim 15]

A therapeutic agent for EGFR-positive tumor, comprising a pyrimidine compound represented by the following formula (I), or a pharmaceutically acceptable salt thereof as an active ingredient:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

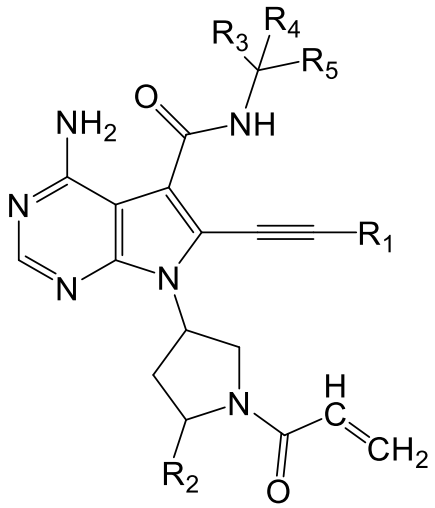
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim 16]

A pharmaceutical composition for use in the treatment of a disease associated with EGFR, the pharmaceutical composition comprising a pyrimidine compound represented by the following formula (I), or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

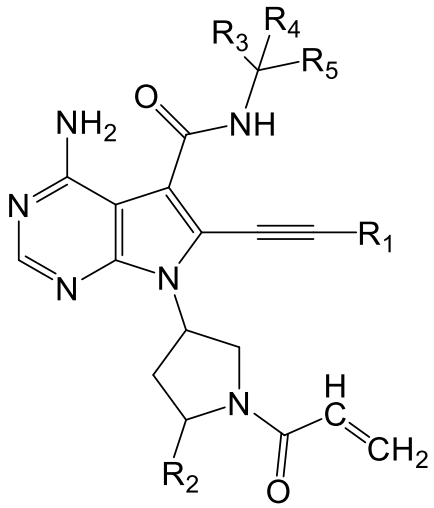
R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim 17]

The pharmaceutical composition according to claim 16, wherein the disease associated with EGFR is malignant tumor having EGFR overexpression, EGFR gene amplification, or an EGFR mutation.

[Claim 18]

A compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of a disease associated with EGFR:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

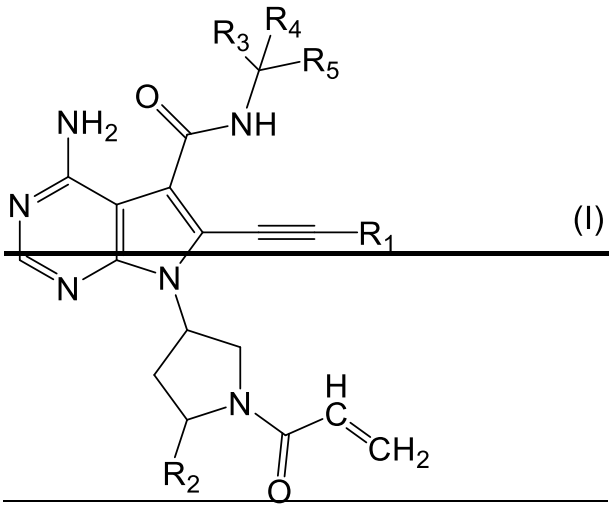
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

~~[Claim 19]~~

~~Use of a compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of a disease associated with EGFR:~~



~~wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;~~

~~R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;~~

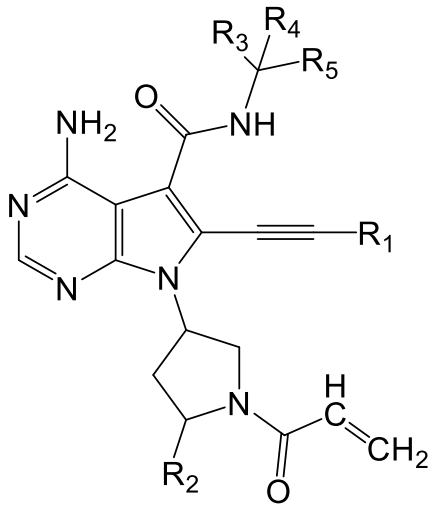
~~R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);~~

~~R_4 represents a hydrogen atom or a C1-C4 alkyl group; and~~

~~R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.~~

[Claim ~~20~~19]

Use of a compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof for the manufacture of a therapeutic agent for use in the treatment of a disease associated with EGFR:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

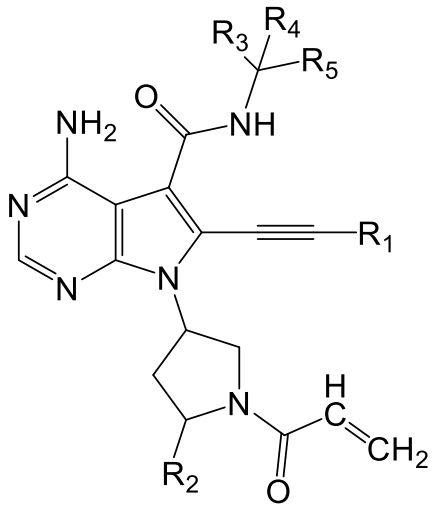
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim ~~21~~20]

A compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of EGFR-positive tumor:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

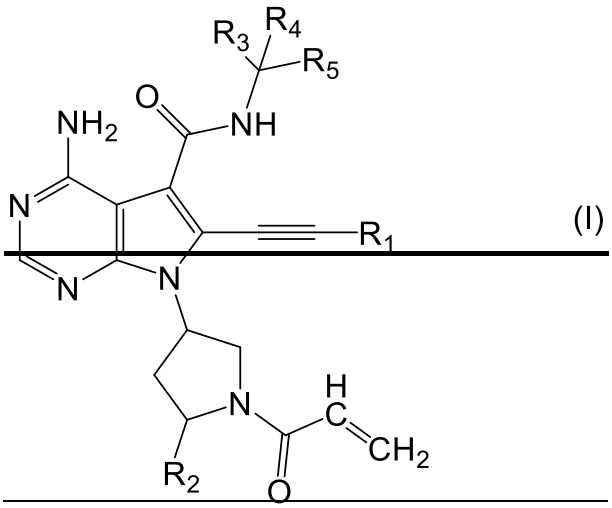
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

~~[Claim 22]~~

~~Use of a compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof for use in the treatment of EGFR-positive tumor:~~



~~wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;~~

~~R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;~~

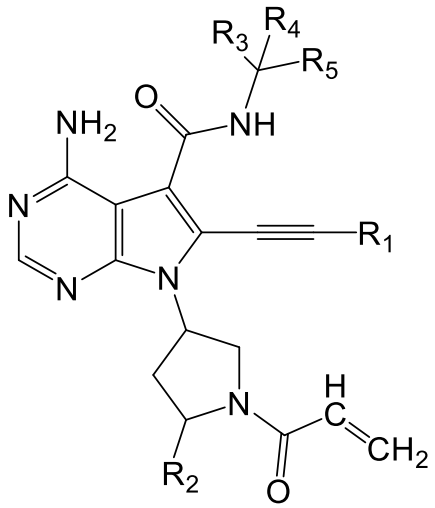
~~R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);~~

~~R_4 represents a hydrogen atom or a C1-C4 alkyl group; and~~

~~R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.~~

[Claim ~~23~~21]

Use of a compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof for the manufacture of a therapeutic agent for use in the treatment of EGFR-positive tumor:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

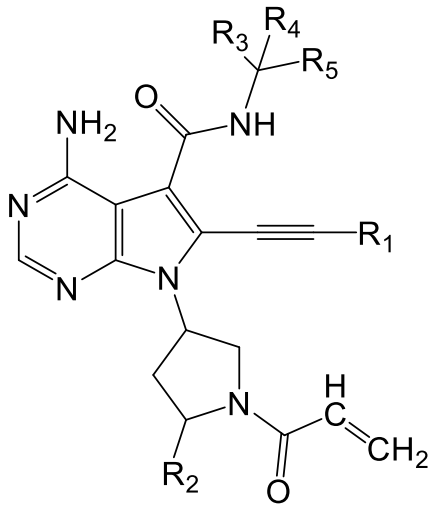
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim ~~24~~22]

~~A method for treatment of a disease associated with EGFR, the method comprising administering~~ Use of an effective amount of a compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a disease associated with EGFR, wherein the medicament is to be administered to a subject in need thereof :



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

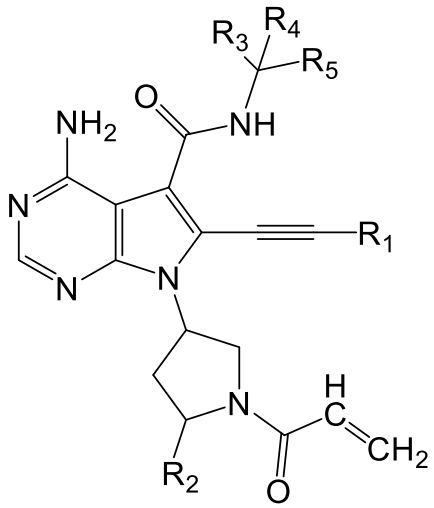
R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.

[Claim ~~25~~23]

~~A method for treatment of EGFR-positive tumor, the method comprising administering~~ Use of an effective amount of a compound represented by the following formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of EGFR-positive tumor, where in the medicament is to be administered to a subject in need thereof~~-~~:



(I)

wherein R_1 represents a C1-C4 alkyl group optionally having a C1-C4 alkoxy group as a substituent, or a C3-C4 cycloalkyl group;

R_2 represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group optionally having 1 to 5 C1-C4 alkoxy groups or fluorine atoms each as a substituent(s), or a C1-C6 alkoxy group;

R_3 represents a hydrogen atom, or a C1-C4 alkyl group optionally having 1 to 5 fluorine atoms as a substituent(s);

R_4 represents a hydrogen atom or a C1-C4 alkyl group; and

R_5 represents a phenyl group optionally having 1 to 3 substituents selected from fluorine atoms and chlorine atoms.