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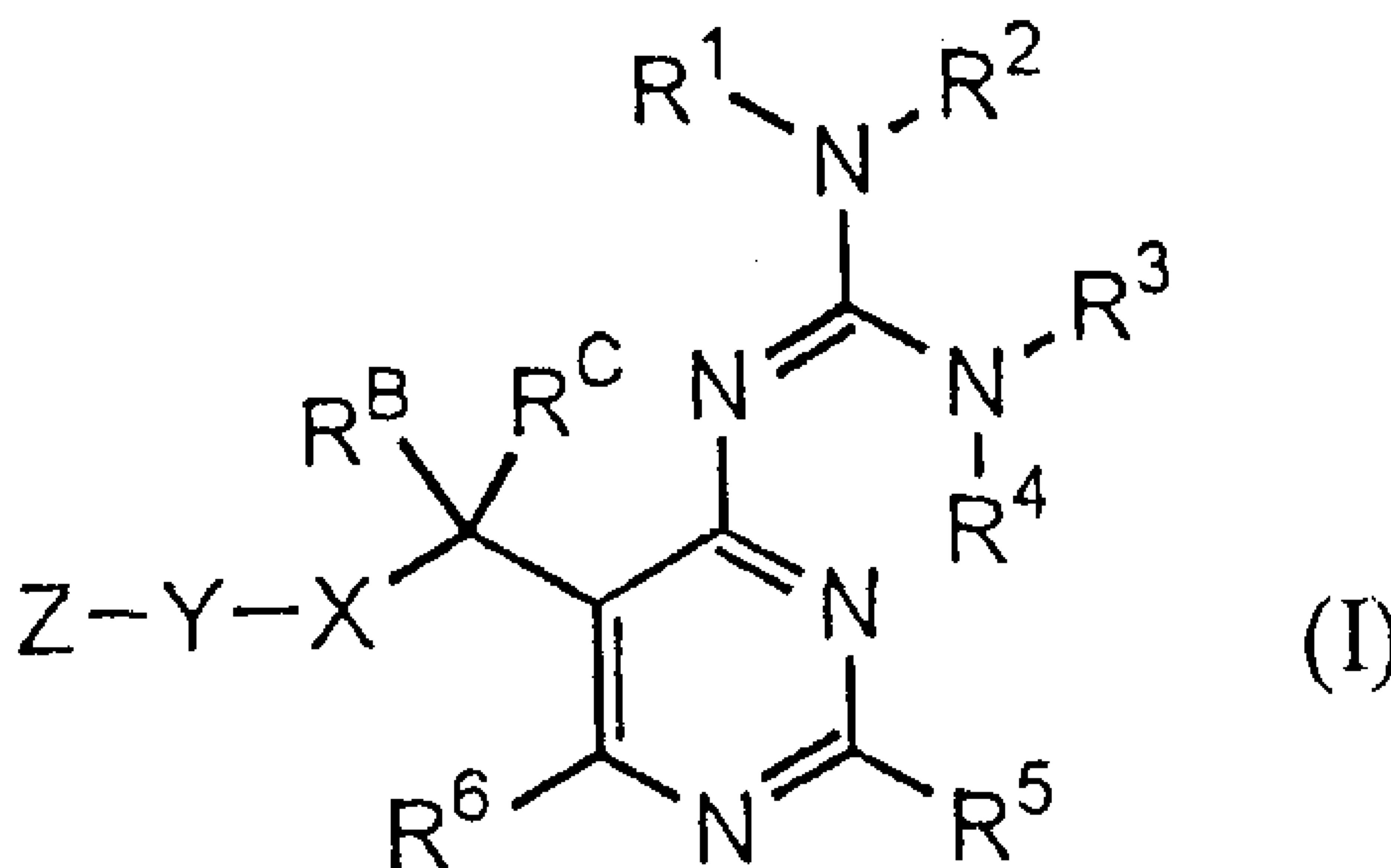
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(54) Titre : DERIVES DE LA PYRIMIDINE AYANT UNE ACTIVITE ANTI-TUMORAL
(54) Title: PYRIMIDINE DERIVATIVES HAVING ANTITUMOR ACTIVITY



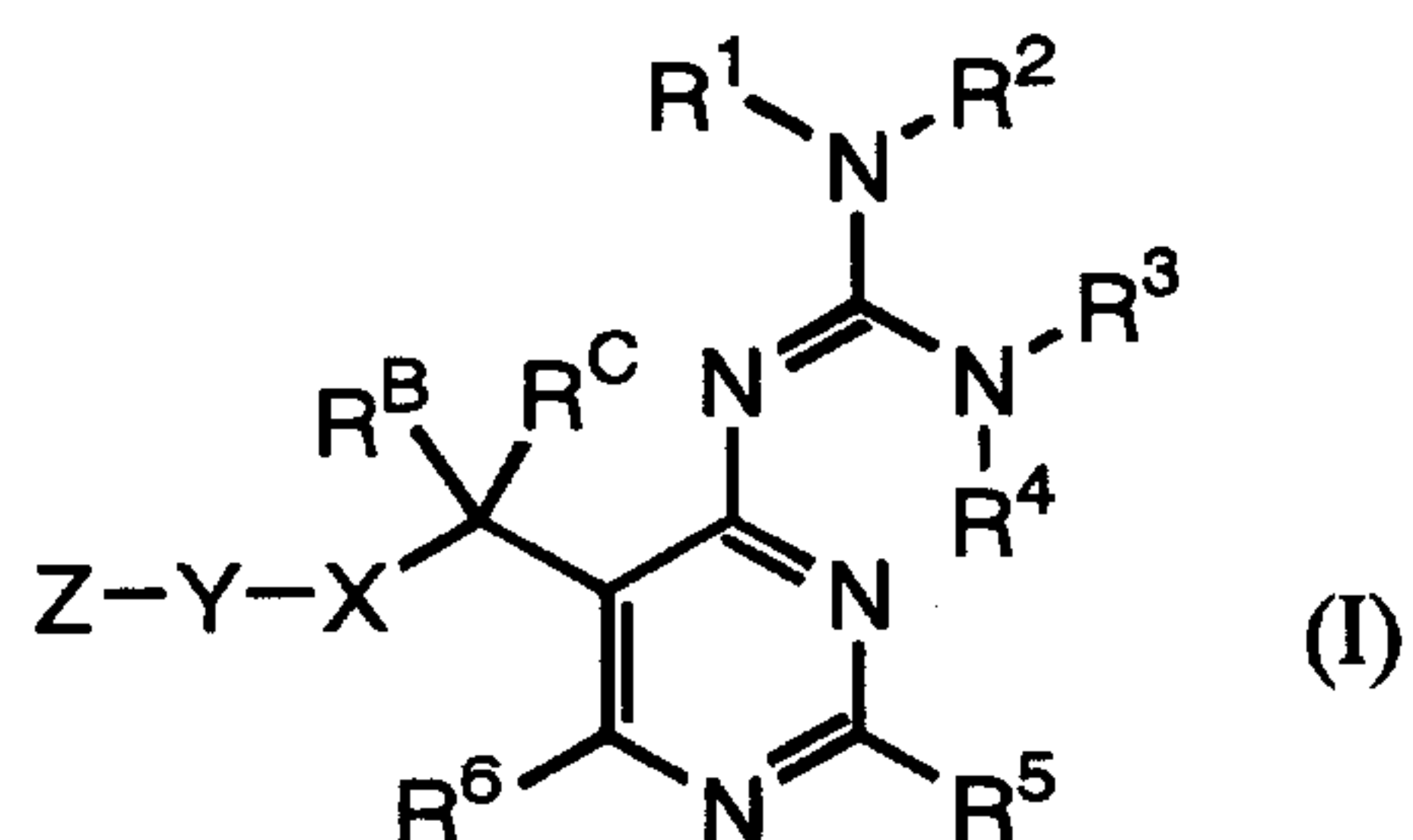
(57) Abrégé/Abstract:

Compounds represented by the general formula (I), pharmaceutically acceptable salts thereof or hydrates of the same; wherein, for example, R^1 , R^2 , R^3 and R^4 independently represent each hydrogen, alkyl, etc.; R^5 and R^6 independently represent each hydrogen, alkyl, etc.; R^B and R^C independently represent each hydrogen, alkyl, etc.; X represents -O-, -S-, etc.; Y represents 5-membered heteroaryl, etc.; and Z represents optionally substituted aryl, etc. These compounds have effects of inhibiting the cancer gene product downstream signal and inhibiting cell proliferation and, therefore, are useful as drugs such as antitumor agents.



ABSTRACT

A compound represented by the formula (I) :



5 wherein, for example, R¹, R², R³, and R⁴ are each independently hydrogen atom, alkyl, and the like, R⁵ and R⁶ are each independently hydrogen atom, alkyl, and the like, R^B and R^C are each independently hydrogen atom, alkyl, and the like, X is -O-, -S-, and the like, Y is 5- membered heteroaryl-diyl and the like, Z is optionally substituted aryl and the like, their pharmaceutically acceptable salts, or their solvates.

DESCRIPTION

PYRIMIDINE DERIVATIVES HAVING ANTITUMOR ACTIVITY

5 **Technical Field**

The present invention relates to a novel pyrimidine derivative having an antitumor activity, a cytostatic activity, and an inhibitory activity against a signal derived from Ras oncogene products.

10 **Background Art**

The oncogene "ras" such as H-ras, K-ras, and N-ras is mutated and activated in many of neoplasms. The "Ras", the products of ras oncogene, strongly concerns tumorigenesis caused by acceleration of cell cycle and induction of expression of many of genes associated with a malignant conversion such as a vascular endothelial growth factor and type-IV collagenase. Especially, it is found that there is highly frequent ras mutation in solid tumor such as pancreatic cancer (> 80%), colon cancer (> 40%), and lung cancer (> 20%) which are difficult to be cured by using existing chemotherapeutics. Therefore, it is considered that Ras is one of the most important target molecules in the development of the chemotherapeutics against them.

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A farnesyl-protein-transferase (FPT) inhibitor (FPTI) is known as chemotherapeutics of which target are Ras (WO95/13059, WO95/25086, WO95/25092, WO95/34535, US5608067, and JP-A-7-112930).

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In the cells expressing activated Ras, the excess signals reach cell nucleus through some signaling pathways and some signal transmitter molecules such as MAPK (Mitogen Activated Protein Kinase) and PI3K (Phosphatidylinositol-3-Kinase). The signals activate the transcription factors such as AP1 (Activator Protein-1) and ETS (E26 transformation specific) in the cell nucleus and then they induce the expression of many genes related to malignant features through transcription activation element such as Ras Responsive

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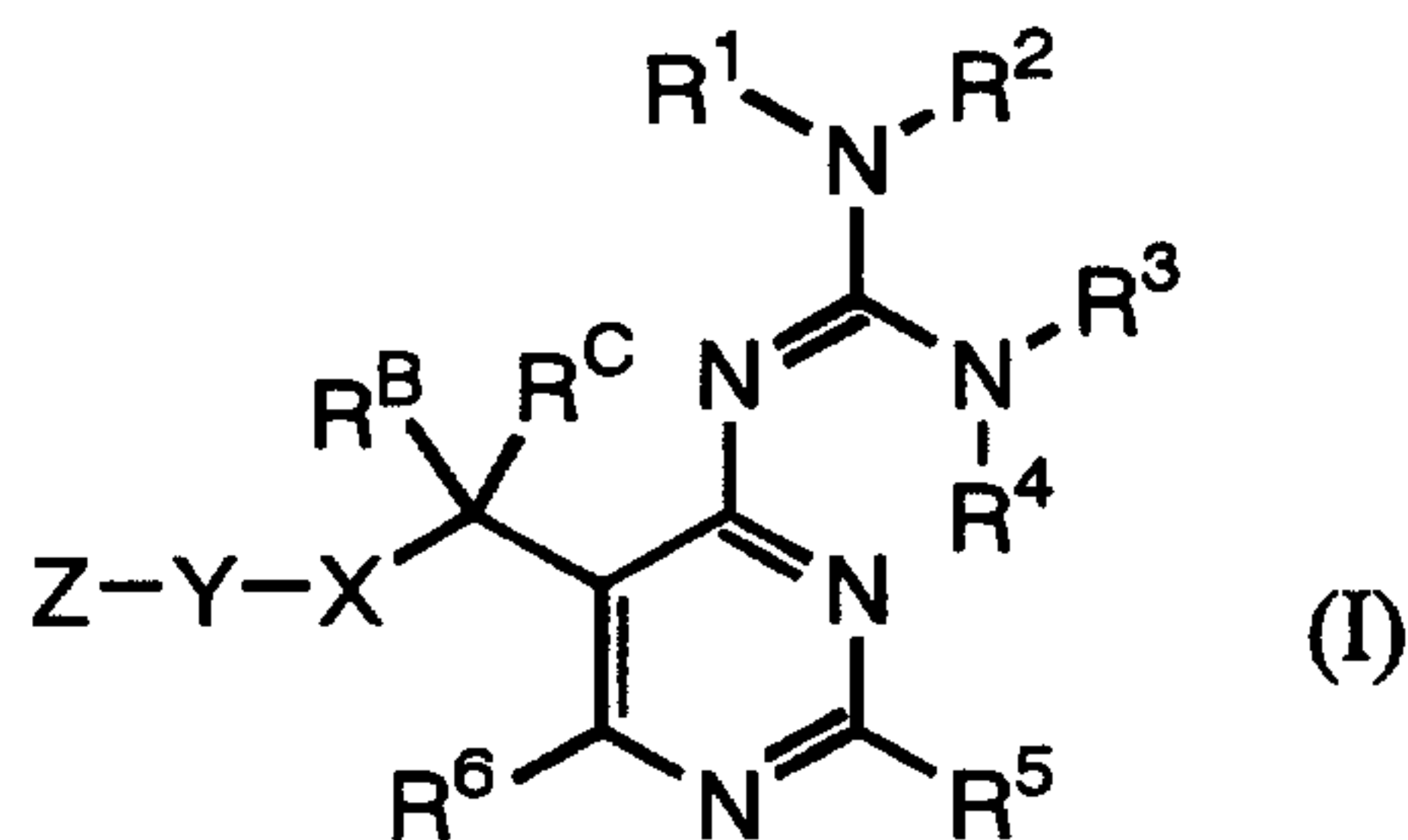
Element (RRE). Therefore, it is possible to repress the malignant conversion of the cancer cells, when the signal transmission (a signal derived from ras oncogene products) is inhibited. Inhibitors of a signal derived from Ras oncogene products, of which basic structure is similar to that of the compounds of the present invention, are described in
 5 WO00/04014.

Disclosure of Invention

In the above situation, the inventors of the present invention have studied on the antitumor agent having an inhibitory activity against a signal derived from Ras oncogene
 10 products.

The activation of gene expression through RRE is in proportion to a signal derived from Ras and the signal can be measured by the amount of its expression. The inventors of the present invention artificially made cells having activated Ras wherein
 15 expression of firefly luciferase gene, reporter gene, is regulated by RRE and carried out a screening of the inhibitors taking luciferase activity shown by the cells as an index of signals through Ras. As a result, the inventors of the present invention found that a series of pyrimidine derivatives have a strong inhibitory activity against a signal derived from Ras oncogene products.

20 The present invention relates to I) a compound represented by the formula (I):



wherein R¹, R², R³, and R⁴ are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted
 25 aryl, optionally substituted heteroaryl, optionally substituted aralkyl, an optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy,

hydroxy, cyano, or nitro; or

R^1 and R^2 , R^3 and R^4 , and R^2 and R^3 each taken together with the adjacent nitrogen atom form the same or different 3- to 7- membered ring optionally containing O, N, or S, provided that R^1 and R^2 , and R^3 and R^4 do not form a ring when R^2 and R^3 taken together
5 form a ring;

R^5 and R^6 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkyloxy, alkylthio, optionally substituted alkyloxycarbonyl, optionally substituted aryl, optionally substituted heteroaryl, halogen, hydroxy, mercapto, optionally substituted amino,
10 carboxy, cyano, or nitro;

R^B and R^C are each independently hydrogen atom, alkyl, or alkyloxy; provided that in the case of both of R^B and R^C are hydrogen atom, R^1 is hydrogen atom or alkyl, R^2 is optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; and R^3 and R^4 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl,
15 optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; or R^3 and R^4 each taken together with the adjacent nitrogen atom form the same or different 3- to 7- membered ring optionally containing O, N, or S;

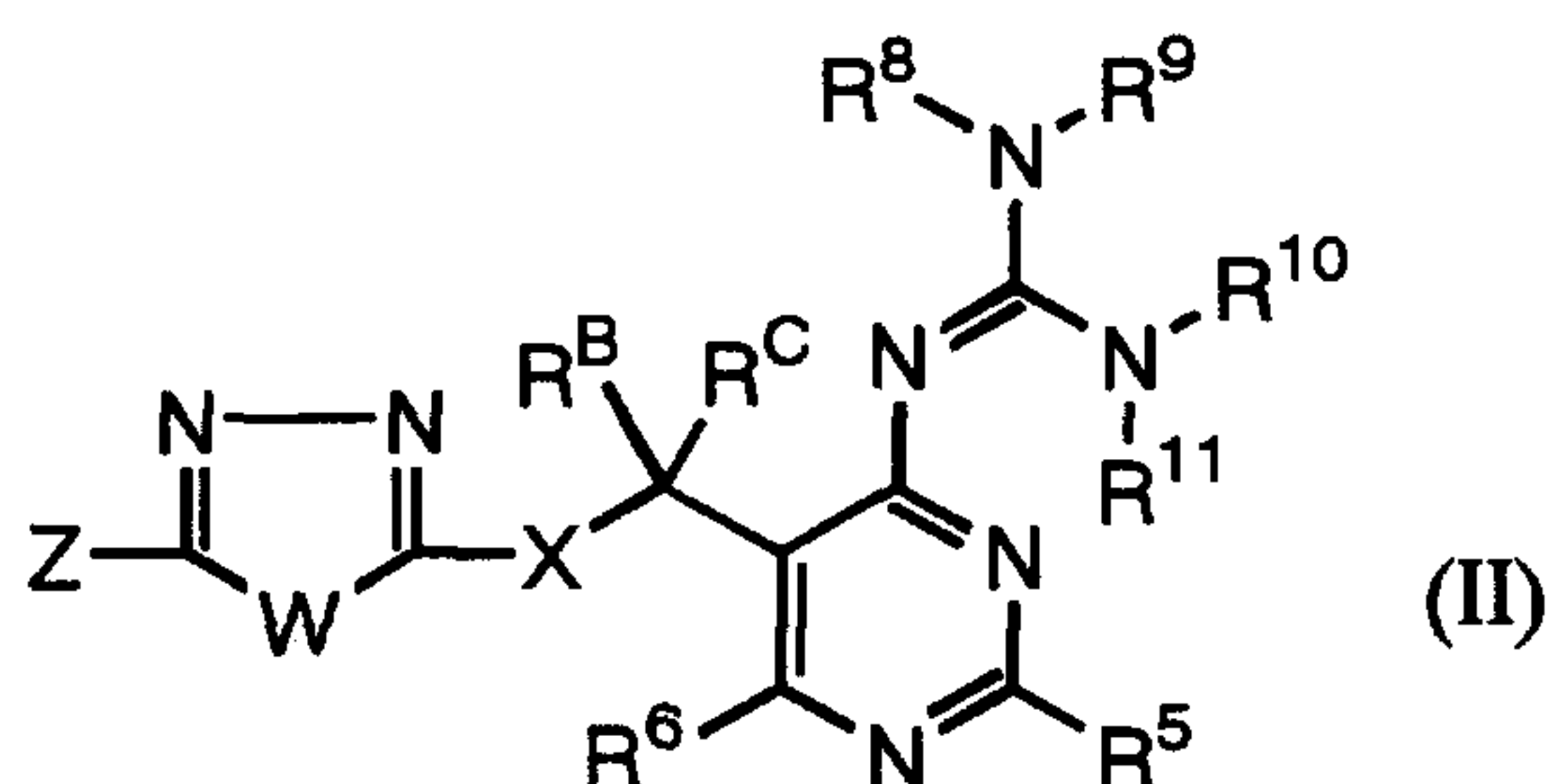
20 X is $-N(R^7)-$, $-NH-NH-$, $-O-$, or $-S-$ wherein R^7 is hydrogen atom or optionally substituted alkyl;

Y is optionally substituted 5- membered non-aromatic heterocycle-diyl or optionally substituted 5- membered heteroaryl-diyl;

Z is optionally substituted aryl or optionally substituted heteroaryl;
25 its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

In more detail, the present invention relates to II)-XVI):

30 II) a compound described in I), represented by the formula (II) :



wherein R^8 , R^9 , R^{10} , and R^{11} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, a non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

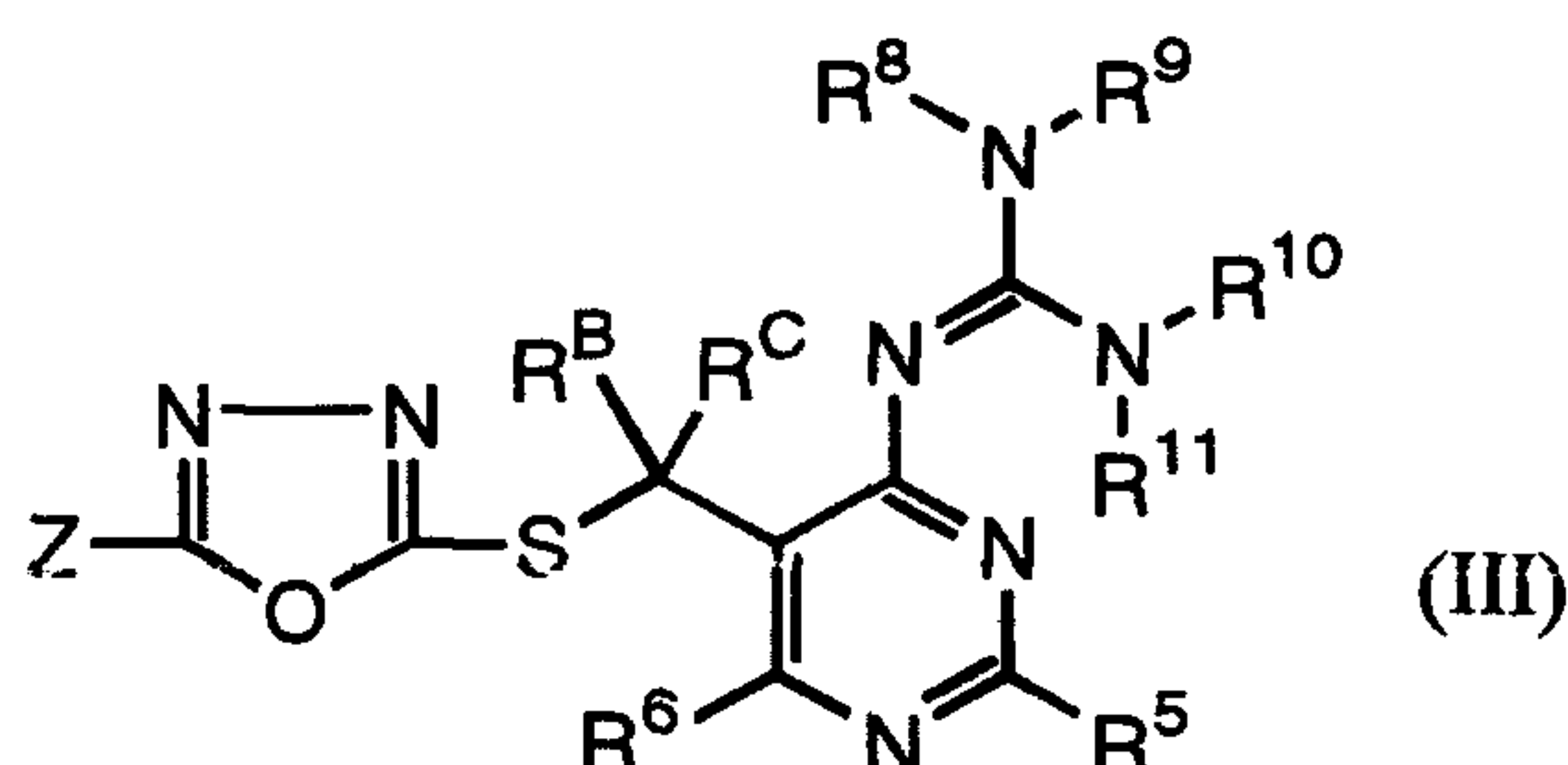
R^B and R^C are each independently hydrogen atom, alkyl, or alkyloxy; provided that in the case of both of R^B and R^C are hydrogen atom, R^8 is hydrogen atom or alkyl, R^9 is substituted amino, alkyloxy, hydroxy, cyano, or nitro; and R^{10} and R^{11} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

W is -O-, -S-, or -N(R^A)- wherein R^A is hydrogen atom or optionally substituted alkyl;

R^5 , R^6 , X, and Z are as defined above mentioned I);

its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

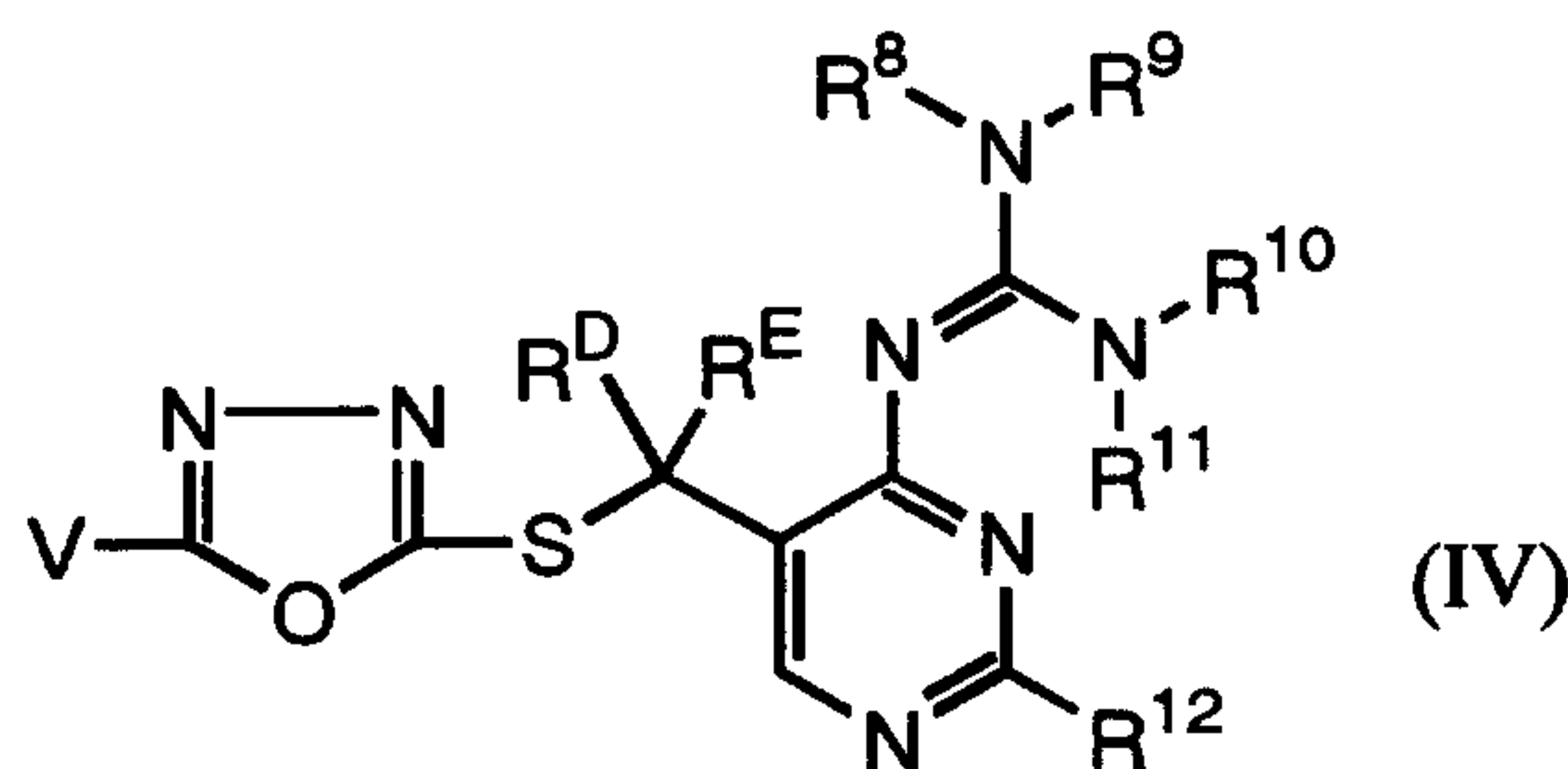
III) a compound described in I), represented by the formula (III) :



wherein R^5 , R^6 , and Z are as defined above mentioned I); R^8 , R^9 , R^{10} , R^{11} , R^B and R^C are as defined above mentioned II);

its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

IV) a compound described in I), represented by the formula (IV) :



wherein R^8 , R^9 , R^{10} and R^{11} are as defined above mentioned II);

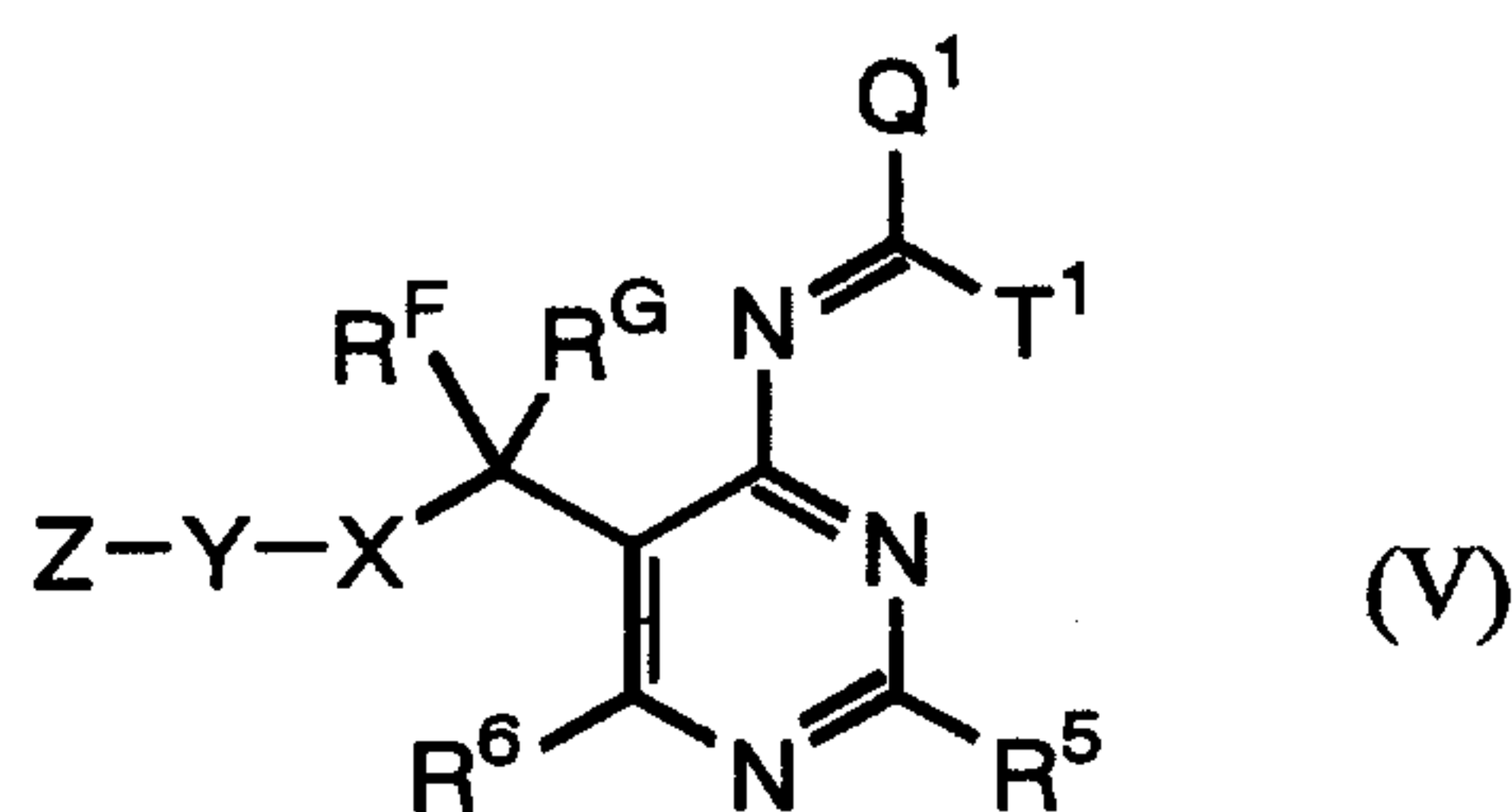
R^{12} is hydrogen atom or alkyl;

R^D and R^E are each independently hydrogen atom or alkyl; provided that in the case of both of R^D and R^E are hydrogen atom, R^8 is hydrogen atom or alkyl, R^9 is optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; and R^{10} and R^{11} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

V is optionally substituted aryl;

its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

V) a compound represented by the formula (V) :



wherein R^5 and R^6 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted

alkyloxy, alkylthio, optionally substituted alkyloxycarbonyl, optionally substituted aryl, optionally substituted heteroaryl, halogen atoms, hydroxy, mercapto, optionally substituted amino, carboxy, cyano, or nitro;

R^F and R^G are each independently hydrogen atom, alkyl, or alkyloxy;

5 X is $-N(R^7)-$, $-NH-NH-$, $-O-$, or $-S-$ wherein R^7 is hydrogen atom or optionally substituted alkyl;

Y is optionally substituted 5- membered non-aromatic heterocycle-diyl or optionally substituted 5- membered heteroaryl-diyl;

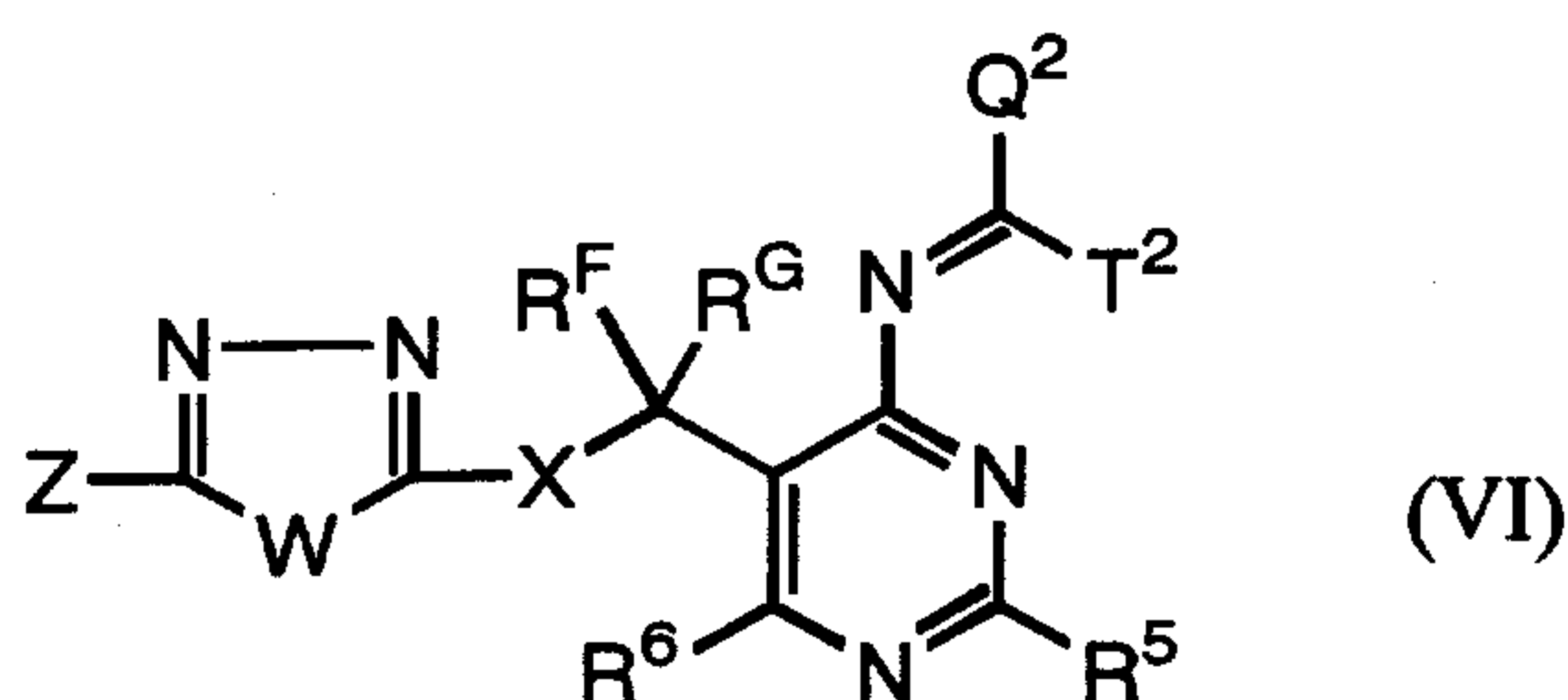
Z is optionally substituted aryl or optionally substituted heteroaryl;

10 Q^1 is $-NR^1R^2$, $-OR^1$, or $-SR^1$, T^1 is $-OR^3$ or $-SR^3$ wherein R^1 , R^2 and R^3 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; or

15 R^1 and R^3 , and R^2 and R^3 each taken together with the adjacent heteroatom form 5- to 7- membered ring;

its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

20 VI) a compound described in V), represented by the formula (VI) :



wherein Q^2 is $-NR^8R^9$, $-OR^8$, or $-SR^8$, T^2 is $-OR^{10}$ or $-SR^{10}$ wherein R^8 , R^9 and R^{10} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

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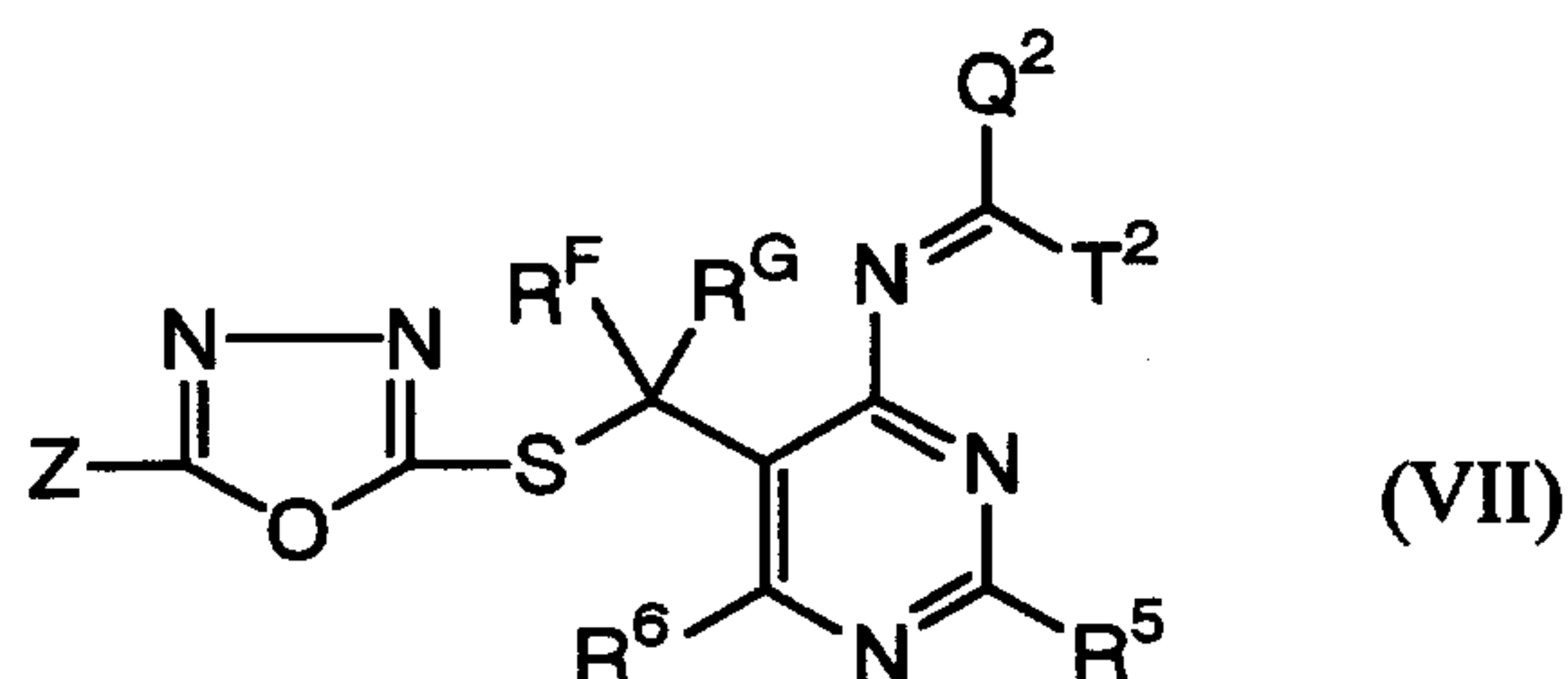
W is -O-, -S-, or -N(R^A)- wherein R^A is hydrogen atom or optionally substituted alkyl;

R⁵, R⁶, R^F, R^G, X, and Z are as defined above mentioned V);

its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

In the case of R⁸ and R¹⁰ are bonded directly with O or S, R⁸ and R¹⁰ preferably are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, non-aromatic heterocyclic group, or acyl;

VII) a compound described in V), represented by the formula (VII) :

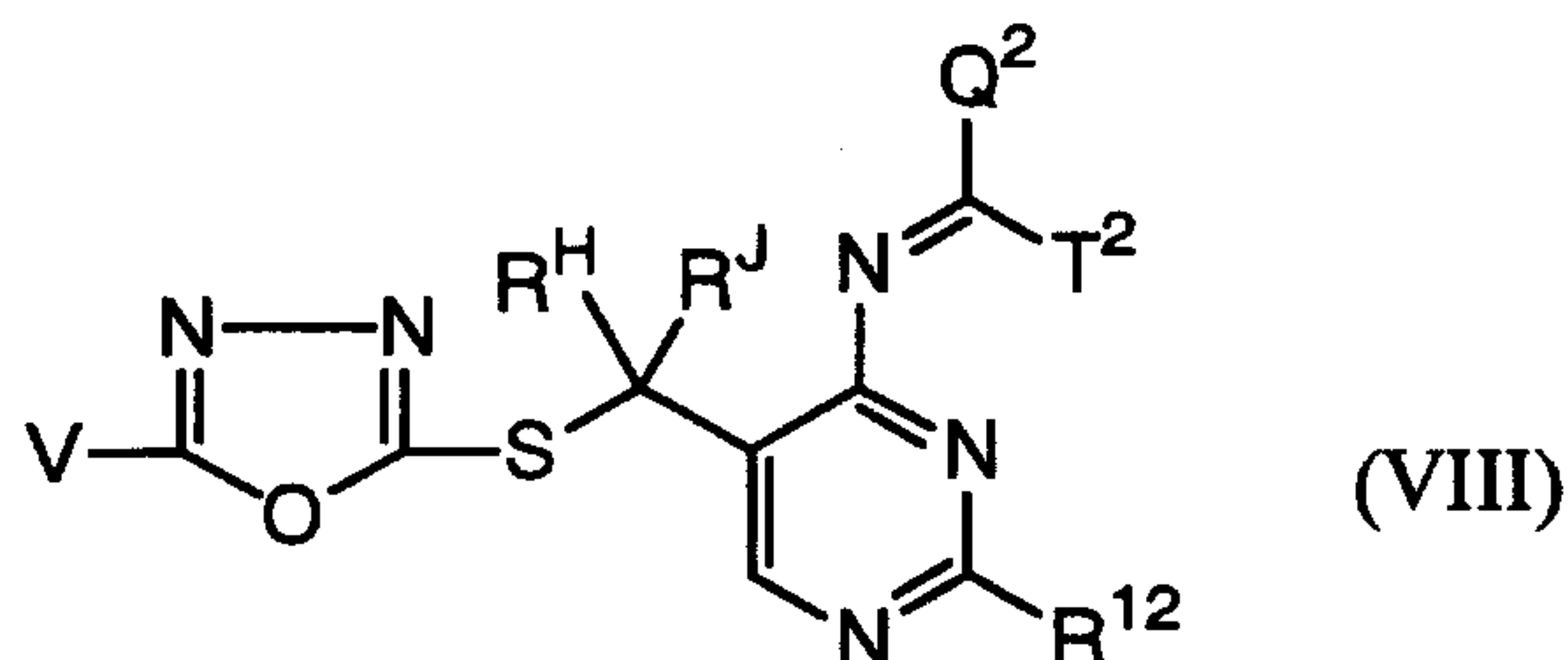


wherein R⁵, R⁶, R^F, R^G, and Z are as defined above mentioned V);

Q² and T² are as defined above mentioned VI)

its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

VIII) a compound described in V), represented by the formula (VIII) :



wherein R¹² is hydrogen or alkyl;

R^H and R^J are each independently hydrogen atom or alkyl;

V is optically substituted aryl;

the other symbols are as defined above mentioned VI);
its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

5 IX) a compound, its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate as described in any one of the above I) to V), wherein R^1 , R^2 , R^3 , and R^4 are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, or acyl,

10 X) a compound, its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate as described in any one of the above VI) to VIII), wherein R^8 , R^9 , R^{10} , and R^{11} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, or acyl,

15 XI) a pharmaceutical composition which contains as active ingredient a compound as described in any one of I) to X),

XII) a pharmaceutical composition for use as an antitumor agent which contains as active ingredient a compound as described in any one of I) to X),

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XIII) a pharmaceutical composition for use as a cytostatic agent which contains as described in any one of I) to X),

XIV) a pharmaceutical composition for use as an inhibitor against a signal derived
25 from Ras oncogene products which contains as active ingredient a compound as described in any one of I) to X),

XV) use of a compound of any one of I) to X) for the preparation of a pharmaceutical composition for treating cancer, and

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XVI) a method of treating a mammal, including a human, to alleviate a pathological effect of cancer, which comprises administration to the mammal of a compound as described in any one of I) to X).

5 The term "alkyl" employed alone or in combination with other terms in the present specification includes a straight or branched chain monovalent hydrocarbon group having 1 to 8 carbon atoms. Examples of the alkyl include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, isohexyl, n-heptyl, n-octyl and the like. Preferably, C1 to C6 alkyl is exemplified. More preferably,
10 C1 to C3 alkyl is exemplified.

 The term "alkenyl" employed alone or in combination with other terms in the present specification includes a straight or branched chain monovalent hydrocarbon group having 2 to 8 carbon atoms and one or more double bonds. An example of the alkenyl
15 includes vinyl, allyl, propenyl, crotonyl, prenyl, a variety of butenyl isomers and the like. Preferably, C2 to C6 alkenyl is exemplified. More preferably, C2 to C3 alkenyl is exemplified.

 The term "alkynyl" employed alone or in combination with other terms in the present specification includes a straight or branched chain monovalent hydrocarbon group having 2 to 8 carbon atoms and one or more triple bonds. The alkynyl may contain (a)
20 double bond(s). An example of the alkenyl includes ethynyl, propynyl, 6-heptynyl, 7-octynyl, and the like. Preferably, C2 to C6 alkynyl is exemplified. More preferably, C2 to C3 alkynyl is exemplified.

25 The term "aryl" employed alone or in combination with other terms in the present specification includes a monocyclic or condensed cyclic aromatic hydrocarbon. An example of the aryl includes phenyl, 1-naphthyl, 2-naphthyl, anthryl and the like. Preferably, phenyl, 1-naphthyl, and 2-naphthyl are exemplified. More preferably, phenyl
30 is exemplified.

The term "aralkyl" in the present specification includes a group wherein the above-mentioned "alkyl" is substituted with the above-mentioned "aryl". An example of aralkyl includes benzyl, phenethyl (e.g., 2-phenylethyl), phenylpropyl (e.g., 3-phenylpropyl),
 5 naphthylmethyl (e.g., 1-naphthylmethyl and 2-naphthylmethyl), anthrylmethyl (e.g., 9-anthrylmethyl) and the like. Preferably, benzyl and phenylethyl are exemplified.

The term "heteroaryl" employed alone or in combination with other terms in the present specification includes a 5- to 6- membered aromatic cyclic group which contains
 10 one or more hetero atoms selected from the group consisting of oxygen, sulfur, and nitrogen atoms in the ring and may be fused with the above mentioned "aryl", the later mentioned "carbocyclic group", and "non-aromatic heterocyclic group", or "heteroaryl". Heteroaryl is bonded at any possible position when the heteroaryl is a condensed ring. Examples of the heteroaryl are pyrrolyl (e.g., 1-pyrrolyl), indolyl (e.g., 3-indolyl),
 15 carbazoyl (e.g., 3-carbazoyl), imidazolyl (e.g., 4-imidazolyl), pyrazolyl (e.g., 3-pyrazolyl and 5-pyrazolyl), benzimidazolyl (e.g., 2-benzimidazolyl), indazolyl (e.g., 3-indazolyl), indoliziny (e.g., 6-indoliziny), pyridyl (e.g., 3-pyridyl and 4-pyridyl), quinolyl (e.g., 5-quinolyl), isoquinolyl (e.g., 3-isoquinolyl), acridinyl (e.g., 1-acridinyl), phenanthridinyl (e.g., 2-phenanthridinyl), pyridazinyl (e.g., 3-pyridazinyl), pyrimidinyl (e.g., 4-pyrimidinyl),
 20 pyrazinyl (e.g., 2-pyrazinyl), cinnolinyl (e.g., 3-cinnolinyl), phthalazinyl (e.g., 2-phthalazinyl), quinazolinyl (e.g., 2-quinazolinyl), isoxazolyl (e.g., 3-isoxazolyl), benzisoxazolyl (e.g., 3-benzisoxazolyl), oxazolyl (e.g., 2-oxazolyl), benzoxazolyl (e.g., 2-benzoxazolyl), benzoxadiazolyl (e.g., 4-benzoxadiazolyl), isothiazolyl (e.g., 3-isothiazolyl), benzisothiazolyl (e.g., 2-benzisothiazolyl), thiazolyl (e.g., 4-thiazolyl), benzothiazolyl (e.g.,
 25 2-benzothiazolyl), furyl (e.g., 2-furyl and 3-furyl), benzofuryl (e.g., 3-benzofuryl), thienyl (e.g., 2-thienyl and 3-thienyl), benzothienyl (e.g., 2-benzothienyl), tetrazolyl, oxadiazolyl (e.g., 1,3,4-oxadiazolyl and 1,2,4-oxadiazolyl), oxazolyl, thiadiazolyl (e.g., 1,3,4-thiadiazolyl and 1,2,4-thiadiazolyl), 4H-1,2,4-triazolyl, quinoxalinyl, 2-pyridon-3-yl, and the like. Preferably, pyridyl, pyrazinyl, furyl, thienyl and the like are exemplified.

The term "5- membered heteroaryl-diyl" herein used includes a 5- membered divalent group derived from above-mentioned "heteroaryl". Examples of the 5- membered heteroaryl-diyl are furan-2,5-diyl, thiophene-2,5-diyl, pyrrole-2,5-diyl, pyrazole-3,5-diyl, 1,3,4-oxadiazole-2,5-diyl, 1,2,4-oxadiazole-3,5-diyl, oxazole-3,5-diyl, isoxazole-3,5-diyl, 1,3,4-thiadiazole-3,5-diyl, 1,2,4-thiadiazole-3,5-diyl, 4H-1,2,4-triazole-3,5-diyl, and the like.

The term "non-aromatic heterocyclic group" employed alone or in combination with other terms in the present specification includes a 5- to 7- membered non-aromatic heterocyclic group which contains one or more hetero atoms selected from the group consisting of oxygen, sulfur, and nitrogen atoms in the ring and a cyclic group wherein two or more of the above-mentioned heterocyclic groups are fused. Examples of the heterocyclic group are pyrrolidinyl (e.g., 1-pyrrolidinyl), pyrazolidinyl (e.g., 1-pyrazolidinyl), piperidinyl (e.g., piperidino and 2-piperidinyl), piperazinyl (e.g., 1-piperazinyl), morpholinyl (e.g., morpholino and 3-morpholinyl), and the like.

The term "5- membered non-aromatic heterocycle-diyl" herein used includes a 5- membered divalent group derived from the above-mentioned "non-aromatic heterocyclic group". Examples of the 5- membered non-aromatic heterocycle-diyl are pyrrolidindiyl (e.g., pyrrolidine-2,5-diyl) and the like.

The term "carbocyclic group" herein used includes a 3- to 7- membered non-aromatic carbocyclic group. Examples of the carbocyclic group are cycloalkyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), cycloalkenyl (e.g., cyclopentenyl and cyclohexenyl), and the like.

In this specification, examples of the ring represented by "R¹ and R², and R³ and R⁴" each taken together with the adjacent nitrogen atom form the same or different 3- to 7- membered non-aromatic heterocyclic ring optionally containing O, N, or S" are aziridine, pyrrolidine, piperidine, piperazine, morpholine, imidazolidine, pyrazolidine, pyrrole,

pyrimidine, triazine, azepine, perhydroazepine, and the like.

In this specification, examples of the ring represented by "R² and R³ each taken together with the adjacent nitrogen atom form the same or different 3- to 7- membered non-aromatic heterocyclic ring optionally containing O, N, or S" are imidazolidine, hexahydropyridine, and perhydro-1,3-diazepine the like.

In this specification, examples of the ring represented by "R¹ and R³, or R² and R³ each taken together with heteroatom form 5- to 7- membered non-aromatic heterocyclic ring optionally containing O, N, or S" are thiazolidine, perhydro-1,3-thiadine, oxazolidine, perhydro-1,3-oxadine, 1,3-dithiolane, 1,3-dithiane, 1,3-oxathiolane, 1,3-oxathiane, perhydro-1,3-oxazepine, perhydro-1,3-thiazepine, and the like.

The term "acyl" employed alone or in combination with other terms in the present specification includes alkylcarbonyl of which alkyl part is the above-mentioned "alkyl" and arylcarbonyl of which aryl part is the above-mentioned "aryl". Examples of the acyl are acetyl, propanoyl, benzoyl, and the like.

The term "halogen" herein used means fluoro, chloro, bromo, and iodo.

Examples of "alkyloxy" herein used are methyloxy, ethyloxy, n-propyloxy, isopropyloxy, n-butyloxy, isobutyloxy, sec-butyloxy, tert-butyloxy, and the like. Preferably, methyloxy, ethyloxy, n-propyloxy, and isopropyloxy are exemplified.

Examples of "alkylthio" herein used are methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, isobutylthio, sec-butylthio, tert-butylthio, and the like. Preferably, methylthio, ethylthio, n-propylthio, and isopropylthio are exemplified.

Examples of "alkyloxycarbonyl" herein used are methyloxycarbonyl, ethyloxycarbonyl, n-propyloxycarbonyl, and the like.

The term "optionally substituted amino" herein used means amino substituted with one or two of the above-mentioned "alkyl", the above-mentioned "aralkyl", the above-mentioned "acyl", optionally substituted arylsulfonyl (e.g., alkyloxyphenylsulfonyl),
 5 arylalkylene (e.g., benzylidene), alkylsulfonyl, carbamoyl and the like or non-substituted amino. Examples of the optionally substituted amino are amino, methylamino, ethylamino, dimethylamino, ethylmethylamino, diethylamino, benzylamino, benzoylamino, acetylamino, propionylamino, tert-butyloxycarbonylamino, benzylidenamino, methylsulfonylamino, 4-methoxyphenylsulfonylamino, and the like. Preferably, amino, methylamino,
 10 dimethylamino, diethylamino, acetylamino are exemplified.

Substituents on the aromatic ring of "optionally substituted aralkyl" are, for example, hydroxy, alkyloxy (e.g., methyloxy and ethyloxy), mercapto, alkylthio (e.g., methylthio), cycloalkyl (e.g., cyclopropyl, cyclobutyl, and cyclopentyl), halogen (e.g.,
 15 fluoro, chloro, bromo, and iodo), carboxy, alkyloxycarbonyl (e.g., methyloxycarbonyl and ethyloxycarbonyl), nitro, cyano, haloalkyl (e.g., trifluoromethyl), aryloxy (e.g., phenyloxy), optionally substituted amino (e.g., amino, methylamino, dimethylamino, diethylamino, and benzylidenamino), alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, and neopentyl), alkenyl (e.g., vinyl and propenyl), alkynyl
 20 (e.g., ethynyl and phenylethynyl), formyl, lower alkanoyl (e.g., acetyl and propionyl), acyloxy (e.g., acetyloxy), acylamino, alkylsulfonyl (e.g., methylsulfonyl), and the like. These substituents may be substituted at one or more possible position(s).

Substituents of "optionally substituted alkyl", "optionally substituted alkyloxy",
 25 and "optionally substituted alkyloxycarbonyl" are, for example, hydroxy, alkyloxy (e.g., methyloxy and ethyloxy), mercapto, alkylthio (e.g., methylthio), cycloalkyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl), halogen (e.g., fluoro, chloro, bromo, and iodo), carboxy, alkyloxycarbonyl (e.g., methyloxycarbonyl and ethyloxycarbonyl), nitro, cyano, haloalkyl (e.g., trifluoromethyl), optionally substituted amino (e.g., amino,
 30 methylamino, dimethylamino, carbamoylamino, and tert-butyloxycarbonylamino), acyloxy

(e.g., acetyloxy), optionally substituted aralkyloxy (e.g., benzyloxy and 4-methoxybenzyloxy), and the like. These substituents may be substituted at one or more possible position(s).

5 Substituents of "optionally substituted alkenyl" and "optionally substituted alkynyl" are, for example, hydroxy, alkyloxy (e.g., methyloxy and ethyloxy), mercapto, alkylthio (e.g., methylthio), cycloalkyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl), halogen (e.g., fluoro, chloro, bromo, and iodo), carboxy, alkyloxycarbonyl (e.g., methyloxycarbonyl and ethyloxycarbonyl), nitro, cyano, haloalkyl (e.g.,
10 trifluoromethyl), optionally substituted amino (e.g., amino, methylamino, dimethylamino, carbamoylamino, and tert-butyloxycarbonylamino), acyloxy (e.g., acetyloxy), optionally substituted aralkyloxy (e.g., benzyloxy and 4-methoxybenzyloxy), optionally substituted aryl (e.g., phenyl), and the like. These substituents may be substituted at one or more possible position(s).

15 The preferable examples of "optionally substituted alkyl" are methyl, ethyl, n-propyl, isopropyl, n-butyl, trifluoromethyl, 2,2,2-trifluoroethyl, hydroxymethyl, cyclohexylmethyl, carboxyethyl, acetyloxyethyl, and benzyloxymethyl. More preferably, methyl, ethyl, n-propyl, isopropyl, n-butyl, trifluoromethyl, 2,2,2-trifluoroethyl are
20 exemplified.

 Substituents of "optionally substituted aryl", "optionally substituted heteroaryl", "optionally substituted 5- membered heteroaryl-diyl", "optionally substituted 5- membered non-aromatic heterocycle-diyl", and "an optionally substituted non-aromatic heterocyclic
25 group" are, for example, hydroxy, optionally substituted alkyloxy (e.g., methyloxy, ethyloxy, n-propyloxy, isopropyloxy, ethyloxycarbonylmethyloxy, carboxymethyloxy and 4-methoxybenzyloxy), mercapto, alkylthio (e.g., methylthio), cycloalkyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl), halogen (e.g., fluoro, chloro, bromo, and iodo), carboxy, alkyloxycarbonyl (e.g., methyloxycarbonyl, ethyloxycarbonyl, and tert-butyloxycarbonyl),
30 nitro, cyano, haloalkyl (e.g., trifluoromethyl), aryloxy (e.g., phenyloxy), optionally

substituted amino (e.g., amino, methylamino, dimethylamino, ethylamino, diethylamino, acetylmethylamino, benzylidenamino, 4-methoxyphenylsulfonylamino, methylsulfonylamino, benzoylamino, acetylamino, propionylamino, and tert-butylloxycarbonylamino), optionally substituted sulfamoyl (e.g., sulfamoyl), optionally substituted alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, t-butylloxycarbonylaminomethyl, and aminomethyl), alkenyl (e.g., vinyl, propenyl, and prenyl), optionally substituted alkynyl (e.g., ethynyl and phenylethynyl), alkenyloxy (e.g., propenyloxy and prenyloxy), formyl, acyl (e.g., acetyl, propionyl, and benzoyl), acyloxy (e.g., acetyloxy), optionally substituted carbamoyl (e.g., carbamoyl and N,N-dimethylcarbamoyl), alkylsulfonyl (e.g., methylsulfonyl), aryl (e.g., phenyl), aralkyl (e.g., benzyl), carbothioamide, optionally substituted heterocyclic group (e.g., dioxolanyl, 2-methyl-1,3-dioxolan-2-yl, pyrrolidinyl, and piperidino), optionally substituted heteroaryl (e.g., 2-pyridyl, 3-pyridyl, 4-pyridyl, pyridine N-oxide-4-yl, 1-methyl-2-pyridon-4-yl, 1-pyrrolyl, 2-pyrrolyl, and 3-pyrrolyl), and the like. These substituents may be substituted at one or more possible position(s). Preferably, optionally substituted amino, halogen, nitro, alkyl, and alkyloxy are exemplified.

Examples of "optionally substituted aryl" are phenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-acetylaminophenyl, 4-acetylaminophenyl, 2-benzoylaminophenyl, 4-benzoylaminophenyl, 2-methylsulfonylaminophenyl, 2-propionylaminophenyl, 2-methylaminophenyl, 4-methylaminophenyl, 2-dimethylaminophenyl, 4-dimethylaminophenyl, 2-ethylaminophenyl, 4-ethylaminophenyl, 4-diethylaminophenyl, 2-(4-methoxyphenylsulfonylamino)phenyl, 2-hydroxyphenyl, 4-hydroxyphenyl, 2-ethyloxycarbonylmethyloxyphenyl, 2-carboxymethyloxyphenyl, 2-chlorophenyl, 4-chlorophenyl, 4-bromophenyl, 4-iodophenyl, 4-trifluoromethylphenyl, 2-methylphenyl, 4-methylphenyl, 4-methyloxyphenyl, 4-ethyloxyphenyl, 4-n-propyloxyphenyl, 4-isopropyloxyphenyl, 4-tert-butylloxycarbonylphenyl, 4-prenyloxyphenyl, 2-nitrophenyl, 4-nitrophenyl, 4-(4-methoxybenzyloxy)phenyl, 4-methyloxycarbonylphenyl, 4-sulfamoylphenyl, 4-(N,N-dimethylcarbamoyl)phenyl, 4-carboxyphenyl, 4-biphenyl, 4-benzoylphenyl, 4-pyrrolidinophenyl, 4-piperidinophenyl, 3-aminonaphthalen-2-yl, 2-amino-

5-chlorophenyl, 2-amino-3-chlorophenyl, 2-amino-4-chlorophenyl, 2-amino-6-chlorophenyl, 4-amino-2-chlorophenyl, 2-amino-4-fluorophenyl, 2-amino-5-fluorophenyl, 2-amino-6-fluorophenyl, 4-amino-2-fluorophenyl, 2-amino-4,5-difluorophenyl, 2-amino-3-methylphenyl, 2-amino-4-methylphenyl, 2-amino-5-methylphenyl, 2-amino-6-methylphenyl, 4-amino-3-methylphenyl, 4-amino-3-methoxyphenyl, 2-amino-4-nitrophenyl, 4-amino-3-hydroxyphenyl, 2-amino-4-carboxyphenyl, 2-amino-4-methoxycarbonylphenyl, 4-amino-2-hydroxyphenyl, 4-amino-3-(4-methoxybenzyloxy)phenyl, 2,4-diaminophenyl, 3,4-diaminophenyl, 2-acetylmethylaminophenyl, 2-acetylamino-4-fluorophenyl, 2-acetylamino-4-chlorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 4-amino-2-methylphenyl, 2-fluoro-4-nitrophenyl, 4-amino-2-methoxyphenyl, 2-methoxy-4-nitrophenyl, 4-fluoro-2-nitrophenyl, 4-amino-2-trifluoromethylphenyl, 4-amino-2-ethoxyphenyl, 4-amino-2-trifluoromethoxyphenyl, 2-chloro-4-nitrophenyl, 2-methyl-4-nitrophenyl, 4-nitro-2-trifluoromethoxyphenyl, 4-nitro-2-trifluoromethylphenyl, 2-ethoxy-4-nitrophenyl, and the like.

Examples of "optionally substituted heteroaryl" are pyridin-3-yl, 2-aminopyridin-3-yl, 2-aminopyridin-5-yl, 3-aminopyrazin-2-yl, 3-aminopyrazol-4-yl, 4-amino-2-methylpyrimidin-5-yl, 2-aminothiophen-3-yl, 3-methylthiophen-2-yl, 5-methylthiophen-2-yl, furan-2-yl, furan-3-yl, 2-methylfuran-3-yl, 2,5-dimethylfuran-3-yl, 5-bromofuran-2-yl, 2-nitrofuran-4-yl, 1-methyl-4-nitropyrizol-3-yl, 1-methyl-4-nitropyrizol-5-yl, 5-nitropyrizol-3-yl, 4-nitropyrizol-3-yl, 2-(3-pyridyl)thiazol-4-yl, 2-(4-pyridyl)thiazol-4-yl, 6-(1-pyrrolyl)pyridin-3-yl, N-methyl-2-pyridon-3-yl, and the like.

Examples of "optionally substituted 5- membered heteroaryl-diyl" are furan-2,5-diyl, thiophene-2,5-diyl, pyrrole-2,5-diyl, pyrazole-3,5-diyl, 1,3,4-oxadiazole-2,5-diyl, 1,2,4-oxadiazole-3,5-diyl, oxazole-2,5-diyl, isooxazole-3,5-diyl, 1,3,4-thiadiazole-2,5-diyl, 1,2,4-thiadiazole-3,5-diyl, 4H-1,2,4-triazole-3,5-diyl, 1-methylpyrazole-3,5-diyl, and the like.

Preferable examples of R^1 to R^6 , R^B , R^C , X, Y, and Z of the compound represented

by the formula (I) are shown below as groups (a) to (t).

R^1 and R^2 are (a) one is hydrogen atom, the other is optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro.

5

R^3 and R^4 are (b) each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; (c) each independently hydrogen atom, alkyl optionally substituted with halogen atom, alkenyl, or alkynyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; and (d) one is
10 hydrogen atom and the other is alkyl optionally substituted with halogen, alkenyl, or alkynyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro.

R^5 is (e) hydrogen atom, alkyloxy, alkylthio, or optionally substituted alkyl; (f) hydrogen atom or alkyl; and (g) hydrogen atom or C1 to C2 alkyl.

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R^6 is (h) hydrogen atom or alkyl; and (i) hydrogen atom.

X is (j) -O- or -S-; and (k) -S-.

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Y is (l) 5- membered heteroaryl-diyl; (m) 1,3,4-oxadiazole-2,5-diyl, 1,2,4-oxadiazole-3,5-diyl, 1,3,4-thiadiazole-2,5-diyl, or 1,2,4-thiadiazole-3,5-diyl; and (n) 1,3,4-oxadiazole-2,5-diyl.

Z is (o) optionally substituted aryl or optionally substituted heteroaryl; (p)
25 optionally substituted phenyl or optionally substituted monocyclic heteroaryl; and (q) phenyl, pyridyl, thienyl, or furyl, which are substituted with 1 to 3 substituents selected from the group consisting of optionally substituted amino, halogen, alkyl, alkyloxy, acyl, phenyl, alkyloxycarbonyl, hydroxy, nitro, or haloalkyl.

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A preferable example of R^B and R^C is (r) (R^B , R^C) is (alkyl, hydrogen atom) or

(hydrogen atom, hydrogen atom); and (s) (R^B , R^C) is (hydrogen atom, hydrogen atom).

A preferred group of compounds represented by the formula (I) is shown below.

5 $[(R^1, R^2), (R^3, R^4), R^5, R^6, X, Y, (R^B, R^C)] = [a, b, e, h, j, l, r], [a, b, e, h, j, l, s], [a, b, e, h, j, m, r], [a, b, e, h, j, m, s], [a, b, e, h, j, n, r], [a, b, e, h, j, n, s], [a, b, e, h, k, l, r], [a, b, e, h, k, l, s], [a, b, e, h, k, m, r], [a, b, e, h, k, m, s], [a, b, e, h, k, n, r], [a, b, e, h, k, n, s], [a, b, e, i, j, l, r], [a, b, e, i, j, l, s], [a, b, e, i, j, m, r], [a, b, e, i, j, m, s], [a, b, e, i, j, n, r], [a, b, e, i, j, n, s], [a, b, e, i, k, l, r], [a, b, e, i, k, l, s], [a, b, e, i, k, m, r], [a, b, e, i, k, m, s], [a, b, e, i, k, n, r], [a, b, e, i, k, n, s], [a, b, f, h, j, l, r], [a, b, f, h, j, l, s], [a, b, f, h, j, m, r], [a, b, f, h, j, m, s], [a, b, f, h, j, n, r], [a, b, f, h, j, n, s], [a, b, f, h, k, l, r], [a, b, f, h, k, l, s], [a, b, f, h, k, m, r], [a, b, f, h, k, m, s], [a, b, f, h, k, n, r], [a, b, f, h, k, n, s], [a, b, f, i, j, l, r], [a, b, f, i, j, l, s], [a, b, f, i, j, m, r], [a, b, f, i, j, m, s], [a, b, f, i, j, n, r], [a, b, f, i, j, n, s], [a, b, f, i, k, l, r], [a, b, f, i, k, l, s], [a, b, f, i, k, m, r], [a, b, f, i, k, m, s], [a, b, f, i, k, n, r], [a, b, f, i, k, n, s], [a, b, g, h, j, l, r], [a, b, g, h, j, l, s], [a, b, g, h, j, m, r], [a, b, g, h, j, m, s], [a, b, g, h, j, n, r], [a, b, g, h, j, n, s], [a, b, g, h, k, l, r], [a, b, g, h, k, l, s], [a, b, g, h, k, m, r], [a, b, g, h, k, m, s], [a, b, g, h, k, n, r], [a, b, g, h, k, n, s], [a, b, g, i, j, l, r], [a, b, g, i, j, l, s], [a, b, g, i, j, m, r], [a, b, g, i, j, m, s], [a, b, g, i, j, n, r], [a, b, g, i, j, n, s], [a, b, g, i, k, l, r], [a, b, g, i, k, l, s], [a, b, g, i, k, m, r], [a, b, g, i, k, m, s], [a, b, g, i, k, n, r], [a, b, g, i, k, n, s], [a, c, e, h, j, l, r], [a, c, e, h, j, l, s], [a, c, e, h, j, m, r], [a, c, e, h, j, m, s], [a, c, e, h, j, n, r], [a, c, e, h, j, n, s], [a, c, e, h, k, l, r], [a, c, e, h, k, l, s], [a, c, e, h, k, m, r], [a, c, e, h, k, m, s], [a, c, e, h, k, n, r], [a, c, e, h, k, n, s], [a, c, e, i, j, l, r], [a, c, e, i, j, l, s], [a, c, e, i, j, m, r], [a, c, e, i, j, m, s], [a, c, e, i, j, n, r], [a, c, e, i, j, n, s], [a, c, e, i, k, l, r], [a, c, e, i, k, l, s], [a, c, e, i, k, m, r], [a, c, e, i, k, m, s], [a, c, e, i, k, n, r], [a, c, e, i, k, n, s], [a, c, f, h, j, l, r], [a, c, f, h, j, l, s], [a, c, f, h, j, m, r], [a, c, f, h, j, m, s], [a, c, f, h, j, n, r], [a, c, f, h, j, n, s], [a, c, f, h, k, l, r], [a, c, f, h, k, l, s], [a, c, f, h, k, m, r], [a, c, f, h, k, m, s], [a, c, f, h, k, n, r], [a, c, f, h, k, n, s], [a, c, f, i, j, l, r], [a, c, f, i, j, l, s], [a, c, f, i, j, m, r], [a, c, f, i, j, m, s], [a, c, f, i, j, n, r], [a, c, f, i, j, n, s], [a, c, f, i, k, l, r], [a, c, f, i, k, l, s], [a, c, f, i, k, m, r], [a, c, f, i, k, m, s], [a, c, f, i, k, n, r], [a, c, f, i, k, n, s], [a, c, g, h, j, l, r], [a, c, g, h, j, l, s], [a, c, g, h, j, m, r], [a, c, g, h, j, m, s], [a, c, g, h, j, n, r], [a, c, g, h, j, n, s], [a, c, g, h, k, l, r], [a, c, g, h, k, l, s], [a, c, g, h, k, m, r], [a, c, g, h,$

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k, m, s], [a, c, g, h, k, n, r], [a, c, g, h, k, n, s], [a, c, g, i, j, l, r], [a, c, g, i, j, l, s], [a, c, g, i, j, m, r], [a, c, g, i, j, m, s], [a, c, g, i, j, n, r], [a, c, g, i, j, n, s], [a, c, g, i, k, l, r], [a, c, g, i, k, l, s], [a, c, g, i, k, m, r], [a, c, g, i, k, m, s], [a, c, g, i, k, n, r], [a, c, g, i, k, n, s], [a, d, e, h, j, l, r], [a, d, e, h, j, l, s], [a, d, e, h, j, m, r], [a, d, e, h, j, m, s], [a, d, e, h, j, n, r], [a, d, e, h, j, n, s], [a, d, e, h, k, l, r], [a, d, e, h, k, l, s], [a, d, e, h, k, m, r], [a, d, e, h, k, m, s], [a, d, e, h, k, n, r], [a, d, e, h, k, n, s], [a, d, e, i, j, l, r], [a, d, e, i, j, l, s], [a, d, e, i, j, m, r], [a, d, e, i, j, m, s], [a, d, e, i, j, n, r], [a, d, e, i, j, n, s], [a, d, e, i, k, l, r], [a, d, e, i, k, l, s], [a, d, e, i, k, m, r], [a, d, e, i, k, m, s], [a, d, e, i, k, n, r], [a, d, e, i, k, n, s], [a, d, f, h, j, l, r], [a, d, f, h, j, l, s], [a, d, f, h, j, m, r], [a, d, f, h, j, m, s], [a, d, f, h, j, n, r], [a, d, f, h, j, n, s], [a, d, f, h, k, l, r], [a, d, f, h, k, l, s], [a, d, f, h, k, m, r], [a, d, f, h, k, m, s], [a, d, f, h, k, n, r], [a, d, f, h, k, n, s], [a, d, f, i, j, l, r], [a, d, f, i, j, l, s], [a, d, f, i, j, m, r], [a, d, f, i, j, m, s], [a, d, f, i, j, n, r], [a, d, f, i, j, n, s], [a, d, f, i, k, l, r], [a, d, f, i, k, l, s], [a, d, f, i, k, m, r], [a, d, f, i, k, m, s], [a, d, f, i, k, n, r], [a, d, f, i, k, n, s], [a, d, g, h, j, l, r], [a, d, g, h, j, l, s], [a, d, g, h, j, m, r], [a, d, g, h, j, m, s], [a, d, g, h, j, n, r], [a, d, g, h, j, n, s], [a, d, g, h, k, l, r], [a, d, g, h, k, l, s], [a, d, g, h, k, m, r], [a, d, g, h, k, m, s], [a, d, g, h, k, n, r], [a, d, g, h, k, n, s], [a, d, g, i, j, l, r], [a, d, g, i, j, l, s], [a, d, g, i, j, m, r], [a, d, g, i, j, m, s], [a, d, g, i, j, n, r], [a, d, g, i, j, n, s], [a, d, g, i, k, l, r], [a, d, g, i, k, l, s], [a, d, g, i, k, m, r], [a, d, g, i, k, m, s], [a, d, g, i, k, n, r], [a, d, g, i, k, n, s]

Preferred embodiments of this invention are compounds wherein Z is any one of (o) to (q) and $[(R^1, R^2), (R^3, R^4), R^5, R^6, X, Y, (R^B, R^C)]$ is any one of the above combinations.

Preferable examples of $R^5, R^6, R^F, R^G, Q^1, T^1, X, Y$, and Z of the compound represented by the formula (V) are shown below as groups (a) to (r).

R^5 is (a) hydrogen atom, alkyloxy, alkylthio, or optionally substituted alkyl; (b) hydrogen atom or alkyl; and (c) hydrogen atom or C1 to C2 alkyl.

R^3 is (d) hydrogen atom or alkyl; and (e) hydrogen atom.

A preferable example of R^F and R^G is (f) (R^B , R^C) is (hydrogen atom, hydrogen atom), (hydrogen atom, alkyl), (alkyl, alkyl), or (hydrogen atom, alkyloxy); and (g) is (hydrogen atom, hydrogen atom), (hydrogen atom, alkyl), or (alkyl, alkyl).

5 Q^1 and T^1 are (h) Q^1 is $-NR^1R^2$ or $-SR^1$ wherein R^1 and R^2 are each independently hydrogen atom, optionally substituted alkyl, alkenyl, or alkynyl, T^1 is $-SR^3$ wherein R^3 is hydrogen atom, optionally substituted alkyl, alkenyl, or alkynyl; (i) Q^1 is $-NR^1R^2$ or $-SR^1$ wherein R^1 and R^2 are each independently hydrogen atom, alkyl optionally substituted with halogen, alkenyl, or alkynyl, T^1 is $-SR^3$ wherein R^3 is hydrogen atom, alkyl optionally substituted with halogen, alkenyl, or alkynyl; (j) Q^1 is $-NR^1R^2$ or $-SR^1$ wherein R^1 and R^2 are one is hydrogen atom and the other is C1 to C3 alkyl optionally substituted with halogen, T^1 is $-SR^3$ wherein R^3 is hydrogen atom or alkyl optionally substituted with halogen.

15 X is (k) -O- or -S-; and (l) -S-.

Y is (m) 5- membered heteroaryl-diyl; (n) 1,3,4-oxadiazole-2,5-diyl, 1,2,4-oxadiazole-3,5-diyl, 1,3,4-thiadiazole-2,5-diyl, or 1,2,4-thiadiazole-3,5-diyl; and (o) 1,3,4-oxadiazole-2,5-diyl.

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Z is (p) optionally substituted aryl or optionally substituted heteroaryl; (q) optionally substituted phenyl or optionally substituted monocyclic heteroaryl; and (r) phenyl, pyridyl, thienyl, or furyl, which are substituted with 1 to 3 substituents selected from the group consisting of optionally substituted amino, halogen, alkyl, alkyloxy, acyl, phenyl, alkyloxycarbonyl, hydroxy, nitro, or haloalkyl.

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A preferred group of compounds represented by the formula (V) is shown below.

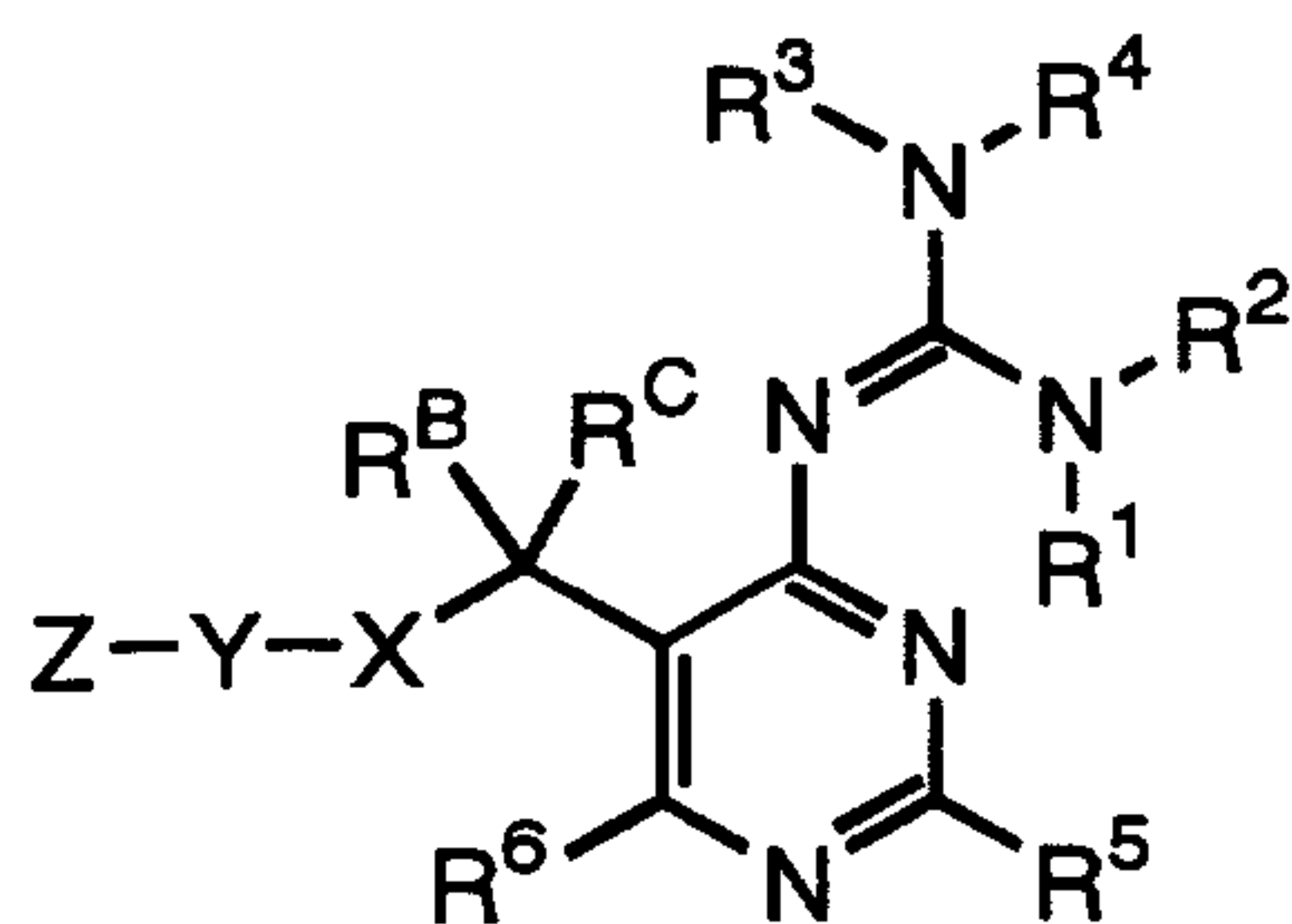
30 $[R^5, R^6, (R^F, R^G), (Q^1, T^1), X, Y] = [a, d, f, h, k, m], [a, d, f, h, k, n], [a, d, f, h, k, o], [a, d, f, h, l, m], [a, d, f, h, l, n], [a, d, f, h, l, o], [a, d, f, i, k, m], [a, d, f, i, k, n], [a, d, f, i, k,$

o], [a, d, f, i, l, m], [a, d, f, i, l, n], [a, d, f, i, l, o], [a, d, f, j, k, m], [a, d, f, j, k, n], [a, d, f, j,
 k, o], [a, d, f, j, l, m], [a, d, f, j, l, n], [a, d, f, j, l, o], [a, d, g, h, k, m], [a, d, g, h, k, n], [a, d,
 g, h, k, o], [a, d, g, h, l, m], [a, d, g, h, l, n], [a, d, g, h, l, o], [a, d, g, i, k, m], [a, d, g, i, k, n],
 [a, d, g, i, k, o], [a, d, g, i, l, m], [a, d, g, i, l, n], [a, d, g, i, l, o], [a, d, g, j, k, m], [a, d, g, j, k,
 5 n], [a, d, g, j, k, o], [a, d, g, j, l, m], [a, d, g, j, l, n], [a, d, g, j, l, o], [a, e, f, h, k, m], [a, e, f,
 h, k, n], [a, e, f, h, k, o], [a, e, f, h, l, m], [a, e, f, h, l, n], [a, e, f, h, l, o], [a, e, f, i, k, m], [a,
 e, f, i, k, n], [a, e, f, i, k, o], [a, e, f, i, l, m], [a, e, f, i, l, n], [a, e, f, i, l, o], [a, e, f, j, k, m], [a,
 e, f, j, k, n], [a, e, f, j, k, o], [a, e, f, j, l, m], [a, e, f, j, l, n], [a, e, f, j, l, o], [a, e, g, h, k, m],
 [a, e, g, h, k, n], [a, e, g, h, k, o], [a, e, g, h, l, m], [a, e, g, h, l, n], [a, e, g, h, l, o], [a, e, g, i,
 10 k, m], [a, e, g, i, k, n], [a, e, g, i, k, o], [a, e, g, i, l, m], [a, e, g, i, l, n], [a, e, g, i, l, o], [a, e,
 g, j, k, m], [a, e, g, j, k, n], [a, e, g, j, k, o], [a, e, g, j, l, m], [a, e, g, j, l, n], [a, e, g, j, l, o], [b,
 d, f, h, k, m], [b, d, f, h, k, n], [b, d, f, h, k, o], [b, d, f, h, l, m], [b, d, f, h, l, n], [b, d, f, h, l,
 o], [b, d, f, i, k, m], [b, d, f, i, k, n], [b, d, f, i, k, o], [b, d, f, i, l, m], [b, d, f, i, l, n], [b, d, f, i,
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 15 j, l, o], [b, d, g, h, k, m], [b, d, g, h, k, n], [b, d, g, h, k, o], [b, d, g, h, l, m], [b, d, g, h, l, n],
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 25 h, k, o], [c, d, f, h, l, m], [c, d, f, h, l, n], [c, d, f, h, l, o], [c, d, f, i, k, m], [c, d, f, i, k, n], [c,
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 30 [c, d, g, j, k, n], [c, d, g, j, k, o], [c, d, g, j, l, m], [c, d, g, j, l, n], [c, d, g, j, l, o], [c, e, f, h, k,

m], [c, e, f, h, k, n], [c, e, f, h, k, o], [c, e, f, h, l, m], [c, e, f, h, l, n], [c, e, f, h, l, o], [c, e, f, i, k, m], [c, e, f, i, k, n], [c, e, f, i, k, o], [c, e, f, i, l, m], [c, e, f, i, l, n], [c, e, f, i, l, o], [c, e, f, j, k, m], [c, e, f, j, k, n], [c, e, f, j, k, o], [c, e, f, j, l, m], [c, e, f, j, l, n], [c, e, f, j, l, o], [c, e, g, h, k, m], [c, e, g, h, k, n], [c, e, g, h, k, o], [c, e, g, h, l, m], [c, e, g, h, l, n], [c, e, g, h, l, o],
 5 [c, e, g, i, k, m], [c, e, g, i, k, n], [c, e, g, i, k, o], [c, e, g, i, l, m], [c, e, g, i, l, n], [c, e, g, i, l, o], [c, e, g, j, k, m], [c, e, g, j, k, n], [c, e, g, j, k, o], [c, e, g, j, l, m], [c, e, g, j, l, n], [c, e, g, j, l, o]

Preferred embodiments of this invention are compounds wherein Z is any one of
 10 (p) to (r) and $[R^5, R^6, (R^F, R^G), (Q^1, T^1), X, Y]$ is any one of the above combinations.

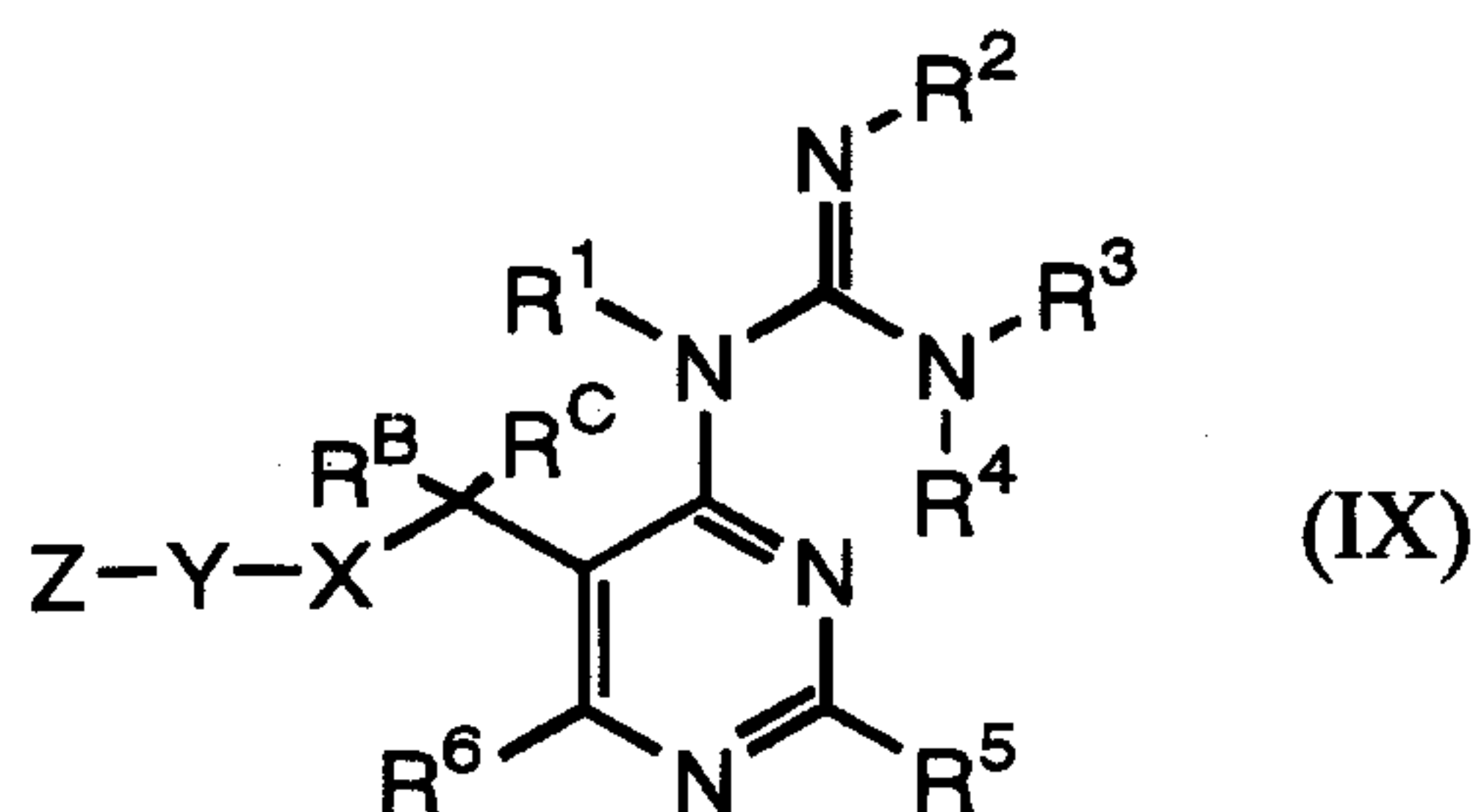
In this specification, the compounds represented by the formula (I) may be represented by the below formula.



15

The compounds represented by the formula (II), (III), and (IV) are as well as the above.

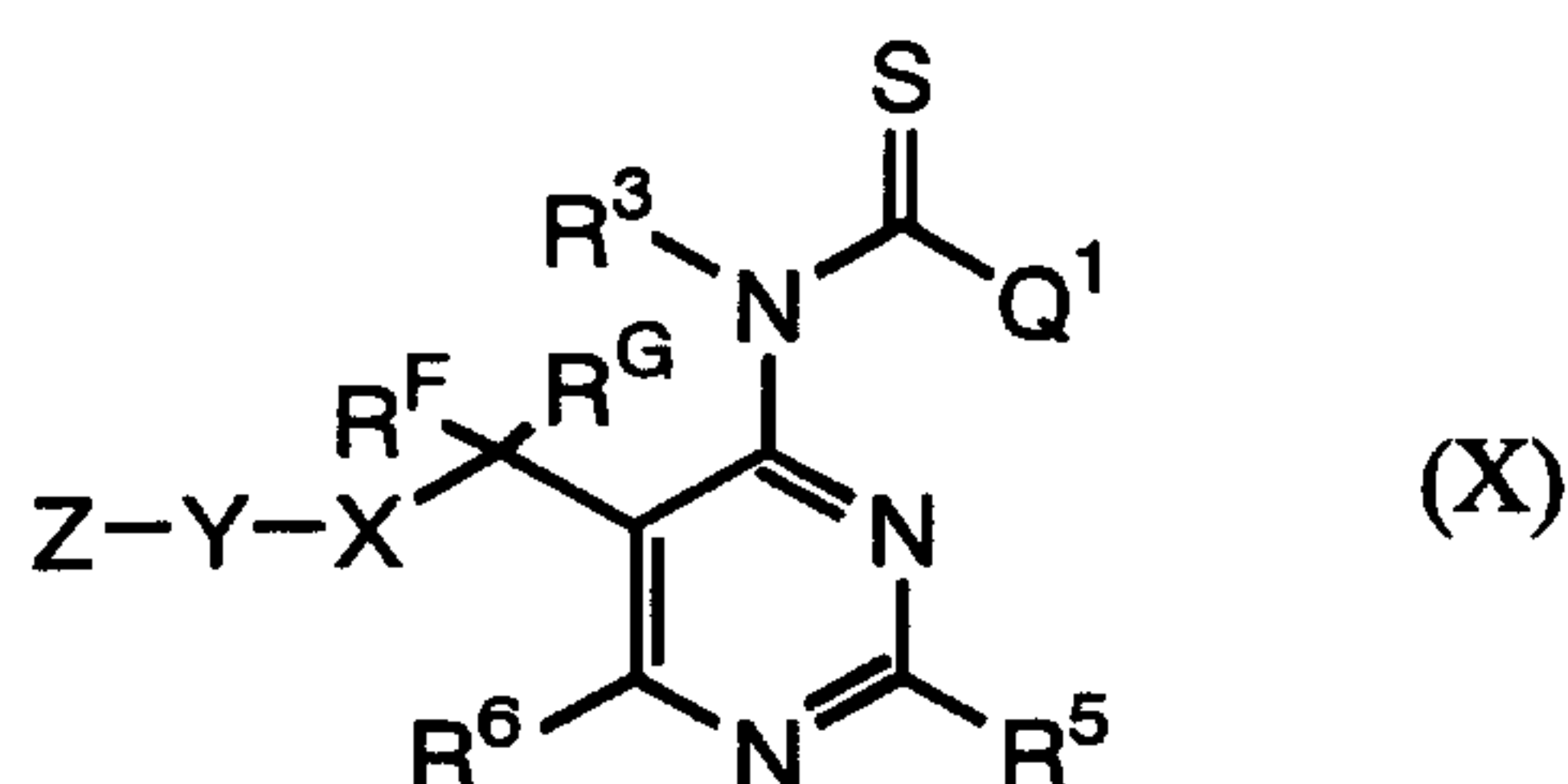
In this specification, a compound of formula (I) wherein R^1 is hydrogen atom may
 20 be represented as an isomer of the formula (IX).



wherein $R^2, R^3, R^4, R^5, R^6, R^B, R^C, X, Y$, and Z are as defined above; R^1 is hydrogen atom.

The compounds represented by the formula (II), (III), and (IV) are as well as the above.

5 In this specification, a compound of formula (V) wherein T^1 is $-SR^3$ wherein R^3 is hydrogen atom may be represented as an isomer of the formula (X). The compounds wherein T^1 is $-OR^3$ wherein R^3 is hydrogen atom are as well as the above.

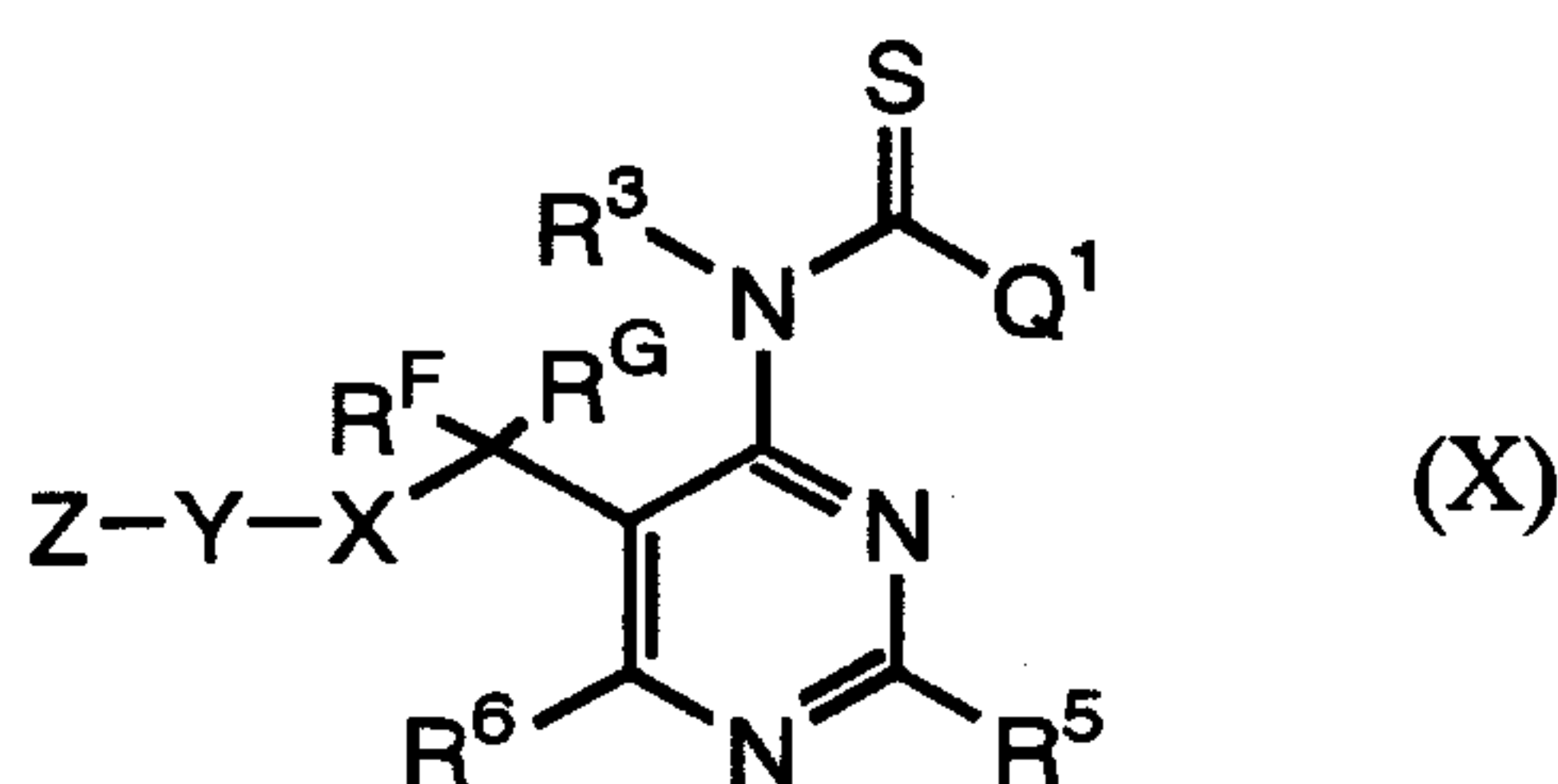


wherein R^5 , R^6 , R^F , R^G , Q^1 , X , Y , and Z are as defined above; R^3 is hydrogen atom.

10

The compounds represented by the formulae (VI), (VII), and (VIII) are as well as the above.

15 In this specification, according to alkylation conditions for synthesis of the compounds (V) wherein T^1 is $-SR^3$ wherein R^3 is alkyl, the compounds represented by the formula (X) may be obtained. The compounds wherein T^1 is $-OR^3$ wherein R^3 is alkyl are as well as the above.



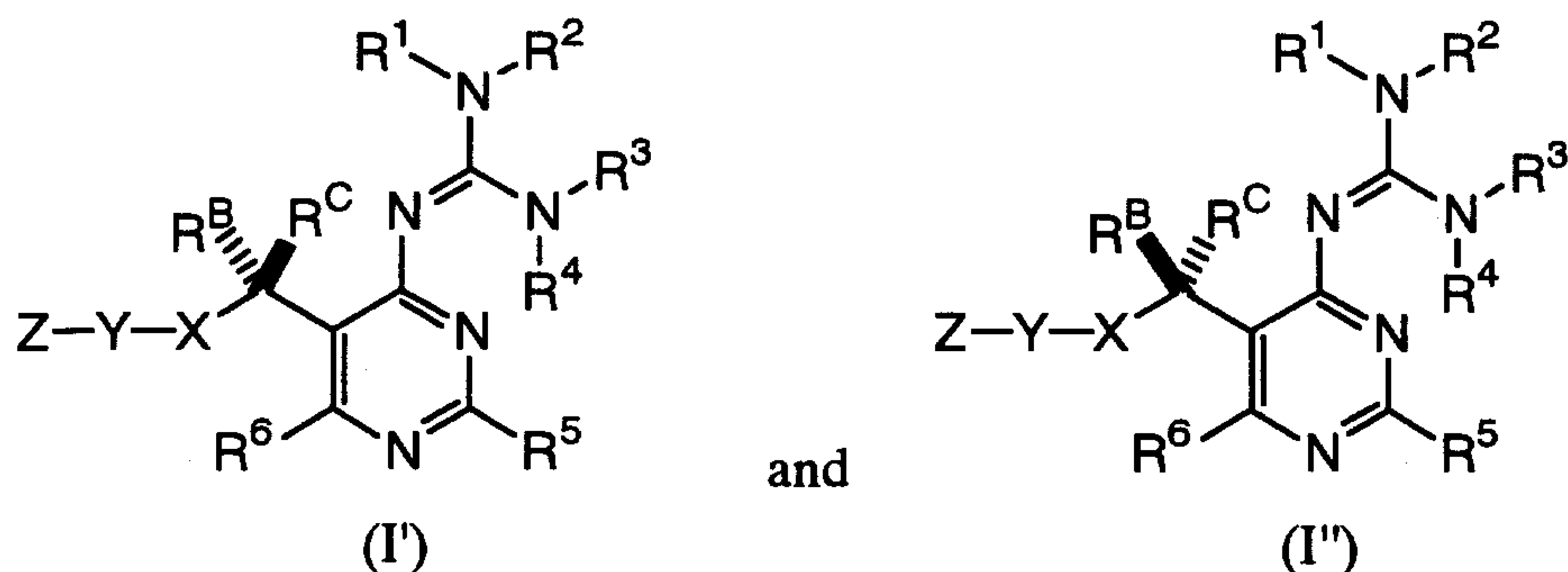
wherein R^5 , R^6 , R^F , R^G , Q^1 , X , Y , and Z are as defined above; R^3 is alkyl.

20

The compounds represented by the formulae (VI), (VII), and (VIII) are as well as the above.

In this specification, the compounds of formula (I) wherein R^B and R^C are different,

are represented as an optical active compound by the formulae (I') and (I'').



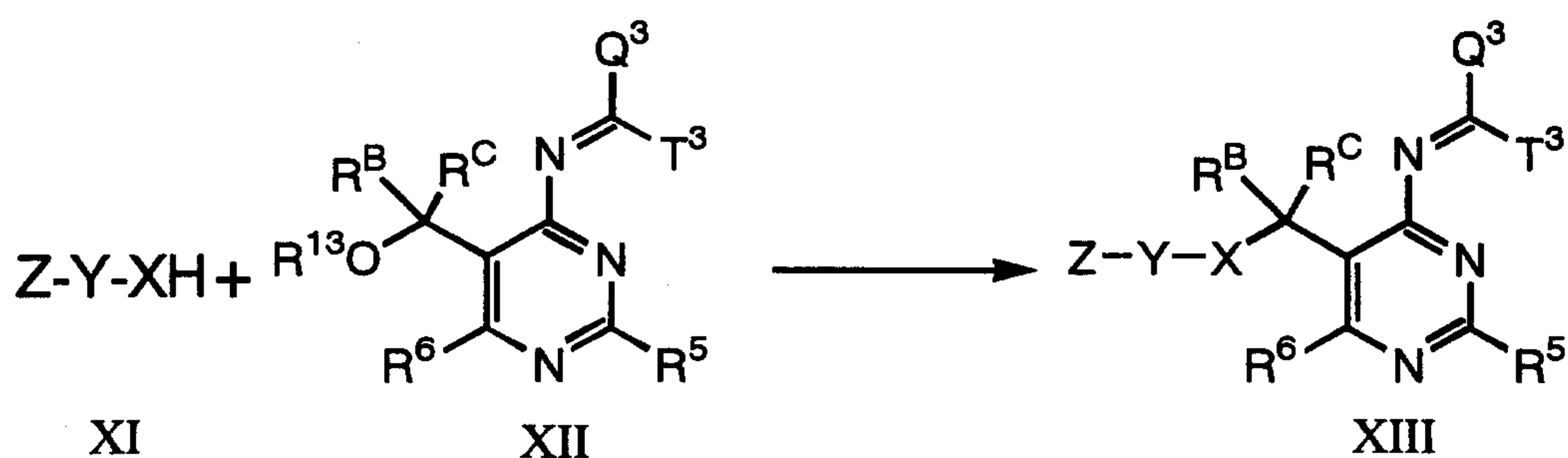
wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^B , R^C , X , Y , and Z are as defined above.

5 The compounds represented by the formulae (II), (III), (IV), (V), (VI), (VII), and (VIII) are as well as the above.

Best Mode for Carrying Out the Invention

10 The compounds of the present invention represented by the formulae (I), (V), or (XIII) can be synthesized by the well-known methods described in a literature of chemistry. A summary of the useful methods for synthesis of the compounds of the present invention is shown below.

(Synthetic method)



15 wherein R^5 , R^6 , R^B , R^C , X , Y , and Z are as defined above; R^{13} is a protective group of a hydroxy group such as methyl, ethyl, trimethylsilyl, and tert-butyldimethylsilyl or hydrogen atom; Q^3 is $-NR^1R^2$, $-OR^1$, or $-SR^1$; T^3 is $-NR^3R^4$, $-OR^1$, or $-SR^1$ wherein R^1 , R^2 , R^3 , and R^4 are as defined above.

20 The compound represented by the formula (XIII) can be synthesized by reacting $Z-Y-XH$ (XI) with the pyrimidine derivatives (XII) mentioned later such as (XII-1) to

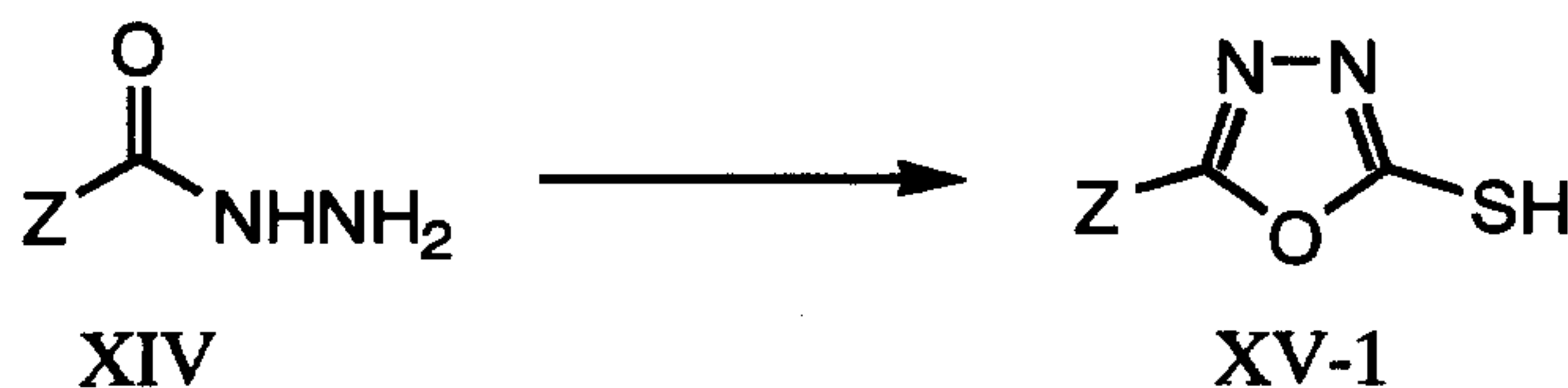
(XII-4). The pyrimidine derivatives (XII) in a solvent such as water, acetic acid, and pyridine are treated with a hydrohalogenic acid such as hydrochloric acid and hydrobromic acid to give hydrogen halide salts of 5-halogenomethylpyrimidine. When R¹³ is hydrogen atom, a halogenation agent such as thionyl halide and phosphorous halide can be used.

5 The obtained salts and Z-Y-XH (XI) in a solvent such as water, methanol, ethanol, N,N-dimethylformamide, dimethylsulfoxide, and tetrahydrofuran are reacted with an appropriate base, for example an inorganic base such as sodium hydroxide, potassium butoxide, sodium hydride, potassium hydride, and potassium carbonate or an organic base such as triethylamine, pyridine, and diisopropylethylamine at -20 °C to 100 °C, preferably 0 °C to
10 30 °C for 1 min to 24 h, preferably 10 min to 12 h to give the aimed compound (XIII).

Compound (XI) and compound (XII) can be synthesized by the methods A to I and the methods J to N as shown below.

15 In the methods A to I, Z represents optionally substituted aryl or optionally substituted heteroaryl. The starting material of each method is commercially available or can be synthesized by well-know method from the compound which is commercially available.

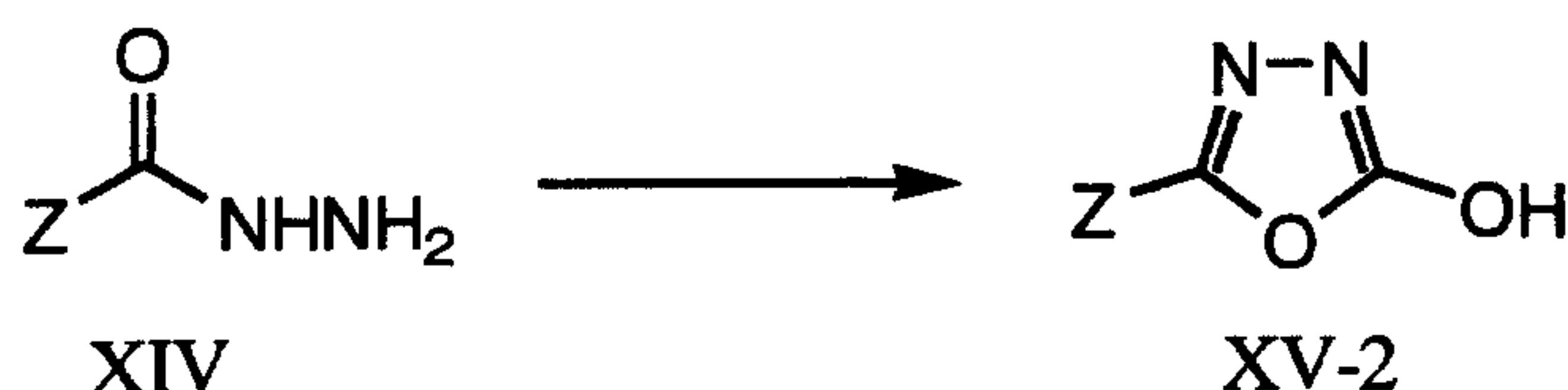
20 Method A : Synthetic method of the compound wherein Y is an oxadiazole ring and X is -S-.



wherein Z is above defined.

Compound (XIV) in a solvent such as ethanol and benzene is reacted with carbon
25 disulfide and a base such as triethylamine, sodium hydroxide, and potassium carbonate at 0 °C to 100 °C, preferably 60 °C to 100 °C for 10 min to 24 h, preferably 2 h to 12 h to give compound (XV-1).

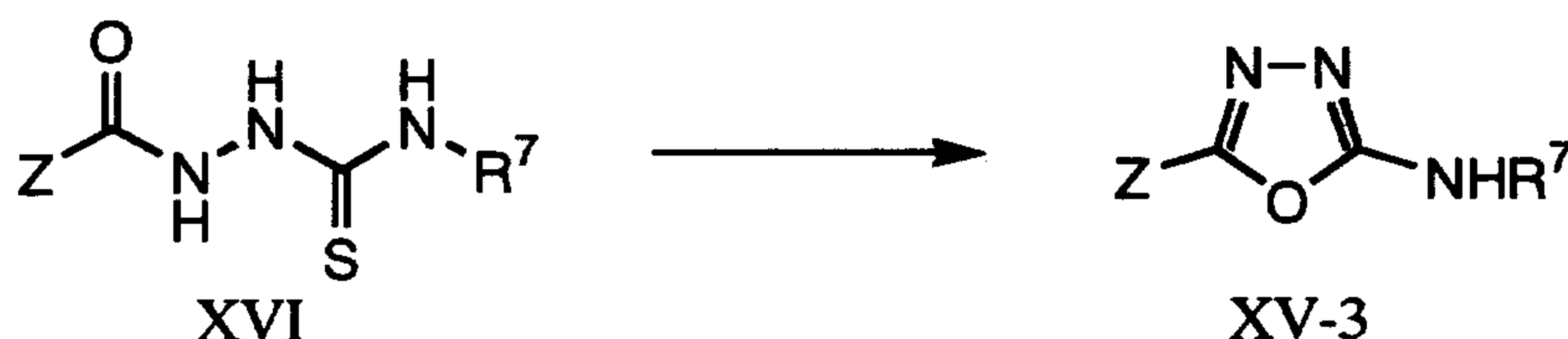
Method B : Synthetic method of the compound wherein Y is an oxadiazole ring and X is -O-.



wherein Z is above defined.

- 5 To a solution of compound (XIV) in a solvent such as tetrahydrofuran and toluene, is added carbonyldiimidazole, and the mixture is reacted at 0 °C to 120 °C, preferably 60 °C to 120 °C for 10 min to 24 h, preferably 2 h to 12 h to give compound (XV-2).

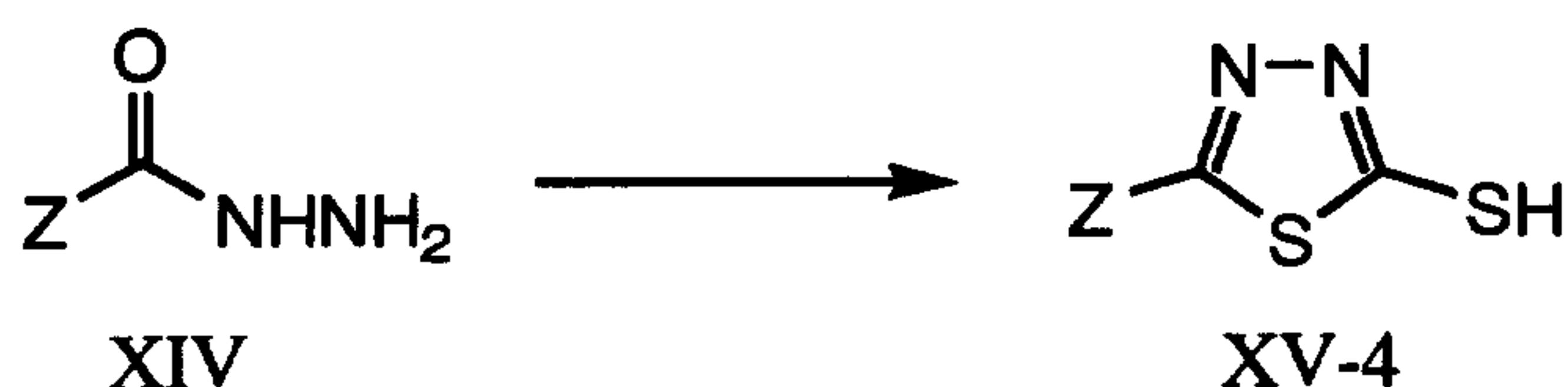
10 Method C : Synthetic method of the compound wherein Y is an oxadiazole ring and X is -N(R⁷)-.



wherein Z is as defined above and R⁷ is as defined above.

- 15 To a solution of compound (XVI) in a solvent such as ethanol and tetrahydrofuran, is added mercury oxide, and the mixture is reacted at 0 °C to 120 °C, preferably 30 °C to 80 °C for 0.5 h to 24 h, preferably 1h to 24 h to give compound (XV-3).

Method D : Synthetic method of the compound wherein Y is a thiadiazole ring and X is -S-.



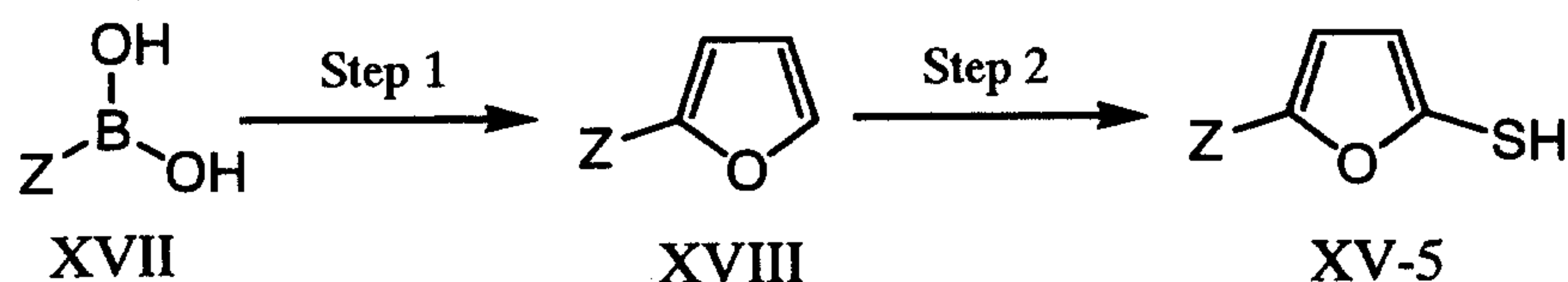
- 20 wherein Z is as defined above.

To a solution of compound (XIV) in a solvent such as ethanol and tetrahydrofuran are added carbon disulfide and a base such as triethylamine and sodium hydroxide and the mixture is reacted at 0 °C to 100 °C, preferably 20 °C to 60 °C for 0.5 h to 24 h, preferably 1 h to 12 h. After the solvent is removed, the residue is reacted with conc. sulfuric acid at

-20 °C to 40 °C, preferably 0 °C to 20 °C for 1 min to 12 h, preferably 10 min to 1 h to give compound (XV-4).

Method E : Synthetic method of the compound wherein Y is a furan ring and X is

5 -S-.



wherein Z is as defined above.

(Step 1)

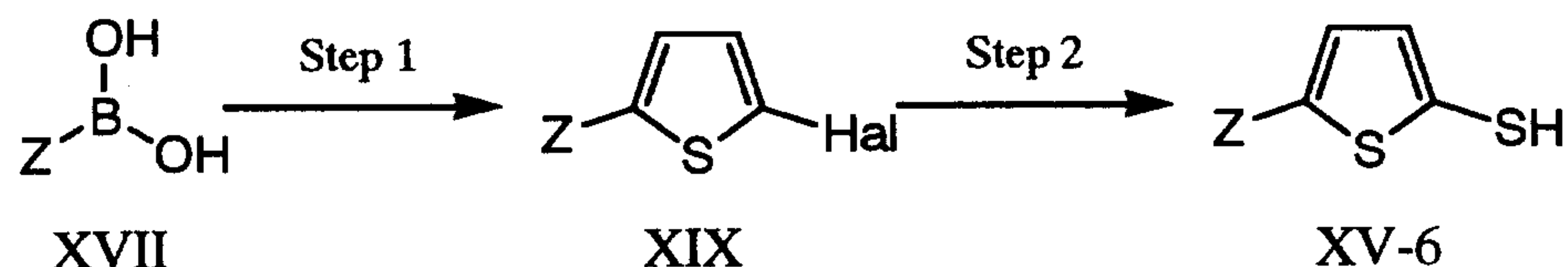
Halogenated furan such as 2-bromofuran is reacted with compound (XVII) in a solvent such as N,N-dimethylformamide, toluene, xylene, benzene, tetrahydrofuran, and ethanol in the presence of palladium catalyst such as $\text{Pd}(\text{Ph}_3\text{P})_4$ and a base such as potassium carbonate, calcium carbonate, triethylamine, and sodium methoxide to give the aimed compound (XVIII) (Suzuki reaction). The reaction temperature is room temperature to 100 °C, preferably room temperature to 80 °C and the reaction time is 5 to 50 h, preferably 15 to 30 h.

(Step 2)

To a solution of compound (XVIII) in a solvent such as tetrahydrofuran, diethyl ether, and toluene is added a base such as n-butyllithium and sec-butyllithium, and the mixture is stirred at -100 °C to 50 °C, preferably -80 °C to 0 °C for 1 min to 24 h, preferably 10 min to 60 min. To the mixture is added sulfur, and the resulting mixture is reacted at -100 °C to 50 °C, preferably -80 °C to 0 °C for 1 h to 24 h, preferably 1 h to 12 h to give the aimed compound (XV-5).

Method F : Synthetic method of the compound wherein Y is a thiophene ring and

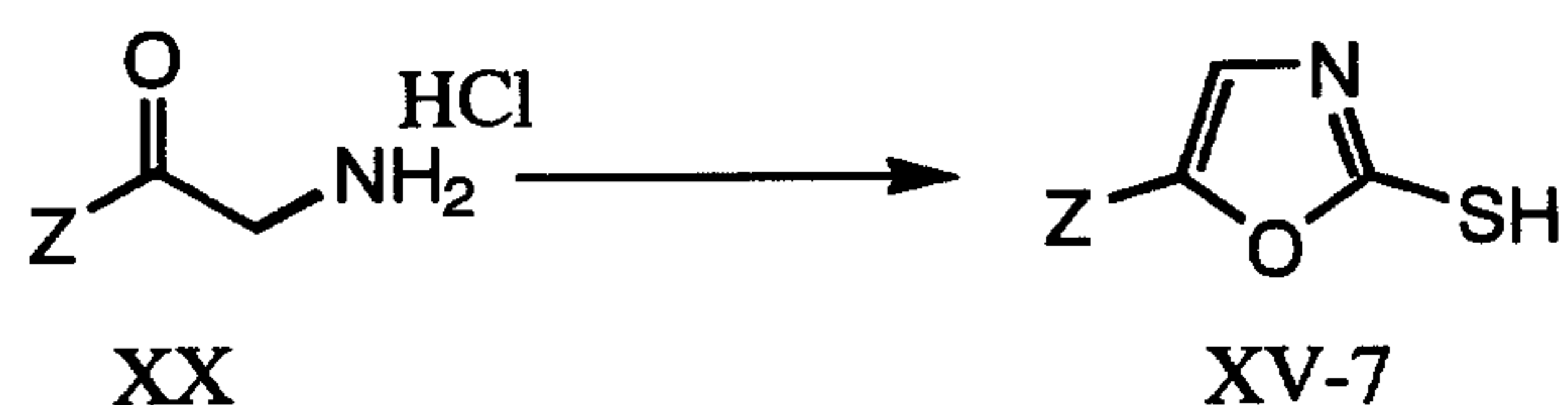
25 X is -S-.



wherein Z is as defined above and Hal is halogen.

The steps 1 and 2 can be carried out in a manner similar to those described in step 1 and 2 of Method E.

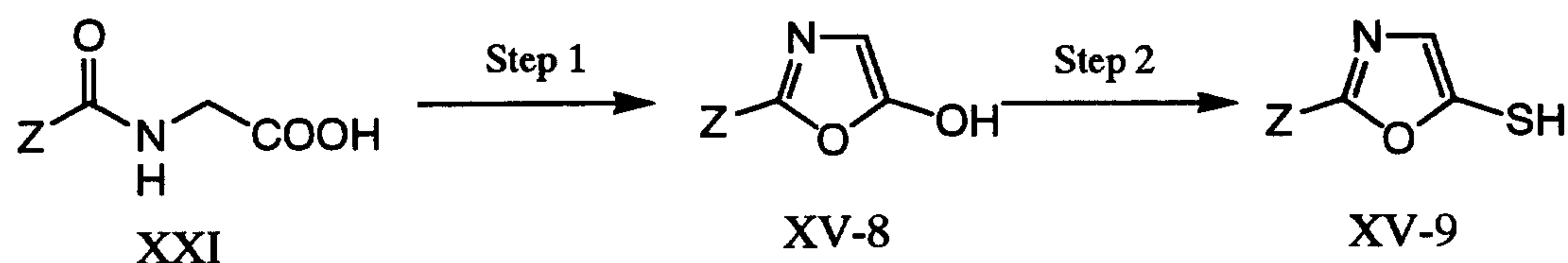
5 Method G : Synthetic method of the compound wherein Y is an oxazole ring and X is -S-.



wherein Z is as defined above.

To a solution of compound (XX) in a solvent such as dichloromethane, toluene,
 10 and diethyl ether is added thiophosgene in the presence of a base such as triethylamine and sodium hydroxide and the mixture is reacted at -20 °C to 100 °C, preferably 0 °C to 40 °C for 1 h to 48 h, preferably 1 h to 24 h to give compound (XV-7).

Method H : Synthetic method of the compound wherein Y is an oxazole ring and
 15 X is -O- or -S-.



wherein Z is as defined above.

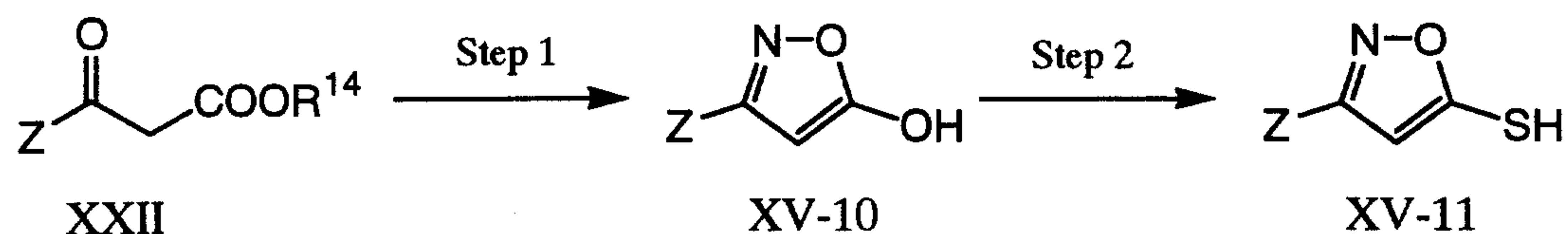
(Step 1)

Compound (XXI) in a solvent such as dichloromethane and acetonitrile is reacted
 20 with a coupling reagent such as dicyclohexylcarbodiimide at -20 °C to 50 °C, preferably 0 °C to 20 °C for 5 min to 24 h, preferably 10 min to 2 h to give compound (XV-8).

(Step 2)

To a solution of compound (XV-8) in a solvent such as toluene and dioxane is
 added Lawesson's reagent, and the mixture is reacted at 60 °C to 150 °C, preferably 80 °C
 25 to 120 °C for 1 h to 24 h, preferably 2 to 12 h to give compound (XV-9).

Method I : Synthetic method of the compound wherein Y is an isoxazole ring and X is -O- or -S-.



wherein Z is as defined above and R¹⁴ is C1 to C3 alkyl.

5 (Step 1)

Compound (XXII) in a solvent such as methanol and tetrahydrofuran is reacted with hydroxylamine at 20 °C to 100°C, preferably 50 °C to 80 °C for 1 h to 24 h, preferably 2 h to 12 h to give compound (XV-10).

(Step 2)

10 Compound (XV-11) can be obtained in a manner similar to that described in step 2
of Method H.

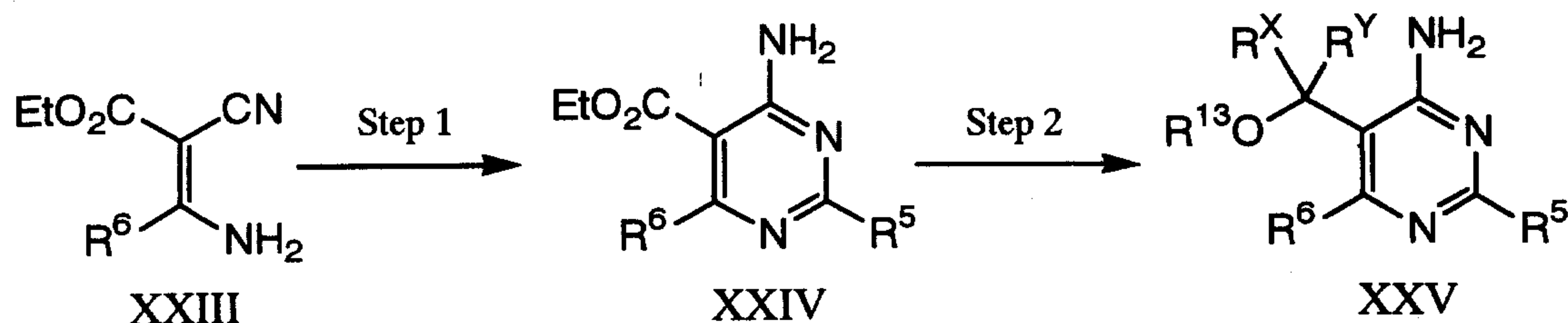
The compounds which are not concretely shown in the above methods can be synthesized by a combination of the above methods A to I and well-know methods.

In the methods J to N, R⁵, R⁶, R¹³, Q³, and T³ (wherein R¹, R², R³, and R⁴ are as defined above) are as defined above. The starting material of each method is commercially available or can be synthesized by well-know methods from the compound which is commercially available.

Methods J and K are processes for construction of a pyrimidine ring, and can be carried out in accordance with well-known methods (see Journal of Chemical Society, 1937, p-364, *ibid.*, 1943, p-388 and J. Pharm. Soc. Japan 1954, p-742).

Methods L to N are processes for introduction a guanidino group to the pyrimidine derivative obtained in the Method J and Method K, and can be carried out in accordance with well-known methods (see Journal of Chemical Society, 1948, p-581, *ibid.*, 1946, p-1063 and *Synthesis*, 1988, p-460).

Method J-1 : Synthesis of a pyrimidine ring wherein both R^X and R^Y are hydrogen atom.



wherein R^5 , R^6 and R^{13} are as defined above; and R^X and R^Y are hydrogen atom.

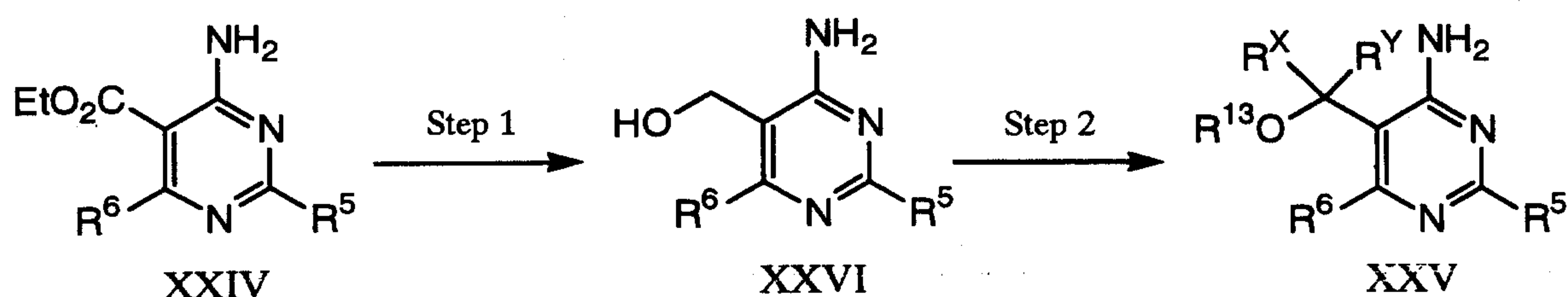
5 (Step 1)

Compound (XXIII) in a solvent such as ethanol, tetrahydrofuran, and N,N-dimethylformamide is reacted with $R^5\text{-C}(=\text{S})\text{-NH}_2$ in the presence of a base such as sodium ethylate and sodium hydroxide at 0°C to 150°C , preferably 60°C to 100°C for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XXIV).

10 (Step 2)

Compound (XXIV) in a solvent such as ether and tetrahydrofuran or in a mixed solvent such as ether-tetrahydrofuran is reacted with a reducing agent such as lithium aluminum hydride and lithium borohydride at -80°C to 100°C , preferably -20°C to 40°C for 0.5 h to 24 h, preferably 1 h to 12 h to give an alcohol derivative. The obtained alcohol derivative is protected by the method described in Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons) and the like, to give compound (XXV).

20 Method J-2 : Synthesis of a pyrimidine ring wherein one of R^X and R^Y is hydrogen atom.



wherein R^5 , R^6 and R^{13} are as defined above; R^X is alkyl; and R^Y are hydrogen atom or alkyl.

(Step 1)

Compound (XXIV) in a solvent such as ether and tetrahydrofuran or in a mixed

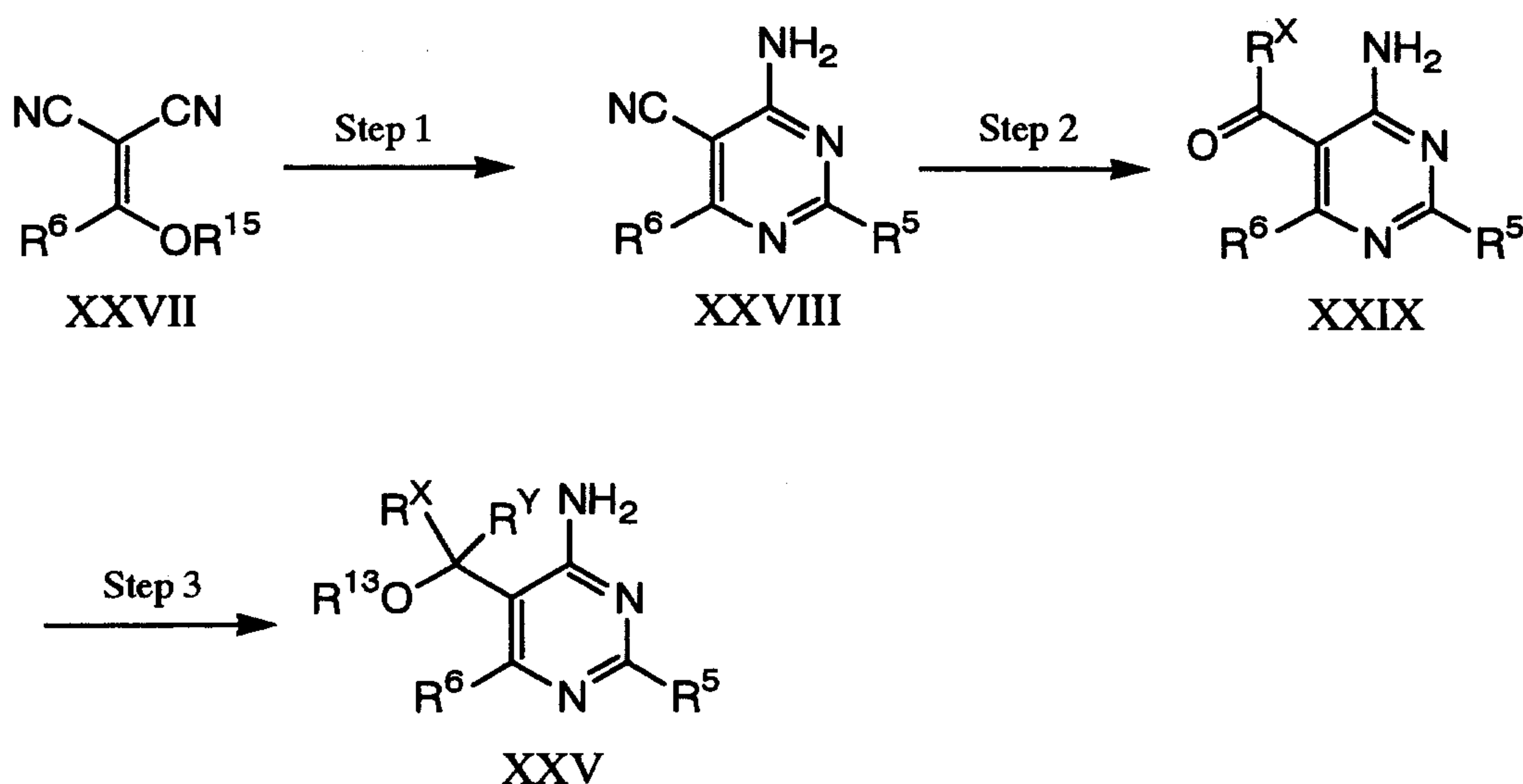
solvent such as ether-tetrahydrofuran is reacted with a reducing agent such as lithium aluminum hydride and lithium borohydride at -80°C to 100°C , preferably -20°C to 40°C for 0.5 h to 24 h, preferably 1 h to 12 h to give compound (XXVI).

(Step 2)

5 Compound (XXVI) in a solvent such as dichloromethane and chloroform is reacted with an oxidizing agent such as manganese dioxide, pyridinium dichromate, and pyridinium chlorochromate at -20°C to 100°C , preferably 0°C to 40°C for 0.5 h to 14 days, preferably 1 h to 7 days to give an aldehyde derivative. The obtained aldehyde derivative in a solvent such as ether and tetrahydrofuran or in a mixed solvent such as
10 ether-tetrahydrofuran is reacted with Grignard reagent such as $\text{R}^{\text{X}}\text{MgBr}$ or organometallic reagent such as $\text{R}^{\text{X}}\text{Li}$ at -80°C to 100°C , preferably -20°C to 40°C for 0.5 h to 24 h, preferably 1 h to 12 h to give an alcohol derivative. The obtained alcohol derivative is protected by the method described in Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons) and the like, to give compound (XXV).

15

Method J-3 : Synthesis of a pyrimidine ring wherein both of R^{X} and R^{Y} are not hydrogen atom.



wherein R^5 , R^6 and R^{13} are as defined above; R^{X} and R^{Y} are each independently alkyl or
20 alkyloxy; R^{15} is alkyl such as methyl and ethyl.

(Step 1)

Compound (XXVII) in a solvent such as ethanol, tetrahydrofuran, and N,N-

dimethylformamide is reacted with $R^5-C(=N)-NH_2$ in the presence of a base such as sodium ethylate and sodium hydroxide, at 0 °C to 150 °C, preferably 60 °C to 100 °C for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XXVIII).

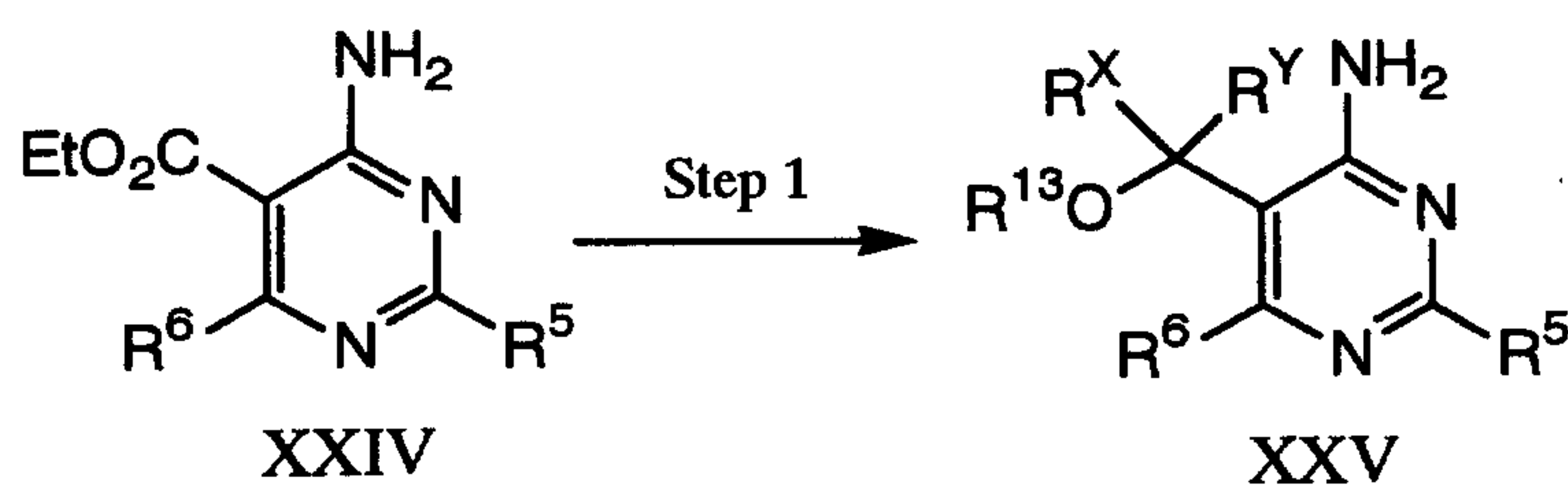
(Step 2)

5 Compound (XXVIII) in a solvent such as ether and tetrahydrofuran or in a mixed solvent such as ether-tetrahydrofuran is reacted with Grignard reagent such as $R^X MgBr$ or organometallic reagent such as $R^X Li$ at -80 °C to 100 °C, preferably -20 °C to 40 °C for 0.5 h to 24 h, preferably 1 h to 12 h. To the mixture an acid aqueous solution such as hydrochloric acid and sulfuric acid is added, and then the resulting mixture is stirred at -20
10 °C to 100 °C, preferably 0 °C to 40 °C for 0.5 h to 24 h, preferably 1 h to 12 h to give compound (XXIX).

(Step 3)

Compound (XXIX) in a solvent such as ether and tetrahydrofuran or in a mixed solvent such as ether-tetrahydrofuran is reacted with Grignard reagent such as $R^X MgBr$ or
15 organometallic reagent such as $R^X Li$ at -80 °C to 100 °C, preferably -20 °C to 40 °C for 0.5 h to 24 h, preferably 1 h to 12 h to give an alcohol derivative. The obtained alcohol derivative is protected by the method described in Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons) and the like, to give compound (XXX).

20 Method J-4 : Synthesis of a pyrimidine ring wherein R^X and R^Y are same.



wherein R^5 , R^6 and R^{13} are as defined above; R^X and R^Y are same as alkyl or alkyloxy.

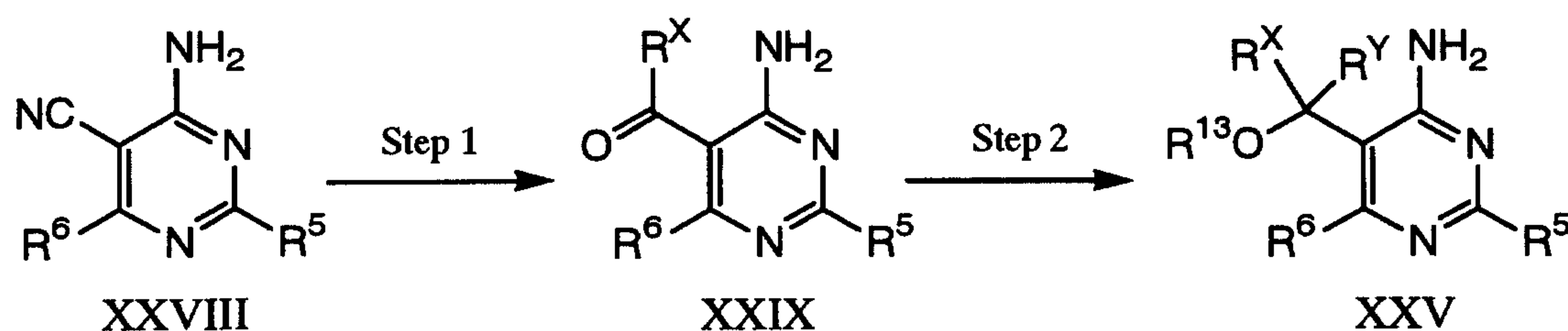
(Step 1)

Compound (XXIV) in a solvent such as ether and tetrahydrofuran or in a mixed
25 solvent such as ether-tetrahydrofuran is reacted with Grignard reagent such as $R^X MgBr$ or organometallic reagent such as $R^X Li$ at -80 °C to 100 °C, preferably -20 °C to 40 °C for 0.5 h to 24 h, preferably 1 h to 12 h to give an alcohol derivative. The obtained alcohol

derivative is protected by the method described in Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons) and the like to give compound (XXV).

Method J-5 : Synthesis of a pyrimidine ring wherein one of R^X and R^Y is hydrogen

5 atom.



wherein R^5 , R^6 and R^{13} are as defined above; one of R^X and R^Y is hydrogen atom and the other is hydrogen atom, alkyl or alkyloxy.

(Step 1)

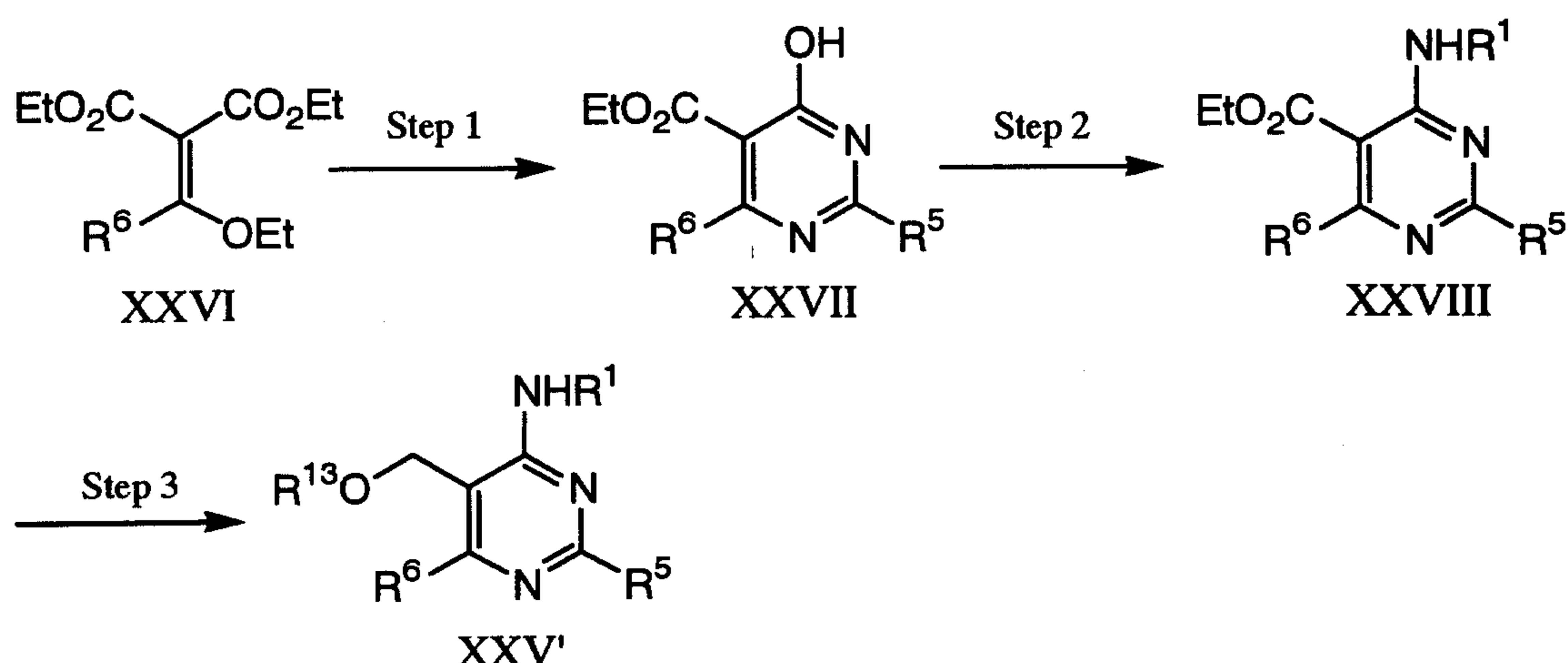
10 Compound (XXVIII) in a solvent such as ether and tetrahydrofuran or a mixed in solvent such as ether-tetrahydrofuran is reacted with Grignard reagent such as $R^X\text{MgBr}$ or organometallic reagent such as $R^X\text{Li}$ at -80°C to 100°C , preferably -20°C to 40°C for 0.5 h to 24 h, preferably 1 h to 12 h. To the mixture an acid aqueous solution such as hydrochloric acid and sulfuric acid is added, and then the resulting mixture is stirred at -20°C to 100°C , preferably 0°C to 40°C for 0.5 h to 24 h, preferably 1 h to 12 h to give compound (XXIX).

(Step 2)

20 Compound (XXIX) in a solvent such as ether, tetrahydrofuran, methanol, and ethanol or their mixed solvent is reacted with a reducing agent such as sodium borohydride, lithium borohydride, and lithium aluminum hydride at -80°C to 100°C , preferably -20°C to 40°C for 0.5 h to 24 h, preferably 1 h to 12 h to give an alcohol derivative. The obtained alcohol derivative is protected by the method described in Protective Groups in Organic Synthesis, Theodora W Green (John Wiley & Sons) and the like to give compound (XXV).

25

Method K : Synthesis of a pyrimidine ring.



wherein R¹, R⁵, R⁶ and R¹³ are as defined above.

(Step 1)

Compound (XXVI) in a solvent such as ethanol, tetrahydrofuran, and N,N-dimethylformamide is reacted with R⁵-C(=NH)-NH₂ or its salt in the presence of a base such as sodium ethylate and sodium hydroxide at 0 °C to 150 °C, preferably 60 °C to 100 °C for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XXVII) or its salt.

(Step 2)

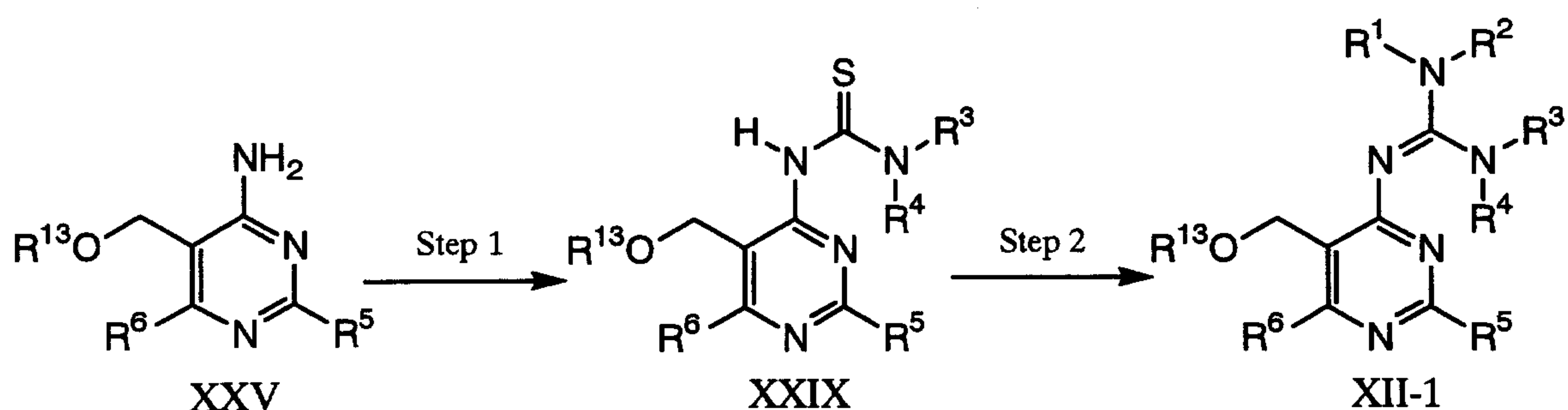
Compound (XXVII) or its salt in a solvent such as toluene and dichloroethane or without solvent is reacted with a halogenating reagent such as thionyl chloride and phosphorus oxychloride at 0 °C to 150 °C, preferably 60 °C to 120 °C for 0.5 h to 12 h, preferably 1 h to 5 h to give a halogenated compound. The obtained halogenated compound in a solvent such as ethanol and tetrahydrofuran is reacted with R¹NH₂ at -80 °C to 100 °C, preferably -20 °C to 30 °C for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XXVIII).

(Step 3)

This step can be carried out in a manner similar to that described in step 2 of Method J-1.

20

Method L : Introduction of a guanidino group



wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 and R^{13} are as defined above.

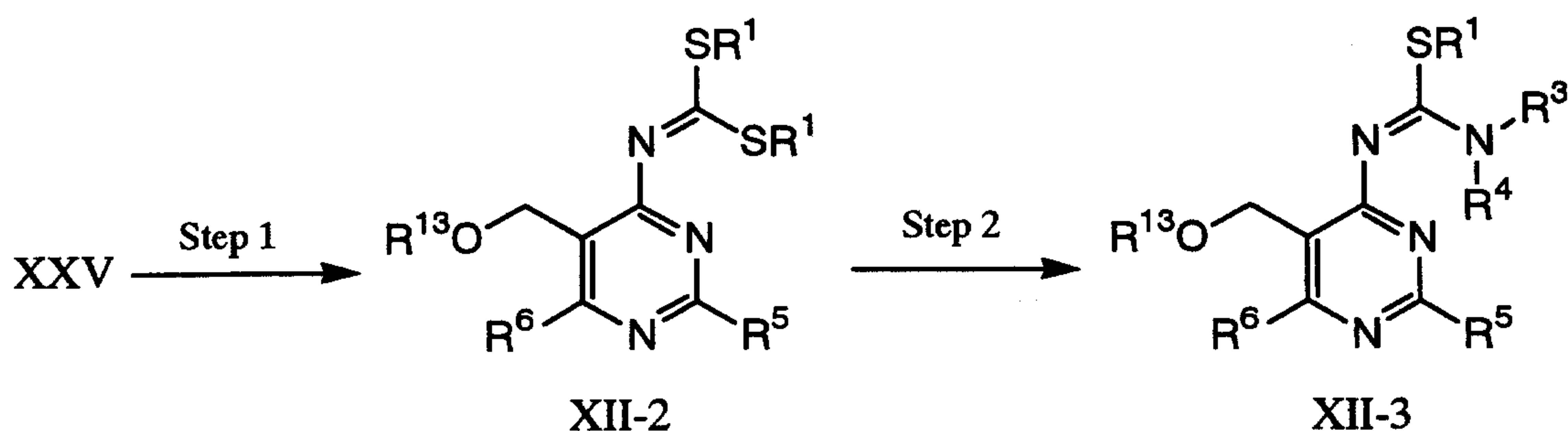
(Step 1)

Compound (XXV) in a solvent such as N,N-dimethylformamide, pyridine, and tetrahydrofuran is reacted with R^3 -NCS or R^3R^4 NCS-Hal wherein Hal is halogen, in the presence or absence of a base such as sodium hydride at $-20\text{ }^\circ\text{C}$ to $120\text{ }^\circ\text{C}$, preferably $0\text{ }^\circ\text{C}$ to $120\text{ }^\circ\text{C}$ for 0.5 h to 48 h, preferably 1 h to 24 h to give compound (XXIX).

(Step 2)

To a solution of compound (XXIX) in a solvent such as methanol and tetrahydrofuran are added a heavy metal salt or heavy metal oxide such as HgO and R^1R^2 NH, and the mixture is reacted at $-20\text{ }^\circ\text{C}$ to $100\text{ }^\circ\text{C}$, preferably $0\text{ }^\circ\text{C}$ to $50\text{ }^\circ\text{C}$ for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XII-1).

Method M : Introduction of a guanidino group



15 XII-4

wherein R^1 , R^3 , R^4 , R^5 , R^6 and R^{13} are as defined above.

(Step 1)

To a solution of compound (XXV) in a solvent such as N,N-dimethylformamide and tetrahydrofuran in the presence of a base such as sodium hydride and potassium butoxide added carbon disulfide and then alkylating reagent such as R^1 I and R^1_2 SO₄, and

the mixture is reacted at 0 °C to 100 °C, preferably 20 °C to 60 °C for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XII-2).

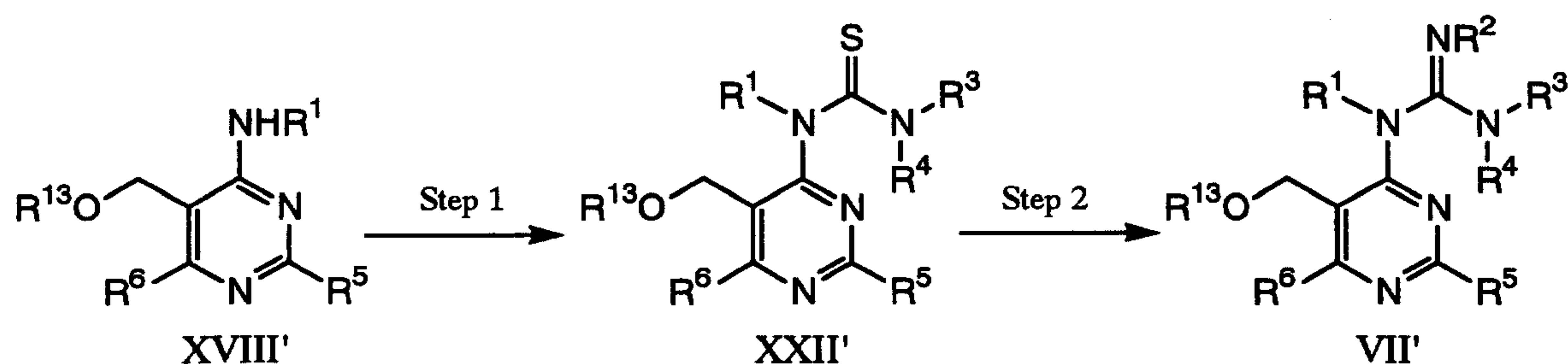
(Step 2)

Compound (XII-2) in a solvent such as methanol and N,N-dimethylformamide is reacted with R^3R^4NH at 0 °C to 150 °C, preferably 0 °C to 100 °C for 0.5 h to 48 h, preferably 1 h to 12 h to give compound (XII-3).

(Step 3)

Compound (XII-3) in a solvent such as methanol and N,N-dimethylformamide is reacted with R^1R^2NH at 20 °C to 150 °C, preferably 40 °C to 80 °C for 0.5 h to 48 h, preferably 4 h to 24 h to give compound (XII-4).

Method N : Introduction of a guanidino group wherein R^1 is not hydrogen atom.



wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 and R^{13} are as defined above.

(Step 1)

This step can be carried out in a manner similar to that described in step 1 of Method L.

(Step 2)

This step can be carried out in a manner similar to that described in step 2 of Method L.

When a compound contains a functional group(s) possibly interfering the reaction such as hydroxy, mercapto, and amino group in the each step of Method A to Method N, it can previously be protected and deprotected at an appropriate stage by the method described Protective Groups in Organic Synthesis, Theodora W. Green (John Wiley & Sons).

The term "the compounds of the present invention" herein used includes pharmaceutically acceptable salts and hydrates of the compounds. For example, salts with alkali metals (e.g., lithium, sodium, and potassium), alkaline earth metals (e.g., magnesium and calcium), ammonium, organic bases, amino acids, mineral acids (e.g., hydrochloric acid, hydrobromic acid, phosphoric acid, and sulfuric acid), or organic acids (e.g., acetic acid, citric acid, maleic acid, fumaric acid, benzenesulfonic acid, and p-toluenesulfonic acid) are exemplified. These salts can be formed by usual methods. The hydrates may coordinate with an arbitrary number of water molecule.

The compounds of the present invention is not restricted to any particular isomers but includes all possible isomers and racemate.

The compounds of the present invention have an inhibitory activity against a signal derived from Ras oncogene products as shown in the experimental examples below.

Consequently, the compounds of the present invention can be used as a therapeutic agent for cancer, preferably solid tumor such as pancreatic cancer, colon cancer, and lung cancer.

When the compounds of this invention is administered to a patient for the treatment of the above diseases, they can be administered by oral administration such as powder, granules, tablets, capsules, pilulae, liquid medicine, or the like, or by parenteral administration such as injections, suppository, percutaneous formulations, insufflation, or the like. An effective amount of the compound of this invention is formulated by being mixed with appropriate medicinal admixture such as excipient, binder, penetrant, disintegrators, lubricant, and the like, if necessary. When parenteral injection is prepared, the compound of this invention and an appropriate carrier are sterilized to formulate.

An appropriate dosage varies with the conditions of the patients, an administration route, their age, and their body weight. In the case of oral administration to an adult, the

dosage can generally be between 0.01 - 100 mg/kg/day, preferably 0.1 - 20 mg/kg/day.

The following examples are provided to further illustrate the present invention and are not to be construed as limiting the scope thereof.

5

In the examples, the following abbreviations are used.

Me : methyl

Et : ethyl

10 Pr : n-propyl

i-Pr : isopropyl

Bu : n-butyl

DMF : dimethylformamide

THF : tetrahydrofuran

15 DMSO : dimethylsulfoxide

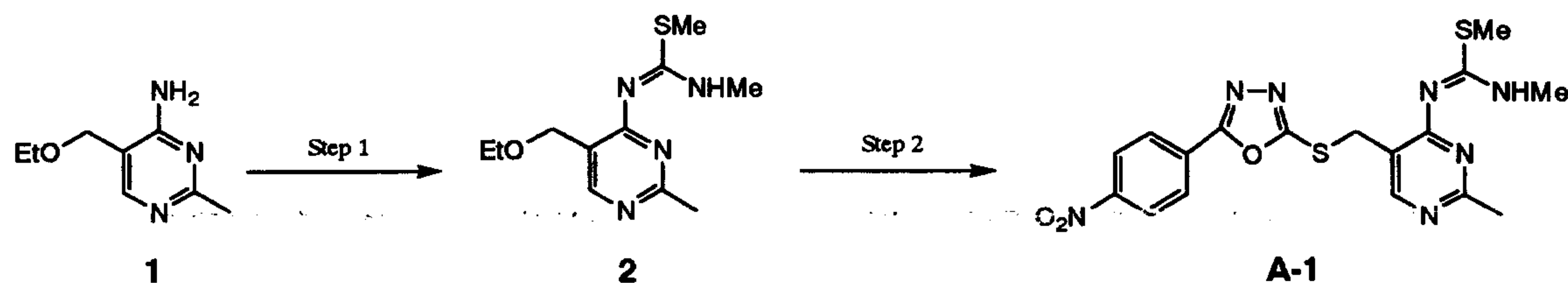
TBS : tert-butyldimethylsilyl

TBDPS ; tert-butyldiphenylsilyl

20 In ¹H-NMR, the value of δ is represented by ppm, s is singlet, d is doublet, t is triplet, q is quartet, qu is quintet, sext is sextet, and br is broad. The value of J is represented by Hz.

Example

Example 1



25 Step 1

To a solution of potassium t-butoxide (8.05 g) in 60 ml of DMF was added dropwise a solution of compound 1 (10.0 g) which was obtained by well-known method

(M. Tomita, S. Uyeo, A. Takamizawa and R. Maeda, Yakugakuzasshi, 74, 742 (1954)), in 29 ml of DMF with stirring at ice-cooling. The reaction mixture was allowed to room temperature and stirred for 1 h. To the resulting mixture was added a solution of methylisothiocyanate (5.25 g) in 7.5 ml of DMF at ice-cooling and stirred for 2 h at room temperature. After confirming the disappearance of compound 1, a solution of methyl iodide (12.7 g) in 1.5 ml of DMF was added to the mixture at ice-cooling. The mixture was stirred for 1 h at room temperature and DMF was removed under reduced pressure, and then water was added to the residue. The mixture was extracted with diethyl ether, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 8.15 g of compound 2.

¹H-NMR(CDCl₃) : 1.26(3H, t, J=6.9 Hz), 2.52(3H, s), 2.56(3H, s), 3.07(3H, d, J=5.3 Hz), 3.60(2H, q, J=6.9 Hz), 4.61(2H, s), 8.41(1H, s).

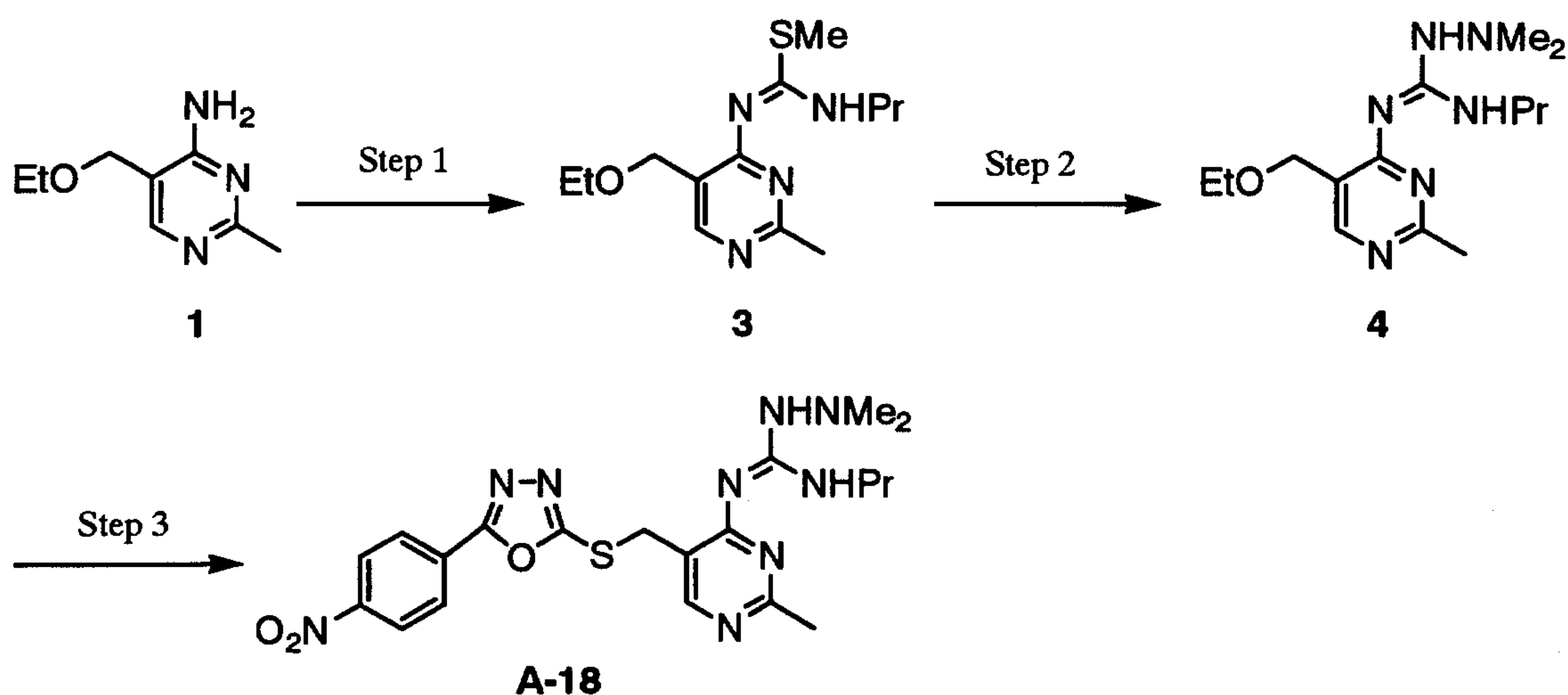
Step 2

A solution of compound 2 (2.50 g) in 25 ml of 25% hydrobromic acid/acetic acid was reacted for 7 h at 70 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 10 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (2.41 g) which was obtained in similar to described (R. W. Young and K. H. Wood. J. Am. Chem. Soc., 77, 400 (1955)) and potassium carbonate (5.43 g) in 25 ml of DMF. The reaction mixture was stirred for 1 h at room temperature and added water. The appeared crystal was filtered to give 2.56 g of compound A-1. The physical data was shown in Table 1.

Example 2 to 17

Compounds A-2 to A-17 were synthesized in a manner similar to described in Example 1. The physical data were shown in Tables 1 to 2.

Example 18



Step 1

To a solution of potassium t-butoxide (3.43 g) in 30 ml of DMF was added dropwise a solution of compound **1** (4.64 g) in 12 ml of DMF with stirring at ice-cooling.

- 5 The reaction mixture was allowed to room temperature and stirred for 30 min. To the resulting mixture was added dropwise a solution of propylisothiocyanate (3.09 g) in 3 ml of DMF at ice-cooling and stirred for 1.5 h at room temperature. After confirming the disappearance of compound **1**, a solution of methyl iodide (5.91 g) in 3 ml of DMF was added to the mixture at ice-cooling. The mixture was stirred for 1 h at room
- 10 temperature. DMF was removed under reduced pressure and added water. The resulting mixture was extracted with diethyl ether, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. To the residue was added hexane, the appeared crystal was filtered to give 2.25 g of compound **3**.

¹H-NMR(CDCl₃) : 1.06(3H, t, J=7.3 Hz), 1.27(3H, t, J=7.3 Hz), 1.71(2H, sext, J=7.3 Hz), 2.51(3H, s), 2.55(3H, s), 3.35(2H, q, J=7.3 Hz), 3.60(2H, q, J=7.3 Hz), 4.61(2H, s), 8.41(1H, s), 11.31(1H, br).

15

Step 2

- A solution of compound **3** (0.10 g) and dimethylhydrazine (0.43 g) in 2 ml of ethanol was stirred for 3 days at 65 °C. The reaction mixture was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography to give 0.03 g of compound **4**.
- 20

$^1\text{H-NMR}(\text{CDCl}_3)$: 0.96(3H, t, $J=7.3$ Hz), 1.26(3H, t, $J=7.3$ Hz), 1.62(2H, sext, $J=7.3$ Hz), 2.50(3H, s), 2.61(6H, s), 3.37(2H, q, $J=7.3$ Hz), 3.60(2H, q, $J=7.3$ Hz), 4.53(2H, s), 6.25(1H, br), 8.21(1H, s), 10.94(1H, br).

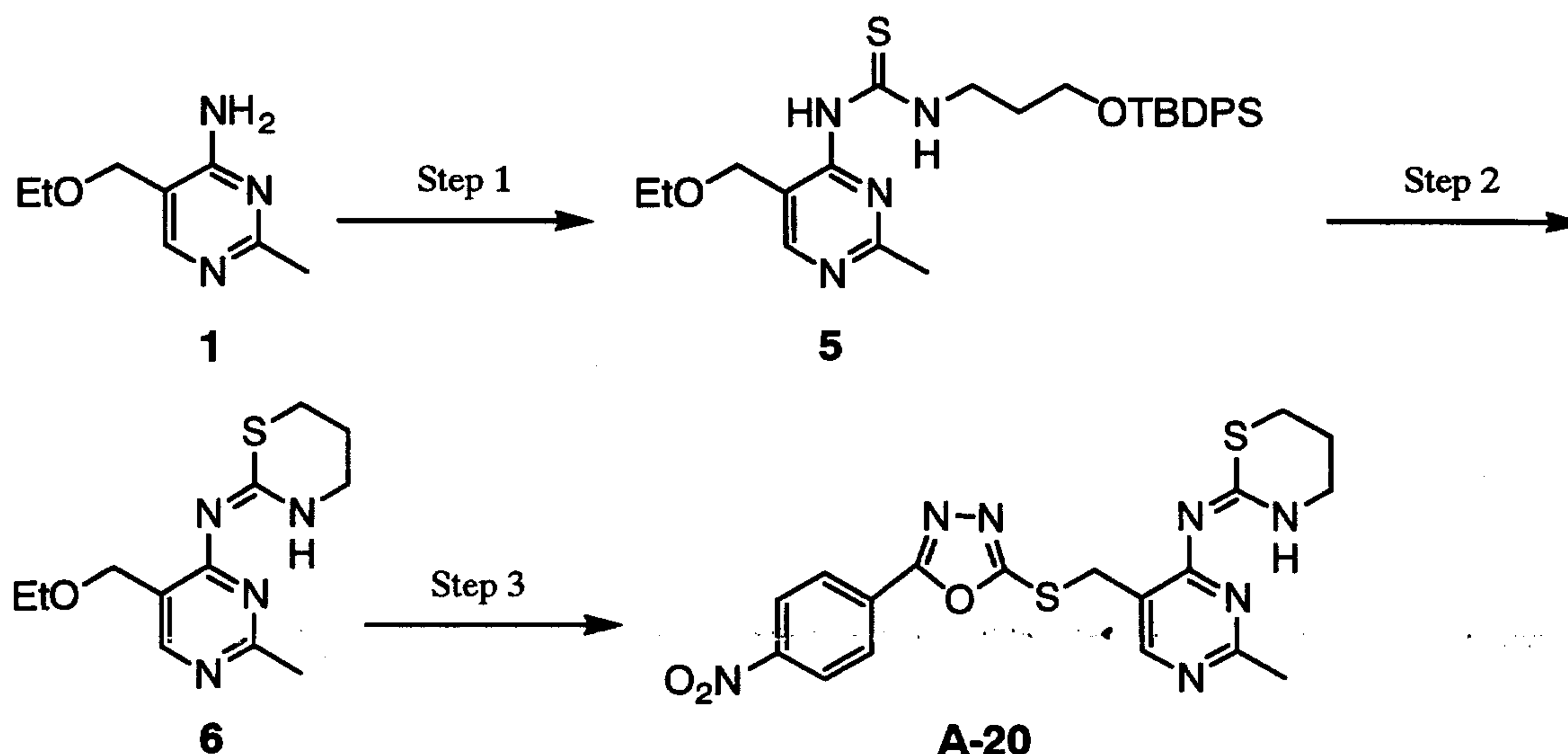
5 Step 3

A solution of compound **4** (0.03 g) in 0.3 ml of 25% hydrobromic acid in acetic acid was reacted for 7 h at 70 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 1 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (0.03 g) and potassium carbonate (0.06 g) in 2 ml of DMF. The reaction mixture was stirred for 1 h at ice-cooling and added water. The appeared crystal was filtered and recrystallized from ethyl acetate/hexane to give 0.02 g of compound **A-18**. The physical data were shown in Table 2.

15 Example 19

Compounds **A-19** was synthesized in a manner similar to described in Example 18. The physical data were shown in Table 3.

Example 20



20 Step 1

To a solution of potassium t-butoxide (0.73 g) in 15 ml of DMF was added

dropwise a solution of compound 1 (1.00 g) in 5 ml of DMF with stirring at ice-cooling. To the resulting mixture was added dropwise 3-t-butylldiphenylsilyloxypropylisothiocyanate (2.33 g) which was obtained easily from 3-amino-1-propanol by usual method and stirred for 17 h. To the reaction mixture was added water, and the mixture was extracted with diethyl ether, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 1.10 g of compound 5.

¹H-NMR(CDCl₃) : 1.05(9H, s), 1.36(3H, t, J=6.9 Hz), 1.98(2H, quint, J=6.6 Hz), 2.42(3H, s), 3.63(2H, q, J=6.9 Hz), 3.81(2H, t, J=6.6 Hz), 3.89(2H, q, J=6.6 Hz), 4.51(2H, s), 7.31 - 7.41(6H, m), 7.64 - 7.68(4H, m), 8.22(1H, s), 9.40(1H, br), 11.48(1H, br).

Step 2

A solution of compound 5 (1.00 g) and p-toluenesulfonic acid monohydrate (0.76 g) in 5 ml of toluene was heated with stirring for 2 h under reflux. To the resulting mixture were added water and saturated sodium hygrocarbonate aqueous solution. The mixture was extracted with ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 0.25 g of compound 6.

¹H-NMR(CDCl₃) : 1.26(3H, t, J=6.9 Hz), 2.13 - 2.21(2H, m), 2.54(3H, s), 3.07 - 3.12(2H, m), 3.55 - 3.62(2H, m), 3.61(2H, q, J=6.9 Hz), 4.57(2H, s), 8.38(1H, s), 11.81(1H, br).

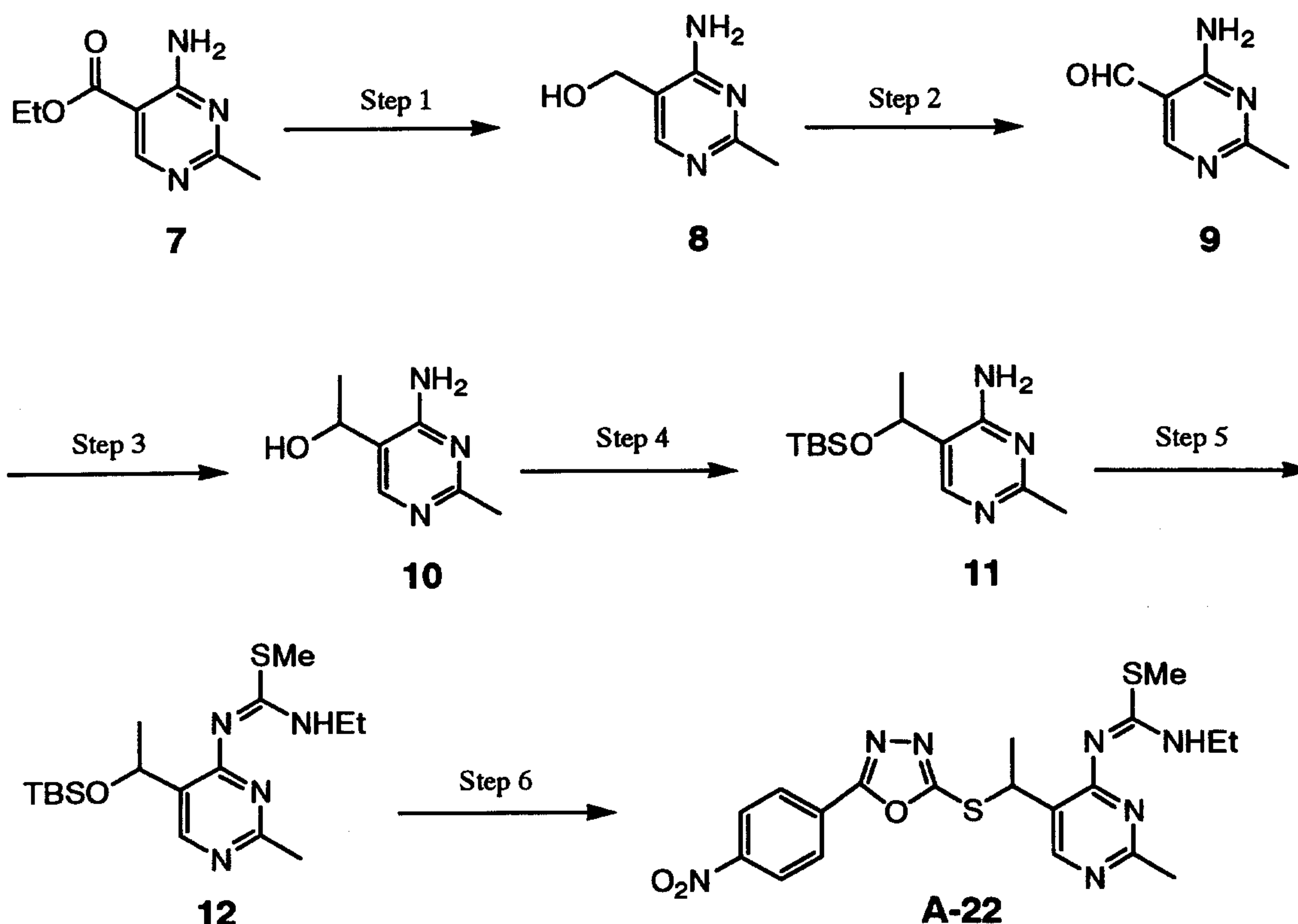
Step 3

A solution of compound 6 (0.10 g) in 0.8 ml of 25% hydrobromic acid/acetic acid was reacted for 14 h at 70 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 1 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (0.09 g) and potassium carbonate (0.21 g) in 2 ml of DMF at ice-cooling. The reaction mixture was stirred for 1 h at ice-cooling and added water. The appeared crystal was filtered and recrystallized from dichloromethane/diethyl ether/hexane to give 0.07 g of compound A-20. The physical data were shown in Table 3.

Example 21

Compounds **A-21** was synthesized in a manner similar to described in Example 20. The physical data were shown in Table 3.

5 Example 22



Step 1

To a suspension of lithium aluminum hydride (4.4 g) in 220ml of THF was added dropwise a solution of 4-amino-5-ethoxycarbonyl-2-methylpyrimidine **7** (22.0 g) which was obtained by the method described in literature (G. W. Kenner, B. Lythgoe, A. R. Todd and A. Topham. J. Chem. Soc., 388 (1943)) in 220 ml of THF with stirring at ice-cooling. The reaction mixture was allowed to room temperature and stirred for 2 h. To the mixture was added excess of ice and the stirring was continued for additional 2 h. To the reaction mixture was added anhydrous sodium sulfate, and the stirring was continued. The THF-insoluble material was filtered off and washed with methanol. The combined filtrate was concentrated completely under reduced pressure and added ethanol. The ethanol solution was heated and the insoluble material was filtered off. The ethanol-soluble filtrate was cooled and the appeared insoluble material was filtered off again. The

filtrate was diluted with diethyl ether and the appeared crystals were filtered to give 14.5 g of compound **8**.

Melting Point :191~192°C,

¹H-NMR(DMSO-d₆) 2.28(3H, s), 4.30(2H, s), 7.90(1H, s).

5

Step 2

To a solution of compound **8** (500 mg) in a combined solvent of 10 ml of dichloromethane and 5 ml of methanol was added active manganese dioxide (2.5 g), and stirred for 6 days at room temperature. The dichloromethane-insoluble material was
10 filtered off and the solvent was removed under reduced pressure. The residue was subjected to silica gel column chromatography and crystalized from diethyl ether to give 284 mg of compound **9**.

¹H-NMR(CDCl₃) : 2.58(3H, s), 5.84(1H, br), 8.13(1H, br), 8.57(1H, s), 9.86(1H, s).

15

Step 3

A solution of compound **9** (280 mg) in 14 ml of THF was heated to dissolve and the mixture was allowed to ice-cooling. To the mixture was added dropwise 0.93 M solution of methylmagnesium bromide in THF (8.8 ml) with stirring at ice-cooling. The reaction mixture was stirred for 20 min at room temperature. Ice-water was added to the
20 mixture, and the mixture was extracted with ethyl acetate. And the aqueous layer was reextracted with methyl ethyl ketone. The combined organic layer was concentrated under reduced pressure, and 10% solution of metanol in dichloromethane was added to the residue, then the insolble material was filtered off. The filtrate was subjected to silica gel column chromatography and then crystalized from diethyl ether/hexane to give 188 mg of
25 compound **10**.

¹H-NMR(CDCl₃) : 1.57(3H, d, J=6.6 Hz), 2.13(1H, br), 2.48(3H, s), 4.86(1H, q, J=6.6 Hz), 5.55(2H, br), 7.94(1H, s).

Step 4

30 A solution of compound **10** (188 mg) and imidazole (100 mg) in 10 ml of DMF

was added a solution of t-butyldimethylchlorosilane (200 mg) in 2 ml of DMF with stirring at ice-cooling. The mixture was stirred at room temperature for 2 h, and then imidazole (50 mg) and t-butyldimethylchlorosilane (100 mg) were added again to the mixture. The reaction mixture was stirred overnight, and added ethyl acetate. The resulting mixture was washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 285 mg of compound **11**.

¹H-NMR(CDCl₃) : 0.01(3H, s), 0.10(3H, s), 0.88(9H, s), 1.46(3H, d, J=6.6 Hz), 2.48(3H, s), 4.79(1H, q, J=6.6 Hz), 5.56(2H, br), 7.87(1H, s).

Step 5

Potassium t-butoxide (140 mg) was added to a solution of compound **11** (285 mg) in 5.0 ml of DMF with stirring at ice-cooling. After stirring for 5 min, ethylisothiocyanate (0.11 ml) was added dropwise. The resulting mixture was stirred for 10 min at ice-cooling and methyl iodide (0.08 ml) was added, and stirred for additional 1 h. To the reaction mixture was added water, extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 176 mg of compound **12**.

¹H-NMR(CDCl₃) : -0.01(3H, s), 0.05(3H, s), 0.90(9H, s), 1.33(3H, t, J=7.3 Hz), 1.40(3H, d, J=6.3 Hz), 2.48(3H, s), 2.55(3H, s), 3.42(2H, dq, J=5.6 Hz, 7.3 Hz), 5.36(1H, q, J=6.3 Hz), 8.54(1H, s), 11.18(1H, br).

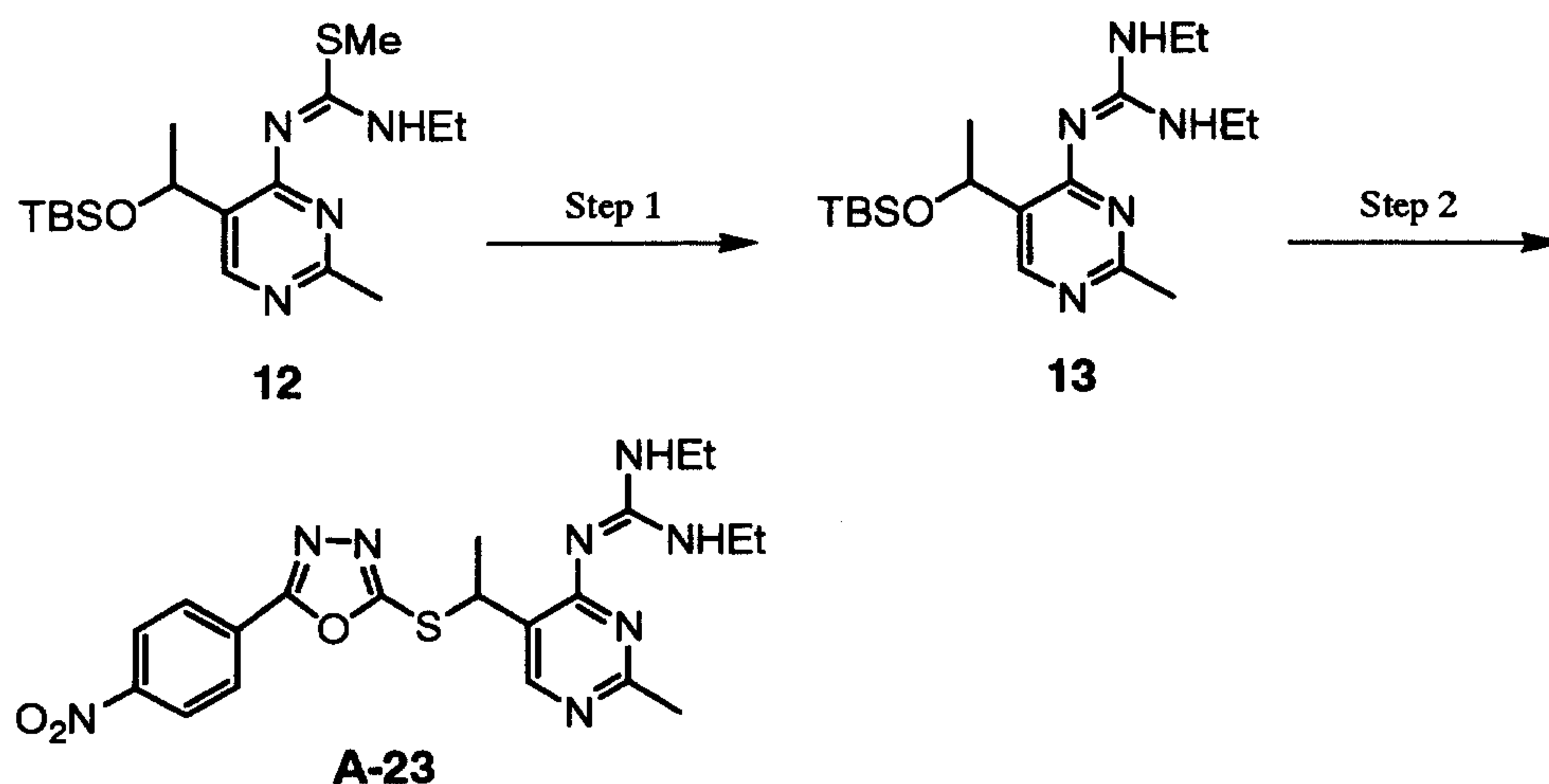
Step 6

A solution of compound **12** (50 mg) in 1.0 ml of 25% hydrobromic acid/acetic acid was reacted for 15 h at 40 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 1 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (50 mg) and potassium carbonate (105 mg) in 2 ml of DMF at ice-cooling. The reaction mixture was stirred for 1 h at ice-cooling and added water. The reaction mixture was extracted with

dichloromethane, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography and crystallized from diethyl ether to give 16.8 mg of compound A-22. The physical data were shown in Table 3.

5

Example 23



Step 1

To a solution of compound **12** (120 mg) in 3.0 ml of ethanol was added 70% ethylamine aqueous solution (0.27 ml), and the mixture was stirred for 5 h at 60 °C. An additional 70% ethylamine aqueous solution (0.54 ml) was added to the reaction mixture, stirred overnight at 80 °C. After cooling, the solvent was removed under reduced pressure to give 114 mg of compound **13**.

¹H-NMR(CDCl₃) : -0.00(3H, s), 0.04(3H, s), 0.91(9H, s), 1.28(6H, t, J=7.2 Hz), 1.39(3H, d, J=6.2 Hz), 2.48(3H, s), 3.33(4H, br), 5.27(1H, q, J=6.2 Hz), 8.35(1H, s).

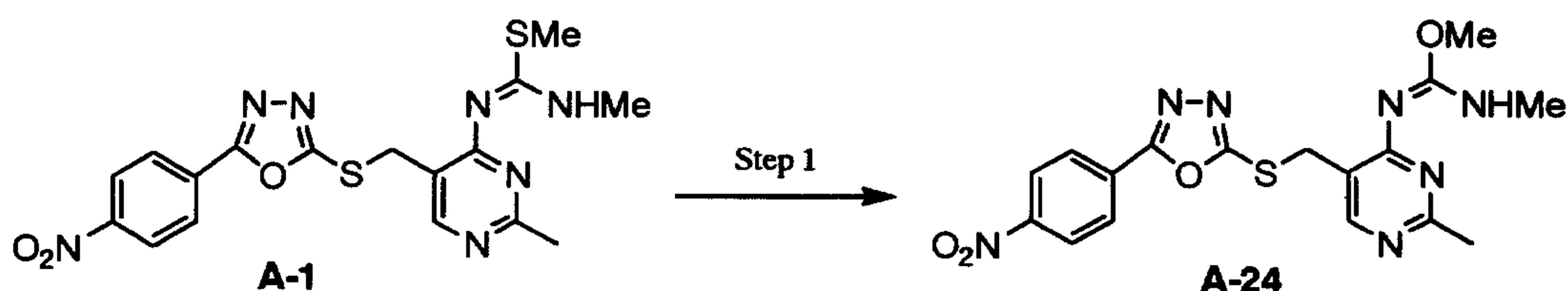
Step 2

A solution of compound **13** (50 m g) in 1.0 ml of 25% hydrobromic acid/acetic acid was reacted for 15 h at 40 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 1 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (50 mg) and potassium carbonate (105 mg) in 2 ml of DMF at ice-cooling. The reaction mixture was stirred for 3 h at ice-cooling and added water. The mixture was extracted with dichloromethane and

successively with 20% 2-propanol/dichloromethane, and the combined organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography and crystallized from methanol to give 24.9 mg of compound **A-23**. The physical data were shown in Table 3.

5

Example 24



Step 1

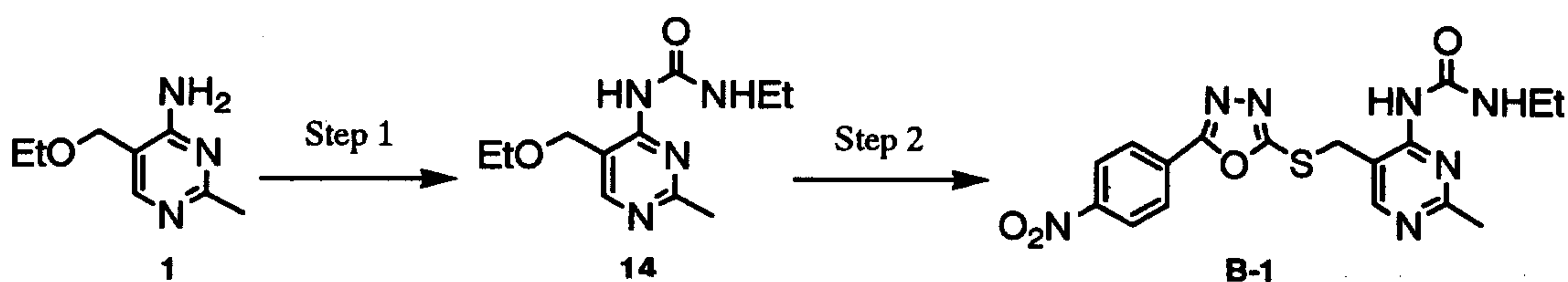
To a solution of compound **A-1** (100 mg) in a mixed solvent of dichloromethane (5.0 ml) and methanol (5.0 ml) was added silver(I) oxide (70 mg), and the reaction mixture was stirred for 4 h at room temperature. The dichloromethane-insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The residue was subjected to silica gel column chromatography and recrystallized from diethyl ether to give 82.9 mg of compound **A-24**. The physical data were shown in Table 3.

15

Example 25 to 27

Compounds **A-25** to **A-27** were synthesized in a manner similar to described in Example 24. The physical data were shown in Table 3.

20 Example 28



Step 1

To a solution of potassium t-butoxide (3.69 g) in 20 ml of DMF was added dropwise a solution of compound **1** (5.00 g) in 32 ml of DMF with stirring at ice-cooling.

The reaction mixture was allowed at room temperature and stirred for 30 min. A solution of ethylisocyanate (2.34 g) in 6 ml of DMF was added dropwise to the mixture at ice-cooling, and the mixture was stirred for 1.5 h at room temperature. After removal of DMF under reduced pressure, water was added to the residue. The mixture was extracted
5 with diethyl ether, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 6.27 g of compound **14**.

¹H-NMR(CDCl₃) : 1.26(3H, t, J=7.3 Hz), 1.27(3H, t, J=7.3 Hz), 2.60(3H, s), 3.43(2H, dq, J=5.6 Hz, 7.3 Hz), 3.55(2H, q, J=7.3 Hz), 4.46(2H, s), 7.99(1H, br), 8.17(1H, s), 9.36(1H,
10 br).

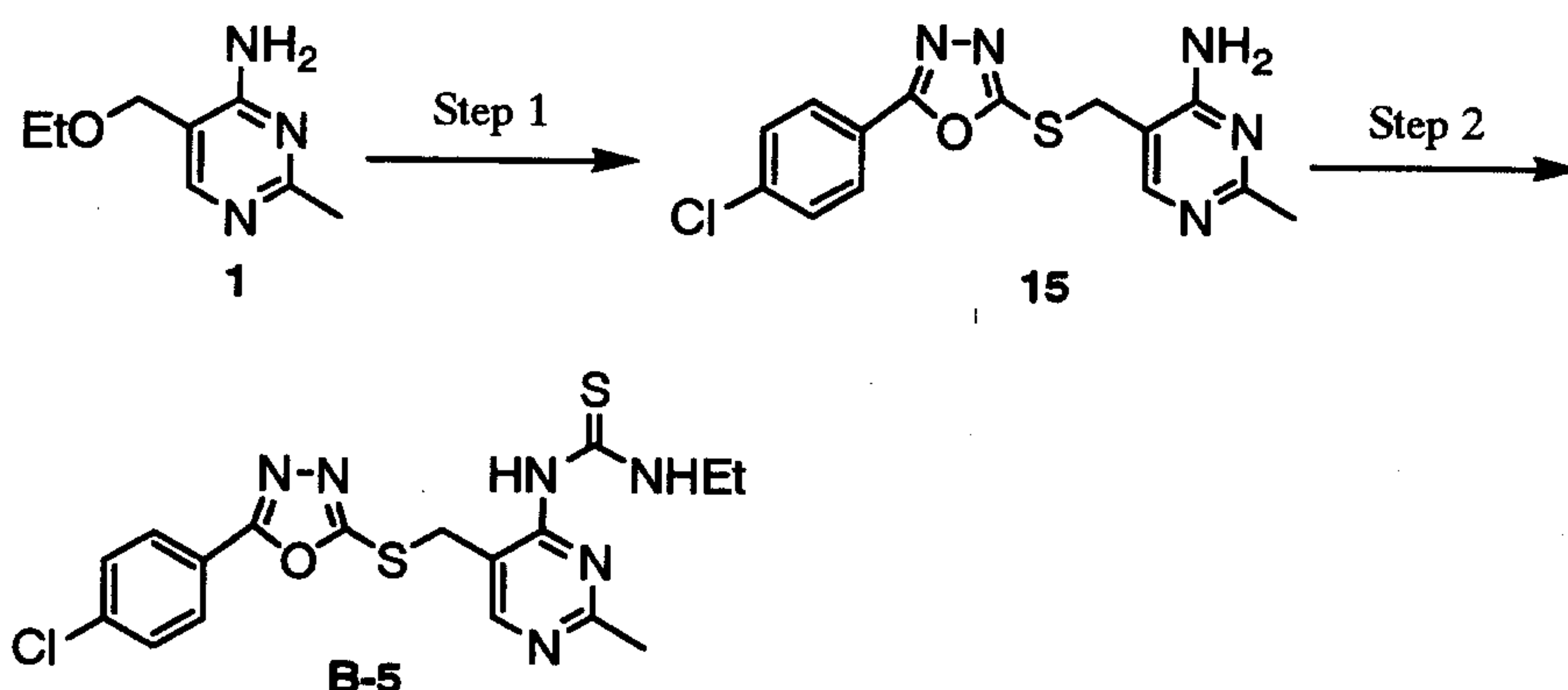
Step 2

A solution of compound **14** (100 mg) in 2.5 ml of 25% hydrobromic acid in acetic acid was reacted for 5 h at 70 °C. The solvent was removed under reduced pressure, and
15 the residue was dissolved in 2 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (120 mg) and potassium carbonate (230 mg) in 3 ml of DMF at ice-cooling. The reaction mixture was stirred for 1 h at ice-cooling, then water was added to the reaction mixture. The insoluble precipitate was filtered, dried, and subjected to silica gel column chromatography and crystallized from
20 methanol to give 126 mg of compound **B-1**. The physical data were shown in Table 5.

Example 29 to 31

Compounds **B-2** to **B-4** were synthesized in a manner similar to described in Example 28. The physical data were shown in Table 5.

Example 32



Step 1

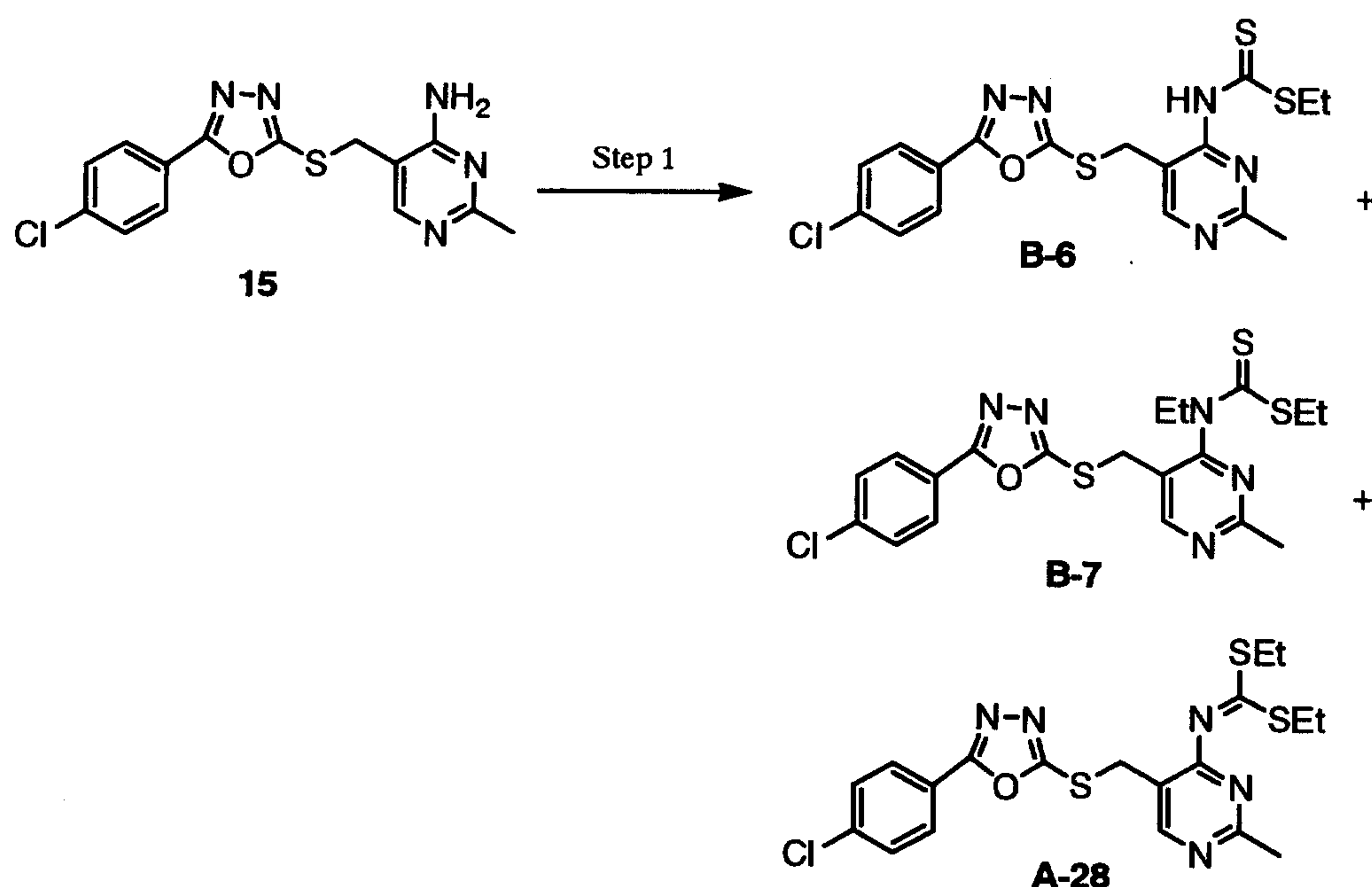
A solution of compound **1** (2.24 g) in 30 ml of 25% hydrobromic acid/acetic acid was reacted for 15.5 h at 70 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 10 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (3.13 g) and potassium carbonate (7.14 g) in 35 ml of DMF at ice-cooling. The reaction mixture was stirred for 1 h at ice-cooling and added water. The appeared crystal was filtered to give 3.99 g of compound **15**.

¹H-NMR(DMSO-d₆) : 2.28(3H, s), 4.37(2H, s), 7.09(2H, br), 7.67(2H, d, J=8.6 Hz), 7.98(2H, d, J=8.6 Hz), 8.06(1H, s).

Step 2

To a solution of compound **15** (200 mg) in 10 ml of DMF was added potassium t-butoxide (70 mg) with stirring at colling with dryice/acetonitrile bath. The reaction mixture was stirred for 5 min and ethylisothiocyanate (0.06 ml) was added to the resulting mixture. The reaction mixture was stirred for 3 min and added acetic acid (0.05 ml). To the reaction mixture was added water at room temperature, extracted with dichloromethane, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography and crystalized from diethyl ether to give 16.3 mg of compound **B-5**. The physical data were shown in Table 5.

Example 33



Step 1

To a solution of compound **15** (200 mg) in 10 ml of DMF were added potassium t-butoxide (140 mg) and carbon disulfide (0.04 ml) with stirring at cooling with dryice/acetonitrile bath. After stirring for 5 min, ethyl iodide (0.1 ml) was added. The reaction mixture was stirred for additional 15 min and water was added at room temperature. The reaction mixture was extracted with ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give a mixture of compounds **B-6**, **B-7**, and **A-28**.

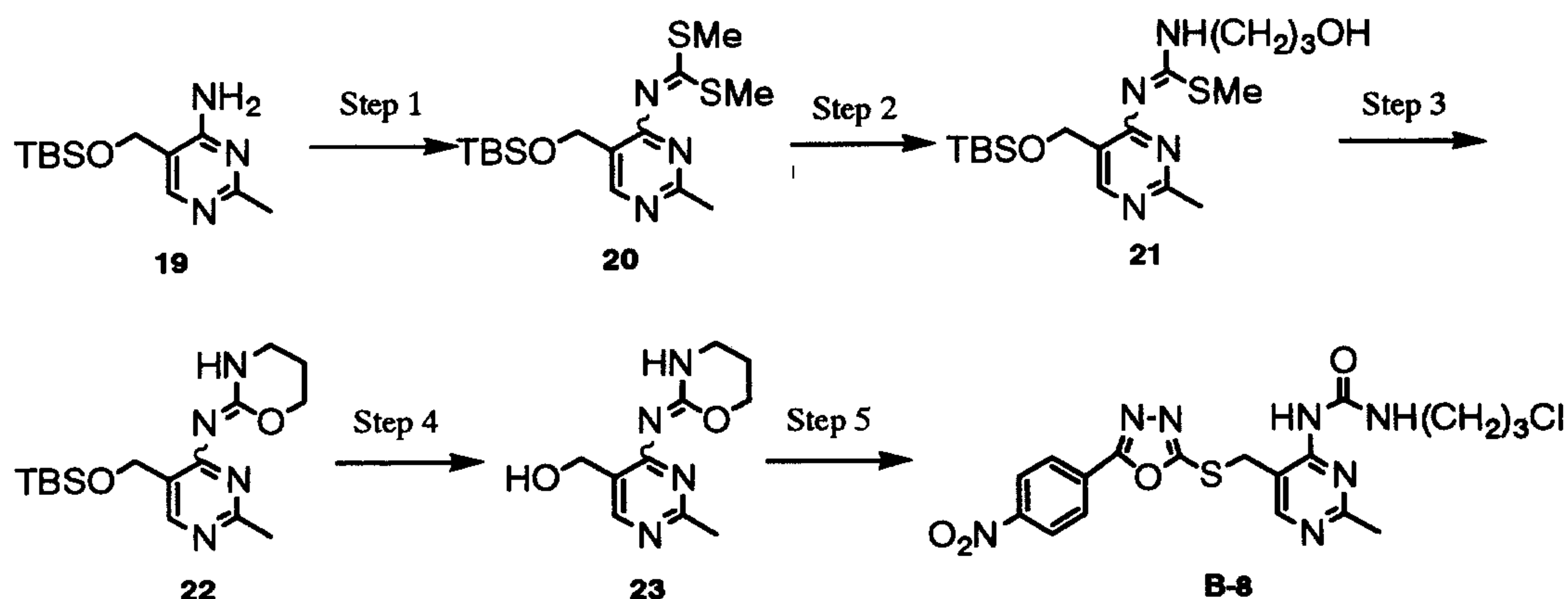
Crystals, which were appeared by addition of diethyl ether to obtained mixture was filtered to give 4.7 mg of compound **B-6**. The physical data was shown in Table 5.

The filtrate was subjected again to silica gel column chromatography to separate compounds **B-7** and **A-28**, and then independently crystalized from diethyl ether/hexane to give 2.2 mg of **B-7** and 6.1 mg of **A-28**, respectively. The physical data of compound **B-7** and **A-26** were shown in Table 5 and Table 3, respectively.

Example 34 to 40

Compounds **A-29** to **A-35** were synthesized in a manner similar to described above. The physical data were shown in Table 4.

Example 41



Step 1

To a suspension of sodium hydride (2.28 g) in 50 ml of DMF was added dropwise a solution of compound **19** (5.56 g) which was obtained by the method described in WO00/04014, and carbon disulfide (3.59 g) in 60 ml of DMF with stirring at ice-cooling. The reaction mixture was allowed to room temperature and stirred for 20 min, and a solution of methyl iodide (9.34 g) in 10ml of DMF was added dropwise to the mixture at ice-cooling. The resulting mixture was stirred for 1.5 h at room temperature, and DMF was removed under reduced pressure. After addition of water the mixture was extracted with ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 4.45 g of compound **20**.

¹H-NMR(CDCl₃) : 0.10(6H, s), 0.94(9H, s), 2.54(6H, s), 2.67(3H, s), 4.64(2H, s), 8.63(1H, s).

Step 2

A solution of compound **20** (0.06 g) and 3-amino-1-propanol (0.02 g) in 1 ml of methanol was stirred for 16 h at 30 °C. The reaction mixture was concentrated under reduced pressure and the residue was subjected to silica gel column chromatography to give 0.06 g of compound **21**.

¹H-NMR(CDCl₃) : 0.10(6H, s), 0.95(9H, s), 1.94(2H, quint, J=6.6 Hz), 2.48(3H, s), 2.55(3H, s), 3.54(2H, q, J=6.6 Hz), 3.83(2H, t, J=6.6 Hz), 4.83(2H, s), 8.48(1H, s), 11.22(1H, br).

Step 3

To a solution of compound **21** (0.06 g) in 0.5 ml of THF was added potassium t-butoxide (0.02 g) with stirring at room temperature, and the reaction mixture was stirred for 4 h. The reaction mixture was concentrated under reduced pressure and the residue

5 was subjected to silica gel column chromatography to give 0.05 g of compound **22**.

¹H-NMR(CDCl₃) : 0.10(6H, s), 0.94(9H, s), 2.11(2H, quint, J=5.3 Hz), 2.55(3H, s), 3.58(2H, t, J=5.3 Hz), 4.40(2H, t, J=5.3 Hz), 4.79(2H, s), 8.45(1H, s), 11.38(1H, br).

Step 4

10 A solution of compound **22** (0.04 g) and tetrabutylammonium fluoride trihydrate (0.04 g) in 1 ml of THF was stirred for 18 h at room temperature. The reaction mixture was concentrated under reduced pressure and the residue was subjected to silica gel column chromatography to give 0.02 g of crude compound **23**. This crude compound **23** was used for Step 5 without purification.

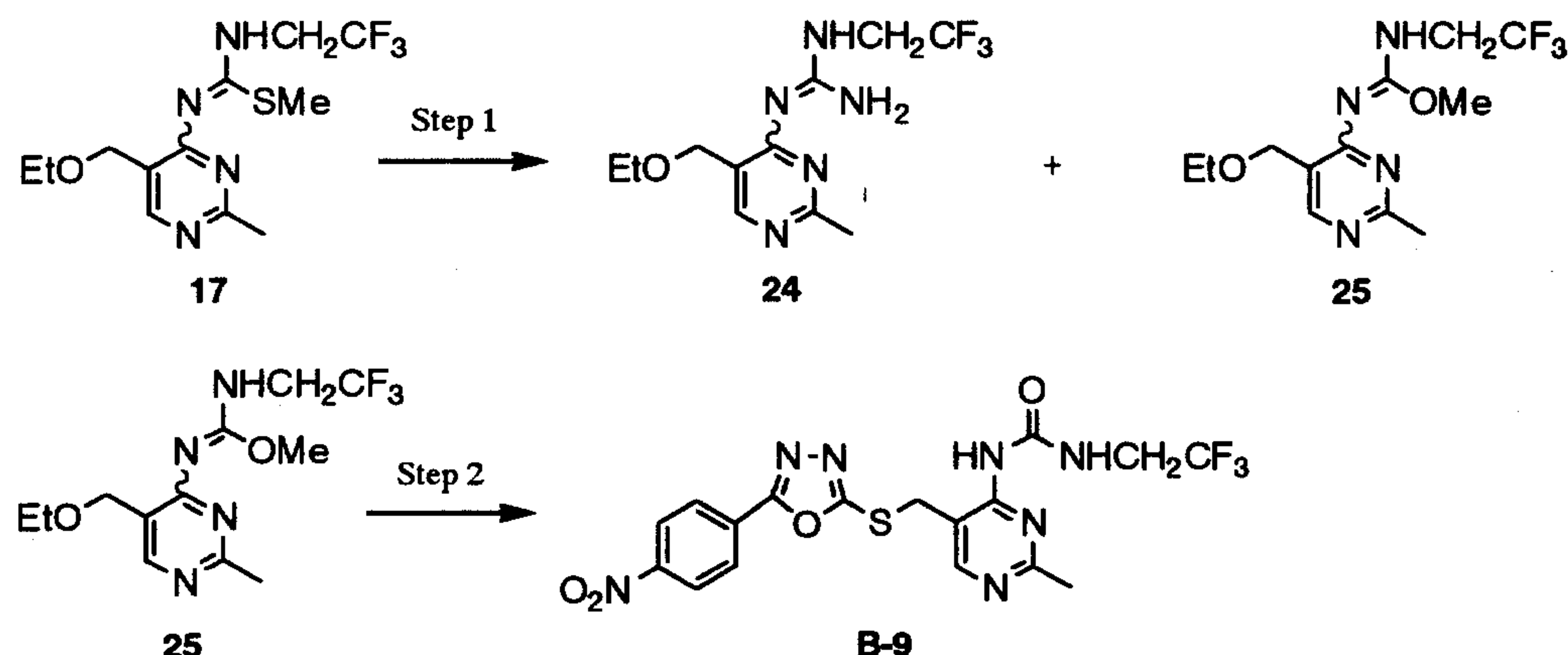
15

Step 5

To a solution of the crude compound **22** (0.02 g) which was obtained at Step 4 in 1 ml of 1,2-dichloroethane were added thionyl chloride (0.01 g) and catalytic amount of DMF with stirring at room temperature. The mixture was stirred for 1 h at room
20 temperature and for 10 min at 80 °C. The solvent was removed under reduced pressure and the residue was dissolved in 1 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (0.02 g) which was obtained by similar method described in a literature (R. W. Young and K. H. Wood. J. Am. Chem. Soc., 77, 400 (1955)) and potassium carbonate (0.06 g) in 1ml of DMF. The reaction
25 mixture was stirred for 1 h at room temperature and added water. The resulting mixture was extracted with ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography and crystalized from methanol/diethyl ether/hexane to give 0.02 g of compound **B-8**. The physical data were shown in Table 5.

30

Example 42



Step 1

A solution of compound **17** (0.95 g), which was obtained by similar method described in reference example 1, in 13 ml of 7N ammonia in methanol was reacted for 4 days at 80 °C in sealed tube. The solvent was removed under reduced pressure and added dichloromethane. The insoluble material was filtered to give 0.21 g of compound **24**. The filtrate was cocentrated under reduced pressure and the residue was subjected to silica gel column chromatography to give 0.39 g of compound **25**.

10 Compound **24**

¹H-NMR(CDCl₃) : 1.27(3H, t, J=7.3), 2.54(3H, s), 3.60(2H, q, J=7.3 Hz), 4.09(2H, q-like, J=8.9 Hz), 4.54(2H, s), 8.34(1H, s).

Compound **25**

¹H-NMR(CDCl₃) : 1.27(3H, t, J=7.3), 2.58(3H, s), 3.61(2H, q, J=7.3 Hz), 3.94(3H, s), 3.91-3.98(2H, m), 4.59(2H, s), 8.44(1H, s), 10.73(1H, br).

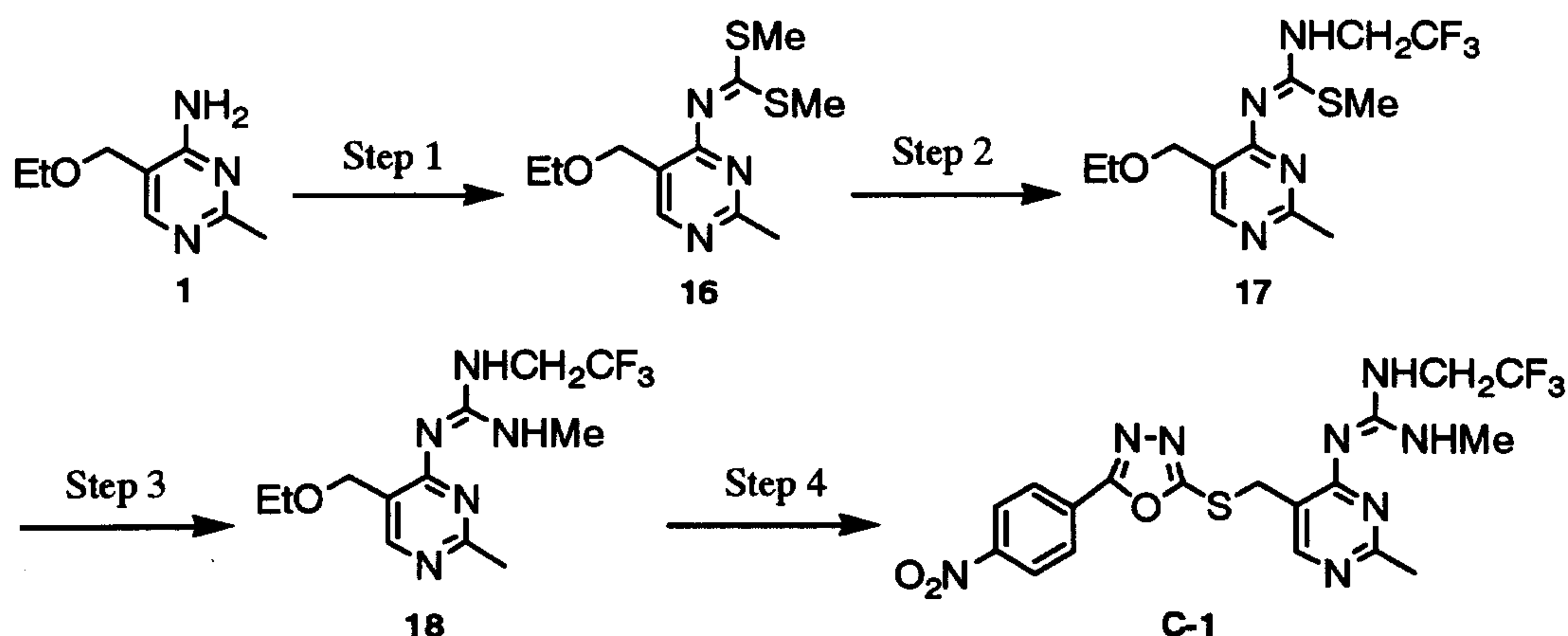
Step 2

A solution of compound **25** (0.10 g) in 1.0 ml of 25% hydrobromic acid/acetic acid was reacted for 7 h at 70 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 1.5 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (0.08 g) and potassium carbonate (0.18 g) in 1 ml of DMF at ice-cooling. The reaction mixture was stirred for 1 h at ice-cooling and added water. The appeared crystal was filtered and crystalized from methanol/dichloromethane/diethyl ether to give 0.06 g of compound **B-9**. The physical

data were shown in Table 5.

Reference

Reference 1



Step 1

To a solution of compound 1 (6.00g) in 40 ml of DMF was added carbon disulfide (6.00 g) and the mixture was added dropwise to a solution of potassium t-butoxide (10.5 g) in 50 ml of DMF at ice-cooling. The reaction mixture was allowed to room temperature and stirred for 1.5 h, and then a solution of methyl iodide (15.3 g) in 10 ml of DMF was added at ice-cooling. The mixture was stirred for 1.5 h at room temperature, and then DMF was removed under reduced pressure and added water. The resulting mixture was extracted with diethyl ether, washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 3.05 g of compound 16.

¹H-NMR(CDCl₃) : 1.24(3H, t, J=7.0 Hz), 2.55(6H, s), 2.67(3H, s), 3.55(2H, q, J=7.0 Hz), 4.43(2H, s), 8.41(1H, s).

Step 2

To a suspension of compound 16 (3.05 g) and 2,2,2-trifluoroethylamine hydrochloride (6.09 g) in 30 ml of DMF was added triethylamine (4.55 g) and the mixture was stirred for 4 days at 50 °C. To the mixture was added water, and then mixture was extracted with diethyl ether, washed with brine, dried over anhydrous magnesium

sulfate, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography to give 2.62 g of compound **17**.

¹H-NMR(CDCl₃) : 1.27(3H, t, J=7.3 Hz), 2.55(3H, s), 2.58(3H, s), 3.60(2H, q, J=7.3 Hz), 4.03(2H, dq, J=8.6 Hz, 6.3 Hz), 4.62(2H, s), 8.50(1H, s).

5

Step 3

A solution of compound **17** (2.62 g) and 40% methylamine in methanol (50 ml) in 15 ml of DMF was stirred for 2 days at 60 °C. The reaction mixture was concentrated under reduced pressure and the residue was subjected to silica gel column chromatography to give 2.10 g of compound **18**.

10

¹H-NMR(CDCl₃) : 1.26(3H, t, J=7.1 Hz), 2.52(3H, s), 2.98(3H, d, J=5.1 Hz), 3.60(2H, q, J=7.1 Hz), 4.20(2H, dq, J=8.9 Hz, 6.4 Hz), 4.52(2H, s), 8.29(1H, s).

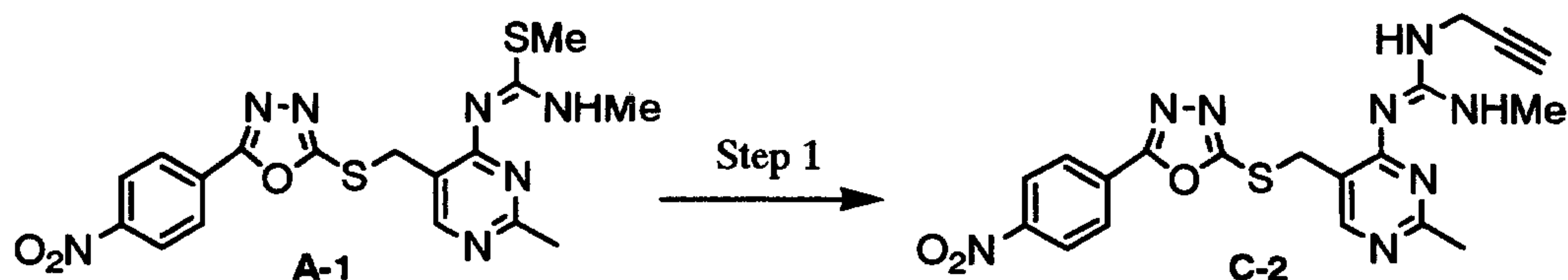
Step 4

A solution of compound **18** (2.10 g) in 20 ml of 25% hydrobromic acid in acetic acid was reacted for 7 h at 70 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 15 ml of DMF. The resulting mixture was added to a suspension of 2-(4-nitrophenyl)-5-mercapto-1,3,4-oxadiazole (1.69 g) and potassium carbonate (3.80 g) in 15 ml of DMF at ice-cooling. The reaction mixture was stirred for 1 h at room temperature and added water. The appeared precipitate was filtered, dried, and subjected to silica gel column chromatography and crystalized from methanol/dichloromethane/diethyl ether to give 3.24 g of compound **C-1**. The physical data was shown in Table 6.

15

20

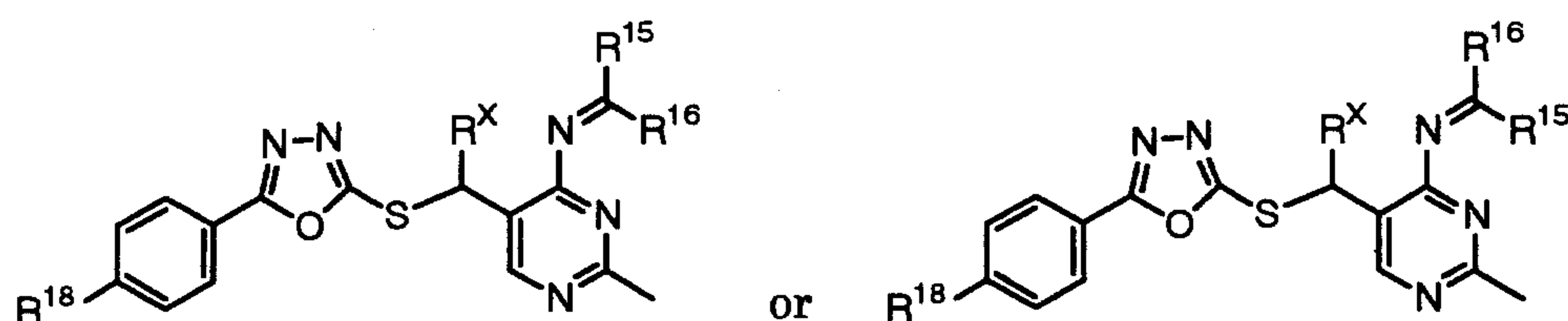
25 Reference 2



Step 1

To a compound **A-1** (4.00 g) were added DMF (200 ml) and propargylamine (7.66 g), and the mixture was stirred for 17 h at 65 °C. DMF was removed under reduced pressure and water and brine were added. The mixture was extracted with ethyl acetate, and the organic layer was dried over anhydrous magnesium sulfate, and concentrated under
5 reduced pressure. The residue was subjected to silica gel column chromatography and crystalized from methanol/dichloromethane/diethyl ether to give 0.74 g of compound **C-2**. The physical data were shown in Table 6.

Table 1



Exam-ple No.	Comp-ound No.	R ¹⁸	R ^X	R ¹⁵	R ¹⁶	¹ H-NMR(CDCl ₃) (δ) ppm
1	A-1	NO ₂	H	SMe	NHMe	2.56(3H, s), 2.57(3H, s), 3.10(3H, d, J = 5.3), 4.58(2H, s), 8.16(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.53(1H, s), 11.18(1H, br)
2	A-2	NO ₂	H	SMe	NH ₂	2.57(3H, s), 2.58(3H, s), 4.60(2H, s), 8.17(2H, d, J = 9.1), 8.36(2H, d, J = 9.1), 8.61(1H, s)
3	A-3	NO ₂	H	SMe	NHEt	1.35(3H, t, J = 7.3), 2.55(3H, s), 2.57(3H, s), 3.45(2H, dq, J = 7.3, 5.3), 4.58(2H, s), 8.16(2H, d, J = 8.7), 8.36(2H, d, J = 8.7), 8.53(1H, s), 11.31(1H, br)
4	A-4	NO ₂	H	SMe	NHPr	1.07(3H, t, J = 7.3), 1.73(2H, sext, J = 7.3), 2.55(3H, s), 2.57(3H, s), 3.38(2H, q, J = 7.3), 4.58(2H, s), 8.16(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.53(1H, s), 11.44(1H, br)
5	A-5	NO ₂	H	SEt	NHMe	1.41(3H, t, J = 7.3), 2.55(3H, s), 3.09(3H, d, J = 5.1), 3.22(2H, q, J = 7.3), 4.57(2H, s), 8.17(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.53(1H, s), 11.23(1H, br)
6	A-6	NO ₂	H	SEt	NHEt	1.34(3H, t, J = 7.3), 1.41(3H, t, J = 7.3), 2.51(3H, s), 3.21(2H, q, J = 7.3), 3.44(2H, dq, J = 7.3, 5.3), 4.57(2H, s), 8.17(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.53(1H, s), 11.39(1H, br)
7	A-7	NO ₂	H	SPr	NHMe	1.05(3H, t, J = 7.3), 1.80(2H, sext, J = 7.3), 2.55(3H, s), 3.10(3H, d, J = 5.1), 3.19(2H, t, J = 7.3), 4.56(2H, s), 8.17(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.53(1H, s), 11.26(1H, br)
8	A-8	NO ₂	H	SPr	NHEt	1.05(3H, t, J = 7.3), 1.34(3H, t, J = 7.3), 1.79(2H, sext, J = 7.3), 2.54(3H, s), 3.18(2H, t, J = 7.3), 3.45(2H, dq, J = 7.3, 5.4), 4.56(2H, s), 8.17(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.53(1H, s), 11.38(1H, br)
9	A-9	NH ₂	H	SMe	NH ₂	2.56(3H, s), 2.58(3H, s), 4.03(2H, s), 4.53(2H, s), 6.71(2H, d, J = 8.7), 7.76(2H, d, J = 8.7), 8.58(1H, s)

Table 2

Exam-ple No.	Comp-ound No.	R ¹⁸	R ^x	R ¹⁵	R ¹⁶	¹ H-NMR(CDCl ₃) (δ) ppm
10	A-10	NH ₂	H	SMe	NHMe	2.55(3H, s), 2.56(3H, s), 3.08(3H, d, J = 5.3), 4.02(2H, br), 4.51(2H, s), 6.70(2H, d, J = 8.9), 7.76(2H, d, J = 8.9), 8.49(1H, s), 11.13(1H, br)
11	A-11	NH ₂	H	SMe	NHEt	1.34(3H, t, J = 7.3), 2.54(3H, s), 2.56(3H, s), 3.43(2H, dq, J = 7.3, 5.4), 3.50(2H, br), 4.01(2H, s), 6.71(2H, d, J = 8.7), 7.76(2H, d, J = 8.7), 8.49(1H, s), 11.30(1H, br)
12	A-12	NH ₂	H	SMe	NHPr	1.06(3H, t, J = 7.3), 1.72(2H, sext, J = 7.3), 2.54(3H, s), 2.56(3H, s), 3.36(2H, q, J = 7.3), 4.02(2H, br), 4.51(2H, s), 6.71(2H, d, J = 8.7), 7.76(2H, d, J = 8.7), 8.49(1H, s)
13	A-13	NH ₂	H	SEt	NHMe	1.41(3H, t, J = 7.3), 2.55(3H, s), 3.08(3H, d, J = 5.1), 3.21(2H, q, J = 7.3), 4.02(2H, br), 4.51(2H, s), 6.70(2H, d, J = 8.5), 7.76(2H, d, J = 8.5), 8.50(1H, s)
14	A-14	NH ₂	H	SEt	NHEt	1.33(3H, t, J = 7.3), 1.39(3H, t, J = 7.3), 2.54(3H, s), 3.20(2H, q, J = 7.3), 3.43(2H, dq, J = 7.3, 5.4), 4.02(2H, br), 4.50(2H, s), 6.71(2H, d, J = 8.9), 7.77(2H, d, J = 8.9), 8.49(1H, s), 11.33(1H, br)
15	A-15	NH ₂	H	SPr	NHMe	1.04(3H, t, J = 7.3), 1.78(2H, sext, J = 7.3), 2.54(3H, s), 3.08(3H, d, J = 5.3), 3.18(2H, t, J = 7.3), 4.03(2H, br), 4.49(2H, s), 6.70(2H, d, J = 8.9), 7.76(2H, d, J = 8.9), 8.49(1H, s), 11.20(1H, br)
16	A-16	NH ₂	H	SPr	NHEt	1.04(3H, t, J = 7.3), 1.33(3H, t, J = 7.3), 1.78(2H, sext, J = 7.3), 2.54(3H, s), 3.18(2H, t, J = 7.3), 3.44(2H, dq, J = 7.3, 5.4), 4.01(2H, br), 4.49(2H, s), 6.71(2H, d, J = 8.9), 7.76(2H, d, J = 8.9), 8.49(1H, s), 11.35(1H, br)
17	A-17	Me	H	SMe	NHPr	1.06(3H, t, J = 7.3), 1.72(2H, sext, J = 7.3), 2.41(3H, s), 2.54(3H, s), 2.56(3H, s), 3.37(2H, dt, J = 5.4, 7.3), 4.54(2H, s), 7.28(2H, d, J = 8.2), 7.86(2H, d, J = 8.2), 8.51(1H, s)
18	A-18	NO ₂	H	NHNMe ₂	NHPr	1.00(3H, t, J = 7.3), 1.67(2H, sext, J = 7.3), 2.51(3H, s), 2.64(6H, s), 3.44(2H, q, J = 7.3), 4.52(2H, s), 6.39(1H, br), 8.18(2H, d, J = 9.0), 8.34(1H, s), 8.36(2H, d, J = 9.0)

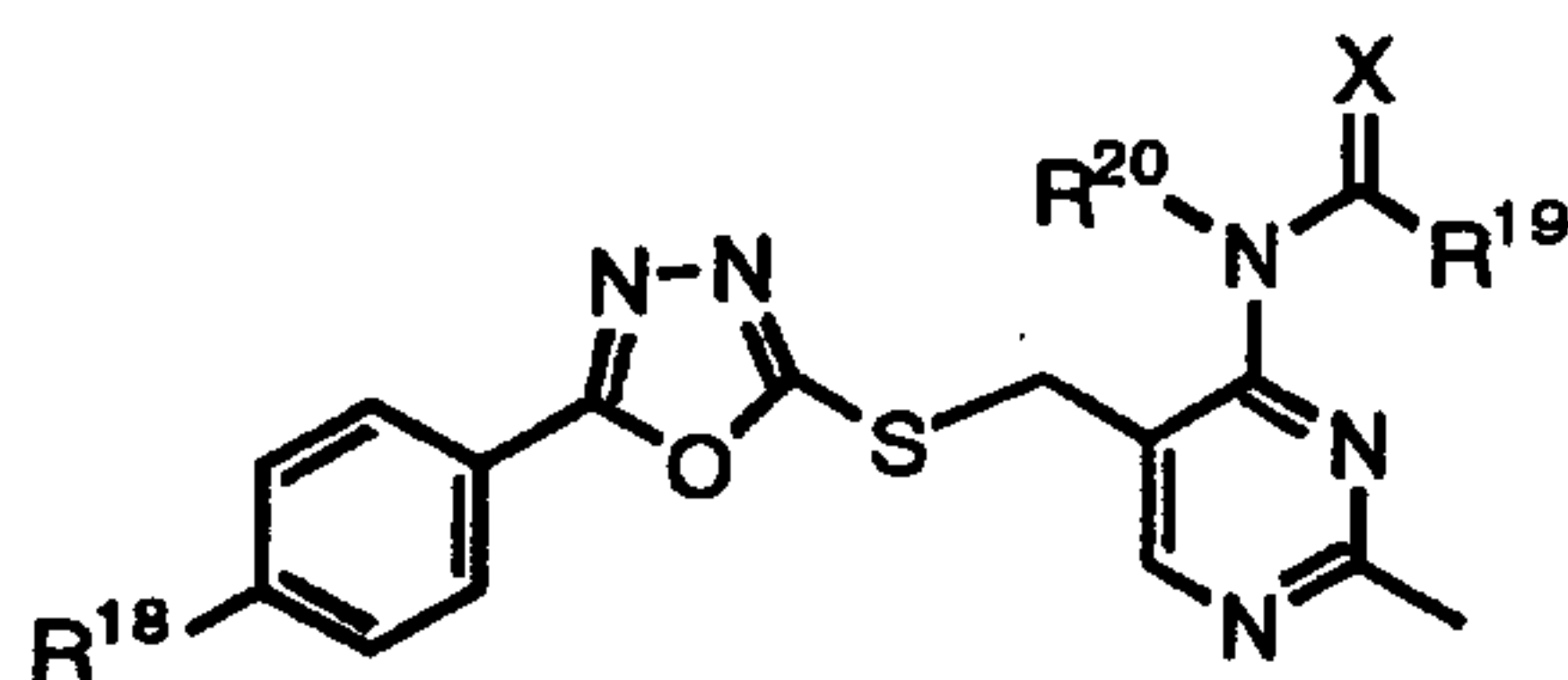
Table 3

Exam -ple No.	Comp -ound No.	R ¹⁸	R ^X	R ¹⁵	R ¹⁶	¹ H-NMR(CDCl ₃) (δ) ppm
19	A-19	NO ₂	H	NHOMe	NHMe	2.52(1.95H, s), 2.58(1.05H, s), 2.83(1.05H, d, J = 5.1), 3.05(1.95H, d, J = 5.1), 3.75(1.05H, s), 3.81(1.95H, s), 4.49(0.7H, s), 4.53(1.3H, s), 5.62(0.65H, br), 7.77(0.35H, br), 8.16(2H, d, J = 8.5), 8.35(2H, d, J = 8.5), 8.36(1H, s)
20	A-20	NO ₂	H	S(CH ₂) ₃ NH		2.13 - 2.25(2H, m), 2.53(3H, s), 3.08 - 3.13(2H, m), 3.55 - 3.65(2H, m), 4.50(2H, s), 8.16(2H, d, J = 8.9), 8.35(2H, d, J = 8.9), 8.49(1H, s), 11.85(1H, br)
21	A-21	NO ₂	H	S(CH ₂) ₂ NH		2.59(3H, s), 3.31(2H, t, J = 7.3), 3.92(2H, br), 4.53(2H, s), 8.16(2H, d, J = 8.9), 8.35(2H, d, J = 8.9), 8.55(1H, s)
22	A-22	NO ₂	Me	SMe	NHEt	1.34(3H, t, J = 7.2), 1.95(3H, d, J = 7.2), 2.56(3H, s), 2.57(3H, s), 3.44(2H, dq, J = 5.4, 7.2), 5.49(1H, q, J = 7.2), 8.16(2H, d, J = 8.8), 8.35(2H, d, J = 8.8), 8.46(1H, s), 11.36(1H, br)
23	A-23	NO ₂	Me	NHEt	NHEt	1.29(6H, t, J = 7.1), 1.95(3H, d, J = 7.1), 2.48(3H, s), 3.39(4H, br), 5.33(1H, q, J = 7.1), 8.17(2H, d, J = 9.0), 8.25(1H, s), 8.34(2H, d, J = 9.0)
24	A-24	NO ₂	H	OMe	NHMe	2.56(3H, s), 2.99(3H, d, J = 5.1), 3.98(3H, s), 4.55(2H, s), 8.16(2H, d, J = 9.2), 8.41(2H, d, J = 9.2), 8.47(1H, s), 9.96(1H, br)
25	A-25	NO ₂	H	OEt	NHMe	1.40(3H, t, J = 7.2), 2.55(3H, s), 2.98(3H, d, J = 4.9), 4.45(2H, q, J = 7.2), 4.53(2H, s), 8.16(2H, d, J = 9.0), 8.35(2H, d, J = 9.0), 8.45(1H, s), 10.01(1H, br)
26	A-26	Me	H	OMe	NHPr	1.02(3H, t, J = 7.3), 1.63(2H, tq, J = 6.8, 7.3), 2.41(3H, s), 2.54(3H, s), 3.31(2H, dt, J = 5.6, 6.8), 3.95(3H, s), 4.51(2H, s), 7.28(2H, d, J = 8.3), 7.86(2H, d, J = 8.3), 8.44(1H, s), 10.18(1H, br)
27	A-27	Me	H	OEt	NHPr	1.02(3H, t, J = 7.3), 1.37(3H, t, J = 7.1), 1.64(2H, sext, J = 7.3), 2.41(3H, s), 2.54(3H, s), 3.32(2H, dt, J = 5.5, 7.3), 4.44(2H, q, J = 7.1), 4.49(2H, s), 7.28(2H, d, J = 8.4), 7.86(2H, d, J = 8.4), 8.43(1H, s)
33	A-28	Cl	H	SEt	SEt	1.37(6H, t, J = 7.4), 2.67(3H, s), 3.16(4H, q, J = 7.4), 4.44(2H, s), 7.47(2H, d, J = 8.9), 7.92(2H, d, J = 8.9), 8.67(1H, s),

Table 4

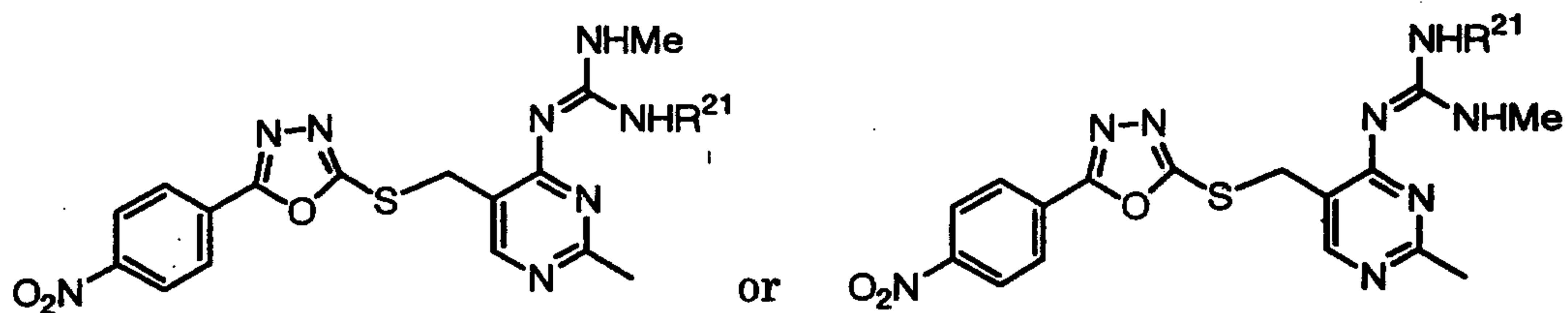
Exam -ple No.	Comp -ound No.	R ¹⁸	R ^x	R ¹⁵	R ¹⁶	¹ H-NMR(CDCl ₃) (δ) ppm
34	A-29	NO ₂	H	SMe	NHC H ₂ CF ₃	2.58(3H, s), 2.61(3H, s), 4.05(2H, dq, J= 6.4, 8.7), 4.60(2H, s), 8.16(2H, d, J = 8.9), 8.35(2H, d, J = 8.9), 8.63(1H, s), 12.03(1H, br).
35	A-30	NH ₂	H	SMe	NHC H ₂ CF ₃	2.57(3H, s), 2.60(3H, s), 4.02(2H, br), 4.03(2H, dq, J= 6.5, 8.7), 4.53(2H, s), 6.71(2H, d, J = 8.8), 7.76(2H, d, J = 8.8), 8.59(1H, s), 12.02(1H, br).
36	A-31	NO ₂	H	SMe	NHPh	2.54(3H, s), 2.59(3H, s), 4.64(2H, s), 7.34(1H, t, J = 7.6), 7.35(2H, d, J = 7.6), 7.44(2H, t, J = 7.6), 8.17(2H, d, J = 9.2), 8.36(2H, d, J = 9.2), 8.63(1H, s), 13.11(1H, br).
37	A-32	NO ₂	H	OMe	NHEt	1.26(3H, t, J = 7.3), 2.55(3H, s), 3.39(2H, dq, J= 5.6, 7.3), 3.97(3H, s), 4.55(2H, s), 8.16(2H, d, J = 9.0), 8.35(2H, d, J = 9.0), 8.46(1H, s), 10.09(1H, t-like, J = 5.6).
38	A-33	NO ₂	H	OEt	NHEt	1.27(3H, t, J = 7.3), 1.39(3H, t, J = 7.1), 2.55(3H, s), 3.40(2H, dq, J= 5.6, 7.3), 4.45(2H, q, J = 7.1), 4.53(2H, s), 8.16(2H, d, J = 9.0), 8.35(2H, d, J = 9.0), 8.45(1H, s), 10.14(1H, t-like, J = 5.6).
39	A-34	NO ₂	H	O ⁱ Pr	NHMe	1.38(6H, d, J = 6.1), 2.55(3H, s), 2.96(3H, d, J= 4.9), 4.52(2H, s), 5.40(1H, sept, J = 6.1), 8.17(2H, d, J = 8.9), 8.35(2H, d, J = 8.9), 8.44(1H, s), 10.06(1H, br).
40	A-35	NO ₂	H	O ⁱ Pr	NHEt	1.26(3H, t, J = 7.3), 1.37(6H, d, J = 6.3), 2.54(3H, s), 3.38(2H, dq, J= 5.4, 7.3), 4.52(2H, s), 5.40(1H, sept, J = 6.3), 8.17(2H, d, J = 9.0), 8.35(2H, d, J = 9.0), 8.44(1H, s), 10.19(1H, br).

Table 5



Exam- ple No.	Comp- ound No.	R ¹⁸	R ²⁰	R ¹⁹	X	¹ H-NMR(CDCl ₃) (δ) ppm
28	B-1	NO ₂	H	NHEt	O	1.28(3H, t, J = 7.3), 2.60(3H, s), 3.45(2H, dq, J = 5.1, 7.3), 4.60(2H, s), 8.17(2H, d, J = 8.8), 8.36(2H, d, J = 8.8), 8.54(1H, s), 8.85(1H, br), 9.64(1H, t-like, J = 5.1)
29	B-2	Cl	H	NHEt	O	1.27(3H, t, J = 7.2), 2.59(3H, s), 3.44(2H, dq, J = 5.2, 7.2), 4.57(2H, s), 7.46(2H, d, J = 8.5), 7.90(2H, d, J = 8.5), 8.52(1H, s), 8.97(1H, br), 9.66(1H, t-like, J = 5.2)
30	B-3	NH ₂	H	NHEt	O	1.27(3H, t, J = 7.3), 2.59(3H, s), 3.44(2H, dq, J = 5.2, 7.3), 4.03(2H, br), 4.49(2H, s), 6.69(2H, d, J = 8.5), 7.75(2H, d, J = 8.5), 8.47(1H, s), 8.67(1H, br), 9.59(1H, t-like, J = 5.2)
31	B-4	NO ₂	H	NHPr	O	1.03(3H, t, J = 7.3), 1.67(2H, sext, J = 7.3), 2.60(3H, s), 3.39(2H, dt, J = 5.2, 7.3), 4.62(2H, s), 8.17(2H, d, J = 8.8), 8.35(2H, d, J = 8.8), 8.57(1H, s), 9.13(1H, br), 9.79(1H, t-like, J = 5.2)
32	B-5	Cl	H	NHEt	S	1.29(3H, t, J = 7.2), 2.64(3H, s), 3.80(2H, dq, J = 5.2, 7.2), 4.43(2H, s), 7.50(2H, d, J = 8.7), 7.98(2H, d, J = 8.7), 8.14(1H, br), 8.28(1H, s)
33	B-6	Cl	H	SEt	S	1.35(3H, t, J = 7.3), 2.62(3H, s), 3.38(2H, q, J = 7.3), 4.65(2H, s), 7.49(2H, d, J = 8.7), 8.01(2H, d, J = 8.7), 8.27(1H, s)
33	B-7	Cl	Et	SEt	S	1.33(3H, t, J = 7.4), 1.45(3H, t, J = 7.2), 2.65(3H, s), 3.36(2H, q, J = 7.4), 4.02(2H, q, J = 7.2), 4.64(2H, s), 7.47(2H, d, J = 8.8), 7.83(2H, d, J = 8.8), 8.48(1H, s)
41	B-8	NO ₂	H	NH(C H ₂) ₃ Cl	O	2.11(2H, quint, J = 6.3), 2.62(3H, s), 3.62(2H, q, J = 6.3), 3.68(2H, t, J = 6.3), 4.62(2H, s), 8.17(2H, d, J = 8.8), 8.36(2H, d, J = 8.8), 9.14(1H, br), 9.91(1H, t, J = 6.1)
42	B-9	NO ₂	H	NHCH 2CF ₃	O	2.62(3H, s), 4.10(2H, dq, J = 8.9, 6.3), 4.63(2H, s), 8.18(2H, d, J = 8.9), 8.36(2H, d, J = 8.9), 8.64(1H, s), 9.48(1H, br), 10.52(1H, t, J = 6.3)

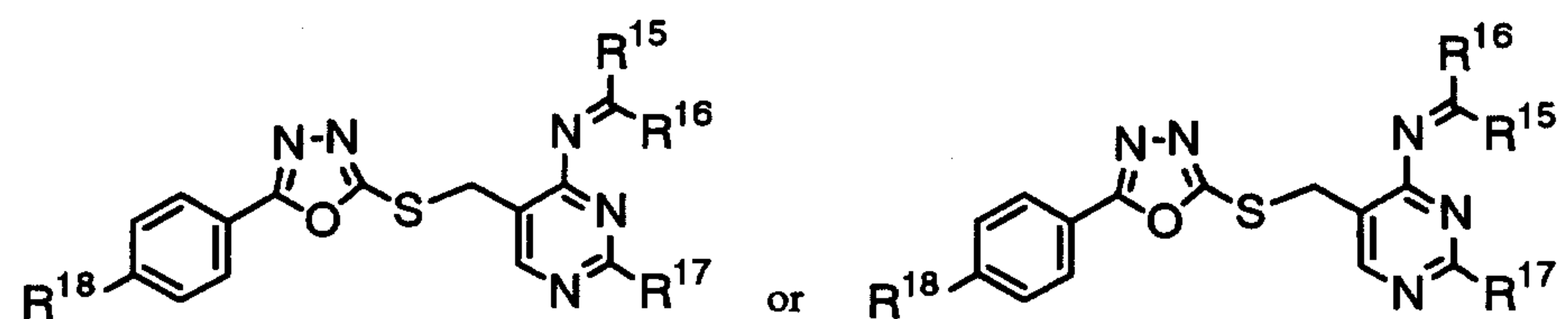
Table 6



Refer- ence No.	Comp- ound No.	R ²¹	¹ H-NMR (δ) ppm
1	C-1	CH ₂ CF ₃	2.41(3H, s), 2.91(3H, d, J = 4.6), 4.24(2H, dq, J = 9.5, 5.7), 4.46(2H, s), 7.37(1H, br), 8.22(2H, d, J = 8.8), 8.28(1H, s), 8.41(2H, d, J = 8.8), 10.20(1H, br) (in DMSO-d ₆)
2	C-2	CH ₂ C=CH	2.33(1H, s), 2.51(3H, s), 3.00(3H, d, J = 4.9), 4.24(2H, br), 4.54(2H, s), 8.16(2H, d, J = 9.1), 8.35(2H, d, J = 9.1), 8.38(1H, s) (in CDCl ₃)

Compounds **D-1** to **D-1700** shown in Table 7 to Table 23 are able to synthesize in a manner similar to those described in Example 1 or Example 18, and were compounds **E-1** to **E-60** shown in Table 24 are able to synthesize in a manner similar to described in Example 20 .

5 Table 7 to Table 24



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Table 7

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1	NH ₂	SH	H	4-NH ₂	D-51	NH-allyl	SH	H	4-NH ₂
D-2	NH ₂	SMe	H	4-NH ₂	D-52	NH-allyl	SMe	H	4-NH ₂
D-3	NH ₂	SEt	H	4-NH ₂	D-53	NH-allyl	SEt	H	4-NH ₂
D-4	NH ₂	S-n-Pr	H	4-NH ₂	D-54	NH-allyl	S-n-Pr	H	4-NH ₂
D-5	NH ₂	S-i-Pr	H	4-NH ₂	D-55	NH-allyl	S-i-Pr	H	4-NH ₂
D-6	NH ₂	S-n-Bu	H	4-NH ₂	D-56	NH-allyl	S-n-Bu	H	4-NH ₂
D-7	NH ₂	S-allyl	H	4-NH ₂	D-57	NH-allyl	S-allyl	H	4-NH ₂
D-8	NH ₂	S-propargyl	H	4-NH ₂	D-58	NH-allyl	S-propargyl	H	4-NH ₂
D-9	NH ₂	SCH ₂ CF ₃	H	4-NH ₂	D-59	NH-allyl	SCH ₂ CF ₃	H	4-NH ₂
D-10	NH ₂	SCH ₂ CH ₂ F	H	4-NH ₂	D-60	NH-allyl	SCH ₂ CH ₂ F	H	4-NH ₂
D-11	NHMe	SH	H	4-NH ₂	D-61	NH-propargyl	SH	H	4-NH ₂
D-12	NHMe	SMe	H	4-NH ₂	D-62	NH-propargyl	SMe	H	4-NH ₂
D-13	NHMe	SEt	H	4-NH ₂	D-63	NH-propargyl	SEt	H	4-NH ₂
D-14	NHMe	S-n-Pr	H	4-NH ₂	D-64	NH-propargyl	S-n-Pr	H	4-NH ₂
D-15	NHMe	S-i-Pr	H	4-NH ₂	D-65	NH-propargyl	S-i-Pr	H	4-NH ₂
D-16	NHMe	S-n-Bu	H	4-NH ₂	D-66	NH-propargyl	S-n-Bu	H	4-NH ₂
D-17	NHMe	S-allyl	H	4-NH ₂	D-67	NH-propargyl	S-allyl	H	4-NH ₂
D-18	NHMe	S-propargyl	H	4-NH ₂	D-68	NH-propargyl	S-propargyl	H	4-NH ₂
D-19	NHMe	SCH ₂ CF ₃	H	4-NH ₂	D-69	NH-propargyl	SCH ₂ CF ₃	H	4-NH ₂
D-20	NHMe	SCH ₂ CH ₂ F	H	4-NH ₂	D-70	NH-propargyl	SCH ₂ CH ₂ F	H	4-NH ₂
D-21	NHEt	SH	H	4-NH ₂	D-71	NHCH ₂ CF ₃	SH	H	4-NH ₂
D-22	NHEt	SMe	H	4-NH ₂	D-72	NHCH ₂ CF ₃	SMe	H	4-NH ₂
D-23	NHEt	SEt	H	4-NH ₂	D-73	NHCH ₂ CF ₃	SEt	H	4-NH ₂
D-24	NHEt	S-n-Pr	H	4-NH ₂	D-74	NHCH ₂ CF ₃	S-n-Pr	H	4-NH ₂
D-25	NHEt	S-i-Pr	H	4-NH ₂	D-75	NHCH ₂ CF ₃	S-i-Pr	H	4-NH ₂
D-26	NHEt	S-n-Bu	H	4-NH ₂	D-76	NHCH ₂ CF ₃	S-n-Bu	H	4-NH ₂
D-27	NHEt	S-allyl	H	4-NH ₂	D-77	NHCH ₂ CF ₃	S-allyl	H	4-NH ₂
D-28	NHEt	S-propargyl	H	4-NH ₂	D-78	NHCH ₂ CF ₃	S-propargyl	H	4-NH ₂
D-29	NHEt	SCH ₂ CF ₃	H	4-NH ₂	D-79	NHCH ₂ CF ₃	SCH ₂ CF ₃	H	4-NH ₂
D-30	NHEt	SCH ₂ CH ₂ F	H	4-NH ₂	D-80	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	H	4-NH ₂
D-31	NHPr	SH	H	4-NH ₂	D-81	NHCH ₂ CH ₂ F	SH	H	4-NH ₂
D-32	NHPr	SMe	H	4-NH ₂	D-82	NHCH ₂ CH ₂ F	SMe	H	4-NH ₂
D-33	NHPr	SEt	H	4-NH ₂	D-83	NHCH ₂ CH ₂ F	SEt	H	4-NH ₂
D-34	NHPr	S-n-Pr	H	4-NH ₂	D-84	NHCH ₂ CH ₂ F	S-n-Pr	H	4-NH ₂
D-35	NHPr	S-i-Pr	H	4-NH ₂	D-85	NHCH ₂ CH ₂ F	S-i-Pr	H	4-NH ₂
D-36	NHPr	S-n-Bu	H	4-NH ₂	D-86	NHCH ₂ CH ₂ F	S-n-Bu	H	4-NH ₂
D-37	NHPr	S-allyl	H	4-NH ₂	D-87	NHCH ₂ CH ₂ F	S-allyl	H	4-NH ₂
D-38	NHPr	S-propargyl	H	4-NH ₂	D-88	NHCH ₂ CH ₂ F	S-propargyl	H	4-NH ₂
D-39	NHPr	SCH ₂ CF ₃	H	4-NH ₂	D-89	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	H	4-NH ₂
D-40	NHPr	SCH ₂ CH ₂ F	H	4-NH ₂	D-90	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	H	4-NH ₂
D-41	NH-i-Pr	SH	H	4-NH ₂	D-91	NH-n-Bu	SH	H	4-NH ₂
D-42	NH-i-Pr	SMe	H	4-NH ₂	D-92	NH-n-Bu	SMe	H	4-NH ₂
D-43	NH-i-Pr	SEt	H	4-NH ₂	D-93	NH-n-Bu	SEt	H	4-NH ₂
D-44	NH-i-Pr	S-n-Pr	H	4-NH ₂	D-94	NH-n-Bu	S-n-Pr	H	4-NH ₂
D-45	NH-i-Pr	S-i-Pr	H	4-NH ₂	D-95	NH-n-Bu	S-i-Pr	H	4-NH ₂
D-46	NH-i-Pr	S-n-Bu	H	4-NH ₂	D-96	NH-n-Bu	S-n-Bu	H	4-NH ₂
D-47	NH-i-Pr	S-allyl	H	4-NH ₂	D-97	NH-n-Bu	S-allyl	H	4-NH ₂
D-48	NH-i-Pr	S-propargyl	H	4-NH ₂	D-98	NH-n-Bu	S-propargyl	H	4-NH ₂
D-49	NH-i-Pr	SCH ₂ CF ₃	H	4-NH ₂	D-99	NH-n-Bu	SCH ₂ CF ₃	H	4-NH ₂
D-50	NH-i-Pr	SCH ₂ CH ₂ F	H	4-NH ₂	D-100	NH-n-Bu	SCH ₂ CH ₂ F	H	4-NH ₂

Table 8

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-101	NH ₂	SH	H	2-NH ₂	D-151	NH-allyl	SH	H	2-NH ₂
D-102	NH ₂	SMe	H	2-NH ₂	D-152	NH-allyl	SMe	H	2-NH ₂
D-103	NH ₂	SEt	H	2-NH ₂	D-153	NH-allyl	SEt	H	2-NH ₂
D-104	NH ₂	S-n-Pr	H	2-NH ₂	D-154	NH-allyl	S-n-Pr	H	2-NH ₂
D-105	NH ₂	S-i-Pr	H	2-NH ₂	D-155	NH-allyl	S-i-Pr	H	2-NH ₂
D-106	NH ₂	S-n-Bu	H	2-NH ₂	D-156	NH-allyl	S-n-Bu	H	2-NH ₂
D-107	NH ₂	S-allyl	H	2-NH ₂	D-157	NH-allyl	S-allyl	H	2-NH ₂
D-108	NH ₂	S-propargyl	H	2-NH ₂	D-158	NH-allyl	S-propargyl	H	2-NH ₂
D-109	NH ₂	SCH ₂ CF ₃	H	2-NH ₂	D-159	NH-allyl	SCH ₂ CF ₃	H	2-NH ₂
D-110	NH ₂	SCH ₂ CH ₂ F	H	2-NH ₂	D-160	NH-allyl	SCH ₂ CH ₂ F	H	2-NH ₂
D-111	NHMe	SH	H	2-NH ₂	D-161	NH-propargyl	SH	H	2-NH ₂
D-112	NHMe	SMe	H	2-NH ₂	D-162	NH-propargyl	SMe	H	2-NH ₂
D-113	NHMe	SEt	H	2-NH ₂	D-163	NH-propargyl	SEt	H	2-NH ₂
D-114	NHMe	S-n-Pr	H	2-NH ₂	D-164	NH-propargyl	S-n-Pr	H	2-NH ₂
D-115	NHMe	S-i-Pr	H	2-NH ₂	D-165	NH-propargyl	S-i-Pr	H	2-NH ₂
D-116	NHMe	S-n-Bu	H	2-NH ₂	D-166	NH-propargyl	S-n-Bu	H	2-NH ₂
D-117	NHMe	S-allyl	H	2-NH ₂	D-167	NH-propargyl	S-allyl	H	2-NH ₂
D-118	NHMe	S-propargyl	H	2-NH ₂	D-168	NH-propargyl	S-propargyl	H	2-NH ₂
D-119	NHMe	SCH ₂ CF ₃	H	2-NH ₂	D-169	NH-propargyl	SCH ₂ CF ₃	H	2-NH ₂
D-120	NHMe	SCH ₂ CH ₂ F	H	2-NH ₂	D-170	NH-propargyl	SCH ₂ CH ₂ F	H	2-NH ₂
D-121	NHEt	SH	H	2-NH ₂	D-171	NHCH ₂ CF ₃	SH	H	2-NH ₂
D-122	NHEt	SMe	H	2-NH ₂	D-172	NHCH ₂ CF ₃	SMe	H	2-NH ₂
D-123	NHEt	SEt	H	2-NH ₂	D-173	NHCH ₂ CF ₃	SEt	H	2-NH ₂
D-124	NHEt	S-n-Pr	H	2-NH ₂	D-174	NHCH ₂ CF ₃	S-n-Pr	H	2-NH ₂
D-125	NHEt	S-i-Pr	H	2-NH ₂	D-175	NHCH ₂ CF ₃	S-i-Pr	H	2-NH ₂
D-126	NHEt	S-n-Bu	H	2-NH ₂	D-176	NHCH ₂ CF ₃	S-n-Bu	H	2-NH ₂
D-127	NHEt	S-allyl	H	2-NH ₂	D-177	NHCH ₂ CF ₃	S-allyl	H	2-NH ₂
D-128	NHEt	S-propargyl	H	2-NH ₂	D-178	NHCH ₂ CF ₃	S-propargyl	H	2-NH ₂
D-129	NHEt	SCH ₂ CF ₃	H	2-NH ₂	D-179	NHCH ₂ CF ₃	SCH ₂ CF ₃	H	2-NH ₂
D-130	NHEt	SCH ₂ CH ₂ F	H	2-NH ₂	D-180	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	H	2-NH ₂
D-131	NHPr	SH	H	2-NH ₂	D-181	NHCH ₂ CH ₂ F	SH	H	2-NH ₂
D-132	NHPr	SMe	H	2-NH ₂	D-182	NHCH ₂ CH ₂ F	SMe	H	2-NH ₂
D-133	NHPr	SEt	H	2-NH ₂	D-183	NHCH ₂ CH ₂ F	SEt	H	2-NH ₂
D-134	NHPr	S-n-Pr	H	2-NH ₂	D-184	NHCH ₂ CH ₂ F	S-n-Pr	H	2-NH ₂
D-135	NHPr	S-i-Pr	H	2-NH ₂	D-185	NHCH ₂ CH ₂ F	S-i-Pr	H	2-NH ₂
D-136	NHPr	S-n-Bu	H	2-NH ₂	D-186	NHCH ₂ CH ₂ F	S-n-Bu	H	2-NH ₂
D-137	NHPr	S-allyl	H	2-NH ₂	D-187	NHCH ₂ CH ₂ F	S-allyl	H	2-NH ₂
D-138	NHPr	S-propargyl	H	2-NH ₂	D-188	NHCH ₂ CH ₂ F	S-propargyl	H	2-NH ₂
D-139	NHPr	SCH ₂ CF ₃	H	2-NH ₂	D-189	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	H	2-NH ₂
D-140	NHPr	SCH ₂ CH ₂ F	H	2-NH ₂	D-190	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	H	2-NH ₂
D-141	NH-i-Pr	SH	H	2-NH ₂	D-191	NH-n-Bu	SH	H	2-NH ₂
D-142	NH-i-Pr	SMe	H	2-NH ₂	D-192	NH-n-Bu	SMe	H	2-NH ₂
D-143	NH-i-Pr	SEt	H	2-NH ₂	D-193	NH-n-Bu	SEt	H	2-NH ₂
D-144	NH-i-Pr	S-n-Pr	H	2-NH ₂	D-194	NH-n-Bu	S-n-Pr	H	2-NH ₂
D-145	NH-i-Pr	S-i-Pr	H	2-NH ₂	D-195	NH-n-Bu	S-i-Pr	H	2-NH ₂
D-146	NH-i-Pr	S-n-Bu	H	2-NH ₂	D-196	NH-n-Bu	S-n-Bu	H	2-NH ₂
D-147	NH-i-Pr	S-allyl	H	2-NH ₂	D-197	NH-n-Bu	S-allyl	H	2-NH ₂
D-148	NH-i-Pr	S-propargyl	H	2-NH ₂	D-198	NH-n-Bu	S-propargyl	H	2-NH ₂
D-149	NH-i-Pr	SCH ₂ CF ₃	H	2-NH ₂	D-199	NH-n-Bu	SCH ₂ CF ₃	H	2-NH ₂
D-150	NH-i-Pr	SCH ₂ CH ₂ F	H	2-NH ₂	D-200	NH-n-Bu	SCH ₂ CH ₂ F	H	2-NH ₂

Table 9

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-201	NH ₂	SH	H	4-Cl	D-251	NH-allyl	SH	H	4-Cl
D-202	NH ₂	SMe	H	4-Cl	D-252	NH-allyl	SMe	H	4-Cl
D-203	NH ₂	SEt	H	4-Cl	D-253	NH-allyl	SEt	H	4-Cl
D-204	NH ₂	S-n-Pr	H	4-Cl	D-254	NH-allyl	S-n-Pr	H	4-Cl
D-205	NH ₂	S-i-Pr	H	4-Cl	D-255	NH-allyl	S-i-Pr	H	4-Cl
D-206	NH ₂	S-n-Bu	H	4-Cl	D-256	NH-allyl	S-n-Bu	H	4-Cl
D-207	NH ₂	S-allyl	H	4-Cl	D-257	NH-allyl	S-allyl	H	4-Cl
D-208	NH ₂	S-propargyl	H	4-Cl	D-258	NH-allyl	S-propargyl	H	4-Cl
D-209	NH ₂	SCH ₂ CF ₃	H	4-Cl	D-259	NH-allyl	SCH ₂ CF ₃	H	4-Cl
D-210	NH ₂	SCH ₂ CH ₂ F	H	4-Cl	D-260	NH-allyl	SCH ₂ CH ₂ F	H	4-Cl
D-211	NHMe	SH	H	4-Cl	D-261	NH-propargyl	SH	H	4-Cl
D-212	NHMe	SMe	H	4-Cl	D-262	NH-propargyl	SMe	H	4-Cl
D-213	NHMe	SEt	H	4-Cl	D-263	NH-propargyl	SEt	H	4-Cl
D-214	NHMe	S-n-Pr	H	4-Cl	D-264	NH-propargyl	S-n-Pr	H	4-Cl
D-215	NHMe	S-i-Pr	H	4-Cl	D-265	NH-propargyl	S-i-Pr	H	4-Cl
D-216	NHMe	S-n-Bu	H	4-Cl	D-266	NH-propargyl	S-n-Bu	H	4-Cl
D-217	NHMe	S-allyl	H	4-Cl	D-267	NH-propargyl	S-allyl	H	4-Cl
D-218	NHMe	S-propargyl	H	4-Cl	D-268	NH-propargyl	S-propargyl	H	4-Cl
D-219	NHMe	SCH ₂ CF ₃	H	4-Cl	D-269	NH-propargyl	SCH ₂ CF ₃	H	4-Cl
D-220	NHMe	SCH ₂ CH ₂ F	H	4-Cl	D-270	NH-propargyl	SCH ₂ CH ₂ F	H	4-Cl
D-221	NHEt	SH	H	4-F	D-271	NHCH ₂ CF ₃	SH	H	4-Cl
D-222	NHEt	SMe	H	4-Cl	D-272	NHCH ₂ CF ₃	SMe	H	4-Cl
D-223	NHEt	SEt	H	4-Cl	D-273	NHCH ₂ CF ₃	SEt	H	4-Cl
D-224	NHEt	S-n-Pr	H	4-Cl	D-274	NHCH ₂ CF ₃	S-n-Pr	H	4-Cl
D-225	NHEt	S-i-Pr	H	4-Cl	D-275	NHCH ₂ CF ₃	S-i-Pr	H	4-Cl
D-226	NHEt	S-n-Bu	H	4-Cl	D-276	NHCH ₂ CF ₃	S-n-Bu	H	4-Cl
D-227	NHEt	S-allyl	H	4-Cl	D-277	NHCH ₂ CF ₃	S-allyl	H	4-Cl
D-228	NHEt	S-propargyl	H	4-Cl	D-278	NHCH ₂ CF ₃	S-propargyl	H	4-Cl
D-229	NHEt	SCH ₂ CF ₃	H	4-Cl	D-279	NHCH ₂ CF ₃	SCH ₂ CF ₃	H	4-Cl
D-230	NHEt	SCH ₂ CH ₂ F	H	4-Cl	D-280	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	H	4-Cl
D-231	NHPr	SH	H	4-Cl	D-281	NHCH ₂ CH ₂ F	SH	H	4-Cl
D-232	NHPr	SMe	H	4-Cl	D-282	NHCH ₂ CH ₂ F	SMe	H	4-Cl
D-233	NHPr	SEt	H	4-Cl	D-283	NHCH ₂ CH ₂ F	SEt	H	4-Cl
D-234	NHPr	S-n-Pr	H	4-Cl	D-284	NHCH ₂ CH ₂ F	S-n-Pr	H	4-Cl
D-235	NHPr	S-i-Pr	H	4-Cl	D-285	NHCH ₂ CH ₂ F	S-i-Pr	H	4-Cl
D-236	NHPr	S-n-Bu	H	4-Cl	D-286	NHCH ₂ CH ₂ F	S-n-Bu	H	4-Cl
D-237	NHPr	S-allyl	H	4-Cl	D-287	NHCH ₂ CH ₂ F	S-allyl	H	4-Cl
D-238	NHPr	S-propargyl	H	4-Cl	D-288	NHCH ₂ CH ₂ F	S-propargyl	H	4-Cl
D-239	NHPr	SCH ₂ CF ₃	H	4-Cl	D-289	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	H	4-Cl
D-240	NHPr	SCH ₂ CH ₂ F	H	4-Cl	D-290	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	H	4-Cl
D-241	NH-i-Pr	SH	H	4-Cl	D-291	NH-n-Bu	SH	H	4-Cl
D-242	NH-i-Pr	SMe	H	4-Cl	D-292	NH-n-Bu	SMe	H	4-Cl
D-243	NH-i-Pr	SEt	H	4-Cl	D-293	NH-n-Bu	SEt	H	4-Cl
D-244	NH-i-Pr	S-n-Pr	H	4-Cl	D-294	NH-n-Bu	S-n-Pr	H	4-Cl
D-245	NH-i-Pr	S-i-Pr	H	4-Cl	D-295	NH-n-Bu	S-i-Pr	H	4-Cl
D-246	NH-i-Pr	S-n-Bu	H	4-Cl	D-296	NH-n-Bu	S-n-Bu	H	4-Cl
D-247	NH-i-Pr	S-allyl	H	4-Cl	D-297	NH-n-Bu	S-allyl	H	4-Cl
D-248	NH-i-Pr	S-propargyl	H	4-Cl	D-298	NH-n-Bu	S-propargyl	H	4-Cl
D-249	NH-i-Pr	SCH ₂ CF ₃	H	4-Cl	D-299	NH-n-Bu	SCH ₂ CF ₃	H	4-Cl
D-250	NH-i-Pr	SCH ₂ CH ₂ F	H	4-Cl	D-300	NH-n-Bu	SCH ₂ CH ₂ F	H	4-Cl

Table 10

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-301	NH ₂	SH	H	4-Me	D-351	NH-allyl	SH	H	4-Me
D-302	NH ₂	SMe	H	4-Me	D-352	NH-allyl	SMe	H	4-Me
D-303	NH ₂	SEt	H	4-Me	D-353	NH-allyl	SEt	H	4-Me
D-304	NH ₂	S-n-Pr	H	4-Me	D-354	NH-allyl	S-n-Pr	H	4-Me
D-305	NH ₂	S-i-Pr	H	4-Me	D-355	NH-allyl	S-i-Pr	H	4-Me
D-306	NH ₂	S-n-Bu	H	4-Me	D-356	NH-allyl	S-n-Bu	H	4-Me
D-307	NH ₂	S-allyl	H	4-Me	D-357	NH-allyl	S-allyl	H	4-Me
D-308	NH ₂	S-propargyl	H	4-Me	D-358	NH-allyl	S-propargyl	H	4-Me
D-309	NH ₂	SCH ₂ CF ₃	H	4-Me	D-359	NH-allyl	SCH ₂ CF ₃	H	4-Me
D-310	NH ₂	SCH ₂ CH ₂ F	H	4-Me	D-360	NH-allyl	SCH ₂ CH ₂ F	H	4-Me
D-311	NHMe	SH	H	4-Me	D-361	NH-propargyl	SH	H	4-Me
D-312	NHMe	SMe	H	4-Me	D-362	NH-propargyl	SMe	H	4-Me
D-313	NHMe	SEt	H	4-Me	D-363	NH-propargyl	SEt	H	4-Me
D-314	NHMe	S-n-Pr	H	4-Me	D-364	NH-propargyl	S-n-Pr	H	4-Me
D-315	NHMe	S-i-Pr	H	4-Me	D-365	NH-propargyl	S-i-Pr	H	4-Me
D-316	NHMe	S-n-Bu	H	4-Me	D-366	NH-propargyl	S-n-Bu	H	4-Me
D-317	NHMe	S-allyl	H	4-Me	D-367	NH-propargyl	S-allyl	H	4-Me
D-318	NHMe	S-propargyl	H	4-Me	D-368	NH-propargyl	S-propargyl	H	4-Me
D-319	NHMe	SCH ₂ CF ₃	H	4-Me	D-369	NH-propargyl	SCH ₂ CF ₃	H	4-Me
D-320	NHMe	SCH ₂ CH ₂ F	H	4-Me	D-370	NH-propargyl	SCH ₂ CH ₂ F	H	4-Me
D-321	NHEt	SH	H	4-Me	D-371	NHCH ₂ CF ₃	SH	H	4-Me
D-322	NHEt	SMe	H	4-Me	D-372	NHCH ₂ CF ₃	SMe	H	4-Me
D-323	NHEt	SEt	H	4-Me	D-373	NHCH ₂ CF ₃	SEt	H	4-Me
D-324	NHEt	S-n-Pr	H	4-Me	D-374	NHCH ₂ CF ₃	S-n-Pr	H	4-Me
D-325	NHEt	S-i-Pr	H	4-Me	D-375	NHCH ₂ CF ₃	S-i-Pr	H	4-Me
D-326	NHEt	S-n-Bu	H	4-Me	D-376	NHCH ₂ CF ₃	S-n-Bu	H	4-Me
D-327	NHEt	S-allyl	H	4-Me	D-377	NHCH ₂ CF ₃	S-allyl	H	4-Me
D-328	NHEt	S-propargyl	H	4-Me	D-378	NHCH ₂ CF ₃	S-propargyl	H	4-Me
D-329	NHEt	SCH ₂ CF ₃	H	4-Me	D-379	NHCH ₂ CF ₃	SCH ₂ CF ₃	H	4-Me
D-330	NHEt	SCH ₂ CH ₂ F	H	4-Me	D-380	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	H	4-Me
D-331	NHPr	SH	H	4-Me	D-381	NHCH ₂ CH ₂ F	SH	H	4-Me
D-332	NHPr	SMe	H	4-Me	D-382	NHCH ₂ CH ₂ F	SMe	H	4-Me
D-333	NHPr	SEt	H	4-Me	D-383	NHCH ₂ CH ₂ F	SEt	H	4-Me
D-334	NHPr	S-n-Pr	H	4-Me	D-384	NHCH ₂ CH ₂ F	S-n-Pr	H	4-Me
D-335	NHPr	S-i-Pr	H	4-Me	D-385	NHCH ₂ CH ₂ F	S-i-Pr	H	4-Me
D-336	NHPr	S-n-Bu	H	4-Me	D-386	NHCH ₂ CH ₂ F	S-n-Bu	H	4-Me
D-337	NHPr	S-allyl	H	4-Me	D-387	NHCH ₂ CH ₂ F	S-allyl	H	4-Me
D-338	NHPr	S-propargyl	H	4-Me	D-388	NHCH ₂ CH ₂ F	S-propargyl	H	4-Me
D-339	NHPr	SCH ₂ CF ₃	H	4-Me	D-389	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	H	4-Me
D-340	NHPr	SCH ₂ CH ₂ F	H	4-Me	D-390	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	H	4-Me
D-341	NH-i-Pr	SH	H	4-Me	D-391	NH-n-Bu	SH	H	4-Me
D-342	NH-i-Pr	SMe	H	4-Me	D-392	NH-n-Bu	SMe	H	4-Me
D-343	NH-i-Pr	SEt	H	4-Me	D-393	NH-n-Bu	SEt	H	4-Me
D-344	NH-i-Pr	S-n-Pr	H	4-Me	D-394	NH-n-Bu	S-n-Pr	H	4-Me
D-345	NH-i-Pr	S-i-Pr	H	4-Me	D-395	NH-n-Bu	S-i-Pr	H	4-Me
D-346	NH-i-Pr	S-n-Bu	H	4-Me	D-396	NH-n-Bu	S-n-Bu	H	4-Me
D-347	NH-i-Pr	S-allyl	H	4-Me	D-397	NH-n-Bu	S-allyl	H	4-Me
D-348	NH-i-Pr	S-propargyl	H	4-Me	D-398	NH-n-Bu	S-propargyl	H	4-Me
D-349	NH-i-Pr	SCH ₂ CF ₃	H	4-Me	D-399	NH-n-Bu	SCH ₂ CF ₃	H	4-Me
D-350	NH-i-Pr	SCH ₂ CH ₂ F	H	4-Me	D-400	NH-n-Bu	SCH ₂ CH ₂ F	H	4-Me

Table 11

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-401	NH ₂	SH	Me	2-NH ₂	D-451	NH-allyl	SH	Me	2-NH ₂
D-402	NH ₂	SMe	Me	2-NH ₂	D-452	NH-allyl	SMe	Me	2-NH ₂
D-403	NH ₂	SEt	Me	2-NH ₂	D-453	NH-allyl	SEt	Me	2-NH ₂
D-404	NH ₂	S-n-Pr	Me	2-NH ₂	D-454	NH-allyl	S-n-Pr	Me	2-NH ₂
D-405	NH ₂	S-i-Pr	Me	2-NH ₂	D-455	NH-allyl	S-i-Pr	Me	2-NH ₂
D-406	NH ₂	S-n-Bu	Me	2-NH ₂	D-456	NH-allyl	S-n-Bu	Me	2-NH ₂
D-407	NH ₂	S-allyl	Me	2-NH ₂	D-457	NH-allyl	S-allyl	Me	2-NH ₂
D-408	NH ₂	S-propargyl	Me	2-NH ₂	D-458	NH-allyl	S-propargyl	Me	2-NH ₂
D-409	NH ₂	SCH ₂ CF ₃	Me	2-NH ₂	D-459	NH-allyl	SCH ₂ CF ₃	Me	2-NH ₂
D-410	NH ₂	SCH ₂ CH ₂ F	Me	2-NH ₂	D-460	NH-allyl	SCH ₂ CH ₂ F	Me	2-NH ₂
D-411	NHMe	SH	Me	2-NH ₂	D-461	NH-propargyl	SH	Me	2-NH ₂
D-412	NHMe	SMe	Me	2-NH ₂	D-462	NH-propargyl	SMe	Me	2-NH ₂
D-413	NHMe	SEt	Me	2-NH ₂	D-463	NH-propargyl	SEt	Me	2-NH ₂
D-414	NHMe	S-n-Pr	Me	2-NH ₂	D-464	NH-propargyl	S-n-Pr	Me	2-NH ₂
D-415	NHMe	S-i-Pr	Me	2-NH ₂	D-465	NH-propargyl	S-i-Pr	Me	2-NH ₂
D-416	NHMe	S-n-Bu	Me	2-NH ₂	D-466	NH-propargyl	S-n-Bu	Me	2-NH ₂
D-417	NHMe	S-allyl	Me	2-NH ₂	D-467	NH-propargyl	S-allyl	Me	2-NH ₂
D-418	NHMe	S-propargyl	Me	2-NH ₂	D-468	NH-propargyl	S-propargyl	Me	2-NH ₂
D-419	NHMe	SCH ₂ CF ₃	Me	2-NH ₂	D-469	NH-propargyl	SCH ₂ CF ₃	Me	2-NH ₂
D-420	NHMe	SCH ₂ CH ₂ F	Me	2-NH ₂	D-470	NH-propargyl	SCH ₂ CH ₂ F	Me	2-NH ₂
D-421	NHEt	SH	Me	2-NH ₂	D-471	NHCH ₂ CF ₃	SH	Me	2-NH ₂
D-422	NHEt	SMe	Me	2-NH ₂	D-472	NHCH ₂ CF ₃	SMe	Me	2-NH ₂
D-423	NHEt	SEt	Me	2-NH ₂	D-473	NHCH ₂ CF ₃	SEt	Me	2-NH ₂
D-424	NHEt	S-n-Pr	Me	2-NH ₂	D-474	NHCH ₂ CF ₃	S-n-Pr	Me	2-NH ₂
D-425	NHEt	S-i-Pr	Me	2-NH ₂	D-475	NHCH ₂ CF ₃	S-i-Pr	Me	2-NH ₂
D-426	NHEt	S-n-Bu	Me	2-NH ₂	D-476	NHCH ₂ CF ₃	S-n-Bu	Me	2-NH ₂
D-427	NHEt	S-allyl	Me	2-NH ₂	D-477	NHCH ₂ CF ₃	S-allyl	Me	2-NH ₂
D-428	NHEt	S-propargyl	Me	2-NH ₂	D-478	NHCH ₂ CF ₃	S-propargyl	Me	2-NH ₂
D-429	NHEt	SCH ₂ CF ₃	Me	2-NH ₂	D-479	NHCH ₂ CF ₃	SCH ₂ CF ₃	Me	2-NH ₂
D-430	NHEt	SCH ₂ CH ₂ F	Me	2-NH ₂	D-480	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Me	2-NH ₂
D-431	NHPr	SH	Me	2-NH ₂	D-481	NHCH ₂ CH ₂ F	SH	Me	2-NH ₂
D-432	NHPr	SMe	Me	2-NH ₂	D-482	NHCH ₂ CH ₂ F	SMe	Me	2-NH ₂
D-433	NHPr	SEt	Me	2-NH ₂	D-483	NHCH ₂ CH ₂ F	SEt	Me	2-NH ₂
D-434	NHPr	S-n-Pr	Me	2-NH ₂	D-484	NHCH ₂ CH ₂ F	S-n-Pr	Me	2-NH ₂
D-435	NHPr	S-i-Pr	Me	2-NH ₂	D-485	NHCH ₂ CH ₂ F	S-i-Pr	Me	2-NH ₂
D-436	NHPr	S-n-Bu	Me	2-NH ₂	D-486	NHCH ₂ CH ₂ F	S-n-Bu	Me	2-NH ₂
D-437	NHPr	S-allyl	Me	2-NH ₂	D-487	NHCH ₂ CH ₂ F	S-allyl	Me	2-NH ₂
D-438	NHPr	S-propargyl	Me	2-NH ₂	D-488	NHCH ₂ CH ₂ F	S-propargyl	Me	2-NH ₂
D-439	NHPr	SCH ₂ CF ₃	Me	2-NH ₂	D-489	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Me	2-NH ₂
D-440	NHPr	SCH ₂ CH ₂ F	Me	2-NH ₂	D-490	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Me	2-NH ₂
D-441	NH-i-Pr	SH	Me	2-NH ₂	D-491	NH-n-Bu	SH	Me	2-NH ₂
D-442	NH-i-Pr	SMe	Me	2-NH ₂	D-492	NH-n-Bu	SMe	Me	2-NH ₂
D-443	NH-i-Pr	SEt	Me	2-NH ₂	D-493	NH-n-Bu	SEt	Me	2-NH ₂
D-444	NH-i-Pr	S-n-Pr	Me	2-NH ₂	D-494	NH-n-Bu	S-n-Pr	Me	2-NH ₂
D-445	NH-i-Pr	S-i-Pr	Me	2-NH ₂	D-495	NH-n-Bu	S-i-Pr	Me	2-NH ₂
D-446	NH-i-Pr	S-n-Bu	Me	2-NH ₂	D-496	NH-n-Bu	S-n-Bu	Me	2-NH ₂
D-447	NH-i-Pr	S-allyl	Me	2-NH ₂	D-497	NH-n-Bu	S-allyl	Me	2-NH ₂
D-448	NH-i-Pr	S-propargyl	Me	2-NH ₂	D-498	NH-n-Bu	S-propargyl	Me	2-NH ₂
D-449	NH-i-Pr	SCH ₂ CF ₃	Me	2-NH ₂	D-499	NH-n-Bu	SCH ₂ CF ₃	Me	2-NH ₂
D-450	NH-i-Pr	SCH ₂ CH ₂ F	Me	2-NH ₂	D-500	NH-n-Bu	SCH ₂ CH ₂ F	Me	2-NH ₂

Table 12

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-501	NH ₂	SH	Et	4-NO ₂	D-551	NH-allyl	SH	Et	4-NO ₂
D-502	NH ₂	SMe	Et	4-NO ₂	D-552	NH-allyl	SMe	Et	4-NO ₂
D-503	NH ₂	SEt	Et	4-NO ₂	D-553	NH-allyl	SEt	Et	4-NO ₂
D-504	NH ₂	S-n-Pr	Et	4-NO ₂	D-554	NH-allyl	S-n-Pr	Et	4-NO ₂
D-505	NH ₂	S-i-Pr	Et	4-NO ₂	D-555	NH-allyl	S-i-Pr	Et	4-NO ₂
D-506	NH ₂	S-n-Bu	Et	4-NO ₂	D-556	NH-allyl	S-n-Bu	Et	4-NO ₂
D-507	NH ₂	S-allyl	Et	4-NO ₂	D-557	NH-allyl	S-allyl	Et	4-NO ₂
D-508	NH ₂	S-propargyl	Et	4-NO ₂	D-558	NH-allyl	S-propargyl	Et	4-NO ₂
D-509	NH ₂	SCH ₂ CF ₃	Et	4-NO ₂	D-559	NH-allyl	SCH ₂ CF ₃	Et	4-NO ₂
D-510	NH ₂	SCH ₂ CH ₂ F	Et	4-NO ₂	D-560	NH-allyl	SCH ₂ CH ₂ F	Et	4-NO ₂
D-511	NHMe	SH	Et	4-NO ₂	D-561	NH-propargyl	SH	Et	4-NO ₂
D-512	NHMe	SMe	Et	4-NO ₂	D-562	NH-propargyl	SMe	Et	4-NO ₂
D-513	NHMe	SEt	Et	4-NO ₂	D-563	NH-propargyl	SEt	Et	4-NO ₂
D-514	NHMe	S-n-Pr	Et	4-NO ₂	D-564	NH-propargyl	S-n-Pr	Et	4-NO ₂
D-515	NHMe	S-i-Pr	Et	4-NO ₂	D-565	NH-propargyl	S-i-Pr	Et	4-NO ₂
D-516	NHMe	S-n-Bu	Et	4-NO ₂	D-566	NH-propargyl	S-n-Bu	Et	4-NO ₂
D-517	NHMe	S-allyl	Et	4-NO ₂	D-567	NH-propargyl	S-allyl	Et	4-NO ₂
D-518	NHMe	S-propargyl	Et	4-NO ₂	D-568	NH-propargyl	S-propargyl	Et	4-NO ₂
D-519	NHMe	SCH ₂ CF ₃	Et	4-NO ₂	D-569	NH-propargyl	SCH ₂ CF ₃	Et	4-NO ₂
D-520	NHMe	SCH ₂ CH ₂ F	Et	4-NO ₂	D-570	NH-propargyl	SCH ₂ CH ₂ F	Et	4-NO ₂
D-521	NHEt	SH	Et	4-NO ₂	D-571	NHCH ₂ CF ₃	SH	Et	4-NO ₂
D-522	NHEt	SMe	Et	4-NO ₂	D-572	NHCH ₂ CF ₃	SMe	Et	4-NO ₂
D-523	NHEt	SEt	Et	4-NO ₂	D-573	NHCH ₂ CF ₃	SEt	Et	4-NO ₂
D-524	NHEt	S-n-Pr	Et	4-NO ₂	D-574	NHCH ₂ CF ₃	S-n-Pr	Et	4-NO ₂
D-525	NHEt	S-i-Pr	Et	4-NO ₂	D-575	NHCH ₂ CF ₃	S-i-Pr	Et	4-NO ₂
D-526	NHEt	S-n-Bu	Et	4-NO ₂	D-576	NHCH ₂ CF ₃	S-n-Bu	Et	4-NO ₂
D-527	NHEt	S-allyl	Et	4-NO ₂	D-577	NHCH ₂ CF ₃	S-allyl	Et	4-NO ₂
D-528	NHEt	S-propargyl	Et	4-NO ₂	D-578	NHCH ₂ CF ₃	S-propargyl	Et	4-NO ₂
D-529	NHEt	SCH ₂ CF ₃	Et	4-NO ₂	D-579	NHCH ₂ CF ₃	SCH ₂ CF ₃	Et	4-NO ₂
D-530	NHEt	SCH ₂ CH ₂ F	Et	4-NO ₂	D-580	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Et	4-NO ₂
D-531	NHPr	SH	Et	4-NO ₂	D-581	NHCH ₂ CH ₂ F	SH	Et	4-NO ₂
D-532	NHPr	SMe	Et	4-NO ₂	D-582	NHCH ₂ CH ₂ F	SMe	Et	4-NO ₂
D-533	NHPr	SEt	Et	4-NO ₂	D-583	NHCH ₂ CH ₂ F	SEt	Et	4-NO ₂
D-534	NHPr	S-n-Pr	Et	4-NO ₂	D-584	NHCH ₂ CH ₂ F	S-n-Pr	Et	4-NO ₂
D-535	NHPr	S-i-Pr	Et	4-NO ₂	D-585	NHCH ₂ CH ₂ F	S-i-Pr	Et	4-NO ₂
D-536	NHPr	S-n-Bu	Et	4-NO ₂	D-586	NHCH ₂ CH ₂ F	S-n-Bu	Et	4-NO ₂
D-537	NHPr	S-allyl	Et	4-NO ₂	D-587	NHCH ₂ CH ₂ F	S-allyl	Et	4-NO ₂
D-538	NHPr	S-propargyl	Et	4-NO ₂	D-588	NHCH ₂ CH ₂ F	S-propargyl	Et	4-NO ₂
D-539	NHPr	SCH ₂ CF ₃	Et	4-NO ₂	D-589	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Et	4-NO ₂
D-540	NHPr	SCH ₂ CH ₂ F	Et	4-NO ₂	D-590	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Et	4-NO ₂
D-541	NH-i-Pr	SH	Et	4-NO ₂	D-591	NH-n-Bu	SH	Et	4-NO ₂
D-542	NH-i-Pr	SMe	Et	4-NO ₂	D-592	NH-n-Bu	SMe	Et	4-NO ₂
D-543	NH-i-Pr	SEt	Et	4-NO ₂	D-593	NH-n-Bu	SEt	Et	4-NO ₂
D-544	NH-i-Pr	S-n-Pr	Et	4-NO ₂	D-594	NH-n-Bu	S-n-Pr	Et	4-NO ₂
D-545	NH-i-Pr	S-i-Pr	Et	4-NO ₂	D-595	NH-n-Bu	S-i-Pr	Et	4-NO ₂
D-546	NH-i-Pr	S-n-Bu	Et	4-NO ₂	D-596	NH-n-Bu	S-n-Bu	Et	4-NO ₂
D-547	NH-i-Pr	S-allyl	Et	4-NO ₂	D-597	NH-n-Bu	S-allyl	Et	4-NO ₂
D-548	NH-i-Pr	S-propargyl	Et	4-NO ₂	D-598	NH-n-Bu	S-propargyl	Et	4-NO ₂
D-549	NH-i-Pr	SCH ₂ CF ₃	Et	4-NO ₂	D-599	NH-n-Bu	SCH ₂ CF ₃	Et	4-NO ₂
D-550	NH-i-Pr	SCH ₂ CH ₂ F	Et	4-NO ₂	D-600	NH-n-Bu	SCH ₂ CH ₂ F	Et	4-NO ₂

Table 13

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-601	NH ₂	SH	Et	4-NH ₂	D-651	NH-allyl	SH	Et	4-NH ₂
D-602	NH ₂	SMe	Et	4-NH ₂	D-652	NH-allyl	SMe	Et	4-NH ₂
D-603	NH ₂	SEt	Et	4-NH ₂	D-653	NH-allyl	SEt	Et	4-NH ₂
D-604	NH ₂	S-n-Pr	Et	4-NH ₂	D-654	NH-allyl	S-n-Pr	Et	4-NH ₂
D-605	NH ₂	S-i-Pr	Et	4-NH ₂	D-655	NH-allyl	S-i-Pr	Et	4-NH ₂
D-606	NH ₂	S-n-Bu	Et	4-NH ₂	D-656	NH-allyl	S-n-Bu	Et	4-NH ₂
D-607	NH ₂	S-allyl	Et	4-NH ₂	D-657	NH-allyl	S-allyl	Et	4-NH ₂
D-608	NH ₂	S-propargyl	Et	4-NH ₂	D-658	NH-allyl	S-propargyl	Et	4-NH ₂
D-609	NH ₂	SCH ₂ CF ₃	Et	4-NH ₂	D-659	NH-allyl	SCH ₂ CF ₃	Et	4-NH ₂
D-610	NH ₂	SCH ₂ CH ₂ F	Et	4-NH ₂	D-660	NH-allyl	SCH ₂ CH ₂ F	Et	4-NH ₂
D-611	NHMe	SH	Et	4-NH ₂	D-661	NH-propargyl	SH	Et	4-NH ₂
D-612	NHMe	SMe	Et	4-NH ₂	D-662	NH-propargyl	SMe	Et	4-NH ₂
D-613	NHMe	SEt	Et	4-NH ₂	D-663	NH-propargyl	SEt	Et	4-NH ₂
D-614	NHMe	S-n-Pr	Et	4-NH ₂	D-664	NH-propargyl	S-n-Pr	Et	4-NH ₂
D-615	NHMe	S-i-Pr	Et	4-NH ₂	D-665	NH-propargyl	S-i-Pr	Et	4-NH ₂
D-616	NHMe	S-n-Bu	Et	4-NH ₂	D-666	NH-propargyl	S-n-Bu	Et	4-NH ₂
D-617	NHMe	S-allyl	Et	4-NH ₂	D-667	NH-propargyl	S-allyl	Et	4-NH ₂
D-618	NHMe	S-propargyl	Et	4-NH ₂	D-668	NH-propargyl	S-propargyl	Et	4-NH ₂
D-619	NHMe	SCH ₂ CF ₃	Et	4-NH ₂	D-669	NH-propargyl	SCH ₂ CF ₃	Et	4-NH ₂
D-620	NHMe	SCH ₂ CH ₂ F	Et	4-NH ₂	D-670	NH-propargyl	SCH ₂ CH ₂ F	Et	4-NH ₂
D-621	NHEt	SH	Et	4-NH ₂	D-671	NHCH ₂ CF ₃	SH	Et	4-NH ₂
D-622	NHEt	SMe	Et	4-NH ₂	D-672	NHCH ₂ CF ₃	SMe	Et	4-NH ₂
D-623	NHEt	SEt	Et	4-NH ₂	D-673	NHCH ₂ CF ₃	SEt	Et	4-NH ₂
D-624	NHEt	S-n-Pr	Et	4-NH ₂	D-674	NHCH ₂ CF ₃	S-n-Pr	Et	4-NH ₂
D-625	NHEt	S-i-Pr	Et	4-NH ₂	D-675	NHCH ₂ CF ₃	S-i-Pr	Et	4-NH ₂
D-626	NHEt	S-n-Bu	Et	4-NH ₂	D-676	NHCH ₂ CF ₃	S-n-Bu	Et	4-NH ₂
D-627	NHEt	S-allyl	Et	4-NH ₂	D-677	NHCH ₂ CF ₃	S-allyl	Et	4-NH ₂
D-628	NHEt	S-propargyl	Et	4-NH ₂	D-678	NHCH ₂ CF ₃	S-propargyl	Et	4-NH ₂
D-629	NHEt	SCH ₂ CF ₃	Et	4-NH ₂	D-679	NHCH ₂ CF ₃	SCH ₂ CF ₃	Et	4-NH ₂
D-630	NHEt	SCH ₂ CH ₂ F	Et	4-NH ₂	D-680	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Et	4-NH ₂
D-631	NHPr	SH	Et	4-NH ₂	D-681	NHCH ₂ CH ₂ F	SH	Et	4-NH ₂
D-632	NHPr	SMe	Et	4-NH ₂	D-682	NHCH ₂ CH ₂ F	SMe	Et	4-NH ₂
D-633	NHPr	SEt	Et	4-NH ₂	D-683	NHCH ₂ CH ₂ F	SEt	Et	4-NH ₂
D-634	NHPr	S-n-Pr	Et	4-NH ₂	D-684	NHCH ₂ CH ₂ F	S-n-Pr	Et	4-NH ₂
D-635	NHPr	S-i-Pr	Et	4-NH ₂	D-685	NHCH ₂ CH ₂ F	S-i-Pr	Et	4-NH ₂
D-636	NHPr	S-n-Bu	Et	4-NH ₂	D-686	NHCH ₂ CH ₂ F	S-n-Bu	Et	4-NH ₂
D-637	NHPr	S-allyl	Et	4-NH ₂	D-687	NHCH ₂ CH ₂ F	S-allyl	Et	4-NH ₂
D-638	NHPr	S-propargyl	Et	4-NH ₂	D-688	NHCH ₂ CH ₂ F	S-propargyl	Et	4-NH ₂
D-639	NHPr	SCH ₂ CF ₃	Et	4-NH ₂	D-689	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Et	4-NH ₂
D-640	NHPr	SCH ₂ CH ₂ F	Et	4-NH ₂	D-690	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Et	4-NH ₂
D-641	NH-i-Pr	SH	Et	4-NH ₂	D-691	NH-n-Bu	SH	Et	4-NH ₂
D-642	NH-i-Pr	SMe	Et	4-NH ₂	D-692	NH-n-Bu	SMe	Et	4-NH ₂
D-643	NH-i-Pr	SEt	Et	4-NH ₂	D-693	NH-n-Bu	SEt	Et	4-NH ₂
D-644	NH-i-Pr	S-n-Pr	Et	4-NH ₂	D-694	NH-n-Bu	S-n-Pr	Et	4-NH ₂
D-645	NH-i-Pr	S-i-Pr	Et	4-NH ₂	D-695	NH-n-Bu	S-i-Pr	Et	4-NH ₂
D-646	NH-i-Pr	S-n-Bu	Et	4-NH ₂	D-696	NH-n-Bu	S-n-Bu	Et	4-NH ₂
D-647	NH-i-Pr	S-allyl	Et	4-NH ₂	D-697	NH-n-Bu	S-allyl	Et	4-NH ₂
D-648	NH-i-Pr	S-propargyl	Et	4-NH ₂	D-698	NH-n-Bu	S-propargyl	Et	4-NH ₂
D-649	NH-i-Pr	SCH ₂ CF ₃	Et	4-NH ₂	D-699	NH-n-Bu	SCH ₂ CF ₃	Et	4-NH ₂
D-650	NH-i-Pr	SCH ₂ CH ₂ F	Et	4-NH ₂	D-700	NH-n-Bu	SCH ₂ CH ₂ F	Et	4-NH ₂

Table 14

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-701	NH ₂	SH	Me	4-NO ₂	D-751	NH-allyl	SH	Me	4-NO ₂
D-702	NH ₂	SMe	Me	4-OMe	D-752	NH-allyl	SMe	Me	4-NO ₂
D-703	NH ₂	SEt	Me	4-NO ₂	D-753	NH-allyl	SEt	Me	4-NO ₂
D-704	NH ₂	S-n-Pr	Me	4-NO ₂	D-754	NH-allyl	S-n-Pr	Me	4-NO ₂
D-705	NH ₂	S-i-Pr	Me	4-NO ₂	D-755	NH-allyl	S-i-Pr	Me	4-NO ₂
D-706	NH ₂	S-n-Bu	Me	4-NO ₂	D-756	NH-allyl	S-n-Bu	Me	4-NO ₂
D-707	NH ₂	S-allyl	Me	4-NO ₂	D-757	NH-allyl	S-allyl	Me	4-NO ₂
D-708	NH ₂	S-propargyl	Me	4-NO ₂	D-758	NH-allyl	S-propargyl	Me	4-NO ₂
D-709	NH ₂	SCH ₂ CF ₃	Me	4-NO ₂	D-759	NH-allyl	SCH ₂ CF ₃	Me	4-NO ₂
D-710	NH ₂	SCH ₂ CH ₂ F	Me	4-NO ₂	D-760	NH-allyl	SCH ₂ CH ₂ F	Me	4-NO ₂
D-711	NHMe	SH	Me	4-NO ₂	D-761	NH-propargyl	SH	Me	4-NO ₂
D-712	NHMe	SMe	Me	4-OMe	D-762	NH-propargyl	SMe	Me	4-NO ₂
D-713	NHMe	SEt	Me	4-OMe	D-763	NH-propargyl	SEt	Me	4-NO ₂
D-714	NHMe	S-n-Pr	Me	4-OMe	D-764	NH-propargyl	S-n-Pr	Me	4-NO ₂
D-715	NHMe	S-i-Pr	Me	4-NO ₂	D-765	NH-propargyl	S-i-Pr	Me	4-NO ₂
D-716	NHMe	S-n-Bu	Me	4-NO ₂	D-766	NH-propargyl	S-n-Bu	Me	4-NO ₂
D-717	NHMe	S-allyl	Me	4-NO ₂	D-767	NH-propargyl	S-allyl	Me	4-NO ₂
D-718	NHMe	S-propargyl	Me	4-NO ₂	D-768	NH-propargyl	S-propargyl	Me	4-NO ₂
D-719	NHMe	SCH ₂ CF ₃	Me	4-NO ₂	D-769	NH-propargyl	SCH ₂ CF ₃	Me	4-NO ₂
D-720	NHMe	SCH ₂ CH ₂ F	Me	4-NO ₂	D-770	NH-propargyl	SCH ₂ CH ₂ F	Me	4-NO ₂
D-721	NHEt	SH	Me	4-NO ₂	D-771	NHCH ₂ CF ₃	SH	Me	4-NO ₂
D-722	NHEt	SMe	Me	4-OMe	D-772	NHCH ₂ CF ₃	SMe	Me	4-OMe
D-723	NHEt	SEt	Me	4-OMe	D-773	NHCH ₂ CF ₃	SEt	Me	4-NO ₂
D-724	NHEt	S-n-Pr	Me	4-OMe	D-774	NHCH ₂ CF ₃	S-n-Pr	Me	4-NO ₂
D-725	NHEt	S-i-Pr	Me	4-NO ₂	D-775	NHCH ₂ CF ₃	S-i-Pr	Me	4-NO ₂
D-726	NHEt	S-n-Bu	Me	4-NO ₂	D-776	NHCH ₂ CF ₃	S-n-Bu	Me	4-NO ₂
D-727	NHEt	S-allyl	Me	4-NO ₂	D-777	NHCH ₂ CF ₃	S-allyl	Me	4-NO ₂
D-728	NHEt	S-propargyl	Me	4-NO ₂	D-778	NHCH ₂ CF ₃	S-propargyl	Me	4-NO ₂
D-729	NHEt	SCH ₂ CF ₃	Me	4-NO ₂	D-779	NHCH ₂ CF ₃	SCH ₂ CF ₃	Me	4-NO ₂
D-730	NHEt	SCH ₂ CH ₂ F	Me	4-NO ₂	D-780	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Me	4-NO ₂
D-731	NHPr	SH	Me	4-NO ₂	D-781	NHCH ₂ CH ₂ F	SH	Me	4-NO ₂
D-732	NHPr	SMe	Me	4-OMe	D-782	NHCH ₂ CH ₂ F	SMe	Me	4-NO ₂
D-733	NHPr	SEt	Me	4-NO ₂	D-783	NHCH ₂ CH ₂ F	SEt	Me	4-NO ₂
D-734	NHPr	S-n-Pr	Me	4-NO ₂	D-784	NHCH ₂ CH ₂ F	S-n-Pr	Me	4-NO ₂
D-735	NHPr	S-i-Pr	Me	4-NO ₂	D-785	NHCH ₂ CH ₂ F	S-i-Pr	Me	4-NO ₂
D-736	NHPr	S-n-Bu	Me	4-NO ₂	D-786	NHCH ₂ CH ₂ F	S-n-Bu	Me	4-NO ₂
D-737	NHPr	S-allyl	Me	4-NO ₂	D-787	NHCH ₂ CH ₂ F	S-allyl	Me	4-NO ₂
D-738	NHPr	S-propargyl	Me	4-NO ₂	D-788	NHCH ₂ CH ₂ F	S-propargyl	Me	4-NO ₂
D-739	NHPr	SCH ₂ CF ₃	Me	4-NO ₂	D-789	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Me	4-NO ₂
D-740	NHPr	SCH ₂ CH ₂ F	Me	4-NO ₂	D-790	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Me	4-NO ₂
D-741	NH-i-Pr	SH	Me	4-NO ₂	D-791	NH-n-Bu	SH	Me	4-NO ₂
D-742	NH-i-Pr	SMe	Me	4-NO ₂	D-792	NH-n-Bu	SMe	Me	4-NO ₂
D-743	NH-i-Pr	SEt	Me	4-NO ₂	D-793	NH-n-Bu	SEt	Me	4-NO ₂
D-744	NH-i-Pr	S-n-Pr	Me	4-NO ₂	D-794	NH-n-Bu	S-n-Pr	Me	4-NO ₂
D-745	NH-i-Pr	S-i-Pr	Me	4-NO ₂	D-795	NH-n-Bu	S-i-Pr	Me	4-NO ₂
D-746	NH-i-Pr	S-n-Bu	Me	4-NO ₂	D-796	NH-n-Bu	S-n-Bu	Me	4-NO ₂
D-747	NH-i-Pr	S-allyl	Me	4-NO ₂	D-797	NH-n-Bu	S-allyl	Me	4-NO ₂
D-748	NH-i-Pr	S-propargyl	Me	4-NO ₂	D-798	NH-n-Bu	S-propargyl	Me	4-NO ₂
D-749	NH-i-Pr	SCH ₂ CF ₃	Me	4-NO ₂	D-799	NH-n-Bu	SCH ₂ CF ₃	Me	4-NO ₂
D-750	NH-i-Pr	SCH ₂ CH ₂ F	Me	4-NO ₂	D-800	NH-n-Bu	SCH ₂ CH ₂ F	Me	4-NO ₂

Table 15

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-801	NH ₂	SH	Me	4-NH ₂	D-851	NH-allyl	SH	Me	4-NH ₂
D-802	NH ₂	SMe	Me	4-OMe	D-852	NH-allyl	SMe	Me	4-NH ₂
D-803	NH ₂	SEt	Me	4-NH ₂	D-853	NH-allyl	SEt	Me	4-NH ₂
D-804	NH ₂	S-n-Pr	Me	4-NH ₂	D-854	NH-allyl	S-n-Pr	Me	4-NH ₂
D-805	NH ₂	S-i-Pr	Me	4-NH ₂	D-855	NH-allyl	S-i-Pr	Me	4-NH ₂
D-806	NH ₂	S-n-Bu	Me	4-NH ₂	D-856	NH-allyl	S-n-Bu	Me	4-NH ₂
D-807	NH ₂	S-allyl	Me	4-NH ₂	D-857	NH-allyl	S-allyl	Me	4-NH ₂
D-808	NH ₂	S-propargyl	Me	4-NH ₂	D-858	NH-allyl	S-propargyl	Me	4-NH ₂
D-809	NH ₂	SCH ₂ CF ₃	Me	4-NH ₂	D-859	NH-allyl	SCH ₂ CF ₃	Me	4-NH ₂
D-810	NH ₂	SCH ₂ CH ₂ F	Me	4-NH ₂	D-860	NH-allyl	SCH ₂ CH ₂ F	Me	4-NH ₂
D-811	NHMe	SH	Me	4-NH ₂	D-861	NH-propargyl	SH	Me	4-NH ₂
D-812	NHMe	SMe	Me	4-OMe	D-862	NH-propargyl	SMe	Me	4-NH ₂
D-813	NHMe	SEt	Me	4-OMe	D-863	NH-propargyl	SEt	Me	4-NH ₂
D-814	NHMe	S-n-Pr	Me	4-OMe	D-864	NH-propargyl	S-n-Pr	Me	4-NH ₂
D-815	NHMe	S-i-Pr	Me	4-NH ₂	D-865	NH-propargyl	S-i-Pr	Me	4-NH ₂
D-816	NHMe	S-n-Bu	Me	4-NH ₂	D-866	NH-propargyl	S-n-Bu	Me	4-NH ₂
D-817	NHMe	S-allyl	Me	4-NH ₂	D-867	NH-propargyl	S-allyl	Me	4-NH ₂
D-818	NHMe	S-propargyl	Me	4-NH ₂	D-868	NH-propargyl	S-propargyl	Me	4-NH ₂
D-819	NHMe	SCH ₂ CF ₃	Me	4-NH ₂	D-869	NH-propargyl	SCH ₂ CF ₃	Me	4-NH ₂
D-820	NHMe	SCH ₂ CH ₂ F	Me	4-NH ₂	D-870	NH-propargyl	SCH ₂ CH ₂ F	Me	4-NH ₂
D-821	NHEt	SH	Me	4-NH ₂	D-871	NHCH ₂ CF ₃	SH	Me	4-NH ₂
D-822	NHEt	SMe	Me	4-OMe	D-872	NHCH ₂ CF ₃	SMe	Me	4-OMe
D-823	NHEt	SEt	Me	4-OMe	D-873	NHCH ₂ CF ₃	SEt	Me	4-NH ₂
D-824	NHEt	S-n-Pr	Me	4-OMe	D-874	NHCH ₂ CF ₃	S-n-Pr	Me	4-NH ₂
D-825	NHEt	S-i-Pr	Me	4-NH ₂	D-875	NHCH ₂ CF ₃	S-i-Pr	Me	4-NH ₂
D-826	NHEt	S-n-Bu	Me	4-NH ₂	D-876	NHCH ₂ CF ₃	S-n-Bu	Me	4-NH ₂
D-827	NHEt	S-allyl	Me	4-NH ₂	D-877	NHCH ₂ CF ₃	S-allyl	Me	4-NH ₂
D-828	NHEt	S-propargyl	Me	4-NH ₂	D-878	NHCH ₂ CF ₃	S-propargyl	Me	4-NH ₂
D-829	NHEt	SCH ₂ CF ₃	Me	4-NH ₂	D-879	NHCH ₂ CF ₃	SCH ₂ CF ₃	Me	4-NH ₂
D-830	NHEt	SCH ₂ CH ₂ F	Me	4-NH ₂	D-880	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Me	4-NH ₂
D-831	NHPr	SH	Me	4-NH ₂	D-881	NHCH ₂ CH ₂ F	SH	Me	4-NH ₂
D-832	NHPr	SMe	Me	4-OMe	D-882	NHCH ₂ CH ₂ F	SMe	Me	4-NH ₂
D-833	NHPr	SEt	Me	4-NH ₂	D-883	NHCH ₂ CH ₂ F	SEt	Me	4-NH ₂
D-834	NHPr	S-n-Pr	Me	4-NH ₂	D-884	NHCH ₂ CH ₂ F	S-n-Pr	Me	4-NH ₂
D-835	NHPr	S-i-Pr	Me	4-NH ₂	D-885	NHCH ₂ CH ₂ F	S-i-Pr	Me	4-NH ₂
D-836	NHPr	S-n-Bu	Me	4-NH ₂	D-886	NHCH ₂ CH ₂ F	S-n-Bu	Me	4-NH ₂
D-837	NHPr	S-allyl	Me	4-NH ₂	D-887	NHCH ₂ CH ₂ F	S-allyl	Me	4-NH ₂
D-838	NHPr	S-propargyl	Me	4-NH ₂	D-888	NHCH ₂ CH ₂ F	S-propargyl	Me	4-NH ₂
D-839	NHPr	SCH ₂ CF ₃	Me	4-NH ₂	D-889	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Me	4-NH ₂
D-840	NHPr	SCH ₂ CH ₂ F	Me	4-NH ₂	D-890	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Me	4-NH ₂
D-841	NH-i-Pr	SH	Me	4-NH ₂	D-891	NH-n-Bu	SH	Me	4-NH ₂
D-842	NH-i-Pr	SMe	Me	4-NH ₂	D-892	NH-n-Bu	SMe	Me	4-NH ₂
D-843	NH-i-Pr	SEt	Me	4-NH ₂	D-893	NH-n-Bu	SEt	Me	4-NH ₂
D-844	NH-i-Pr	S-n-Pr	Me	4-NH ₂	D-894	NH-n-Bu	S-n-Pr	Me	4-NH ₂
D-845	NH-i-Pr	S-i-Pr	Me	4-NH ₂	D-895	NH-n-Bu	S-i-Pr	Me	4-NH ₂
D-846	NH-i-Pr	S-n-Bu	Me	4-NH ₂	D-896	NH-n-Bu	S-n-Bu	Me	4-NH ₂
D-847	NH-i-Pr	S-allyl	Me	4-NH ₂	D-897	NH-n-Bu	S-allyl	Me	4-NH ₂
D-848	NH-i-Pr	S-propargyl	Me	4-NH ₂	D-898	NH-n-Bu	S-propargyl	Me	4-NH ₂
D-849	NH-i-Pr	SCH ₂ CF ₃	Me	4-NH ₂	D-899	NH-n-Bu	SCH ₂ CF ₃	Me	4-NH ₂
D-850	NH-i-Pr	SCH ₂ CH ₂ F	Me	4-NH ₂	D-900	NH-n-Bu	SCH ₂ CH ₂ F	Me	4-NH ₂

Table 16

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-901	NH ₂	OH	H	4-NH ₂	D-951	NH-allyl	OH	H	4-NH ₂
D-902	NH ₂	OMe	H	4-NH ₂	D-952	NH-allyl	OMe	H	4-NH ₂
D-903	NH ₂	OEt	H	4-NH ₂	D-953	NH-allyl	OEt	H	4-NH ₂
D-904	NH ₂	O-n-Pr	H	4-NH ₂	D-954	NH-allyl	O-n-Pr	H	4-NH ₂
D-905	NH ₂	O-i-Pr	H	4-NH ₂	D-955	NH-allyl	O-i-Pr	H	4-NH ₂
D-906	NH ₂	O-n-Bu	H	4-NH ₂	D-956	NH-allyl	O-n-Bu	H	4-NH ₂
D-907	NH ₂	O-allyl	H	4-NH ₂	D-957	NH-allyl	O-allyl	H	4-NH ₂
D-908	NH ₂	O-propargyl	H	4-NH ₂	D-958	NH-allyl	O-propargyl	H	4-NH ₂
D-909	NH ₂	OCH ₂ CF ₃	H	4-NH ₂	D-959	NH-allyl	OCH ₂ CF ₃	H	4-NH ₂
D-910	NH ₂	OCH ₂ CH ₂ F	H	4-NH ₂	D-960	NH-allyl	OCH ₂ CH ₂ F	H	4-NH ₂
D-911	NHMe	OH	H	4-NH ₂	D-961	NH-propargyl	OH	H	4-NH ₂
D-912	NHMe	OMe	H	4-NH ₂	D-962	NH-propargyl	OMe	H	4-NH ₂
D-913	NHMe	OEt	H	4-NH ₂	D-963	NH-propargyl	OEt	H	4-NH ₂
D-914	NHMe	O-n-Pr	H	4-NH ₂	D-964	NH-propargyl	O-n-Pr	H	4-NH ₂
D-915	NHMe	O-i-Pr	H	4-NH ₂	D-965	NH-propargyl	O-i-Pr	H	4-NH ₂
D-916	NHMe	O-n-Bu	H	4-NH ₂	D-966	NH-propargyl	O-n-Bu	H	4-NH ₂
D-917	NHMe	O-allyl	H	4-NH ₂	D-967	NH-propargyl	O-allyl	H	4-NH ₂
D-918	NHMe	O-propargyl	H	4-NH ₂	D-968	NH-propargyl	O-propargyl	H	4-NH ₂
D-919	NHMe	OCH ₂ CF ₃	H	4-NH ₂	D-969	NH-propargyl	OCH ₂ CF ₃	H	4-NH ₂
D-920	NHMe	OCH ₂ CH ₂ F	H	4-NH ₂	D-970	NH-propargyl	OCH ₂ CH ₂ F	H	4-NH ₂
D-921	NHEt	OH	H	4-NH ₂	D-971	NHCH ₂ CF ₃	OH	H	4-NH ₂
D-922	NHEt	OMe	H	4-NH ₂	D-972	NHCH ₂ CF ₃	OMe	H	4-NH ₂
D-923	NHEt	OEt	H	4-NH ₂	D-973	NHCH ₂ CF ₃	OEt	H	4-NH ₂
D-924	NHEt	O-n-Pr	H	4-NH ₂	D-974	NHCH ₂ CF ₃	O-n-Pr	H	4-NH ₂
D-925	NHEt	O-i-Pr	H	4-NH ₂	D-975	NHCH ₂ CF ₃	O-i-Pr	H	4-NH ₂
D-926	NHEt	O-n-Bu	H	4-NH ₂	D-976	NHCH ₂ CF ₃	O-n-Bu	H	4-NH ₂
D-927	NHEt	O-allyl	H	4-NH ₂	D-977	NHCH ₂ CF ₃	O-allyl	H	4-NH ₂
D-928	NHEt	O-propargyl	H	4-NH ₂	D-978	NHCH ₂ CF ₃	O-propargyl	H	4-NH ₂
D-929	NHEt	OCH ₂ CF ₃	H	4-NH ₂	D-979	NHCH ₂ CF ₃	OCH ₂ CF ₃	H	4-NH ₂
D-930	NHEt	OCH ₂ CH ₂ F	H	4-NH ₂	D-980	NHCH ₂ CF ₃	OCH ₂ CH ₂ F	H	4-NH ₂
D-931	NHPr	OH	H	4-NH ₂	D-981	NHCH ₂ CH ₂ F	OH	H	4-NH ₂
D-932	NHPr	OMe	H	4-NH ₂	D-982	NHCH ₂ CH ₂ F	OMe	H	4-NH ₂
D-933	NHPr	OEt	H	4-NH ₂	D-983	NHCH ₂ CH ₂ F	OEt	H	4-NH ₂
D-934	NHPr	O-n-Pr	H	4-NH ₂	D-984	NHCH ₂ CH ₂ F	O-n-Pr	H	4-NH ₂
D-935	NHPr	O-i-Pr	H	4-NH ₂	D-985	NHCH ₂ CH ₂ F	O-i-Pr	H	4-NH ₂
D-936	NHPr	O-n-Bu	H	4-NH ₂	D-986	NHCH ₂ CH ₂ F	O-n-Bu	H	4-NH ₂
D-937	NHPr	O-allyl	H	4-NH ₂	D-987	NHCH ₂ CH ₂ F	O-allyl	H	4-NH ₂
D-938	NHPr	O-propargyl	H	4-NH ₂	D-988	NHCH ₂ CH ₂ F	O-propargyl	H	4-NH ₂
D-939	NHPr	OCH ₂ CF ₃	H	4-NH ₂	D-989	NHCH ₂ CH ₂ F	OCH ₂ CF ₃	H	4-NH ₂
D-940	NHPr	OCH ₂ CH ₂ F	H	4-NH ₂	D-990	NHCH ₂ CH ₂ F	OCH ₂ CH ₂ F	H	4-NH ₂
D-941	NH-i-Pr	OH	H	4-NH ₂	D-991	NH-n-Bu	OH	H	4-NH ₂
D-942	NH-i-Pr	OMe	H	4-NH ₂	D-992	NH-n-Bu	OMe	H	4-NH ₂
D-943	NH-i-Pr	OEt	H	4-NH ₂	D-993	NH-n-Bu	OEt	H	4-NH ₂
D-944	NH-i-Pr	O-n-Pr	H	4-NH ₂	D-994	NH-n-Bu	O-n-Pr	H	4-NH ₂
D-945	NH-i-Pr	O-i-Pr	H	4-NH ₂	D-995	NH-n-Bu	O-i-Pr	H	4-NH ₂
D-946	NH-i-Pr	O-n-Bu	H	4-NH ₂	D-996	NH-n-Bu	O-n-Bu	H	4-NH ₂
D-947	NH-i-Pr	O-allyl	H	4-NH ₂	D-997	NH-n-Bu	O-allyl	H	4-NH ₂
D-948	NH-i-Pr	O-propargyl	H	4-NH ₂	D-998	NH-n-Bu	O-propargyl	H	4-NH ₂
D-949	NH-i-Pr	OCH ₂ CF ₃	H	4-NH ₂	D-999	NH-n-Bu	OCH ₂ CF ₃	H	4-NH ₂
D-950	NH-i-Pr	OCH ₂ CH ₂ F	H	4-NH ₂	D-1000	NH-n-Bu	OCH ₂ CH ₂ F	H	4-NH ₂

Table 17

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1001	NH ₂	OH	H	4-NO ₂	D-1051	NH-allyl	OH	H	4-NO ₂
D-1002	NH ₂	OMe	H	4-NO ₂	D-1052	NH-allyl	OMe	H	4-NO ₂
D-1003	NH ₂	OEt	H	4-NO ₂	D-1053	NH-allyl	OEt	H	4-NO ₂
D-1004	NH ₂	O-n-Pr	H	4-NO ₂	D-1054	NH-allyl	O-n-Pr	H	4-NO ₂
D-1005	NH ₂	O-i-Pr	H	4-NO ₂	D-1055	NH-allyl	O-i-Pr	H	4-NO ₂
D-1006	NH ₂	O-n-Bu	H	4-NO ₂	D-1056	NH-allyl	O-n-Bu	H	4-NO ₂
D-1007	NH ₂	O-allyl	H	4-NO ₂	D-1057	NH-allyl	O-allyl	H	4-NO ₂
D-1008	NH ₂	O-propargyl	H	4-NO ₂	D-1058	NH-allyl	O-propargyl	H	4-NO ₂
D-1009	NH ₂	OCH ₂ CF ₃	H	4-NO ₂	D-1059	NH-allyl	OCH ₂ CF ₃	H	4-NO ₂
D-1010	NH ₂	OCH ₂ CH ₂ F	H	4-NO ₂	D-1060	NH-allyl	OCH ₂ CH ₂ F	H	4-NO ₂
D-1011	NHMe	OH	H	4-NO ₂	D-1061	NH-propargyl	OH	H	4-NO ₂
D-1012	NHMe	OMe	H	4-NO ₂	D-1062	NH-propargyl	OMe	H	4-NO ₂
D-1013	NHMe	OEt	H	4-NO ₂	D-1063	NH-propargyl	OEt	H	4-NO ₂
D-1014	NHMe	O-n-Pr	H	4-NO ₂	D-1064	NH-propargyl	O-n-Pr	H	4-NO ₂
D-1015	NHMe	O-i-Pr	H	4-NO ₂	D-1065	NH-propargyl	O-i-Pr	H	4-NO ₂
D-1016	NHMe	O-n-Bu	H	4-NO ₂	D-1066	NH-propargyl	O-n-Bu	H	4-NO ₂
D-1017	NHMe	O-allyl	H	4-NO ₂	D-1067	NH-propargyl	O-allyl	H	4-NO ₂
D-1018	NHMe	O-propargyl	H	4-NO ₂	D-1068	NH-propargyl	O-propargyl	H	4-NO ₂
D-1019	NHMe	OCH ₂ CF ₃	H	4-NO ₂	D-1069	NH-propargyl	OCH ₂ CF ₃	H	4-NO ₂
D-1020	NHMe	OCH ₂ CH ₂ F	H	4-NO ₂	D-1070	NH-propargyl	OCH ₂ CH ₂ F	H	4-NO ₂
D-1021	NHEt	OH	H	4-NO ₂	D-1071	NHCH ₂ CF ₃	OH	H	4-NO ₂
D-1022	NHEt	OMe	H	4-NO ₂	D-1072	NHCH ₂ CF ₃	OMe	H	4-NO ₂
D-1023	NHEt	OEt	H	4-NO ₂	D-1073	NHCH ₂ CF ₃	OEt	H	4-NO ₂
D-1024	NHEt	O-n-Pr	H	4-NO ₂	D-1074	NHCH ₂ CF ₃	O-n-Pr	H	4-NO ₂
D-1025	NHEt	O-i-Pr	H	4-NO ₂	D-1075	NHCH ₂ CF ₃	O-i-Pr	H	4-NO ₂
D-1026	NHEt	O-n-Bu	H	4-NO ₂	D-1076	NHCH ₂ CF ₃	O-n-Bu	H	4-NO ₂
D-1027	NHEt	O-allyl	H	4-NO ₂	D-1077	NHCH ₂ CF ₃	O-allyl	H	4-NO ₂
D-1028	NHEt	O-propargyl	H	4-NO ₂	D-1078	NHCH ₂ CF ₃	O-propargyl	H	4-NO ₂
D-1029	NHEt	OCH ₂ CF ₃	H	4-NO ₂	D-1079	NHCH ₂ CF ₃	OCH ₂ CF ₃	H	4-NO ₂
D-1030	NHEt	OCH ₂ CH ₂ F	H	4-NO ₂	D-1080	NHCH ₂ CF ₃	OCH ₂ CH ₂ F	H	4-NO ₂
D-1031	NHPr	OH	H	4-NO ₂	D-1081	NHCH ₂ CH ₂ F	OH	H	4-NO ₂
D-1032	NHPr	OMe	H	4-NO ₂	D-1082	NHCH ₂ CH ₂ F	OMe	H	4-NO ₂
D-1033	NHPr	OEt	H	4-NO ₂	D-1083	NHCH ₂ CH ₂ F	OEt	H	4-NO ₂
D-1034	NHPr	O-n-Pr	H	4-NO ₂	D-1084	NHCH ₂ CH ₂ F	O-n-Pr	H	4-NO ₂
D-1035	NHPr	O-i-Pr	H	4-NO ₂	D-1085	NHCH ₂ CH ₂ F	O-i-Pr	H	4-NO ₂
D-1036	NHPr	O-n-Bu	H	4-NO ₂	D-1086	NHCH ₂ CH ₂ F	O-n-Bu	H	4-NO ₂
D-1037	NHPr	O-allyl	H	4-NO ₂	D-1087	NHCH ₂ CH ₂ F	O-allyl	H	4-NO ₂
D-1038	NHPr	O-propargyl	H	4-NO ₂	D-1088	NHCH ₂ CH ₂ F	O-propargyl	H	4-NO ₂
D-1039	NHPr	OCH ₂ CF ₃	H	4-NO ₂	D-1089	NHCH ₂ CH ₂ F	OCH ₂ CF ₃	H	4-NO ₂
D-1040	NHPr	OCH ₂ CH ₂ F	H	4-NO ₂	D-1090	NHCH ₂ CH ₂ F	OCH ₂ CH ₂ F	H	4-NO ₂
D-1041	NH-i-Pr	OH	H	4-NO ₂	D-1091	NH-n-Bu	OH	H	4-NO ₂
D-1042	NH-i-Pr	OMe	H	4-NO ₂	D-1092	NH-n-Bu	OMe	H	4-NO ₂
D-1043	NH-i-Pr	OEt	H	4-NO ₂	D-1093	NH-n-Bu	OEt	H	4-NO ₂
D-1044	NH-i-Pr	O-n-Pr	H	4-NO ₂	D-1094	NH-n-Bu	O-n-Pr	H	4-NO ₂
D-1045	NH-i-Pr	O-i-Pr	H	4-NO ₂	D-1095	NH-n-Bu	O-i-Pr	H	4-NO ₂
D-1046	NH-i-Pr	O-n-Bu	H	4-NO ₂	D-1096	NH-n-Bu	O-n-Bu	H	4-NO ₂
D-1047	NH-i-Pr	O-allyl	H	4-NO ₂	D-1097	NH-n-Bu	O-allyl	H	4-NO ₂
D-1048	NH-i-Pr	O-propargyl	H	4-NO ₂	D-1098	NH-n-Bu	O-propargyl	H	4-NO ₂
D-1049	NH-i-Pr	OCH ₂ CF ₃	H	4-NO ₂	D-1099	NH-n-Bu	OCH ₂ CF ₃	H	4-NO ₂
D-1050	NH-i-Pr	OCH ₂ CH ₂ F	H	4-NO ₂	D-1100	NH-n-Bu	OCH ₂ CH ₂ F	H	4-NO ₂

Table 18

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1101	NH ₂	OH	Me	4-NH ₂	D-1151	NH-allyl	OH	Me	4-NH ₂
D-1102	NH ₂	OMe	Me	4-NH ₂	D-1152	NH-allyl	OMe	Me	4-NH ₂
D-1103	NH ₂	OEt	Me	4-NH ₂	D-1153	NH-allyl	OEt	Me	4-NH ₂
D-1104	NH ₂	O-n-Pr	Me	4-NH ₂	D-1154	NH-allyl	O-n-Pr	Me	4-NH ₂
D-1105	NH ₂	O-i-Pr	Me	4-NH ₂	D-1155	NH-allyl	O-i-Pr	Me	4-NH ₂
D-1106	NH ₂	O-n-Bu	Me	4-NH ₂	D-1156	NH-allyl	O-n-Bu	Me	4-NH ₂
D-1107	NH ₂	O-allyl	Me	4-NH ₂	D-1157	NH-allyl	O-allyl	Me	4-NH ₂
D-1108	NH ₂	O-propargyl	Me	4-NH ₂	D-1158	NH-allyl	O-propargyl	Me	4-NH ₂
D-1109	NH ₂	OCH ₂ CF ₃	Me	4-NH ₂	D-1159	NH-allyl	OCH ₂ CF ₃	Me	4-NH ₂
D-1110	NH ₂	OCH ₂ CH ₂ F	Me	4-NH ₂	D-1160	NH-allyl	OCH ₂ CH ₂ F	Me	4-NH ₂
D-1111	NHMe	OH	Me	4-NH ₂	D-1161	NH-propargyl	OH	Me	4-NH ₂
D-1112	NHMe	OMe	Me	4-NH ₂	D-1162	NH-propargyl	OMe	Me	4-NH ₂
D-1113	NHMe	OEt	Me	4-NH ₂	D-1163	NH-propargyl	OEt	Me	4-NH ₂
D-1114	NHMe	O-n-Pr	Me	4-NH ₂	D-1164	NH-propargyl	O-n-Pr	Me	4-NH ₂
D-1115	NHMe	O-i-Pr	Me	4-NH ₂	D-1165	NH-propargyl	O-i-Pr	Me	4-NH ₂
D-1116	NHMe	O-n-Bu	Me	4-NH ₂	D-1166	NH-propargyl	O-n-Bu	Me	4-NH ₂
D-1117	NHMe	O-allyl	Me	4-NH ₂	D-1167	NH-propargyl	O-allyl	Me	4-NH ₂
D-1118	NHMe	O-propargyl	Me	4-NH ₂	D-1168	NH-propargyl	O-propargyl	Me	4-NH ₂
D-1119	NHMe	OCH ₂ CF ₃	Me	4-NH ₂	D-1169	NH-propargyl	OCH ₂ CF ₃	Me	4-NH ₂
D-1120	NHMe	OCH ₂ CH ₂ F	Me	4-NH ₂	D-1170	NH-propargyl	OCH ₂ CH ₂ F	Me	4-NH ₂
D-1121	NHEt	OH	Me	2-NH ₂	D-1171	NHCH ₂ CF ₃	OH	Me	4-NH ₂
D-1122	NHEt	OMe	Me	4-NH ₂	D-1172	NHCH ₂ CF ₃	OMe	Me	4-NH ₂
D-1123	NHEt	OEt	Me	4-NH ₂	D-1173	NHCH ₂ CF ₃	OEt	Me	4-NH ₂
D-1124	NHEt	O-n-Pr	Me	4-NH ₂	D-1174	NHCH ₂ CF ₃	O-n-Pr	Me	4-NH ₂
D-1125	NHEt	O-i-Pr	Me	4-NH ₂	D-1175	NHCH ₂ CF ₃	O-i-Pr	Me	4-NH ₂
D-1126	NHEt	O-n-Bu	Me	4-NH ₂	D-1176	NHCH ₂ CF ₃	O-n-Bu	Me	4-NH ₂
D-1127	NHEt	O-allyl	Me	4-NH ₂	D-1177	NHCH ₂ CF ₃	O-allyl	Me	4-NH ₂
D-1128	NHEt	O-propargyl	Me	4-NH ₂	D-1178	NHCH ₂ CF ₃	O-propargyl	Me	4-NH ₂
D-1129	NHEt	OCH ₂ CF ₃	Me	4-NH ₂	D-1179	NHCH ₂ CF ₃	OCH ₂ CF ₃	Me	4-NH ₂
D-1130	NHEt	OCH ₂ CH ₂ F	Me	4-NH ₂	D-1180	NHCH ₂ CF ₃	OCH ₂ CH ₂ F	Me	4-NH ₂
D-1131	NHPr	OH	Me	4-NH ₂	D-1181	NHCH ₂ CH ₂ F	OH	Me	4-NH ₂
D-1132	NHPr	OMe	Me	4-NH ₂	D-1182	NHCH ₂ CH ₂ F	OMe	Me	4-NH ₂
D-1133	NHPr	OEt	Me	4-NH ₂	D-1183	NHCH ₂ CH ₂ F	OEt	Me	4-NH ₂
D-1134	NHPr	O-n-Pr	Me	4-NH ₂	D-1184	NHCH ₂ CH ₂ F	O-n-Pr	Me	4-NH ₂
D-1135	NHPr	O-i-Pr	Me	4-NH ₂	D-1185	NHCH ₂ CH ₂ F	O-i-Pr	Me	4-NH ₂
D-1136	NHPr	O-n-Bu	Me	4-NH ₂	D-1186	NHCH ₂ CH ₂ F	O-n-Bu	Me	4-NH ₂
D-1137	NHPr	O-allyl	Me	4-NH ₂	D-1187	NHCH ₂ CH ₂ F	O-allyl	Me	4-NH ₂
D-1138	NHPr	O-propargyl	Me	4-NH ₂	D-1188	NHCH ₂ CH ₂ F	O-propargyl	Me	4-NH ₂
D-1139	NHPr	OCH ₂ CF ₃	Me	4-NH ₂	D-1189	NHCH ₂ CH ₂ F	OCH ₂ CF ₃	Me	4-NH ₂
D-1140	NHPr	OCH ₂ CH ₂ F	Me	4-NH ₂	D-1190	NHCH ₂ CH ₂ F	OCH ₂ CH ₂ F	Me	4-NH ₂
D-1141	NH-i-Pr	OH	Me	4-NH ₂	D-1191	NH-n-Bu	OH	Me	4-NH ₂
D-1142	NH-i-Pr	OMe	Me	4-NH ₂	D-1192	NH-n-Bu	OMe	Me	4-NH ₂
D-1143	NH-i-Pr	OEt	Me	4-NH ₂	D-1193	NH-n-Bu	OEt	Me	4-NH ₂
D-1144	NH-i-Pr	O-n-Pr	Me	4-NH ₂	D-1194	NH-n-Bu	O-n-Pr	Me	4-NH ₂
D-1145	NH-i-Pr	O-i-Pr	Me	4-NH ₂	D-1195	NH-n-Bu	O-i-Pr	Me	4-NH ₂
D-1146	NH-i-Pr	O-n-Bu	Me	4-NH ₂	D-1196	NH-n-Bu	O-n-Bu	Me	4-NH ₂
D-1147	NH-i-Pr	O-allyl	Me	4-NH ₂	D-1197	NH-n-Bu	O-allyl	Me	4-NH ₂
D-1148	NH-i-Pr	O-propargyl	Me	4-NH ₂	D-1198	NH-n-Bu	O-propargyl	Me	4-NH ₂
D-1149	NH-i-Pr	OCH ₂ CF ₃	Me	4-NH ₂	D-1199	NH-n-Bu	OCH ₂ CF ₃	Me	4-NH ₂
D-1150	NH-i-Pr	OCH ₂ CH ₂ F	Me	4-NH ₂	D-1200	NH-n-Bu	OCH ₂ CH ₂ F	Me	4-NH ₂

Table 19

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1201	NH ₂	OH	Me	4-NO ₂	D-1251	NH-allyl	OH	Me	4-NO ₂
D-1202	NH ₂	OMe	Me	4-NO ₂	D-1252	NH-allyl	OMe	Me	4-NO ₂
D-1203	NH ₂	OEt	Me	4-NO ₂	D-1253	NH-allyl	OEt	Me	4-NO ₂
D-1204	NH ₂	O-n-Pr	Me	4-NO ₂	D-1254	NH-allyl	O-n-Pr	Me	4-NO ₂
D-1205	NH ₂	O-i-Pr	Me	4-NO ₂	D-1255	NH-allyl	O-i-Pr	Me	4-NO ₂
D-1206	NH ₂	O-n-Bu	Me	4-NO ₂	D-1256	NH-allyl	O-n-Bu	Me	4-NO ₂
D-1207	NH ₂	O-allyl	Me	4-NO ₂	D-1257	NH-allyl	O-allyl	Me	4-NO ₂
D-1208	NH ₂	O-propargyl	Me	4-NO ₂	D-1258	NH-allyl	O-propargyl	Me	4-NO ₂
D-1209	NH ₂	OCH ₂ CF ₃	Me	4-NO ₂	D-1259	NH-allyl	OCH ₂ CF ₃	Me	4-NO ₂
D-1210	NH ₂	OCH ₂ CH ₂ F	Me	4-NO ₂	D-1260	NH-allyl	OCH ₂ CH ₂ F	Me	4-NO ₂
D-1211	NHMe	OH	Me	4-NO ₂	D-1261	NH-propargyl	OH	Me	4-NO ₂
D-1212	NHMe	OMe	Me	4-OMe	D-1262	NH-propargyl	OMe	Me	4-NO ₂
D-1213	NHMe	OEt	Me	4-Cl	D-1263	NH-propargyl	OEt	Me	4-NO ₂
D-1214	NHMe	O-n-Pr	Me	4-NO ₂	D-1264	NH-propargyl	O-n-Pr	Me	4-NO ₂
D-1215	NHMe	O-i-Pr	Me	4-OMe	D-1265	NH-propargyl	O-i-Pr	Me	4-NO ₂
D-1216	NHMe	O-n-Bu	Me	4-NO ₂	D-1266	NH-propargyl	O-n-Bu	Me	4-NO ₂
D-1217	NHMe	O-allyl	Me	4-NO ₂	D-1267	NH-propargyl	O-allyl	Me	4-NO ₂
D-1218	NHMe	O-propargyl	Me	4-NO ₂	D-1268	NH-propargyl	O-propargyl	Me	4-NO ₂
D-1219	NHMe	OCH ₂ CF ₃	Me	4-NO ₂	D-1269	NH-propargyl	OCH ₂ CF ₃	Me	4-NO ₂
D-1220	NHMe	OCH ₂ CH ₂ F	Me	4-NO ₂	D-1270	NH-propargyl	OCH ₂ CH ₂ F	Me	4-NO ₂
D-1221	NHEt	OH	Me	4-Me	D-1271	NHCH ₂ CF ₃	OH	Me	4-NH ₂
D-1222	NHEt	OMe	Me	4-OMe	D-1272	NHCH ₂ CF ₃	OMe	Me	4-NO ₂
D-1223	NHEt	OEt	Me	4-OMe	D-1273	NHCH ₂ CF ₃	OEt	Me	4-NO ₂
D-1224	NHEt	O-n-Pr	Me	4-NO ₂	D-1274	NHCH ₂ CF ₃	O-n-Pr	Me	4-NO ₂
D-1225	NHEt	O-i-Pr	Me	4-OMe	D-1275	NHCH ₂ CF ₃	O-i-Pr	Me	4-NO ₂
D-1226	NHEt	O-n-Bu	Me	4-NO ₂	D-1276	NHCH ₂ CF ₃	O-n-Bu	Me	4-NO ₂
D-1227	NHEt	O-allyl	Me	4-NO ₂	D-1277	NHCH ₂ CF ₃	O-allyl	Me	4-NO ₂
D-1228	NHEt	O-propargyl	Me	4-NO ₂	D-1278	NHCH ₂ CF ₃	O-propargyl	Me	4-NO ₂
D-1229	NHEt	OCH ₂ CF ₃	Me	4-NO ₂	D-1279	NHCH ₂ CF ₃	OCH ₂ CF ₃	Me	4-NO ₂
D-1230	NHEt	OCH ₂ CH ₂ F	Me	4-NO ₂	D-1280	NHCH ₂ CF ₃	OCH ₂ CH ₂ F	Me	4-NO ₂
D-1231	NHPr	OH	Me	4-OMe	D-1281	NHCH ₂ CH ₂ F	OH	Me	4-NO ₂
D-1232	NHPr	OMe	Me	4-NO ₂	D-1282	NHCH ₂ CH ₂ F	OMe	Me	4-NO ₂
D-1233	NHPr	OEt	Me	4-NO ₂	D-1283	NHCH ₂ CH ₂ F	OEt	Me	4-NO ₂
D-1234	NHPr	O-n-Pr	Me	4-NO ₂	D-1284	NHCH ₂ CH ₂ F	O-n-Pr	Me	4-NO ₂
D-1235	NHPr	O-i-Pr	Me	4-NO ₂	D-1285	NHCH ₂ CH ₂ F	O-i-Pr	Me	4-NO ₂
D-1236	NHPr	O-n-Bu	Me	4-NO ₂	D-1286	NHCH ₂ CH ₂ F	O-n-Bu	Me	4-NO ₂
D-1237	NHPr	O-allyl	Me	4-NO ₂	D-1287	NHCH ₂ CH ₂ F	O-allyl	Me	4-NO ₂
D-1238	NHPr	O-propargyl	Me	4-NO ₂	D-1288	NHCH ₂ CH ₂ F	O-propargyl	Me	4-NO ₂
D-1239	NHPr	OCH ₂ CF ₃	Me	4-NO ₂	D-1289	NHCH ₂ CH ₂ F	OCH ₂ CF ₃	Me	4-NO ₂
D-1240	NHPr	OCH ₂ CH ₂ F	Me	4-NO ₂	D-1290	NHCH ₂ CH ₂ F	OCH ₂ CH ₂ F	Me	4-NO ₂
D-1241	NH-i-Pr	OH	Me	4-NO ₂	D-1291	NH-n-Bu	OH	Me	4-NO ₂
D-1242	NH-i-Pr	OMe	Me	4-NO ₂	D-1292	NH-n-Bu	OMe	Me	4-NO ₂
D-1243	NH-i-Pr	OEt	Me	4-NO ₂	D-1293	NH-n-Bu	OEt	Me	4-NO ₂
D-1244	NH-i-Pr	O-n-Pr	Me	4-NO ₂	D-1294	NH-n-Bu	O-n-Pr	Me	4-NO ₂
D-1245	NH-i-Pr	O-i-Pr	Me	4-NO ₂	D-1295	NH-n-Bu	O-i-Pr	Me	4-NO ₂
D-1246	NH-i-Pr	O-n-Bu	Me	4-NO ₂	D-1296	NH-n-Bu	O-n-Bu	Me	4-NO ₂
D-1247	NH-i-Pr	O-allyl	Me	4-NO ₂	D-1297	NH-n-Bu	O-allyl	Me	4-NO ₂
D-1248	NH-i-Pr	O-propargyl	Me	4-NO ₂	D-1298	NH-n-Bu	O-propargyl	Me	4-NO ₂
D-1249	NH-i-Pr	OCH ₂ CF ₃	Me	4-NO ₂	D-1299	NH-n-Bu	OCH ₂ CF ₃	Me	4-NO ₂
D-1250	NH-i-Pr	OCH ₂ CH ₂ F	Me	4-NO ₂	D-1300	NH-n-Bu	OCH ₂ CH ₂ F	Me	4-NO ₂

Table 20

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1301	NH ₂	NHOH	Me	4-NH ₂	D-1351	NH-propargyl	NHOH	Me	4-NH ₂
D-1302	NH ₂	NHOMe	Me	4-NH ₂	D-1352	NH-propargyl	NHOMe	Me	4-NH ₂
D-1303	NH ₂	NHOEt	Me	4-NH ₂	D-1353	NH-propargyl	NHOEt	Me	4-NH ₂
D-1304	NH ₂	NHNH ₂	Me	4-NH ₂	D-1354	NH-propargyl	NHNH ₂	Me	4-NH ₂
D-1305	NH ₂	NHNMe ₂	Me	4-NH ₂	D-1355	NH-propargyl	NHNMe ₂	Me	4-NH ₂
D-1306	NH ₂	NHNHMe	Me	4-NH ₂	D-1356	NH-propargyl	NHNHMe	Me	4-NH ₂
D-1307	NH ₂	NHNHEt	Me	4-NH ₂	D-1357	NH-propargyl	NHNHEt	Me	4-NH ₂
D-1308	NH ₂	NMeNH ₂	Me	4-NH ₂	D-1358	NH-propargyl	NMeNH ₂	Me	4-NH ₂
D-1309	NH ₂	NHCN	Me	4-NH ₂	D-1359	NH-propargyl	NHCN	Me	4-NH ₂
D-1310	NH ₂	NHNO ₂	Me	4-NH ₂	D-1360	NH-propargyl	NHNO ₂	Me	4-NH ₂
D-1311	NHMe	NHOH	Me	4-NH ₂	D-1361	NHCH ₂ CH ₂ F	NHOH	Me	4-NH ₂
D-1312	NHMe	NHOMe	Me	4-NH ₂	D-1362	NHCH ₂ CH ₂ F	NHOMe	Me	4-NH ₂
D-1313	NHMe	NHOEt	Me	4-NH ₂	D-1363	NHCH ₂ CH ₂ F	NHOEt	Me	4-NH ₂
D-1314	NHMe	NHNH ₂	Me	4-NH ₂	D-1364	NHCH ₂ CH ₂ F	NHNH ₂	Me	4-NH ₂
D-1315	NHMe	NHNMe ₂	Me	4-NH ₂	D-1365	NHCH ₂ CH ₂ F	NHNMe ₂	Me	4-NH ₂
D-1316	NHMe	NHNHMe	Me	4-NH ₂	D-1366	NHCH ₂ CH ₂ F	NHNHMe	Me	4-NH ₂
D-1317	NHMe	NHNHEt	Me	4-NH ₂	D-1367	NHCH ₂ CH ₂ F	NHNHEt	Me	4-NH ₂
D-1318	NHMe	NMeNH ₂	Me	4-NH ₂	D-1368	NHCH ₂ CH ₂ F	NMeNH ₂	Me	4-NH ₂
D-1319	NHMe	NHCN	Me	4-NH ₂	D-1369	NHCH ₂ CH ₂ F	NHCN	Me	4-NH ₂
D-1320	NHMe	NHNO ₂	Me	4-NH ₂	D-1370	NHCH ₂ CH ₂ F	NHNO ₂	Me	4-NH ₂
D-1321	NHEt	NHOH	Me	4-NH ₂	D-1371	NHCH ₂ CF ₃	NHOH	Me	4-NH ₂
D-1322	NHEt	NHOMe	Me	4-NH ₂	D-1372	NHCH ₂ CF ₃	NHOMe	Me	4-NH ₂
D-1323	NHEt	NHOEt	Me	4-NH ₂	D-1373	NHCH ₂ CF ₃	NHOEt	Me	4-NH ₂
D-1324	NHEt	NHNH ₂	Me	4-NH ₂	D-1374	NHCH ₂ CF ₃	NHNH ₂	Me	4-NH ₂
D-1325	NHEt	NHNMe ₂	Me	4-NH ₂	D-1375	NHCH ₂ CF ₃	NHNMe ₂	Me	4-NH ₂
D-1326	NHEt	NHNHMe	Me	4-NH ₂	D-1376	NHCH ₂ CF ₃	NHNHMe	Me	4-NH ₂
D-1327	NHEt	NHNHEt	Me	4-NH ₂	D-1377	NHCH ₂ CF ₃	NHNHEt	Me	4-NH ₂
D-1328	NHEt	NMeNH ₂	Me	4-NH ₂	D-1378	NHCH ₂ CF ₃	NMeNH ₂	Me	4-NH ₂
D-1329	NHEt	NHCN	Me	4-NH ₂	D-1379	NHCH ₂ CF ₃	NHCN	Me	4-NH ₂
D-1330	NHEt	NHNO ₂	Me	4-NH ₂	D-1380	NHCH ₂ CF ₃	NHNO ₂	Me	4-NH ₂
D-1331	NH-i-Pr	NHOH	Me	4-NH ₂	D-1381	SMe	NHOH	Me	4-NH ₂
D-1332	NH-i-Pr	NHOMe	Me	4-NH ₂	D-1382	SMe	NHOMe	Me	4-NH ₂
D-1333	NH-i-Pr	NHOEt	Me	4-NH ₂	D-1383	SMe	NHOEt	Me	4-NH ₂
D-1334	NH-i-Pr	NHNH ₂	Me	4-NH ₂	D-1384	SMe	NHNH ₂	Me	4-NH ₂
D-1335	NH-i-Pr	NHNMe ₂	Me	4-NH ₂	D-1385	SMe	NHNMe ₂	Me	4-NH ₂
D-1336	NH-i-Pr	NHNHMe	Me	4-NH ₂	D-1386	SMe	NHNHMe	Me	4-NH ₂
D-1337	NH-i-Pr	NHNHEt	Me	4-NH ₂	D-1387	SMe	NHNHEt	Me	4-NH ₂
D-1338	NH-i-Pr	NMeNH ₂	Me	4-NH ₂	D-1388	SMe	NMeNH ₂	Me	4-NH ₂
D-1339	NH-i-Pr	NHCN	Me	4-NH ₂	D-1389	SMe	NHCN	Me	4-NH ₂
D-1340	NH-i-Pr	NHNO ₂	Me	4-NH ₂	D-1390	SMe	NHNO ₂	Me	4-NH ₂
D-1341	NH-allyl	NHOH	Me	4-NH ₂	D-1391	SEt	NHOH	Me	4-NH ₂
D-1342	NH-allyl	NHOMe	Me	4-NH ₂	D-1392	SEt	NHOMe	Me	4-NH ₂
D-1343	NH-allyl	NHOEt	Me	4-NH ₂	D-1393	SEt	NHOEt	Me	4-NH ₂
D-1344	NH-allyl	NHNH ₂	Me	4-NH ₂	D-1394	SEt	NHNH ₂	Me	4-NH ₂
D-1345	NH-allyl	NHNMe ₂	Me	4-NH ₂	D-1395	SEt	NHNMe ₂	Me	4-NH ₂
D-1346	NH-allyl	NHNHMe	Me	4-NH ₂	D-1396	SEt	NHNHMe	Me	4-NH ₂
D-1347	NH-allyl	NHNHEt	Me	4-NH ₂	D-1397	SEt	NHNHEt	Me	4-NH ₂
D-1348	NH-allyl	NMeNH ₂	Me	4-NH ₂	D-1398	SEt	NMeNH ₂	Me	4-NH ₂
D-1349	NH-allyl	NHCN	Me	4-NH ₂	D-1399	SEt	NHCN	Me	4-NH ₂
D-1350	NH-allyl	NHNO ₂	Me	4-NH ₂	D-1400	SEt	NHNO ₂	Me	4-NH ₂

Table 21

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1401	NH ₂	NHOH	Me	4-NO ₂	D-1451	NH-propargyl	NHOH	Me	4-NO ₂
D-1402	NH ₂	NHOMe	Me	4-NO ₂	D-1452	NH-propargyl	NHOMe	Me	4-NO ₂
D-1403	NH ₂	NHOEt	Me	4-NO ₂	D-1453	NH-propargyl	NHOEt	Me	4-NO ₂
D-1404	NH ₂	NHNH ₂	Me	4-NO ₂	D-1454	NH-propargyl	NHNH ₂	Me	4-NO ₂
D-1405	NH ₂	NHNMe ₂	Me	4-NO ₂	D-1455	NH-propargyl	NHNMe ₂	Me	4-NO ₂
D-1406	NH ₂	NHNHMe	Me	4-NO ₂	D-1456	NH-propargyl	NHNHMe	Me	4-NO ₂
D-1407	NH ₂	NHNHEt	Me	4-NO ₂	D-1457	NH-propargyl	NHNHEt	Me	4-NO ₂
D-1408	NH ₂	NMeNH ₂	Me	4-NO ₂	D-1458	NH-propargyl	NMeNH ₂	Me	4-NO ₂
D-1409	NH ₂	NHCN	Me	4-NO ₂	D-1459	NH-propargyl	NHCN	Me	4-NO ₂
D-1410	NH ₂	NHNO ₂	Me	4-NO ₂	D-1460	NH-propargyl	NHNO ₂	Me	4-NO ₂
D-1411	NHMe	NHOH	Me	4-NO ₂	D-1461	NHCH ₂ CH ₂ F	NHOH	Me	4-NO ₂
D-1412	NHMe	NHOMe	Me	4-Cl	D-1462	NHCH ₂ CH ₂ F	NHOMe	Me	4-NO ₂
D-1413	NHMe	NHOEt	Me	4-NO ₂	D-1463	NHCH ₂ CH ₂ F	NHOEt	Me	4-NO ₂
D-1414	NHMe	NHNH ₂	Me	4-NO ₂	D-1464	NHCH ₂ CH ₂ F	NHNH ₂	Me	4-NO ₂
D-1415	NHMe	NHNMe ₂	Me	4-NO ₂	D-1465	NHCH ₂ CH ₂ F	NHNMe ₂	Me	4-NO ₂
D-1416	NHMe	NHNHMe	Me	4-NO ₂	D-1466	NHCH ₂ CH ₂ F	NHNHMe	Me	4-NO ₂
D-1417	NHMe	NHNHEt	Me	4-NO ₂	D-1467	NHCH ₂ CH ₂ F	NHNHEt	Me	4-NO ₂
D-1418	NHMe	NMeNH ₂	Me	4-NO ₂	D-1468	NHCH ₂ CH ₂ F	NMeNH ₂	Me	4-NO ₂
D-1419	NHMe	NHCN	Me	4-NO ₂	D-1469	NHCH ₂ CH ₂ F	NHCN	Me	4-NO ₂
D-1420	NHMe	NHNO ₂	Me	4-NO ₂	D-1470	NHCH ₂ CH ₂ F	NHNO ₂	Me	4-NO ₂
D-1421	NHEt	NHOH	Me	4-NO ₂	D-1471	NHCH ₂ CF ₃	NHOH	Me	4-NO ₂
D-1422	NHEt	NHOMe	Me	4-NO ₂	D-1472	NHCH ₂ CF ₃	NHOMe	Me	4-NO ₂
D-1423	NHEt	NHOEt	Me	4-NO ₂	D-1473	NHCH ₂ CF ₃	NHOEt	Me	4-NO ₂
D-1424	NHEt	NHNH ₂	Me	4-NO ₂	D-1474	NHCH ₂ CF ₃	NHNH ₂	Me	4-NO ₂
D-1425	NHEt	NHNMe ₂	Me	4-NO ₂	D-1475	NHCH ₂ CF ₃	NHNMe ₂	Me	4-NO ₂
D-1426	NHEt	NHNHMe	Me	4-NO ₂	D-1476	NHCH ₂ CF ₃	NHNHMe	Me	4-NO ₂
D-1427	NHEt	NHNHEt	Me	4-NO ₂	D-1477	NHCH ₂ CF ₃	NHNHEt	Me	4-NO ₂
D-1428	NHEt	NMeNH ₂	Me	4-NO ₂	D-1478	NHCH ₂ CF ₃	NMeNH ₂	Me	4-NO ₂
D-1429	NHEt	NHCN	Me	4-NO ₂	D-1479	NHCH ₂ CF ₃	NHCN	Me	4-NO ₂
D-1430	NHEt	NHNO ₂	Me	4-NO ₂	D-1480	NHCH ₂ CF ₃	NHNO ₂	Me	4-NO ₂
D-1431	NH-i-Pr	NHOH	Me	4-NO ₂	D-1481	SMe	NHOH	Me	4-NO ₂
D-1432	NH-i-Pr	NHOMe	Me	4-NO ₂	D-1482	SMe	NHOMe	Me	4-NO ₂
D-1433	NH-i-Pr	NHOEt	Me	4-NO ₂	D-1483	SMe	NHOEt	Me	4-NO ₂
D-1434	NH-i-Pr	NHNH ₂	Me	4-NO ₂	D-1484	SMe	NHNH ₂	Me	4-NO ₂
D-1435	NH-i-Pr	NHNMe ₂	Me	4-NO ₂	D-1485	SMe	NHNMe ₂	Me	4-NO ₂
D-1436	NH-i-Pr	NHNHMe	Me	4-NO ₂	D-1486	SMe	NHNHMe	Me	4-NO ₂
D-1437	NH-i-Pr	NHNHEt	Me	4-NO ₂	D-1487	SMe	NHNHEt	Me	4-NO ₂
D-1438	NH-i-Pr	NMeNH ₂	Me	4-NO ₂	D-1488	SMe	NMeNH ₂	Me	4-NO ₂
D-1439	NH-i-Pr	NHCN	Me	4-NO ₂	D-1489	SMe	NHCN	Me	4-NO ₂
D-1440	NH-i-Pr	NHNO ₂	Me	4-NO ₂	D-1490	SMe	NHNO ₂	Me	4-NO ₂
D-1441	NH-allyl	NHOH	Me	4-NO ₂	D-1491	SEt	NHOH	Me	4-NO ₂
D-1442	NH-allyl	NHOMe	Me	4-NO ₂	D-1492	SEt	NHOMe	Me	4-NO ₂
D-1443	NH-allyl	NHOEt	Me	4-NO ₂	D-1493	SEt	NHOEt	Me	4-NO ₂
D-1444	NH-allyl	NHNH ₂	Me	4-NO ₂	D-1494	SEt	NHNH ₂	Me	4-NO ₂
D-1445	NH-allyl	NHNMe ₂	Me	4-NO ₂	D-1495	SEt	NHNMe ₂	Me	4-NO ₂
D-1446	NH-allyl	NHNHMe	Me	4-NO ₂	D-1496	SEt	NHNHMe	Me	4-NO ₂
D-1447	NH-allyl	NHNHEt	Me	4-NO ₂	D-1497	SEt	NHNHEt	Me	4-NO ₂
D-1448	NH-allyl	NMeNH ₂	Me	4-NO ₂	D-1498	SEt	NMeNH ₂	Me	4-NO ₂
D-1449	NH-allyl	NHCN	Me	4-NO ₂	D-1499	SEt	NHCN	Me	4-NO ₂
D-1450	NH-allyl	NHNO ₂	Me	4-NO ₂	D-1500	SEt	NHNO ₂	Me	4-NO ₂

Table 22

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1501	NH ₂	NHOH	H	4-NH ₂	D-1551	NH-propargyl	NHOH	H	4-NH ₂
D-1502	NH ₂	NHOMe	H	4-NH ₂	D-1552	NH-propargyl	NHOMe	H	4-NH ₂
D-1503	NH ₂	NHOEt	H	4-NH ₂	D-1553	NH-propargyl	NHOEt	H	4-NH ₂
D-1504	NH ₂	NHNH ₂	H	4-NH ₂	D-1554	NH-propargyl	NHNH ₂	H	4-NH ₂
D-1505	NH ₂	NHNMe ₂	H	4-NH ₂	D-1555	NH-propargyl	NHNMe ₂	H	4-NH ₂
D-1506	NH ₂	NHNHMe	H	4-NH ₂	D-1556	NH-propargyl	NHNHMe	H	4-NH ₂
D-1507	NH ₂	NHNHEt	H	4-NH ₂	D-1557	NH-propargyl	NHNHEt	H	4-NH ₂
D-1508	NH ₂	NMeNH ₂	H	4-NH ₂	D-1558	NH-propargyl	NMeNH ₂	H	4-NH ₂
D-1509	NH ₂	NHCN	H	4-NH ₂	D-1559	NH-propargyl	NHCN	H	4-NH ₂
D-1510	NH ₂	NHNO ₂	H	4-NH ₂	D-1560	NH-propargyl	NHNO ₂	H	4-NH ₂
D-1511	NHMe	NHOH	H	4-NH ₂	D-1561	NHCH ₂ CH ₂ F	NHOH	H	4-NH ₂
D-1512	NHMe	NHOMe	H	4-NH ₂	D-1562	NHCH ₂ CH ₂ F	NHOMe	H	4-NH ₂
D-1513	NHMe	NHOEt	H	4-NH ₂	D-1563	NHCH ₂ CH ₂ F	NHOEt	H	4-NH ₂
D-1514	NHMe	NHNH ₂	H	4-NH ₂	D-1564	NHCH ₂ CH ₂ F	NHNH ₂	H	4-NH ₂
D-1515	NHMe	NHNMe ₂	H	4-NH ₂	D-1565	NHCH ₂ CH ₂ F	NHNMe ₂	H	4-NH ₂
D-1516	NHMe	NHNHMe	H	4-NH ₂	D-1566	NHCH ₂ CH ₂ F	NHNHMe	H	4-NH ₂
D-1517	NHMe	NHNHEt	H	4-NH ₂	D-1567	NHCH ₂ CH ₂ F	NHNHEt	H	4-NH ₂
D-1518	NHMe	NMeNH ₂	H	4-NH ₂	D-1568	NHCH ₂ CH ₂ F	NMeNH ₂	H	4-NH ₂
D-1519	NHMe	NHCN	H	4-NH ₂	D-1569	NHCH ₂ CH ₂ F	NHCN	H	4-NH ₂
D-1520	NHMe	NHNO ₂	H	4-NH ₂	D-1570	NHCH ₂ CH ₂ F	NHNO ₂	H	4-NH ₂
D-1521	NHEt	NHOH	H	4-NH ₂	D-1571	NHCH ₂ CF ₃	NHOH	H	4-NH ₂
D-1522	NHEt	NHOMe	H	4-NH ₂	D-1572	NHCH ₂ CF ₃	NHOMe	H	4-NH ₂
D-1523	NHEt	NHOEt	H	4-NH ₂	D-1573	NHCH ₂ CF ₃	NHOEt	H	4-NH ₂
D-1524	NHEt	NHNH ₂	H	4-NH ₂	D-1574	NHCH ₂ CF ₃	NHNH ₂	H	4-NH ₂
D-1525	NHEt	NHNMe ₂	H	4-NH ₂	D-1575	NHCH ₂ CF ₃	NHNMe ₂	H	4-NH ₂
D-1526	NHEt	NHNHMe	H	4-NH ₂	D-1576	NHCH ₂ CF ₃	NHNHMe	H	4-NH ₂
D-1527	NHEt	NHNHEt	H	4-NH ₂	D-1577	NHCH ₂ CF ₃	NHNHEt	H	4-NH ₂
D-1528	NHEt	NMeNH ₂	H	4-NH ₂	D-1578	NHCH ₂ CF ₃	NMeNH ₂	H	4-NH ₂
D-1529	NHEt	NHCN	H	4-NH ₂	D-1579	NHCH ₂ CF ₃	NHCN	H	4-NH ₂
D-1530	NHEt	NHNO ₂	H	4-NH ₂	D-1580	NHCH ₂ CF ₃	NHNO ₂	H	4-NH ₂
D-1531	NH-i-Pr	NHOH	H	4-NH ₂	D-1581	SMe	NHOH	H	4-NH ₂
D-1532	NH-i-Pr	NHOMe	H	4-NH ₂	D-1582	SMe	NHOMe	H	4-NH ₂
D-1533	NH-i-Pr	NHOEt	H	4-NH ₂	D-1583	SMe	NHOEt	H	4-NH ₂
D-1534	NH-i-Pr	NHNH ₂	H	4-NH ₂	D-1584	SMe	NHNH ₂	H	4-NH ₂
D-1535	NH-i-Pr	NHNMe ₂	H	4-NH ₂	D-1585	SMe	NHNMe ₂	H	4-NH ₂
D-1536	NH-i-Pr	NHNHMe	H	4-NH ₂	D-1586	SMe	NHNHMe	H	4-NH ₂
D-1537	NH-i-Pr	NHNHEt	H	4-NH ₂	D-1587	SMe	NHNHEt	H	4-NH ₂
D-1538	NH-i-Pr	NMeNH ₂	H	4-NH ₂	D-1588	SMe	NMeNH ₂	H	4-NH ₂
D-1539	NH-i-Pr	NHCN	H	4-NH ₂	D-1589	SMe	NHCN	H	4-NH ₂
D-1540	NH-i-Pr	NHNO ₂	H	4-NH ₂	D-1590	SMe	NHNO ₂	H	4-NH ₂
D-1541	NH-allyl	NHOH	H	4-NH ₂	D-1591	SEt	NHOH	H	4-NH ₂
D-1542	NH-allyl	NHOMe	H	4-NH ₂	D-1592	SEt	NHOMe	H	4-NH ₂
D-1543	NH-allyl	NHOEt	H	4-NH ₂	D-1593	SEt	NHOEt	H	4-NH ₂
D-1544	NH-allyl	NHNH ₂	H	4-NH ₂	D-1594	SEt	NHNH ₂	H	4-NH ₂
D-1545	NH-allyl	NHNMe ₂	H	4-NH ₂	D-1595	SEt	NHNMe ₂	H	4-NH ₂
D-1546	NH-allyl	NHNHMe	H	4-NH ₂	D-1596	SEt	NHNHMe	H	4-NH ₂
D-1547	NH-allyl	NHNHEt	H	4-NH ₂	D-1597	SEt	NHNHEt	H	4-NH ₂
D-1548	NH-allyl	NMeNH ₂	H	4-NH ₂	D-1598	SEt	NMeNH ₂	H	4-NH ₂
D-1549	NH-allyl	NHCN	H	4-NH ₂	D-1599	SEt	NHCN	H	4-NH ₂
D-1550	NH-allyl	NHNO ₂	H	4-NH ₂	D-1600	SEt	NHNO ₂	H	4-NH ₂

Table 23

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
D-1601	NH ₂	NHOH	H	4-NO ₂	D-1651	NH-propargyl	NHOH	H	4-NO ₂
D-1602	NH ₂	NHOMe	H	4-NO ₂	D-1652	NH-propargyl	NHOMe	H	4-NO ₂
D-1603	NH ₂	NHOEt	H	4-NO ₂	D-1653	NH-propargyl	NHOEt	H	4-NO ₂
D-1604	NH ₂	NHNH ₂	H	4-NO ₂	D-1654	NH-propargyl	NHNH ₂	H	4-NO ₂
D-1605	NH ₂	NHNMe ₂	H	4-NO ₂	D-1655	NH-propargyl	NHNMe ₂	H	4-NO ₂
D-1606	NH ₂	NHNHMe	H	4-NO ₂	D-1656	NH-propargyl	NHNHMe	H	4-NO ₂
D-1607	NH ₂	NHNHEt	H	4-NO ₂	D-1657	NH-propargyl	NHNHEt	H	4-NO ₂
D-1608	NH ₂	NMeNH ₂	H	4-NO ₂	D-1658	NH-propargyl	NMeNH ₂	H	4-NO ₂
D-1609	NH ₂	NHCN	H	4-NO ₂	D-1659	NH-propargyl	NHCN	H	4-NO ₂
D-1610	NH ₂	NHNO ₂	H	4-NO ₂	D-1660	NH-propargyl	NHNO ₂	H	4-NO ₂
D-1611	NHMe	NHOH	H	4-NO ₂	D-1661	NHCH ₂ CH ₂ F	NHOH	H	4-NO ₂
D-1612	NHMe	NHOMe	H	4-Cl	D-1662	NHCH ₂ CH ₂ F	NHOMe	H	4-NO ₂
D-1613	NHMe	NHOEt	H	4-NO ₂	D-1663	NHCH ₂ CH ₂ F	NHOEt	H	4-NO ₂
D-1614	NHMe	NHNH ₂	H	4-NO ₂	D-1664	NHCH ₂ CH ₂ F	NHNH ₂	H	4-NO ₂
D-1615	NHMe	NHNMe ₂	H	4-NO ₂	D-1665	NHCH ₂ CH ₂ F	NHNMe ₂	H	4-NO ₂
D-1616	NHMe	NHNHMe	H	4-NO ₂	D-1666	NHCH ₂ CH ₂ F	NHNHMe	H	4-NO ₂
D-1617	NHMe	NHNHEt	H	4-NO ₂	D-1667	NHCH ₂ CH ₂ F	NHNHEt	H	4-NO ₂
D-1618	NHMe	NMeNH ₂	H	4-NO ₂	D-1668	NHCH ₂ CH ₂ F	NMeNH ₂	H	4-NO ₂
D-1619	NHMe	NHCN	H	4-NO ₂	D-1669	NHCH ₂ CH ₂ F	NHCN	H	4-NO ₂
D-1620	NHMe	NHNO ₂	H	4-NO ₂	D-1670	NHCH ₂ CH ₂ F	NHNO ₂	H	4-NO ₂
D-1621	NHEt	NHOH	H	4-NO ₂	D-1671	NHCH ₂ CF ₃	NHOH	H	4-NO ₂
D-1622	NHEt	NHOMe	H	4-NO ₂	D-1672	NHCH ₂ CF ₃	NHOMe	H	4-NO ₂
D-1623	NHEt	NHOEt	H	4-NO ₂	D-1673	NHCH ₂ CF ₃	NHOEt	H	4-NO ₂
D-1624	NHEt	NHNH ₂	H	4-NO ₂	D-1674	NHCH ₂ CF ₃	NHNH ₂	H	4-NO ₂
D-1625	NHEt	NHNMe ₂	H	4-NO ₂	D-1675	NHCH ₂ CF ₃	NHNMe ₂	H	4-NO ₂
D-1626	NHEt	NHNHMe	H	4-NO ₂	D-1676	NHCH ₂ CF ₃	NHNHMe	H	4-NO ₂
D-1627	NHEt	NHNHEt	H	4-NO ₂	D-1677	NHCH ₂ CF ₃	NHNHEt	H	4-NO ₂
D-1628	NHEt	NMeNH ₂	H	4-NO ₂	D-1678	NHCH ₂ CF ₃	NMeNH ₂	H	4-NO ₂
D-1629	NHEt	NHCN	H	4-NO ₂	D-1679	NHCH ₂ CF ₃	NHCN	H	4-NO ₂
D-1630	NHEt	NHNO ₂	H	4-NO ₂	D-1680	NHCH ₂ CF ₃	NHNO ₂	H	4-NO ₂
D-1631	NH-i-Pr	NHOH	H	4-NO ₂	D-1681	SMe	NHOH	H	4-NO ₂
D-1632	NH-i-Pr	NHOMe	H	4-NO ₂	D-1682	SMe	NHOMe	H	4-NO ₂
D-1633	NH-i-Pr	NHOEt	H	4-NO ₂	D-1683	SMe	NHOEt	H	4-NO ₂
D-1634	NH-i-Pr	NHNH ₂	H	4-NO ₂	D-1684	SMe	NHNH ₂	H	4-NO ₂
D-1635	NH-i-Pr	NHNMe ₂	H	4-NO ₂	D-1685	SMe	NHNMe ₂	H	4-NO ₂
D-1636	NH-i-Pr	NHNHMe	H	4-NO ₂	D-1686	SMe	NHNHMe	H	4-NO ₂
D-1637	NH-i-Pr	NHNHEt	H	4-NO ₂	D-1687	SMe	NHNHEt	H	4-NO ₂
D-1638	NH-i-Pr	NMeNH ₂	H	4-NO ₂	D-1688	SMe	NMeNH ₂	H	4-NO ₂
D-1639	NH-i-Pr	NHCN	H	4-NO ₂	D-1689	SMe	NHCN	H	4-NO ₂
D-1640	NH-i-Pr	NHNO ₂	H	4-NO ₂	D-1690	SMe	NHNO ₂	H	4-NO ₂
D-1641	NH-allyl	NHOH	H	4-NO ₂	D-1691	SEt	NHOH	H	4-NO ₂
D-1642	NH-allyl	NHOMe	H	4-NO ₂	D-1692	SEt	NHOMe	H	4-NO ₂
D-1643	NH-allyl	NHOEt	H	4-NO ₂	D-1693	SEt	NHOEt	H	4-NO ₂
D-1644	NH-allyl	NHNH ₂	H	4-NO ₂	D-1694	SEt	NHNH ₂	H	4-NO ₂
D-1645	NH-allyl	NHNMe ₂	H	4-NO ₂	D-1695	SEt	NHNMe ₂	H	4-NO ₂
D-1646	NH-allyl	NHNHMe	H	4-NO ₂	D-1696	SEt	NHNHMe	H	4-NO ₂
D-1647	NH-allyl	NHNHEt	H	4-NO ₂	D-1697	SEt	NHNHEt	H	4-NO ₂
D-1648	NH-allyl	NMeNH ₂	H	4-NO ₂	D-1698	SEt	NMeNH ₂	H	4-NO ₂
D-1649	NH-allyl	NHCN	H	4-NO ₂	D-1699	SEt	NHCN	H	4-NO ₂
D-1650	NH-allyl	NHNO ₂	H	4-NO ₂	D-1700	SEt	NHNO ₂	H	4-NO ₂

Table 24

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
E-1	-S(CH ₂) ₃ NH-		H	4-NO ₂	E-31	-O(CH ₂) ₃ NH-		H	4-NO ₂
E-2	-S(CH ₂) ₃ NH-		H	4-NH ₂	E-32	-O(CH ₂) ₃ NH-		H	4-NH ₂
E-3	-S(CH ₂) ₃ NH-		H	4-Cl	E-33	-O(CH ₂) ₃ NH-		H	4-Cl
E-4	-S(CH ₂) ₃ NH-		H	4-OMe	E-34	-O(CH ₂) ₃ NH-		H	4-OMe
E-5	-S(CH ₂) ₃ NH-		H	4-Me	E-35	-O(CH ₂) ₃ NH-		H	4-Me
E-6	-S(CH ₂) ₃ NH-		Me	2-NH ₂	E-36	-O(CH ₂) ₃ NH-		Me	4-NO ₂
E-7	-S(CH ₂) ₃ NH-		Me	4-NH ₂	E-37	-O(CH ₂) ₃ NH-		Me	4-NH ₂
E-8	-S(CH ₂) ₃ NH-		Me	4-Cl	E-38	-O(CH ₂) ₃ NH-		Me	4-Cl
E-9	-S(CH ₂) ₃ NH-		Me	4-OMe	E-39	-O(CH ₂) ₃ NH-		Me	4-OMe
E-10	-S(CH ₂) ₃ NH-		Me	4-Me	E-40	-O(CH ₂) ₃ NH-		Me	4-Me
E-11	-S(CH ₂) ₃ NH-		Et	4-NO ₂	E-41	-O(CH ₂) ₃ NH-		Et	4-NO ₂
E-12	-S(CH ₂) ₃ NH-		Et	4-NH ₂	E-42	-O(CH ₂) ₃ NH-		Et	4-NH ₂
E-13	-S(CH ₂) ₃ NH-		Et	4-Cl	E-43	-O(CH ₂) ₃ NH-		Et	4-Cl
E-14	-S(CH ₂) ₃ NH-		Et	4-OMe	E-44	-O(CH ₂) ₃ NH-		Et	4-OMe
E-15	-S(CH ₂) ₃ NH-		Et	4-Me	E-45	-O(CH ₂) ₃ NH-		Et	4-Me
E-16	-S(CH ₂) ₂ NH-		H	4-NO ₂	E-46	-O(CH ₂) ₂ NH-		H	4-NO ₂
E-17	-S(CH ₂) ₂ NH-		H	4-NH ₂	E-47	-O(CH ₂) ₂ NH-		H	4-NH ₂
E-18	-S(CH ₂) ₂ NH-		H	4-Cl	E-48	-O(CH ₂) ₂ NH-		H	4-Cl
E-19	-S(CH ₂) ₂ NH-		H	4-OMe	E-49	-O(CH ₂) ₂ NH-		H	4-OMe
E-20	-S(CH ₂) ₂ NH-		H	4-Me	E-50	-O(CH ₂) ₂ NH-		H	4-Me
E-21	-S(CH ₂) ₂ NH-		Me	2-NH ₂	E-51	-O(CH ₂) ₂ NH-		Me	4-NO ₂
E-22	-S(CH ₂) ₂ NH-		Me	4-NH ₂	E-52	-O(CH ₂) ₂ NH-		Me	4-NH ₂
E-23	-S(CH ₂) ₂ NH-		Me	4-Cl	E-53	-O(CH ₂) ₂ NH-		Me	4-Cl
E-24	-S(CH ₂) ₂ NH-		Me	4-OMe	E-54	-O(CH ₂) ₂ NH-		Me	4-OMe
E-25	-S(CH ₂) ₂ NH-		Me	4-Me	E-55	-O(CH ₂) ₂ NH-		Me	4-Me
E-26	-S(CH ₂) ₂ NH-		Et	4-NO ₂	E-56	-O(CH ₂) ₂ NH-		Et	4-NO ₂
E-27	-S(CH ₂) ₂ NH-		Et	4-NH ₂	E-57	-O(CH ₂) ₂ NH-		Et	4-NH ₂
E-28	-S(CH ₂) ₂ NH-		Et	4-Cl	E-58	-O(CH ₂) ₂ NH-		Et	4-Cl
E-29	-S(CH ₂) ₂ NH-		Et	4-OMe	E-59	-O(CH ₂) ₂ NH-		Et	4-OMe
E-30	-S(CH ₂) ₂ NH-		Et	4-Me	E-60	-O(CH ₂) ₂ NH-		Et	4-Me

Compounds **F-1** to **F-800** shown in Table 25 to Table 32 are able to synthesize in a manner similar to those described in Example 22 or Example 23.

Table 25 to Table 32

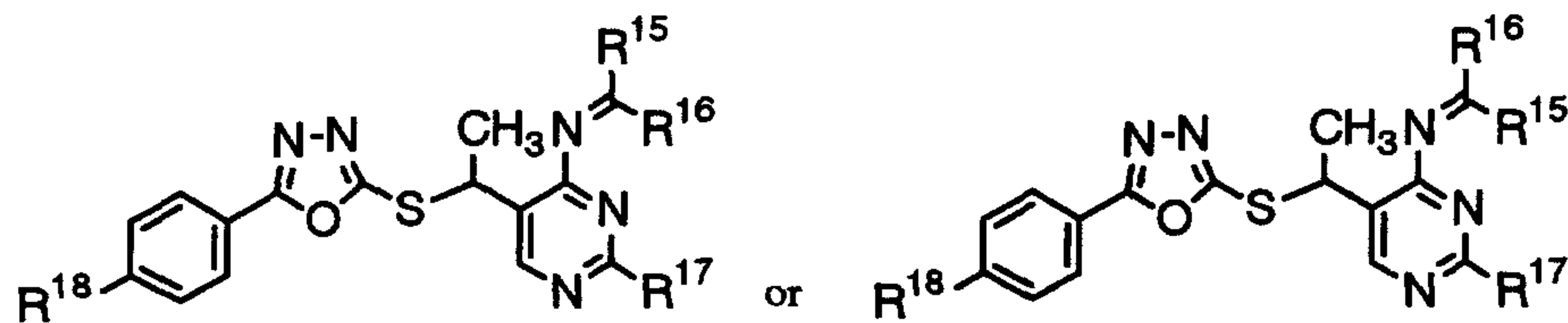


Table 25

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-1	NH ₂	SH	H	4-NH ₂	F-51	NH-allyl	SH	H	4-NH ₂
F-2	NH ₂	SMe	H	4-NH ₂	F-52	NH-allyl	SMe	H	4-NH ₂
F-3	NH ₂	SEt	H	4-NH ₂	F-53	NH-allyl	SEt	H	4-NH ₂
F-4	NH ₂	S-n-Pr	H	4-NH ₂	F-54	NH-allyl	S-n-Pr	H	4-NH ₂
F-5	NH ₂	S-i-Pr	H	4-NH ₂	F-55	NH-allyl	S-i-Pr	H	4-NH ₂
F-6	NH ₂	S-n-Bu	H	4-NH ₂	F-56	NH-allyl	S-n-Bu	H	4-NH ₂
F-7	NH ₂	S-allyl	H	4-NH ₂	F-57	NH-allyl	S-allyl	H	4-NH ₂
F-8	NH ₂	S-propargyl	H	4-NH ₂	F-58	NH-allyl	S-propargyl	H	4-NH ₂
F-9	NH ₂	SCH ₂ CF ₃	H	4-NH ₂	F-59	NH-allyl	SCH ₂ CF ₃	H	4-NH ₂
F-10	NH ₂	SCH ₂ CH ₂ F	H	4-NH ₂	F-60	NH-allyl	SCH ₂ CH ₂ F	H	4-NH ₂
F-11	NHMe	SH	H	4-NH ₂	F-61	NH-propargyl	SH	H	4-NH ₂
F-12	NHMe	SMe	H	4-NH ₂	F-62	NH-propargyl	SMe	H	4-NH ₂
F-13	NHMe	SEt	H	4-NH ₂	F-63	NH-propargyl	SEt	H	4-NH ₂
F-14	NHMe	S-n-Pr	H	4-NH ₂	F-64	NH-propargyl	S-n-Pr	H	4-NH ₂
F-15	NHMe	S-i-Pr	H	4-NH ₂	F-65	NH-propargyl	S-i-Pr	H	4-NH ₂
F-16	NHMe	S-n-Bu	H	4-NH ₂	F-66	NH-propargyl	S-n-Bu	H	4-NH ₂
F-17	NHMe	S-allyl	H	4-NH ₂	F-67	NH-propargyl	S-allyl	H	4-NH ₂
F-18	NHMe	S-propargyl	H	4-NH ₂	F-68	NH-propargyl	S-propargyl	H	4-NH ₂
F-19	NHMe	SCH ₂ CF ₃	H	4-NH ₂	F-69	NH-propargyl	SCH ₂ CF ₃	H	4-NH ₂
F-20	NHMe	SCH ₂ CH ₂ F	H	4-NH ₂	F-70	NH-propargyl	SCH ₂ CH ₂ F	H	4-NH ₂
F-21	NHEt	SH	H	4-NH ₂	F-71	NHCH ₂ CF ₃	SH	H	4-NH ₂
F-22	NHEt	SMe	H	4-NH ₂	F-72	NHCH ₂ CF ₃	SMe	H	4-NH ₂
F-23	NHEt	SEt	H	4-NH ₂	F-73	NHCH ₂ CF ₃	SEt	H	4-NH ₂
F-24	NHEt	S-n-Pr	H	4-NH ₂	F-74	NHCH ₂ CF ₃	S-n-Pr	H	4-NH ₂
F-25	NHEt	S-i-Pr	H	4-NH ₂	F-75	NHCH ₂ CF ₃	S-i-Pr	H	4-NH ₂
F-26	NHEt	S-n-Bu	H	4-NH ₂	F-76	NHCH ₂ CF ₃	S-n-Bu	H	4-NH ₂
F-27	NHEt	S-allyl	H	4-NH ₂	F-77	NHCH ₂ CF ₃	S-allyl	H	4-NH ₂
F-28	NHEt	S-propargyl	H	4-NH ₂	F-78	NHCH ₂ CF ₃	S-propargyl	H	4-NH ₂
F-29	NHEt	SCH ₂ CF ₃	H	4-NH ₂	F-79	NHCH ₂ CF ₃	SCH ₂ CF ₃	H	4-NH ₂
F-30	NHEt	SCH ₂ CH ₂ F	H	4-NH ₂	F-80	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	H	4-NH ₂
F-31	NHPr	SH	H	4-NH ₂	F-81	NHCH ₂ CH ₂ F	SH	H	4-NH ₂
F-32	NHPr	SMe	H	4-NH ₂	F-82	NHCH ₂ CH ₂ F	SMe	H	4-NH ₂
F-33	NHPr	SEt	H	4-NH ₂	F-83	NHCH ₂ CH ₂ F	SEt	H	4-NH ₂
F-34	NHPr	S-n-Pr	H	4-NH ₂	F-84	NHCH ₂ CH ₂ F	S-n-Pr	H	4-NH ₂
F-35	NHPr	S-i-Pr	H	4-NH ₂	F-85	NHCH ₂ CH ₂ F	S-i-Pr	H	4-NH ₂
F-36	NHPr	S-n-Bu	H	4-NH ₂	F-86	NHCH ₂ CH ₂ F	S-n-Bu	H	4-NH ₂
F-37	NHPr	S-allyl	H	4-NH ₂	F-87	NHCH ₂ CH ₂ F	S-allyl	H	4-NH ₂
F-38	NHPr	S-propargyl	H	4-NH ₂	F-88	NHCH ₂ CH ₂ F	S-propargyl	H	4-NH ₂
F-39	NHPr	SCH ₂ CF ₃	H	4-NH ₂	F-89	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	H	4-NH ₂
F-40	NHPr	SCH ₂ CH ₂ F	H	4-NH ₂	F-90	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	H	4-NH ₂
F-41	NH-i-Pr	SH	H	4-NH ₂	F-91	NH-n-Bu	SH	H	4-NH ₂
F-42	NH-i-Pr	SMe	H	4-NH ₂	F-92	NH-n-Bu	SMe	H	4-NH ₂
F-43	NH-i-Pr	SEt	H	4-NH ₂	F-93	NH-n-Bu	SEt	H	4-NH ₂
F-44	NH-i-Pr	S-n-Pr	H	4-NH ₂	F-94	NH-n-Bu	S-n-Pr	H	4-NH ₂
F-45	NH-i-Pr	S-i-Pr	H	4-NH ₂	F-95	NH-n-Bu	S-i-Pr	H	4-NH ₂
F-46	NH-i-Pr	S-n-Bu	H	4-NH ₂	F-96	NH-n-Bu	S-n-Bu	H	4-NH ₂
F-47	NH-i-Pr	S-allyl	H	4-NH ₂	F-97	NH-n-Bu	S-allyl	H	4-NH ₂
F-48	NH-i-Pr	S-propargyl	H	4-NH ₂	F-98	NH-n-Bu	S-propargyl	H	4-NH ₂
F-49	NH-i-Pr	SCH ₂ CF ₃	H	4-NH ₂	F-99	NH-n-Bu	SCH ₂ CF ₃	H	4-NH ₂
F-50	NH-i-Pr	SCH ₂ CH ₂ F	H	4-NH ₂	F-100	NH-n-Bu	SCH ₂ CH ₂ F	H	4-NH ₂

Table 26

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-101	NH ₂	SH	H	4-NO ₂	F-151	NH-allyl	SH	H	4-NO ₂
F-102	NH ₂	SMe	H	4-NO ₂	F-152	NH-allyl	SMe	H	4-NO ₂
F-103	NH ₂	SEt	H	4-NO ₂	F-153	NH-allyl	SEt	H	4-NO ₂
F-104	NH ₂	S-n-Pr	H	4-NO ₂	F-154	NH-allyl	S-n-Pr	H	4-NO ₂
F-105	NH ₂	S-i-Pr	H	4-NO ₂	F-155	NH-allyl	S-i-Pr	H	4-NO ₂
F-106	NH ₂	S-n-Bu	H	4-NO ₂	F-156	NH-allyl	S-n-Bu	H	4-NO ₂
F-107	NH ₂	S-allyl	H	4-NO ₂	F-157	NH-allyl	S-allyl	H	4-NO ₂
F-108	NH ₂	S-propargyl	H	4-NO ₂	F-158	NH-allyl	S-propargyl	H	4-NO ₂
F-109	NH ₂	SCH ₂ CF ₃	H	4-NO ₂	F-159	NH-allyl	SCH ₂ CF ₃	H	4-NO ₂
F-110	NH ₂	SCH ₂ CH ₂ F	H	4-NO ₂	F-160	NH-allyl	SCH ₂ CH ₂ F	H	4-NO ₂
F-111	NHMe	SH	H	4-NO ₂	F-161	NH-propargyl	SH	H	4-NO ₂
F-112	NHMe	SMe	H	4-NO ₂	F-162	NH-propargyl	SMe	H	4-NO ₂
F-113	NHMe	SEt	H	4-NO ₂	F-163	NH-propargyl	SEt	H	4-NO ₂
F-114	NHMe	S-n-Pr	H	4-NO ₂	F-164	NH-propargyl	S-n-Pr	H	4-NO ₂
F-115	NHMe	S-i-Pr	H	4-NO ₂	F-165	NH-propargyl	S-i-Pr	H	4-NO ₂
F-116	NHMe	S-n-Bu	H	4-NO ₂	F-166	NH-propargyl	S-n-Bu	H	4-NO ₂
F-117	NHMe	S-allyl	H	4-NO ₂	F-167	NH-propargyl	S-allyl	H	4-NO ₂
F-118	NHMe	S-propargyl	H	4-NO ₂	F-168	NH-propargyl	S-propargyl	H	4-NO ₂
F-119	NHMe	SCH ₂ CF ₃	H	4-NO ₂	F-169	NH-propargyl	SCH ₂ CF ₃	H	4-NO ₂
F-120	NHMe	SCH ₂ CH ₂ F	H	4-NO ₂	F-170	NH-propargyl	SCH ₂ CH ₂ F	H	4-NO ₂
F-121	NHEt	SH	H	4-NO ₂	F-171	NHCH ₂ CF ₃	SH	H	4-NO ₂
F-122	NHEt	SMe	H	4-NO ₂	F-172	NHCH ₂ CF ₃	SMe	H	4-NO ₂
F-123	NHEt	SEt	H	4-NO ₂	F-173	NHCH ₂ CF ₃	SEt	H	4-NO ₂
F-124	NHEt	S-n-Pr	H	4-NO ₂	F-174	NHCH ₂ CF ₃	S-n-Pr	H	4-NO ₂
F-125	NHEt	S-i-Pr	H	4-NO ₂	F-175	NHCH ₂ CF ₃	S-i-Pr	H	4-NO ₂
F-126	NHEt	S-n-Bu	H	4-NO ₂	F-176	NHCH ₂ CF ₃	S-n-Bu	H	4-NO ₂
F-127	NHEt	S-allyl	H	4-NO ₂	F-177	NHCH ₂ CF ₃	S-allyl	H	4-NO ₂
F-128	NHEt	S-propargyl	H	4-NO ₂	F-178	NHCH ₂ CF ₃	S-propargyl	H	4-NO ₂
F-129	NHEt	SCH ₂ CF ₃	H	4-NO ₂	F-179	NHCH ₂ CF ₃	SCH ₂ CF ₃	H	4-NO ₂
F-130	NHEt	SCH ₂ CH ₂ F	H	4-NO ₂	F-180	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	H	4-NO ₂
F-131	NHPr	SH	H	4-NO ₂	F-181	NHCH ₂ CH ₂ F	SH	H	4-NO ₂
F-132	NHPr	SMe	H	4-NO ₂	F-182	NHCH ₂ CH ₂ F	SMe	H	4-NO ₂
F-133	NHPr	SEt	H	4-NO ₂	F-183	NHCH ₂ CH ₂ F	SEt	H	4-NO ₂
F-134	NHPr	S-n-Pr	H	4-NO ₂	F-184	NHCH ₂ CH ₂ F	S-n-Pr	H	4-NO ₂
F-135	NHPr	S-i-Pr	H	4-NO ₂	F-185	NHCH ₂ CH ₂ F	S-i-Pr	H	4-NO ₂
F-136	NHPr	S-n-Bu	H	4-NO ₂	F-186	NHCH ₂ CH ₂ F	S-n-Bu	H	4-NO ₂
F-137	NHPr	S-allyl	H	4-NO ₂	F-187	NHCH ₂ CH ₂ F	S-allyl	H	4-NO ₂
F-138	NHPr	S-propargyl	H	4-NO ₂	F-188	NHCH ₂ CH ₂ F	S-propargyl	H	4-NO ₂
F-139	NHPr	SCH ₂ CF ₃	H	4-NO ₂	F-189	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	H	4-NO ₂
F-140	NHPr	SCH ₂ CH ₂ F	H	4-NO ₂	F-190	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	H	4-NO ₂
F-141	NH-i-Pr	SH	H	4-NO ₂	F-191	NH-n-Bu	SH	H	4-NO ₂
F-142	NH-i-Pr	SMe	H	4-NO ₂	F-192	NH-n-Bu	SMe	H	4-NO ₂
F-143	NH-i-Pr	SEt	H	4-NO ₂	F-193	NH-n-Bu	SEt	H	4-NO ₂
F-144	NH-i-Pr	S-n-Pr	H	4-NO ₂	F-194	NH-n-Bu	S-n-Pr	H	4-NO ₂
F-145	NH-i-Pr	S-i-Pr	H	4-NO ₂	F-195	NH-n-Bu	S-i-Pr	H	4-NO ₂
F-146	NH-i-Pr	S-n-Bu	H	4-NO ₂	F-196	NH-n-Bu	S-n-Bu	H	4-NO ₂
F-147	NH-i-Pr	S-allyl	H	4-NO ₂	F-197	NH-n-Bu	S-allyl	H	4-NO ₂
F-148	NH-i-Pr	S-propargyl	H	4-NO ₂	F-198	NH-n-Bu	S-propargyl	H	4-NO ₂
F-149	NH-i-Pr	SCH ₂ CF ₃	H	4-NO ₂	F-199	NH-n-Bu	SCH ₂ CF ₃	H	4-NO ₂
F-150	NH-i-Pr	SCH ₂ CH ₂ F	H	4-NO ₂	F-200	NH-n-Bu	SCH ₂ CH ₂ F	H	4-NO ₂

Table 27

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-201	NH ₂	SH	Me	4-NH ₂	F-251	NH-allyl	SH	Me	4-NH ₂
F-202	NH ₂	SMe	Me	4-NH ₂	F-252	NH-allyl	SMe	Me	4-NH ₂
F-203	NH ₂	SEt	Me	4-NH ₂	F-253	NH-allyl	SEt	Me	4-NH ₂
F-204	NH ₂	S-n-Pr	Me	4-NH ₂	F-254	NH-allyl	S-n-Pr	Me	4-NH ₂
F-205	NH ₂	S-i-Pr	Me	4-NH ₂	F-255	NH-allyl	S-i-Pr	Me	4-NH ₂
F-206	NH ₂	S-n-Bu	Me	4-NH ₂	F-256	NH-allyl	S-n-Bu	Me	4-NH ₂
F-207	NH ₂	S-allyl	Me	4-NH ₂	F-257	NH-allyl	S-allyl	Me	4-NH ₂
F-208	NH ₂	S-propargyl	Me	4-NH ₂	F-258	NH-allyl	S-propargyl	Me	4-NH ₂
F-209	NH ₂	SCH ₂ CF ₃	Me	4-NH ₂	F-259	NH-allyl	SCH ₂ CF ₃	Me	4-NH ₂
F-210	NH ₂	SCH ₂ CH ₂ F	Me	4-NH ₂	F-260	NH-allyl	SCH ₂ CH ₂ F	Me	4-NH ₂
F-211	NHMe	SH	Me	4-NH ₂	F-261	NH-propargyl	SH	Me	4-NH ₂
F-212	NHMe	SMe	Me	4-NH ₂	F-262	NH-propargyl	SMe	Me	4-NH ₂
F-213	NHMe	SEt	Me	4-NH ₂	F-263	NH-propargyl	SEt	Me	4-NH ₂
F-214	NHMe	S-n-Pr	Me	4-NH ₂	F-264	NH-propargyl	S-n-Pr	Me	4-NH ₂
F-215	NHMe	S-i-Pr	Me	4-NH ₂	F-265	NH-propargyl	S-i-Pr	Me	4-NH ₂
F-216	NHMe	S-n-Bu	Me	4-NH ₂	F-266	NH-propargyl	S-n-Bu	Me	4-NH ₂
F-217	NHMe	S-allyl	Me	4-NH ₂	F-267	NH-propargyl	S-allyl	Me	4-NH ₂
F-218	NHMe	S-propargyl	Me	4-NH ₂	F-268	NH-propargyl	S-propargyl	Me	4-NH ₂
F-219	NHMe	SCH ₂ CF ₃	Me	4-NH ₂	F-269	NH-propargyl	SCH ₂ CF ₃	Me	4-NH ₂
F-220	NHMe	SCH ₂ CH ₂ F	Me	4-NH ₂	F-270	NH-propargyl	SCH ₂ CH ₂ F	Me	4-NH ₂
F-221	NHEt	SH	Me	4-NH ₂	F-271	NHCH ₂ CF ₃	SH	Me	4-NH ₂
F-222	NHEt	SMe	Me	4-NH ₂	F-272	NHCH ₂ CF ₃	SMe	Me	4-NH ₂
F-223	NHEt	SEt	Me	4-NH ₂	F-273	NHCH ₂ CF ₃	SEt	Me	4-NH ₂
F-224	NHEt	S-n-Pr	Me	4-NH ₂	F-274	NHCH ₂ CF ₃	S-n-Pr	Me	4-NH ₂
F-225	NHEt	S-i-Pr	Me	4-NH ₂	F-275	NHCH ₂ CF ₃	S-i-Pr	Me	4-NH ₂
F-226	NHEt	S-n-Bu	Me	4-NH ₂	F-276	NHCH ₂ CF ₃	S-n-Bu	Me	4-NH ₂
F-227	NHEt	S-allyl	Me	4-NH ₂	F-277	NHCH ₂ CF ₃	S-allyl	Me	4-NH ₂
F-228	NHEt	S-propargyl	Me	4-NH ₂	F-278	NHCH ₂ CF ₃	S-propargyl	Me	4-NH ₂
F-229	NHEt	SCH ₂ CF ₃	Me	4-NH ₂	F-279	NHCH ₂ CF ₃	SCH ₂ CF ₃	Me	4-NH ₂
F-230	NHEt	SCH ₂ CH ₂ F	Me	4-NH ₂	F-280	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Me	4-NH ₂
F-231	NHPr	SH	Me	4-NH ₂	F-281	NHCH ₂ CH ₂ F	SH	Me	4-NH ₂
F-232	NHPr	SMe	Me	4-NH ₂	F-282	NHCH ₂ CH ₂ F	SMe	Me	4-NH ₂
F-233	NHPr	SEt	Me	4-NH ₂	F-283	NHCH ₂ CH ₂ F	SEt	Me	4-NH ₂
F-234	NHPr	S-n-Pr	Me	4-NH ₂	F-284	NHCH ₂ CH ₂ F	S-n-Pr	Me	4-NH ₂
F-235	NHPr	S-i-Pr	Me	4-NH ₂	F-285	NHCH ₂ CH ₂ F	S-i-Pr	Me	4-NH ₂
F-236	NHPr	S-n-Bu	Me	4-NH ₂	F-286	NHCH ₂ CH ₂ F	S-n-Bu	Me	4-NH ₂
F-237	NHPr	S-allyl	Me	4-NH ₂	F-287	NHCH ₂ CH ₂ F	S-allyl	Me	4-NH ₂
F-238	NHPr	S-propargyl	Me	4-NH ₂	F-288	NHCH ₂ CH ₂ F	S-propargyl	Me	4-NH ₂
F-239	NHPr	SCH ₂ CF ₃	Me	4-NH ₂	F-289	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Me	4-NH ₂
F-240	NHPr	SCH ₂ CH ₂ F	Me	4-NH ₂	F-290	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Me	4-NH ₂
F-241	NH-i-Pr	SH	Me	4-NH ₂	F-291	NH-n-Bu	SH	Me	4-NH ₂
F-242	NH-i-Pr	SMe	Me	4-NH ₂	F-292	NH-n-Bu	SMe	Me	4-NH ₂
F-243	NH-i-Pr	SEt	Me	4-NH ₂	F-293	NH-n-Bu	SEt	Me	4-NH ₂
F-244	NH-i-Pr	S-n-Pr	Me	4-NH ₂	F-294	NH-n-Bu	S-n-Pr	Me	4-NH ₂
F-245	NH-i-Pr	S-i-Pr	Me	4-NH ₂	F-295	NH-n-Bu	S-i-Pr	Me	4-NH ₂
F-246	NH-i-Pr	S-n-Bu	Me	4-NH ₂	F-296	NH-n-Bu	S-n-Bu	Me	4-NH ₂
F-247	NH-i-Pr	S-allyl	Me	4-NH ₂	F-297	NH-n-Bu	S-allyl	Me	4-NH ₂
F-248	NH-i-Pr	S-propargyl	Me	4-NH ₂	F-298	NH-n-Bu	S-propargyl	Me	4-NH ₂
F-249	NH-i-Pr	SCH ₂ CF ₃	Me	4-NH ₂	F-299	NH-n-Bu	SCH ₂ CF ₃	Me	4-NH ₂
F-250	NH-i-Pr	SCH ₂ CH ₂ F	Me	4-NH ₂	F-300	NH-n-Bu	SCH ₂ CH ₂ F	Me	4-NH ₂

Table 28

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-301	NH ₂	SH	Me	4-NO ₂	F-351	NH-allyl	SH	Me	4-NO ₂
F-302	NH ₂	SMe	Me	4-NO ₂	F-352	NH-allyl	SMe	Me	4-NO ₂
F-303	NH ₂	SEt	Me	4-NO ₂	F-353	NH-allyl	SEt	Me	4-NO ₂
F-304	NH ₂	S-n-Pr	Me	4-NO ₂	F-354	NH-allyl	S-n-Pr	Me	4-NO ₂
F-305	NH ₂	S-i-Pr	Me	4-NO ₂	F-355	NH-allyl	S-i-Pr	Me	4-NO ₂
F-306	NH ₂	S-n-Bu	Me	4-NO ₂	F-356	NH-allyl	S-n-Bu	Me	4-NO ₂
F-307	NH ₂	S-allyl	Me	4-NO ₂	F-357	NH-allyl	S-allyl	Me	4-NO ₂
F-308	NH ₂	S-propargyl	Me	4-NO ₂	F-358	NH-allyl	S-propargyl	Me	4-NO ₂
F-309	NH ₂	SCH ₂ CF ₃	Me	4-NO ₂	F-359	NH-allyl	SCH ₂ CF ₃	Me	4-NO ₂
F-310	NH ₂	SCH ₂ CH ₂ F	Me	4-NO ₂	F-360	NH-allyl	SCH ₂ CH ₂ F	Me	4-NO ₂
F-311	NHMe	SH	Me	4-NO ₂	F-361	NH-propargyl	SH	Me	4-NO ₂
F-312	NHMe	SMe	Me	4-NO ₂	F-362	NH-propargyl	SMe	Me	4-NO ₂
F-313	NHMe	SEt	Me	4-NO ₂	F-363	NH-propargyl	SEt	Me	4-NO ₂
F-314	NHMe	S-n-Pr	Me	4-NO ₂	F-364	NH-propargyl	S-n-Pr	Me	4-NO ₂
F-315	NHMe	S-i-Pr	Me	4-NO ₂	F-365	NH-propargyl	S-i-Pr	Me	4-NO ₂
F-316	NHMe	S-n-Bu	Me	4-NO ₂	F-366	NH-propargyl	S-n-Bu	Me	4-NO ₂
F-317	NHMe	S-allyl	Me	4-NO ₂	F-367	NH-propargyl	S-allyl	Me	4-NO ₂
F-318	NHMe	S-propargyl	Me	4-NO ₂	F-368	NH-propargyl	S-propargyl	Me	4-NO ₂
F-319	NHMe	SCH ₂ CF ₃	Me	4-NO ₂	F-369	NH-propargyl	SCH ₂ CF ₃	Me	4-NO ₂
F-320	NHMe	SCH ₂ CH ₂ F	Me	4-NO ₂	F-370	NH-propargyl	SCH ₂ CH ₂ F	Me	4-NO ₂
F-321	NHEt	SH	Me	4-NO ₂	F-371	NHCH ₂ CF ₃	SH	Me	4-NO ₂
F-322	NHEt	SMe	Me	4-OMe	F-372	NHCH ₂ CF ₃	SMe	Me	4-NO ₂
F-323	NHEt	SEt	Me	4-Cl	F-373	NHCH ₂ CF ₃	SEt	Me	4-NO ₂
F-324	NHEt	S-n-Pr	Me	4-NO ₂	F-374	NHCH ₂ CF ₃	S-n-Pr	Me	4-NO ₂
F-325	NHEt	S-i-Pr	Me	4-NO ₂	F-375	NHCH ₂ CF ₃	S-i-Pr	Me	4-NO ₂
F-326	NHEt	S-n-Bu	Me	4-NO ₂	F-376	NHCH ₂ CF ₃	S-n-Bu	Me	4-NO ₂
F-327	NHEt	S-allyl	Me	4-NO ₂	F-377	NHCH ₂ CF ₃	S-allyl	Me	4-NO ₂
F-328	NHEt	S-propargyl	Me	4-NO ₂	F-378	NHCH ₂ CF ₃	S-propargyl	Me	4-NO ₂
F-329	NHEt	SCH ₂ CF ₃	Me	4-NO ₂	F-379	NHCH ₂ CF ₃	SCH ₂ CF ₃	Me	4-NO ₂
F-330	NHEt	SCH ₂ CH ₂ F	Me	4-NO ₂	F-380	NHCH ₂ CF ₃	SCH ₂ CH ₂ F	Me	4-NO ₂
F-331	NHPr	SH	Me	4-NO ₂	F-381	NHCH ₂ CH ₂ F	SH	Me	4-NO ₂
F-332	NHPr	SMe	Me	4-NO ₂	F-382	NHCH ₂ CH ₂ F	SMe	Me	4-NO ₂
F-333	NHPr	SEt	Me	4-NO ₂	F-383	NHCH ₂ CH ₂ F	SEt	Me	4-NO ₂
F-334	NHPr	S-n-Pr	Me	4-NO ₂	F-384	NHCH ₂ CH ₂ F	S-n-Pr	Me	4-NO ₂
F-335	NHPr	S-i-Pr	Me	4-NO ₂	F-385	NHCH ₂ CH ₂ F	S-i-Pr	Me	4-NO ₂
F-336	NHPr	S-n-Bu	Me	4-NO ₂	F-386	NHCH ₂ CH ₂ F	S-n-Bu	Me	4-NO ₂
F-337	NHPr	S-allyl	Me	4-NO ₂	F-387	NHCH ₂ CH ₂ F	S-allyl	Me	4-NO ₂
F-338	NHPr	S-propargyl	Me	4-NO ₂	F-388	NHCH ₂ CH ₂ F	S-propargyl	Me	4-NO ₂
F-339	NHPr	SCH ₂ CF ₃	Me	4-NO ₂	F-389	NHCH ₂ CH ₂ F	SCH ₂ CF ₃	Me	4-NO ₂
F-340	NHPr	SCH ₂ CH ₂ F	Me	4-NO ₂	F-390	NHCH ₂ CH ₂ F	SCH ₂ CH ₂ F	Me	4-NO ₂
F-341	NH-i-Pr	SH	Me	4-NO ₂	F-391	NH-n-Bu	SH	Me	4-NO ₂
F-342	NH-i-Pr	SMe	Me	4-NO ₂	F-392	NH-n-Bu	SMe	Me	4-NO ₂
F-343	NH-i-Pr	SEt	Me	4-NO ₂	F-393	NH-n-Bu	SEt	Me	4-NO ₂
F-344	NH-i-Pr	S-n-Pr	Me	4-NO ₂	F-394	NH-n-Bu	S-n-Pr	Me	4-NO ₂
F-345	NH-i-Pr	S-i-Pr	Me	4-NO ₂	F-395	NH-n-Bu	S-i-Pr	Me	4-NO ₂
F-346	NH-i-Pr	S-n-Bu	Me	4-NO ₂	F-396	NH-n-Bu	S-n-Bu	Me	4-NO ₂
F-347	NH-i-Pr	S-allyl	Me	4-NO ₂	F-397	NH-n-Bu	S-allyl	Me	4-NO ₂
F-348	NH-i-Pr	S-propargyl	Me	4-NO ₂	F-398	NH-n-Bu	S-propargyl	Me	4-NO ₂
F-349	NH-i-Pr	SCH ₂ CF ₃	Me	4-NO ₂	F-399	NH-n-Bu	SCH ₂ CF ₃	Me	4-NO ₂
F-350	NH-i-Pr	SCH ₂ CH ₂ F	Me	4-NO ₂	F-400	NH-n-Bu	SCH ₂ CH ₂ F	Me	4-NO ₂

Table 29

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-401	NH ₂	NH ₂	Me	4-NO ₂	F-451	NH-propargyl	NHCH ₂ CF ₃	Me	4-NO ₂
F-402	NH ₂	NHMe	Me	4-NO ₂	F-452	NH-propargyl	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-403	NH ₂	NHEt	Me	4-NO ₂	F-453	NHCH ₂ CF ₃	NHCH ₂ CF ₃	Me	4-NO ₂
F-404	NH ₂	NHPr	Me	4-NO ₂	F-454	NHCH ₂ CF ₃	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-405	NH ₂	NH-i-Pr	Me	4-NO ₂	F-455	NHCH ₂ CH ₂ F	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-406	NH ₂	NH-n-Bu	Me	4-NO ₂	F-456	NHOMe	NH ₂	Me	4-NO ₂
F-407	NH ₂	NH-allyl	Me	4-NO ₂	F-457	NHOMe	NHMe	Me	4-NO ₂
F-408	NH ₂	NH-propargyl	Me	4-NO ₂	F-458	NHOMe	NHEt	Me	4-NO ₂
F-409	NH ₂	NHCH ₂ CF ₃	Me	4-NO ₂	F-459	NHOMe	NHPr	Me	4-NO ₂
F-410	NH ₂	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-460	NHOMe	NH-i-Pr	Me	4-NO ₂
F-411	NHMe	NHMe	Me	4-NO ₂	F-461	NHOMe	NH-n-Bu	Me	4-NO ₂
F-412	NHMe	NHEt	Me	4-NO ₂	F-462	NHOMe	NH-allyl	Me	4-NO ₂
F-413	NHMe	NHPr	Me	4-NO ₂	F-463	NHOMe	NH-propargyl	Me	4-NO ₂
F-414	NHMe	NH-i-Pr	Me	4-NO ₂	F-464	NHOMe	NHCH ₂ CF ₃	Me	4-NO ₂
F-415	NHMe	NH-n-Bu	Me	4-NO ₂	F-465	NHOMe	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-416	NHMe	NH-allyl	Me	4-NO ₂	F-466	NHOEt	NH ₂	Me	4-NO ₂
F-417	NHMe	NH-propargyl	Me	4-NO ₂	F-467	NHOEt	NHMe	Me	4-NO ₂
F-418	NHMe	NHCH ₂ CF ₃	Me	4-NO ₂	F-468	NHOEt	NHEt	Me	4-NO ₂
F-419	NHMe	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-469	NHOEt	NHPr	Me	4-NO ₂
F-420	NHEt	NHEt	Me	4-Cl	F-470	NHOEt	NH-i-Pr	Me	4-NO ₂
F-421	NHEt	NHPr	Me	4-NO ₂	F-471	NHOEt	NH-n-Bu	Me	4-NO ₂
F-422	NHEt	NH-i-Pr	Me	4-NO ₂	F-472	NHOEt	NH-allyl	Me	4-NO ₂
F-423	NHEt	NH-n-Bu	Me	4-NO ₂	F-473	NHOEt	NH-propargyl	Me	4-NO ₂
F-424	NHEt	NH-allyl	Me	4-NO ₂	F-474	NHOEt	NHCH ₂ CF ₃	Me	4-NO ₂
F-425	NHEt	NH-propargyl	Me	4-NO ₂	F-475	NHOEt	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-426	NHEt	NHCH ₂ CF ₃	Me	4-NO ₂	F-476	NHNMe ₂	NH ₂	Me	4-NO ₂
F-427	NHEt	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-477	NHNMe ₂	NHMe	Me	4-NO ₂
F-428	NHPr	NHPr	Me	4-NO ₂	F-478	NHNMe ₂	NHEt	Me	4-NO ₂
F-429	NHPr	NH-i-Pr	Me	4-NO ₂	F-479	NHNMe ₂	NHPr	Me	4-NO ₂
F-430	NHPr	NH-n-Bu	Me	4-NO ₂	F-480	NHNMe ₂	NH-i-Pr	Me	4-NO ₂
F-431	NHPr	NH-allyl	Me	4-NO ₂	F-481	NHNMe ₂	NH-n-Bu	Me	4-NO ₂
F-432	NHPr	NH-propargyl	Me	4-NO ₂	F-482	NHNMe ₂	NH-allyl	Me	4-NO ₂
F-433	NHPr	NHCH ₂ CF ₃	Me	4-NO ₂	F-483	NHNMe ₂	NH-propargyl	Me	4-NO ₂
F-434	NHPr	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-484	NHNMe ₂	NHCH ₂ CF ₃	Me	4-NO ₂
F-435	NH-i-Pr	NH-i-Pr	Me	4-NO ₂	F-485	NHNMe ₂	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-436	NH-i-Pr	NH-n-Bu	Me	4-NO ₂	F-486	NHNH ₂	NH ₂	Me	4-NO ₂
F-437	NH-i-Pr	NH-allyl	Me	4-NO ₂	F-487	NHNH ₂	NHMe	Me	4-NO ₂
F-438	NH-i-Pr	NH-propargyl	Me	4-NO ₂	F-488	NHNH ₂	NHEt	Me	4-NO ₂
F-439	NH-i-Pr	NHCH ₂ CF ₃	Me	4-NO ₂	F-489	NHNH ₂	NHPr	Me	4-NO ₂
F-440	NH-i-Pr	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-490	NHNH ₂	NH-i-Pr	Me	4-NO ₂
F-441	NH-n-Bu	NH-n-Bu	Me	4-NO ₂	F-491	NHNH ₂	NH-n-Bu	Me	4-NO ₂
F-442	NH-n-Bu	NH-allyl	Me	4-NO ₂	F-492	NHNH ₂	NH-allyl	Me	4-NO ₂
F-443	NH-n-Bu	NH-propargyl	Me	4-NO ₂	F-493	NHNH ₂	NH-propargyl	Me	4-NO ₂
F-444	NH-n-Bu	NHCH ₂ CF ₃	Me	4-NO ₂	F-494	NHNH ₂	NHCH ₂ CF ₃	Me	4-NO ₂
F-445	NH-n-Bu	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-495	NHNH ₂	NHCH ₂ CH ₂ F	Me	4-NO ₂
F-446	NH-allyl	NH-allyl	Me	4-NO ₂	F-496	NHNHMe	NHMe	Me	4-NO ₂
F-447	NH-allyl	NH-propargyl	Me	4-NO ₂	F-497	NHNHMe	NHEt	Me	4-NO ₂
F-448	NH-allyl	NHCH ₂ CF ₃	Me	4-NO ₂	F-498	NHNHMe	NHPr	Me	4-NO ₂
F-449	NH-allyl	NHCH ₂ CH ₂ F	Me	4-NO ₂	F-499	NHNHMe	NH-i-Pr	Me	4-NO ₂
F-450	NH-propargyl	NH-propargyl	Me	4-NO ₂	F-500	NHNHMe	NHCH ₂ CF ₃	Me	4-NO ₂

Table 30

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-501	NH ₂	NH ₂	H	4-NO ₂	F-551	NH-propargyl	NHCH ₂ CF ₃	H	4-NO ₂
F-502	NH ₂	NHMe	H	4-NO ₂	F-552	NH-propargyl	NHCH ₂ CH ₂ F	H	4-NO ₂
F-503	NH ₂	NHEt	H	4-NO ₂	F-553	NHCH ₂ CF ₃	NHCH ₂ CF ₃	H	4-NO ₂
F-504	NH ₂	NHPr	H	4-NO ₂	F-554	NHCH ₂ CF ₃	NHCH ₂ CH ₂ F	H	4-NO ₂
F-505	NH ₂	NH-i-Pr	H	4-NO ₂	F-555	NHCH ₂ CH ₂ F	NHCH ₂ CH ₂ F	H	4-NO ₂
F-506	NH ₂	NH-n-Bu	H	4-NO ₂	F-556	NHOMe	NH ₂	H	4-NO ₂
F-507	NH ₂	NH-allyl	H	4-NO ₂	F-557	NHOMe	NHMe	H	4-NO ₂
F-508	NH ₂	NH-propargyl	H	4-NO ₂	F-558	NHOMe	NHEt	H	4-NO ₂
F-509	NH ₂	NHCH ₂ CF ₃	H	4-NO ₂	F-559	NHOMe	NHPr	H	4-NO ₂
F-510	NH ₂	NHCH ₂ CH ₂ F	H	4-NO ₂	F-560	NHOMe	NH-i-Pr	H	4-NO ₂
F-511	NHMe	NHMe	H	4-NO ₂	F-561	NHOMe	NH-n-Bu	H	4-NO ₂
F-512	NHMe	NHEt	H	4-NO ₂	F-562	NHOMe	NH-allyl	H	4-NO ₂
F-513	NHMe	NHPr	H	4-NO ₂	F-563	NHOMe	NH-propargyl	H	4-NO ₂
F-514	NHMe	NH-i-Pr	H	4-NO ₂	F-564	NHOMe	NHCH ₂ CF ₃	H	4-NO ₂
F-515	NHMe	NH-n-Bu	H	4-NO ₂	F-565	NHOMe	NHCH ₂ CH ₂ F	H	4-NO ₂
F-516	NHMe	NH-allyl	H	4-NO ₂	F-566	NHOEt	NH ₂	H	4-NO ₂
F-517	NHMe	NH-propargyl	H	4-NO ₂	F-567	NHOEt	NHMe	H	4-NO ₂
F-518	NHMe	NHCH ₂ CF ₃	H	4-NO ₂	F-568	NHOEt	NHEt	H	4-NO ₂
F-519	NHMe	NHCH ₂ CH ₂ F	H	4-NO ₂	F-569	NHOEt	NHPr	H	4-NO ₂
F-520	NHEt	NHEt	H	4-NO ₂	F-570	NHOEt	NH-i-Pr	H	4-NO ₂
F-521	NHEt	NHPr	H	4-NO ₂	F-571	NHOEt	NH-n-Bu	H	4-NO ₂
F-522	NHEt	NH-i-Pr	H	4-NO ₂	F-572	NHOEt	NH-allyl	H	4-NO ₂
F-523	NHEt	NH-n-Bu	H	4-NO ₂	F-573	NHOEt	NH-propargyl	H	4-NO ₂
F-524	NHEt	NH-allyl	H	4-NO ₂	F-574	NHOEt	NHCH ₂ CF ₃	H	4-NO ₂
F-525	NHEt	NH-propargyl	H	4-NO ₂	F-575	NHOEt	NHCH ₂ CH ₂ F	H	4-NO ₂
F-526	NHEt	NHCH ₂ CF ₃	H	4-NO ₂	F-576	NHNMe ₂	NH ₂	H	4-NO ₂
F-527	NHEt	NHCH ₂ CH ₂ F	H	4-NO ₂	F-577	NHNMe ₂	NHMe	H	4-NO ₂
F-528	NHPr	NHPr	H	4-NO ₂	F-578	NHNMe ₂	NHEt	H	4-NO ₂
F-529	NHPr	NH-i-Pr	H	4-NO ₂	F-579	NHNMe ₂	NHPr	H	4-NO ₂
F-530	NHPr	NH-n-Bu	H	4-NO ₂	F-580	NHNMe ₂	NH-i-Pr	H	4-NO ₂
F-531	NHPr	NH-allyl	H	4-NO ₂	F-581	NHNMe ₂	NH-n-Bu	H	4-NO ₂
F-532	NHPr	NH-propargyl	H	4-NO ₂	F-582	NHNMe ₂	NH-allyl	H	4-NO ₂
F-533	NHPr	NHCH ₂ CF ₃	H	4-NO ₂	F-583	NHNMe ₂	NH-propargyl	H	4-NO ₂
F-534	NHPr	NHCH ₂ CH ₂ F	H	4-NO ₂	F-584	NHNMe ₂	NHCH ₂ CF ₃	H	4-NO ₂
F-535	NH-i-Pr	NH-i-Pr	H	4-NO ₂	F-585	NHNMe ₂	NHCH ₂ CH ₂ F	H	4-NO ₂
F-536	NH-i-Pr	NH-n-Bu	H	4-NO ₂	F-586	NHNH ₂	NH ₂	H	4-NO ₂
F-537	NH-i-Pr	NH-allyl	H	4-NO ₂	F-587	NHNH ₂	NHMe	H	4-NO ₂
F-538	NH-i-Pr	NH-propargyl	H	4-NO ₂	F-588	NHNH ₂	NHEt	H	4-NO ₂
F-539	NH-i-Pr	NHCH ₂ CF ₃	H	4-NO ₂	F-589	NHNH ₂	NHPr	H	4-NO ₂
F-540	NH-i-Pr	NHCH ₂ CH ₂ F	H	4-NO ₂	F-590	NHNH ₂	NH-i-Pr	H	4-NO ₂
F-541	NH-n-Bu	NH-n-Bu	H	4-NO ₂	F-591	NHNH ₂	NH-n-Bu	H	4-NO ₂
F-542	NH-n-Bu	NH-allyl	H	4-NO ₂	F-592	NHNH ₂	NH-allyl	H	4-NO ₂
F-543	NH-n-Bu	NH-propargyl	H	4-NO ₂	F-593	NHNH ₂	NH-propargyl	H	4-NO ₂
F-544	NH-n-Bu	NHCH ₂ CF ₃	H	4-NO ₂	F-594	NHNH ₂	NHCH ₂ CF ₃	H	4-NO ₂
F-545	NH-n-Bu	NHCH ₂ CH ₂ F	H	4-NO ₂	F-595	NHNH ₂	NHCH ₂ CH ₂ F	H	4-NO ₂
F-546	NH-allyl	NH-allyl	H	4-NO ₂	F-596	NHNHMe	NHMe	H	4-NO ₂
F-547	NH-allyl	NH-propargyl	H	4-NO ₂	F-597	NHNHMe	NHEt	H	4-NO ₂
F-548	NH-allyl	NHCH ₂ CF ₃	H	4-NO ₂	F-598	NHNHMe	NHPr	H	4-NO ₂
F-549	NH-allyl	NHCH ₂ CH ₂ F	H	4-NO ₂	F-599	NHNHMe	NH-i-Pr	H	4-NO ₂
F-550	NH-propargyl	NH-propargyl	H	4-NO ₂	F-600	NHNHMe	NHCH ₂ CF ₃	H	4-NO ₂

Table 31

Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Compound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-601	NH ₂	NH ₂	Me	4-NH ₂	F-651	NH-propargyl	NHCH ₂ CF ₃	Me	4-NH ₂
F-602	NH ₂	NHMe	Me	4-NH ₂	F-652	NH-propargyl	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-603	NH ₂	NHEt	Me	4-NH ₂	F-653	NHCH ₂ CF ₃	NHCH ₂ CF ₃	Me	4-NH ₂
F-604	NH ₂	NHPr	Me	4-NH ₂	F-654	NHCH ₂ CF ₃	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-605	NH ₂	NH-i-Pr	Me	4-NH ₂	F-655	NHCH ₂ CH ₂ F	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-606	NH ₂	NH-n-Bu	Me	4-NH ₂	F-656	NHOMe	NH ₂	Me	4-NH ₂
F-607	NH ₂	NH-allyl	Me	4-NH ₂	F-657	NHOMe	NHMe	Me	4-NH ₂
F-608	NH ₂	NH-propargyl	Me	4-NH ₂	F-658	NHOMe	NHEt	Me	4-NH ₂
F-609	NH ₂	NHCH ₂ CF ₃	Me	4-NH ₂	F-659	NHOMe	NHPr	Me	4-NH ₂
F-610	NH ₂	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-660	NHOMe	NH-i-Pr	Me	4-NH ₂
F-611	NHMe	NHMe	Me	4-NH ₂	F-661	NHOMe	NH-n-Bu	Me	4-NH ₂
F-612	NHMe	NHEt	Me	4-NH ₂	F-662	NHOMe	NH-allyl	Me	4-NH ₂
F-613	NHMe	NHPr	Me	4-NH ₂	F-663	NHOMe	NH-propargyl	Me	4-NH ₂
F-614	NHMe	NH-i-Pr	Me	4-NH ₂	F-664	NHOMe	NHCH ₂ CF ₃	Me	4-NH ₂
F-615	NHMe	NH-n-Bu	Me	4-NH ₂	F-665	NHOMe	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-616	NHMe	NH-allyl	Me	4-NH ₂	F-666	NHOEt	NH ₂	Me	4-NH ₂
F-617	NHMe	NH-propargyl	Me	4-NH ₂	F-667	NHOEt	NHMe	Me	4-NH ₂
F-618	NHMe	NHCH ₂ CF ₃	Me	4-NH ₂	F-668	NHOEt	NHEt	Me	4-NH ₂
F-619	NHMe	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-669	NHOEt	NHPr	Me	4-NH ₂
F-620	NHEt	NHEt	Me	4-NH ₂	F-670	NHOEt	NH-i-Pr	Me	4-NH ₂
F-621	NHEt	NHPr	Me	4-NH ₂	F-671	NHOEt	NH-n-Bu	Me	4-NH ₂
F-622	NHEt	NH-i-Pr	Me	4-NH ₂	F-672	NHOEt	NH-allyl	Me	4-NH ₂
F-623	NHEt	NH-n-Bu	Me	4-NH ₂	F-673	NHOEt	NH-propargyl	Me	4-NH ₂
F-624	NHEt	NH-allyl	Me	4-NH ₂	F-674	NHOEt	NHCH ₂ CF ₃	Me	4-NH ₂
F-625	NHEt	NH-propargyl	Me	4-NH ₂	F-675	NHOEt	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-626	NHEt	NHCH ₂ CF ₃	Me	4-NH ₂	F-676	NHNMe ₂	NH ₂	Me	4-NH ₂
F-627	NHEt	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-677	NHNMe ₂	NHMe	Me	4-NH ₂
F-628	NHPr	NHPr	Me	4-NH ₂	F-678	NHNMe ₂	NHEt	Me	4-NH ₂
F-629	NHPr	NH-i-Pr	Me	4-NH ₂	F-679	NHNMe ₂	NHPr	Me	4-NH ₂
F-630	NHPr	NH-n-Bu	Me	4-NH ₂	F-680	NHNMe ₂	NH-i-Pr	Me	4-NH ₂
F-631	NHPr	NH-allyl	Me	4-NH ₂	F-681	NHNMe ₂	NH-n-Bu	Me	4-NH ₂
F-632	NHPr	NH-propargyl	Me	4-NH ₂	F-682	NHNMe ₂	NH-allyl	Me	4-NH ₂
F-633	NHPr	NHCH ₂ CF ₃	Me	4-NH ₂	F-683	NHNMe ₂	NH-propargyl	Me	4-NH ₂
F-634	NHPr	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-684	NHNMe ₂	NHCH ₂ CF ₃	Me	4-NH ₂
F-635	NH-i-Pr	NH-i-Pr	Me	4-NH ₂	F-685	NHNMe ₂	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-636	NH-i-Pr	NH-n-Bu	Me	4-NH ₂	F-686	NHNH ₂	NH ₂	Me	4-NH ₂
F-637	NH-i-Pr	NH-allyl	Me	4-NH ₂	F-687	NHNH ₂	NHMe	Me	4-NH ₂
F-638	NH-i-Pr	NH-propargyl	Me	4-NH ₂	F-688	NHNH ₂	NHEt	Me	4-NH ₂
F-639	NH-i-Pr	NHCH ₂ CF ₃	Me	4-NH ₂	F-689	NHNH ₂	NHPr	Me	4-NH ₂
F-640	NH-i-Pr	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-690	NHNH ₂	NH-i-Pr	Me	4-NH ₂
F-641	NH-n-Bu	NH-n-Bu	Me	4-NH ₂	F-691	NHNH ₂	NH-n-Bu	Me	4-NH ₂
F-642	NH-n-Bu	NH-allyl	Me	4-NH ₂	F-692	NHNH ₂	NH-allyl	Me	4-NH ₂
F-643	NH-n-Bu	NH-propargyl	Me	4-NH ₂	F-693	NHNH ₂	NH-propargyl	Me	4-NH ₂
F-644	NH-n-Bu	NHCH ₂ CF ₃	Me	4-NH ₂	F-694	NHNH ₂	NHCH ₂ CF ₃	Me	4-NH ₂
F-645	NH-n-Bu	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-695	NHNH ₂	NHCH ₂ CH ₂ F	Me	4-NH ₂
F-646	NH-allyl	NH-allyl	Me	4-NH ₂	F-696	NHNHMe	NHMe	Me	4-NH ₂
F-647	NH-allyl	NH-propargyl	Me	4-NH ₂	F-697	NHNHMe	NHEt	Me	4-NH ₂
F-648	NH-allyl	NHCH ₂ CF ₃	Me	4-NH ₂	F-698	NHNHMe	NHPr	Me	4-NH ₂
F-649	NH-allyl	NHCH ₂ CH ₂ F	Me	4-NH ₂	F-699	NHNHMe	NH-i-Pr	Me	4-NH ₂
F-650	NH-propargyl	NH-propargyl	Me	4-NH ₂	F-700	NHNHMe	NHCH ₂ CF ₃	Me	4-NH ₂

Table 32

Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸	Comp- ound No.	R ¹⁵	R ¹⁶	R ¹⁷	R ¹⁸
F-701	NH ₂	NH ₂	H	4-NH ₂	F-751	NH-propargyl	NHCH ₂ CF ₃	H	4-NH ₂
F-702	NH ₂	NHMe	H	4-NH ₂	F-752	NH-propargyl	NHCH ₂ CH ₂ F	H	4-NH ₂
F-703	NH ₂	NHEt	H	4-NH ₂	F-753	NHCH ₂ CF ₃	NHCH ₂ CF ₃	H	4-NH ₂
F-704	NH ₂	NHPr	H	4-NH ₂	F-754	NHCH ₂ CF ₃	NHCH ₂ CH ₂ F	H	4-NH ₂
F-705	NH ₂	NH-i-Pr	H	4-NH ₂	F-755	NHCH ₂ CH ₂ F	NHCH ₂ CH ₂ F	H	4-NH ₂
F-706	NH ₂	NH-n-Bu	H	4-NH ₂	F-756	NHOMe	NH ₂	H	4-NH ₂
F-707	NH ₂	NH-allyl	H	4-NH ₂	F-757	NHOMe	NHMe	H	4-NH ₂
F-708	NH ₂	NH-propargyl	H	4-NH ₂	F-758	NHOMe	NHEt	H	4-NH ₂
F-709	NH ₂	NHCH ₂ CF ₃	H	4-NH ₂	F-759	NHOMe	NHPr	H	4-NH ₂
F-710	NH ₂	NHCH ₂ CH ₂ F	H	4-NH ₂	F-760	NHOMe	NH-i-Pr	H	4-NH ₂
F-711	NHMe	NHMe	H	4-NH ₂	F-761	NHOMe	NH-n-Bu	H	4-NH ₂
F-712	NHMe	NHEt	H	4-NH ₂	F-762	NHOMe	NH-allyl	H	4-NH ₂
F-713	NHMe	NHPr	H	4-NH ₂	F-763	NHOMe	NH-propargyl	H	4-NH ₂
F-714	NHMe	NH-i-Pr	H	4-NH ₂	F-764	NHOMe	NHCH ₂ CF ₃	H	4-NH ₂
F-715	NHMe	NH-n-Bu	H	4-NH ₂	F-765	NHOMe	NHCH ₂ CH ₂ F	H	4-NH ₂
F-716	NHMe	NH-allyl	H	4-NH ₂	F-766	NHOEt	NH ₂	H	4-NH ₂
F-717	NHMe	NH-propargyl	H	4-NH ₂	F-767	NHOEt	NHMe	H	4-NH ₂
F-718	NHMe	NHCH ₂ CF ₃	H	4-NH ₂	F-768	NHOEt	NHEt	H	4-NH ₂
F-719	NHMe	NHCH ₂ CH ₂ F	H	4-NH ₂	F-769	NHOEt	NHPr	H	4-NH ₂
F-720	NHEt	NHEt	H	4-NH ₂	F-770	NHOEt	NH-i-Pr	H	4-NH ₂
F-721	NHEt	NHPr	H	4-NH ₂	F-771	NHOEt	NH-n-Bu	H	4-NH ₂
F-722	NHEt	NH-i-Pr	H	4-NH ₂	F-772	NHOEt	NH-allyl	H	4-NH ₂
F-723	NHEt	NH-n-Bu	H	4-NH ₂	F-773	NHOEt	NH-propargyl	H	4-NH ₂
F-724	NHEt	NH-allyl	H	4-NH ₂	F-774	NHOEt	NHCH ₂ CF ₃	H	4-NH ₂
F-725	NHEt	NH-propargyl	H	4-NH ₂	F-775	NHOEt	NHCH ₂ CH ₂ F	H	4-NH ₂
F-726	NHEt	NHCH ₂ CF ₃	H	4-NH ₂	F-776	NHNMe ₂	NH ₂	H	4-NH ₂
F-727	NHEt	NHCH ₂ CH ₂ F	H	4-NH ₂	F-777	NHNMe ₂	NHMe	H	4-NH ₂
F-728	NHPr	NHPr	H	4-NH ₂	F-778	NHNMe ₂	NHEt	H	4-NH ₂
F-729	NHPr	NH-i-Pr	H	4-NH ₂	F-779	NHNMe ₂	NHPr	H	4-NH ₂
F-730	NHPr	NH-n-Bu	H	4-NH ₂	F-780	NHNMe ₂	NH-i-Pr	H	4-NH ₂
F-731	NHPr	NH-allyl	H	4-NH ₂	F-781	NHNMe ₂	NH-n-Bu	H	4-NH ₂
F-732	NHPr	NH-propargyl	H	4-NH ₂	F-782	NHNMe ₂	NH-allyl	H	4-NH ₂
F-733	NHPr	NHCH ₂ CF ₃	H	4-NH ₂	F-783	NHNMe ₂	NH-propargyl	H	4-NH ₂
F-734	NHPr	NHCH ₂ CH ₂ F	H	4-NH ₂	F-784	NHNMe ₂	NHCH ₂ CF ₃	H	4-NH ₂
F-735	NH-i-Pr	NH-i-Pr	H	4-NH ₂	F-785	NHNMe ₂	NHCH ₂ CH ₂ F	H	4-NH ₂
F-736	NH-i-Pr	NH-n-Bu	H	4-NH ₂	F-786	NHNH ₂	NH ₂	H	4-NH ₂
F-737	NH-i-Pr	NH-allyl	H	4-NH ₂	F-787	NHNH ₂	NHMe	H	4-NH ₂
F-738	NH-i-Pr	NH-propargyl	H	4-NH ₂	F-788	NHNH ₂	NHEt	H	4-NH ₂
F-739	NH-i-Pr	NHCH ₂ CF ₃	H	4-NH ₂	F-789	NHNH ₂	NHPr	H	4-NH ₂
F-740	NH-i-Pr	NHCH ₂ CH ₂ F	H	4-NH ₂	F-790	NHNH ₂	NH-i-Pr	H	4-NH ₂
F-741	NH-n-Bu	NH-n-Bu	H	4-NH ₂	F-791	NHNH ₂	NH-n-Bu	H	4-NH ₂
F-742	NH-n-Bu	NH-allyl	H	4-NH ₂	F-792	NHNH ₂	NH-allyl	H	4-NH ₂
F-743	NH-n-Bu	NH-propargyl	H	4-NH ₂	F-793	NHNH ₂	NH-propargyl	H	4-NH ₂
F-744	NH-n-Bu	NHCH ₂ CF ₃	H	4-NH ₂	F-794	NHNH ₂	NHCH ₂ CF ₃	H	4-NH ₂
F-745	NH-n-Bu	NHCH ₂ CH ₂ F	H	4-NH ₂	F-795	NHNH ₂	NHCH ₂ CH ₂ F	H	4-NH ₂
F-746	NH-allyl	NH-allyl	H	4-NH ₂	F-796	NHNHMe	NHMe	H	4-NH ₂
F-747	NH-allyl	NH-propargyl	H	4-NH ₂	F-797	NHNHMe	NHEt	H	4-NH ₂
F-748	NH-allyl	NHCH ₂ CF ₃	H	4-NH ₂	F-798	NHNHMe	NHPr	H	4-NH ₂
F-749	NH-allyl	NHCH ₂ CH ₂ F	H	4-NH ₂	F-799	NHNHMe	NH-i-Pr	H	4-NH ₂
F-750	NH-propargyl	NH-propargyl	H	4-NH ₂	F-800	NHNHMe	NHCH ₂ CF ₃	H	4-NH ₂

Test Example 1 Inhibitory effect against cellular signaling derived from Ras oncogene products

1) Establishment of cell lines used in assay

5 Based on the reporter plasmid (pGV-P (Toyo Ink, Japan)), in which luciferase gene was ligated to SV40-derived minimal promoter, we constructed a plasmid designated pRRE3-luc by inserting 3 copies of chemically synthesized oligonucleotides (Sequence : CAGGATATGACTCT, derived from mouse NVL-3 (M.A.Reddy et al.(1992)Mol. Endocrinol., 6, 1051)) into upstream of the promoter. v-ki-ras-transformed NIH3T3 cells
10 (DT cells, provided by Dr. Makoto Noda (Kyoto Univ., School of medicine)) were transfected with this plasmid by liposome-mediated transfection and transfected cell lines stably incorporated and maintained each plasmid were obtained. We named pGV-P and pRRE3-transfected cell line as DT-C and DT-R, respectively and used in the assay described below.

15

2) Preparation of samples

- i) All the cell lines were cultured in Dulbecco's Modified Essential Medium (DMEM : 10% Fetal Calf Serum(FCS : Hyclone, USA)) including 60 mg/ml kanamycin (Meiji Seika, Japan) in humidified incubator under condition of 5% CO₂ at 37 °C.
- 20 ii) DT-C and DT-R cells were seeded at 2500 cells/well into flat-bottom 96 well multiplate (Sumitomo bakelite) and incubated for 24 hours.
- iii) Test compounds were prepared as 1 mg/ml DMSO solution.
- iv) The solution of test compounds were added to the culture. Tested compounds are used at the concentration from 10 mg/ml to 0.51 ng/ml with 3-fold dilution.
- 25 v) After 24 hours, the culture supernatant was completely aspirated and 20 µl of cell-lysing solution (PGC-50 (Toyo Ink, Japan)) was added before cells were dried up. In order to lyse the cells completely, multiwell plates were left at room temperature for 10 to 30 min. The plates were wrapped up and stored at -20 °C till the day of measurement.

30 3) Measurement of samples

- i) Melt the samples by putting 96 well multiplate at 37 °C and add 90 µl/well 25 mM Tris (pH 7.5).
 - ii) Transfer 50 µl of the sample (110 µl) to the 96 well microplate (Microlite 1 (Dynatech)) for measurement.
 - 5 iii) Measure the samples by the luminometer, LUMINOUS CT9000D (Dia-Yatron, Japan). We used Pickagene luminescence kit PGL2000 or LT2.0 (Toyo Ink, Japan) as enzyme substrates for luminescence measurement (50 µl/well).
- 4) Judgment of the results
- 10 i) The luciferase activity of DT-C cells and DT-R cells were plotted in the graph where the relative activity and the compound concentration were expressed as Y-axis and X-axis, respectively. We judged by the degree of dissociation between the activities of DT-C cells and DT-R cells as an index.
 - ii) Concretely, efficacy of the compound was expressed by two values described below.
 - 15 a) Among the points of concentration tested, the minimal concentration (Minimal Active Concentration : MAC), at which the activities of DT-C cells and DT-R cells dissociated, was shown as an index of efficacy of the compound.
 - b) Among the points of concentration tested, the concentration which is the nearest to 50% inhibition concentration at DT-C cells (IC₅₀-C), was shown as an index of non-specific transcription-inhibitory effect or of cytotoxicity. In case of positive
20 compounds, 50% inhibition concentration in DT-C cells which was higher than the active concentration was expressed as IC₅₀-C.

The results of the assay were shown in table 33.

Table 33

Compound No.	MAC ($\mu\text{g/ml}$)	IC50 ($\mu\text{g/ml}$)	Compound No.	MAC ($\mu\text{g/ml}$)	IC50 ($\mu\text{g/ml}$)
A-1	1.11	>10	A-16	<0.000508	>10
A-2	1.11	>10	A-17	0.0412	>10
A-3	0.37	>10	A-18	0.00457	>10
A-4	0.37	>10	A-19	0.37	>10
A-5	0.123	10	A-21	0.37	10
A-6	0.0412	10	A-22	1.11	>10
A-7	0.123	3.33	A-23	3.33	>10
A-8	0.123	>10	A-32	0.123	>10
A-10	1.11	>10	A-33	0.0412	>10
A-11	0.0412	>10	A-34	0.0137	>10
A-12	0.0137	>10	A-35	0.0412	>10
A-13	0.0137	10	C-1	0.0412	10
A-14	0.0412	>10	C-2	0.0137	>10
A-15	0.00152	>10			

Test Example 2 In vitro cell growth inhibition test

Cells and MTT assay

Human squamous lung cancer RERF-RC-AI, human squamous lung cancer Ma44, human lung adenocarcinoma A549, human colon cancer HT29 and human pancreas cancer PANC-1 were used. All cell lines were cultured with Eagle's Modified Essential Medium (EMEM, supplemented with 10% fetal calf serum (FCS: Hyclone, USA) and 60 µg/ml Kanamycin (Meiji-seika, Japan) at 37 °C in a humidified incubator (5% CO₂). The cells were plated in 96-well microcultureplate. Twenty-four hours later, compound were added at the concentration from 10 µg/ml to 0.1 ng/ml with 2-fold dilution. MTT assay was performed 4 days later and IC₅₀ values were determined. The results were shown in Table 34 in terms of concentration at ng/ml.

Table 34

Compound No.	A549	HT-29	Ma44	PANC-1	RERF-LC-AI	H460
A-1	0.9	45	120	46		
A-2	34	140	370	160		
A-3	63	52	56	51	46	
A-4	38	23	51	26	30	
A-5	70	48.4	44.6	66.5	33	89
A-6	25.6	24.4	18.2	14.8	15	25.6
A-7	2.1	3.6	1.6	0.6	1.3	3.8
A-8	9.3	41.4	34.1	37.1	27.8	6.8
A-10			80			
A-11	14	6.7	77	6.4		
A-12	8	6.3	9.5	9.1	5.7	11.5
A-13	15	8.9	30	7.7		
A-14	12	11	32	9.8	12	
A-15	11.1	10.3	12.7	12.4	6.5	15.3
A-16	14.6	8.1	13.6	6.5	7.3	10.7
A-17	17.4	15	24.1	10.7	13.2	15
A-18	51.4	0.4	0.4	0.4	0.4	27.5
A-19			83			
A-21			22			
A-22			42			
A-32	64	31	42	34	31	
A-33	23	6.6	9.1	8.6	9.3	
A-34	21	4.6	9.1	7.5	13	
A-35	11	3.3	6.9	5.4	6.7	
C-1	16	6.6	11	6.4		
C-2	4.4	2	3.4	2		

5

10

15

Formulation example

Formulation example 1

Granules are prepared using the following ingredients.

	Ingredients	The compound represented by the formula (I)	10 mg
5		Lactose	700 mg
		Corn starch	274 mg
		HPC-L	16 mg
			1000 mg

The compound represented by the formula (I) and lactose were made pass
 10 through a 60 mesh sieve. Corn starch was made pass through a 120 mesh sieve. They
 were mixed by a twin shell blender. An aqueous solution of HPC-L (low mucosity
 hydroxypropylcellulose) was added to the mixture and the resulting mixture was kneaded,
 granulated (by the extrusion with pore size 0.5 to 1 mm mesh), and dried. The dried
 granules thus obtained were sieved by a swing sieve (12/60 mesh) to yield the granules.

15

Formulation 2

Powders for filling capsules are prepared using the following ingredients.

	Ingredients	The compound represented by the formula (I)	10 mg
		Lactose	79 mg
20		Corn starch	10 mg
		Magnesium stearate	1 mg
			100 mg

The compound represented by the formula (I) and lactose were made pass
 through a 60 mesh sieve. Corn starch was made pass through a 120 mesh sieve. These
 25 ingredients and magnesium stearate were mixed by a twin shell blender. 100 mg of the
 10-fold trituration was filled into a No. 5 hard gelatin capsule.

Formulation 3

Granules for filling capsules are prepared using the following ingredients.

30	Ingredients	The compound represented by the formula (I)	15 mg
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Lactose	90 mg
Corn starch	42 mg
HPC-L	3 mg
	150 mg

The compound represented by the formula (I) and lactose were made pass through a 60 mesh sieve. Corn starch was made pass through a 120 mesh sieve. After mixing them, an aqueous solution of HPC-L was added to the mixture and the resulting mixture was kneaded, granulated, and dried. After the dried granules were lubricated, 150 mg of that were filled into a No. 4 hard gelatin capsule.

Formulation 4

Tablets are prepared using the following ingredients.

Ingredients	The compound represented by the formula (I)	10 mg
	Lactose	90 mg
	Microcrystal cellulose	30 mg
	CMC-Na	15 mg
	Magnesium stearate	5 mg
		150 mg

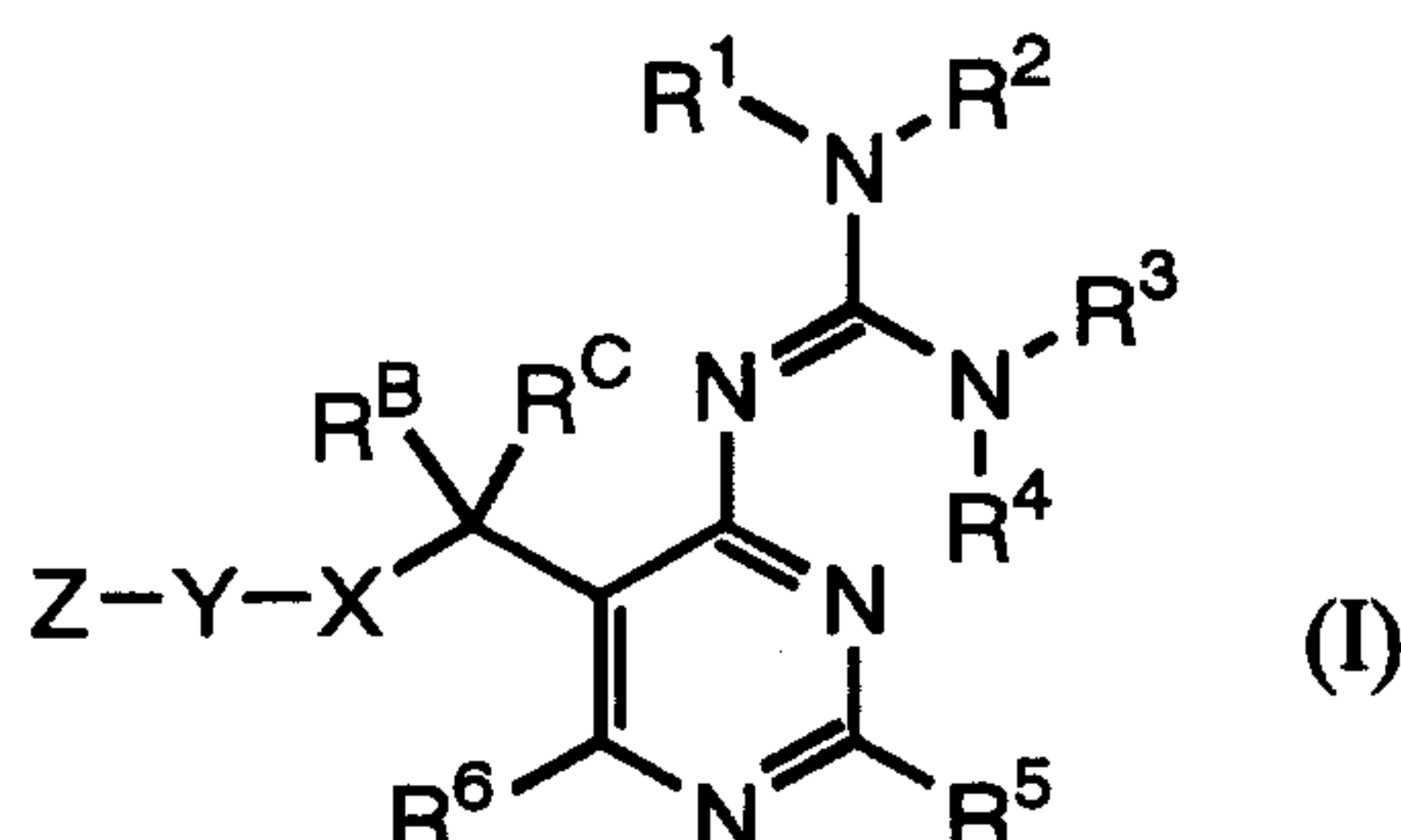
The compound represented by the formula (I), lactose, microcrystal cellulose, and CMC-Na (carboxymethylcellulose sodium salt) were made pass through a 60 mesh sieve and then mixed. The resulting mixture was mixed with magnesium stearate to obtain the mixed powder for the tablet formulation. The mixed powder was compressed to yield tablets of 150 mg.

Industrial Applicability

The pyrimidine derivatives of the present invention have an inhibitory activity against a signal derived from Ras oncogene products, whereby they are effective for solid cancer having high frequency ras activation such as pancreatic cancer, colon cancer, and lung cancer.

CLAIMS

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



- 5 wherein R^1 , R^2 , R^3 , and R^4 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, an optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; or
- 10 R^1 and R^2 , R^3 and R^4 , and R^2 and R^3 each taken together with the adjacent nitrogen atom form the same or different 3- to 7- membered ring optionally containing O, N, or S, provided that R^1 and R^2 and R^3 and R^4 do not form a ring when R^2 and R^3 taken together form a ring;
- R^5 and R^6 are each independently hydrogen atom, optionally substituted alkyl,
- 15 optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkyloxy, alkylthio, optionally substituted alkyloxycarbonyl, optionally substituted aryl, optionally substituted heteroaryl, halogen, hydroxy, mercapto, optionally substituted amino, carboxy, cyano, or nitro;
- R^B and R^C are each independently hydrogen atom, alkyl, or alkyloxy; provided
- 20 that in the case of both of R^B and R^C are hydrogen atom, R^1 is hydrogen atom or alkyl, R^2 is substituted amino, alkyloxy, hydroxy, cyano, or nitro; and R^3 and R^4 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted non-aromatic heterocyclic group, acyl,
- 25 optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; or R^3 and R^4 each taken together with the adjacent nitrogen atom form the same or different 3- to 7- membered ring

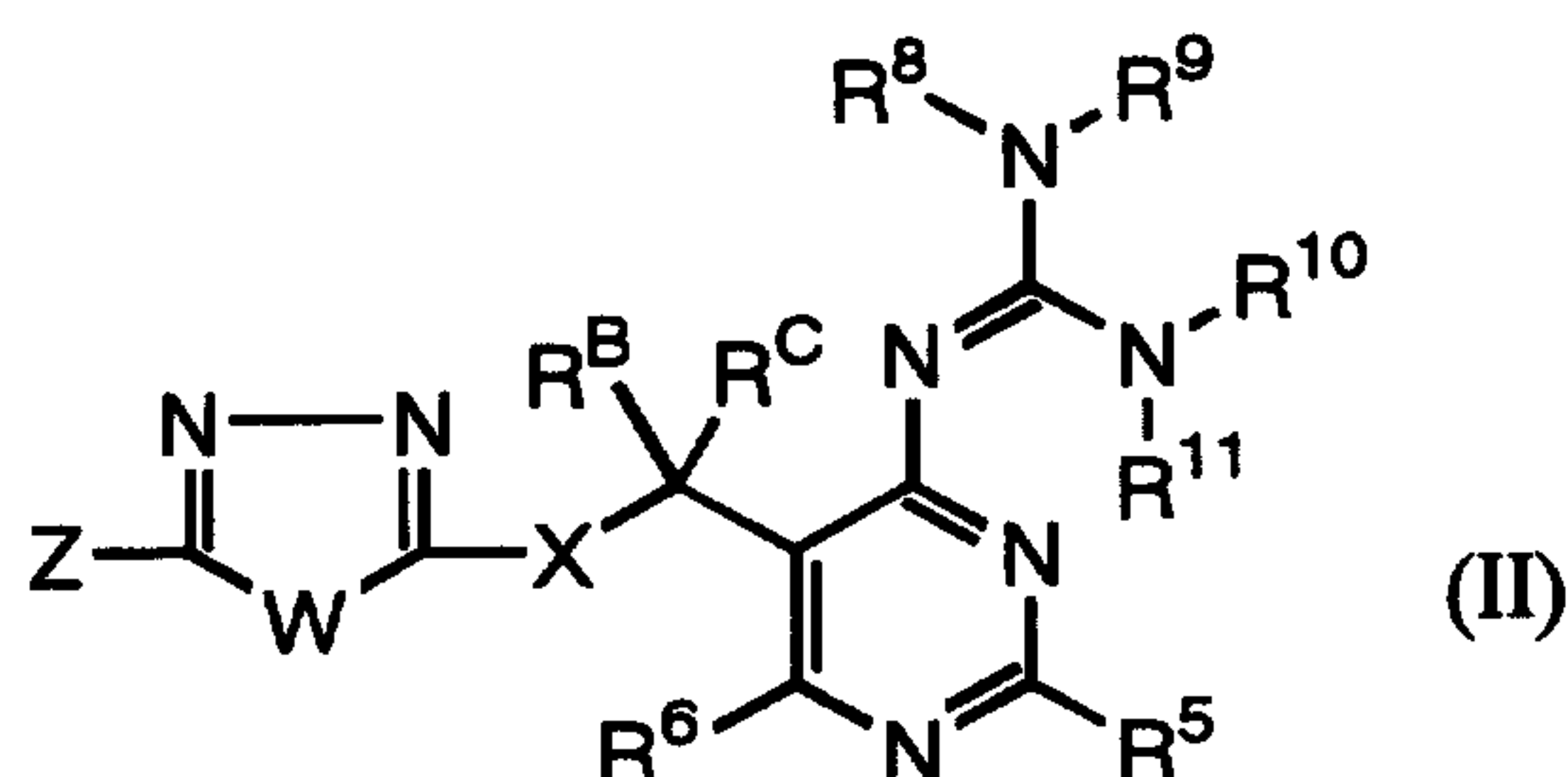
optionally containing O, S, or N;

X is -N(R⁷)-, -NH-NH-, -O-, or -S- wherein R⁷ is hydrogen atom or optionally substituted alkyl;

Y is optionally substituted 5- membered non-aromatic heterocycle-diyl or
5 optionally substituted 5- membered heteroaryl-diyl;

Z is optionally substituted aryl or optionally substituted heteroaryl;
it optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

10 2. A compound of claim 1, represented by the formula (II):



wherein R⁸, R⁹, R¹⁰, and R¹¹ are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, a non-aromatic heterocyclic group, acyl, substituted amino,
15 alkyloxy, hydroxy, cyano, or nitro;

R^B and R^C are each independently hydrogen atom, alkyl, or alkyloxy; provided that in the case of both of R^B and R^C are hydrogen atom, R⁸ is hydrogen atom or alkyl, R⁹ is substituted amino, alkyloxy, hydroxy, cyano, or nitro; and R¹⁰ and R¹¹ are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally
20 substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

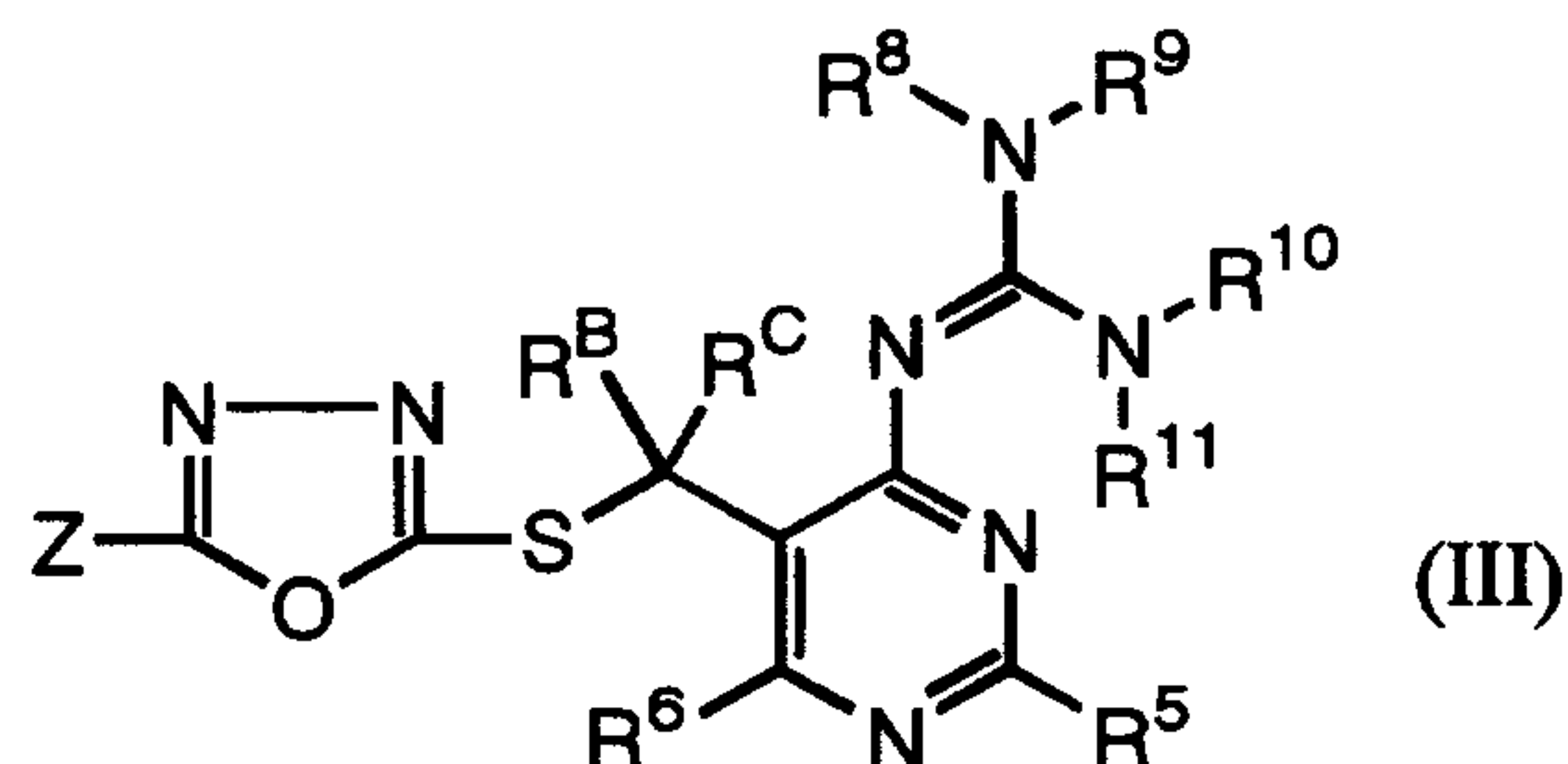
W is -O-, -S-, or -N(R^A)- wherein R^A is hydrogen atom or optionally substituted alkyl;

25 R⁵, R⁶, X, and Z are as defined in claim 1;

it optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or

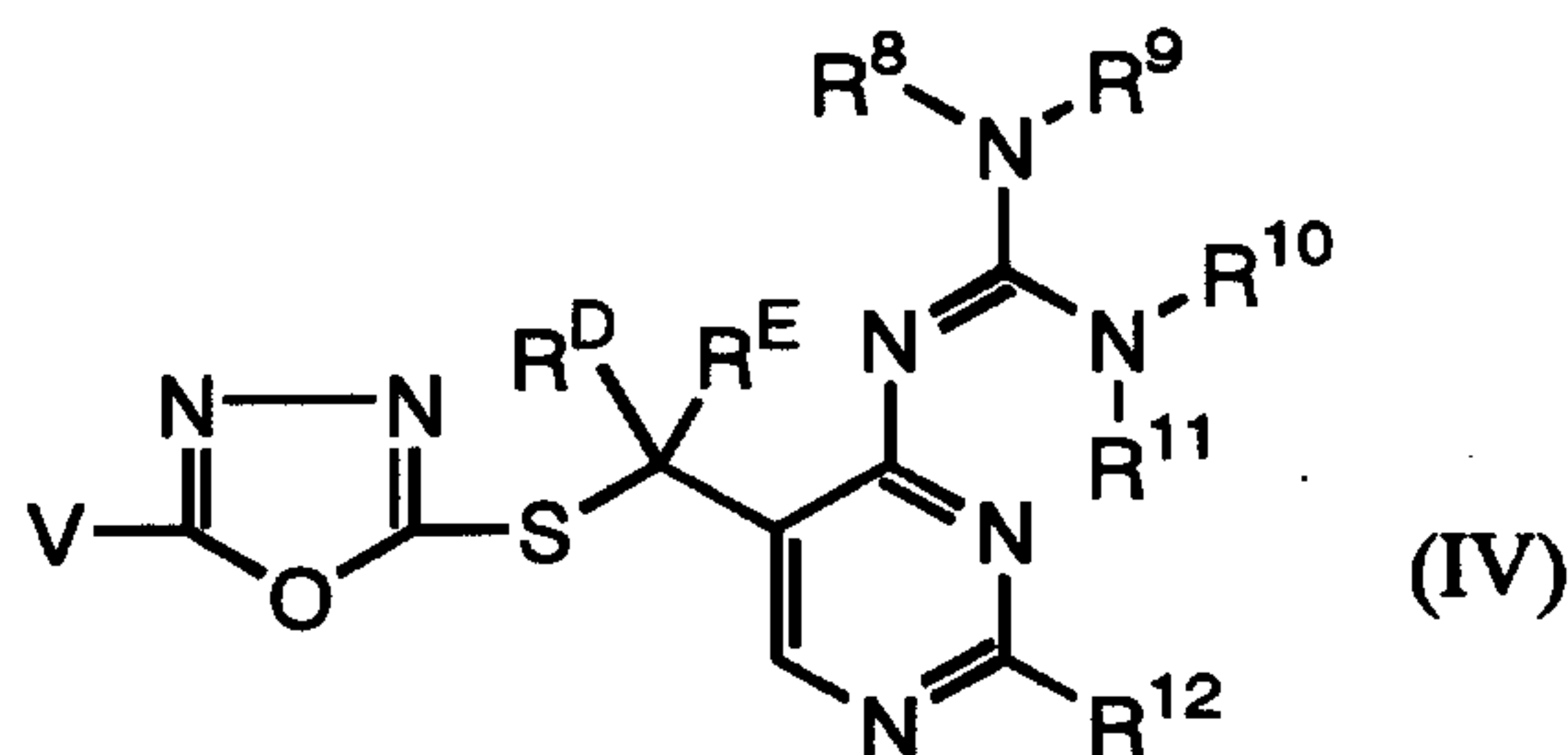
their solvate.

3. A compound of claim 1, represented by the formula (III):



5 wherein R^5 , R^6 , and Z are as defined in claim 1, R^8 , R^9 , R^{10} , R^{11} , R^B and R^C are as defined in claim 2, their optical active compounds, the prodrugs thereof, or their pharmaceutically acceptable salts, or their solvates,

4. A compound of claim 1, represented by the formula (IV):



10 wherein R^8 , R^9 , R^{10} and R^{11} are as defined in claim 2;

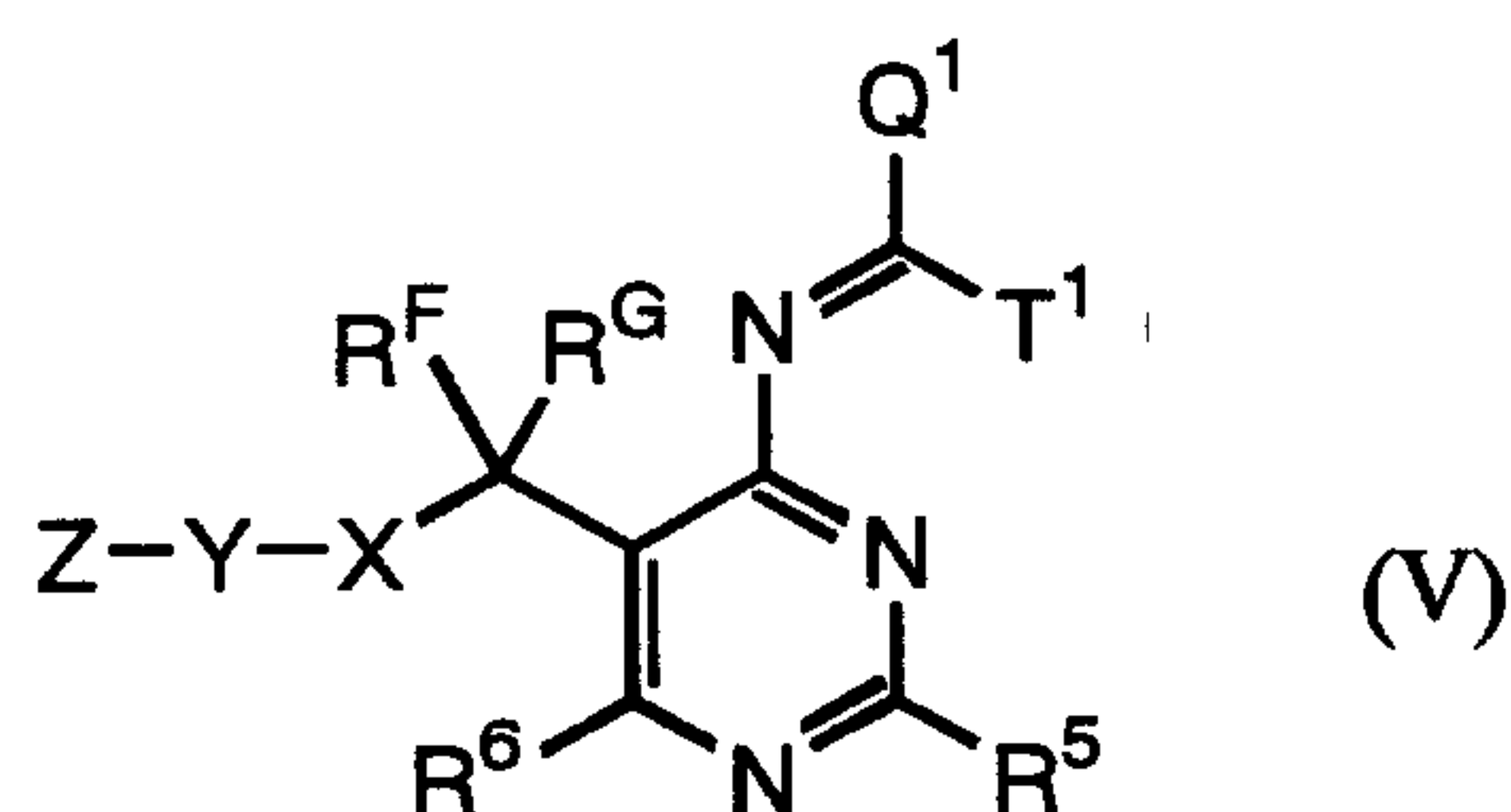
R^{12} is hydrogen atom or alkyl;

R^D and R^E are each independently hydrogen atom or alkyl; provided that in the case of both of R^D and R^E are hydrogen atom, R^8 is hydrogen atom or alkyl, R^9 is substituted amino, alkyloxy, hydroxy, cyano, or nitro; and R^{10} and R^{11} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

20 V is optionally substituted aryl;

it optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

5. A compound of claim 1 represented by the formula (V):



wherein R^5 and R^6 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkyloxy, alkylthio, optionally substituted alkyloxycarbonyl, optionally substituted aryl, optionally substituted heteroaryl, halogen atoms, hydroxy, mercapto, optionally substituted amino, carboxy, cyano, or nitro;

R^F and R^G are each independently hydrogen atom, alkyl, or alkyloxy;

X is $-N(R^7)-$, $-NH-NH-$, $-O-$, or $-S-$ wherein R^7 is hydrogen atom or optionally substituted alkyl;

Y is optionally substituted 5- membered non-aromatic heterocycle-diyl or optionally substituted 5- membered heteroaryl-diyl;

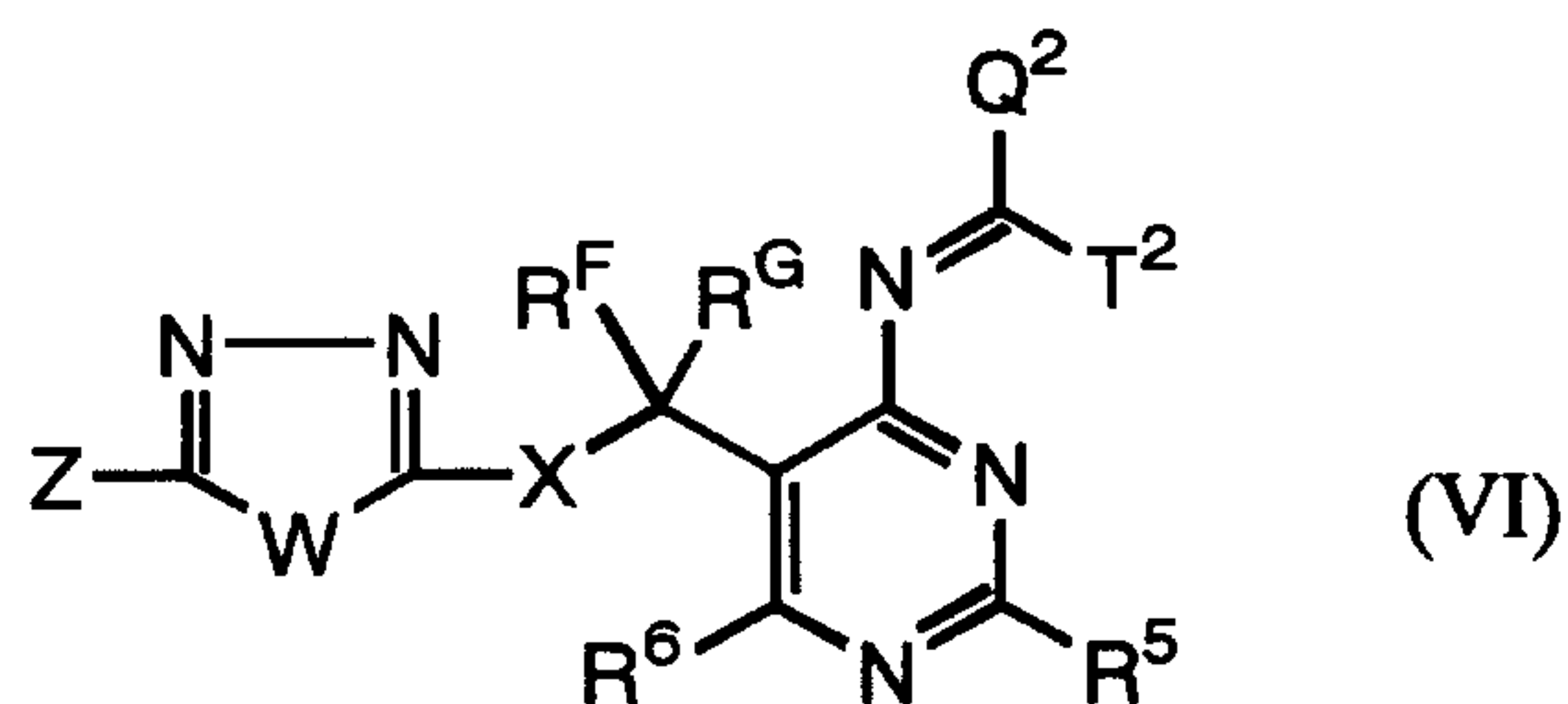
Z is optionally substituted aryl or optionally substituted heteroaryl;

Q^1 is $-NR^1R^2$, $-OR^1$, or $-SR^1$, T^1 is $-OR^3$ or $-SR^3$ wherein R^1 , R^2 and R^3 are each independently hydrogen atom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro; or

R^1 and R^3 , and R^2 and R^3 each taken together with the adjacent heteroatom form 5- to 7- membered ring;

it optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

6. A compound of claim 5, represented by the formula (VI):



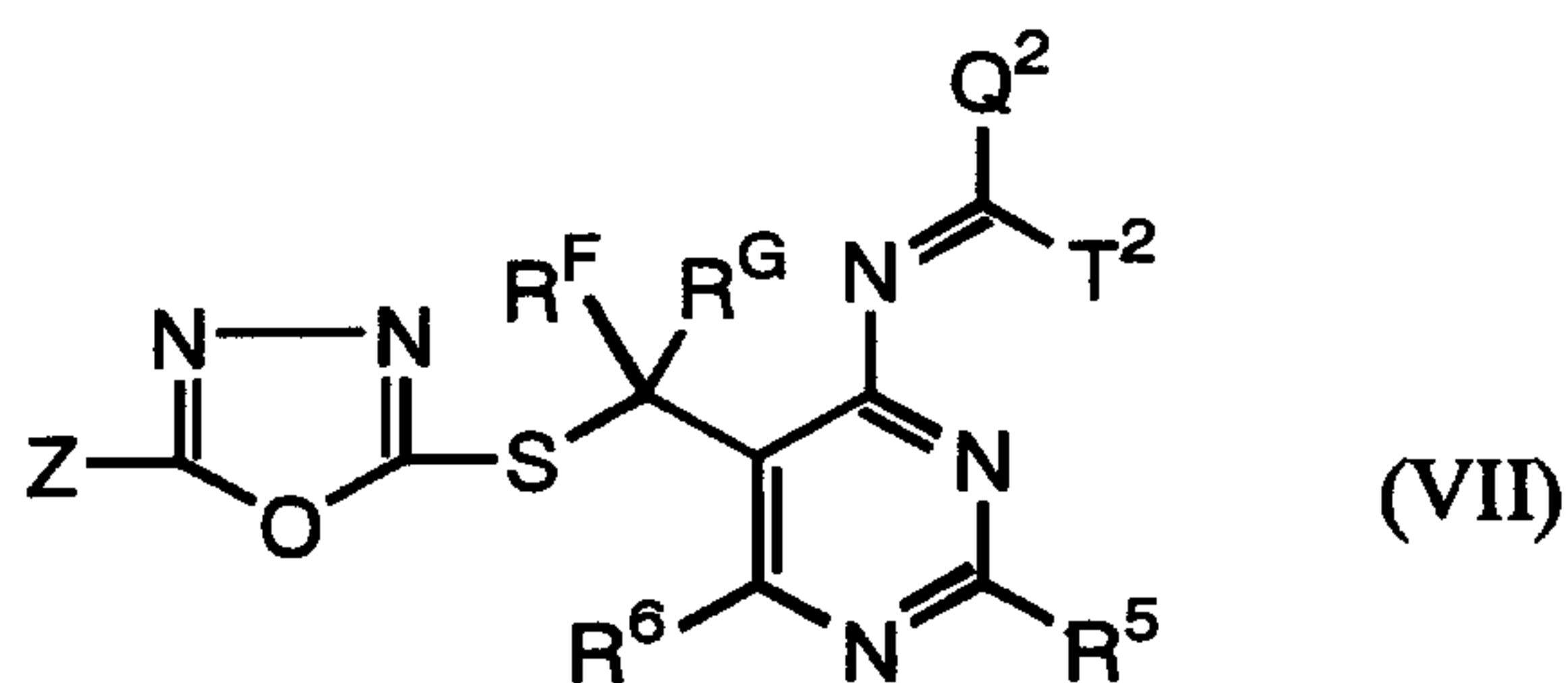
wherein Q^2 is $-NR^8R^9$, $-OR^8$, or $-SR^8$, T^2 is $-OR^{10}$ or $-SR^{10}$ wherein R^8 , R^9 and R^{10} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted non-aromatic heterocyclic group, acyl, optionally substituted amino, alkyloxy, hydroxy, cyano, or nitro;

W is $-O-$, $-S-$, or $-N(R^A)-$ wherein R^A is hydrogen atom or optionally substituted alkyl;

R^5 , R^6 , R^F , R^G , X, and Z are as defined in claim 5;

its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

7. A compound of claim 5, represented by the formula (VII):

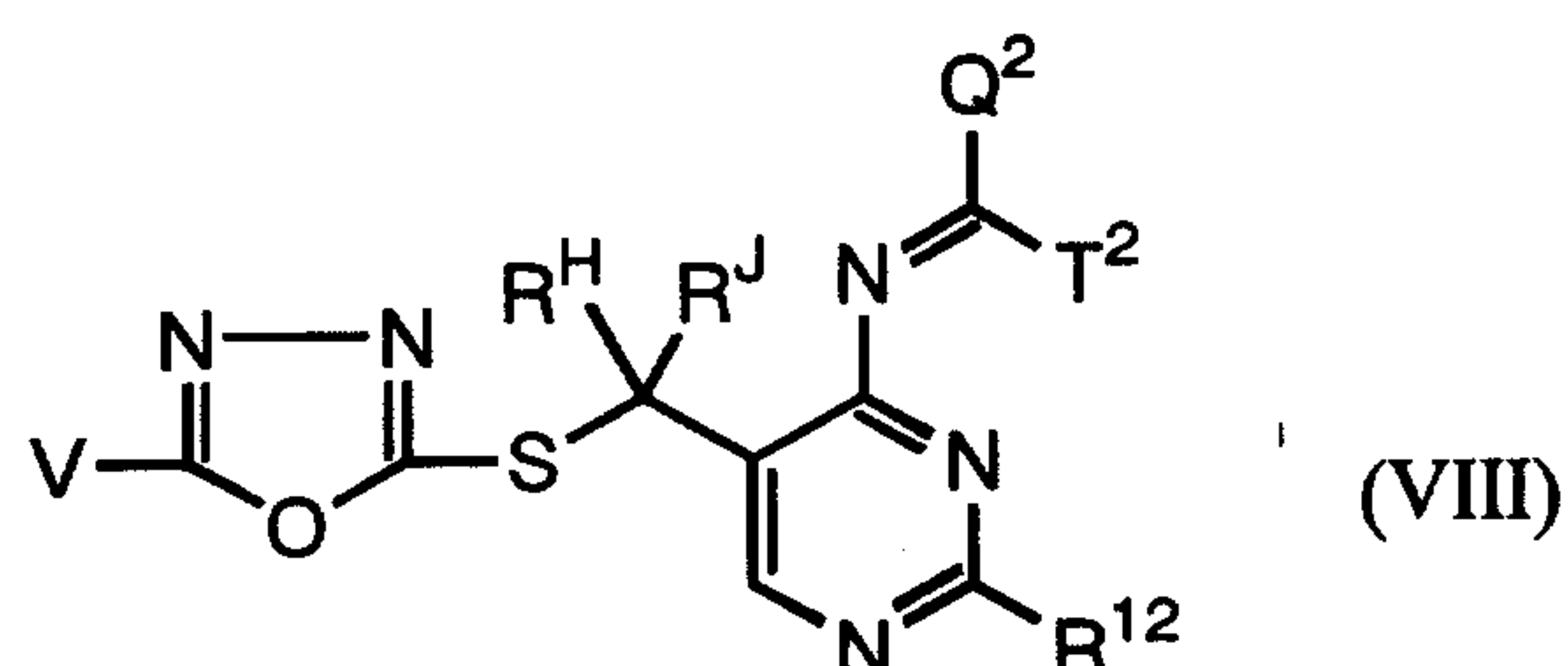


wherein R^5 , R^6 , R^F , R^G , and Z are as defined in claim 5;

Q^2 and T^2 are as defined in claim 6;

its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.

8. A compound of claim 5, represented by the formula (VIII):



wherein R^{12} is hydrogen or alkyl;

R^H and R^J are each independently hydrogen atom or alkyl;

the other symbols are as defined in claim 6:

- 5 its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate.
9. A compound, its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate of claim 1 or 5, wherein R^1 , R^2 , R^3 ,
10 and R^4 are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, or acyl.
10. A compound, its regioisomer, its optical active compound, its prodrug thereof, or their pharmaceutically acceptable salt, or their solvate of any one of claims 2 to 4 or claims
15 6 to 8, wherein R^8 , R^9 , R^{10} , and R^{11} are each independently hydrogen atom, optionally substituted alkyl, alkenyl, alkynyl, or acyl.
11. A pharmaceutical composition which contains as active ingredient a compound as described in any one of claims 1 to 10.
- 20 12. A pharmaceutical composition for use as an antitumor agent which contains as active ingredient a compound as described in any one of claims 1 to 10.
13. A pharmaceutical composition for use as a cytostatic agent which contains as active
25 ingredient a compound as described in any one of claims 1 to 10.

14. A pharmaceutical composition for use as an inhibitor against a signal derived from Ras oncogene products which contains as active ingredient a compound as described in any one of claims 1 to 10.

5 15. Use of a compound of any one of claims 1 to 10 for the preparation of a pharmaceutical composition for treating cancer.

16. A method of treating a mammal, including a human, to alleviate a pathological effect of cancer, which comprises administration to the mammal of a compound as described in
10 any one of claims 1 to 10.

