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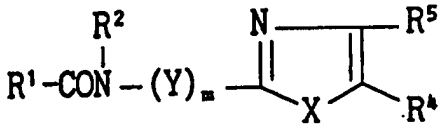
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(54) Title: NEW AMIDE COMPOUNDS

(57) Abstract

A compound of formula (I) wherein each symbol is as defined in the specification, and pharmaceutically acceptable salts thereof. The compound (I) of the present invention and pharmaceutically acceptable salts thereof possess a strong inhibitory activity on the production of nitric oxide (NO), and are useful for prevention and/or treatment of NO–mediated diseases such as adult respiratory distress syndrome, cardiovascular ischemia, myocarditis, heart failure, synovitis, shock, diabetes, diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, glomerulonephritis, peptic ulcer, inflammatory bowel disease, cerebral infarction, cerebral ischemia, cerebral hemorrhage, migraine, rheumatoid arthritis, gout, neuritis, postherpetic neuralgia, osteoarthritis, osteoporosis, systemic lupus erythematosus, rejection by organ transplantation, asthma, metastasis, Alzheimer's disease, arthritis, CNS disorders, dermatitis, hepatitis, liver cirrhosis, multiple sclerosis, pancreatitis, atherosclerosis, and the like in human being and animals.



(I)

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DESCRIPTION

NEW AMIDE COMPOUNDS

TECHNICAL FIELD

This invention relates to new amide compounds and pharmaceutically acceptable salts thereof which are useful as medicament.

BACKGROUND ART

Some peptide compounds have been known as described, for example, in EP 0 394 989 A2.

DISCLOSURE OF INVENTION

This invention relates to new amide compounds.

One object of this invention is to provide the new and useful amide compounds and pharmaceutically acceptable salts thereof which possess a strong inhibitory activity on the production of nitric oxide (NO).

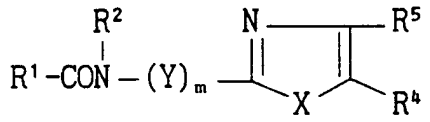
Another object of this invention is to provide a process for the preparation of the amide compounds and salts thereof.

A further object of this invention is to provide a pharmaceutical composition comprising said amide compound or a pharmaceutically acceptable salt thereof.

Still further object of this invention is to provide a use of said amide compounds or pharmaceutically acceptable salts thereof as a medicament for prophylactic and therapeutic treatment of NO-mediated diseases such as adult respiratory distress syndrome, cardiovascular ischemia, myocarditis, heart failure, synovitis, shock (e.g., septic shock, etc.), diabetes (e.g., insulin-dependent diabetes mellitus, etc.), diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, glomerulonephritis, peptic ulcer, inflammatory bowel disease (e.g., ulcerative colitis, chronic colitis, etc.), cerebral

infarction, cerebral ischemia, cerebral hemorrhage, migraine, rheumatoid arthritis, gout, neuritis, postherpetic neuralgia, osteoarthritis, osteoporosis, systemic lupus erythematosus, rejection by organ transplantation, asthma, metastasis, Alzheimer's disease, arthritis, CNS disorders, dermatitis, hepatitis, liver cirrhosis, multiple sclerosis, pancreatitis, atherosclerosis, and the like in human being and animals.

The object amide compounds of the present invention are novel and can be represented by the following general formula (I)



(I)

wherein

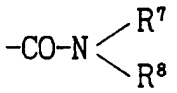
R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro, benzofuranyl, phenyl which may have one or two suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl, pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halogen, trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl,

morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy, quinolyl or 3,4-methylenedioxyphenyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula

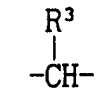


in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

$$-CH=CH-CH=CH-$$

Y is a group of the formula

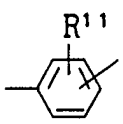


in which R^3 is hydrogen or a group of the formula

$$-(CH_2)_n-R^6$$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

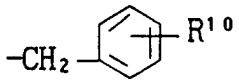
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula

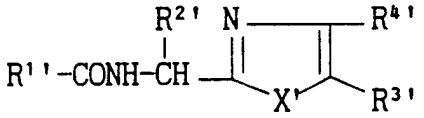


in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a pharmaceutically acceptable salt thereof,

provided that the compound shown below is excluded:

a compound of the formula

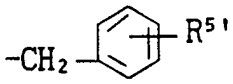


(A)

wherein

$R^{1'}$ is indolyl or benzofuranyl;

$R^{2'}$ is hydrogen, lower alkylthio(lower)alkyl or a group of the formula



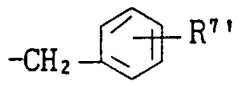
in which $R^{5'}$ is hydrogen, lower alkoxy or halogen;

$R^{3'}$ is hydrogen, quinolyl or phenyl which may have a suitable substituent selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen;

$R^{4'}$ is hydrogen or optionally esterified carboxy; and

X' is S or $NR^{6'}$

in which $R^{6'}$ is hydrogen, lower alkyl or a group of the formula



in which $R^{7'}$ is lower alkyl or lower alkoxy,
and a pharmaceutically acceptable salt thereof.

Suitable pharmaceutically acceptable salts of the object compound (I) are conventional non-toxic salts and include, for example, a salt with a base or an acid addition salt such as a salt with an inorganic base, for example, an alkali metal salt (e.g., sodium salt, potassium salt, etc.), an alkaline earth metal salt (e.g., calcium salt, magnesium salt, etc.), an ammonium salt; a salt with an organic base, for example, an organic amine salt (e.g., triethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt, etc.); an inorganic acid addition salt (e.g., hydrochloride, hydrobromide, sulfate, phosphate, etc.); an organic carboxylic or sulfonic acid addition salt (e.g., formate, acetate, trifluoroacetate, maleate, tartrate, citrate, fumarate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.); and a salt with a basic or acidic amino acid (e.g., arginine, aspartic acid, gultamic acid, etc.).

In the above and subsequent descriptions of the present specification, suitable examples and illustration of the various definitions which the present invention intends to include within the scope thereof are explained in detail as follows.

The term "lower" is used to intend a group having 1 to 6, preferably 1 to 4, carbon atom(s), unless otherwise provided.

Suitable "lower alkyl" and "lower alkyl moiety" in the terms "lower alkylthio", "lower alkylthio(lower)alkyl", "N-(lower)-alkylindolyl", "lower alkylamino", "di(lower)alkylamino",

"phenyl(lower)alkyl", "amino(lower)alkyl", "acylamino(lower)alkyl", "hydroxy(lower)alkyl" and "lower alkylpiperazinyl" include straight or branched one having 1 to 6 carbon atom(s), such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, tert-pentyl and hexyl, in which more preferred one is C_1-C_4 alkyl.

Suitable "lower alkoxy" and "lower alkoxy moiety" in the terms "lower alkoxy(lower)alkoxy" and "phenyl(lower)alkoxy" include, for example, methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, tert-butoxy, pentyloxy, tert-pentyloxy and hexyloxy, in which more preferred one is C_1-C_4 alkoxy.

Suitable "halogen" includes, for example, fluorine, bromine, chlorine and iodine.

"Optionally esterified carboxy" includes carboxy and esterified carboxy. Suitable examples of said ester include lower alkyl ester (e.g., methyl ester, ethyl ester, propyl ester, isopropyl ester, butyl ester, isobutyl ester, tert-butyl ester, pentyl ester, tert-pentyl ester, hexyl ester, etc.); lower alkenyl ester (e.g., vinyl ester, allyl ester, etc.); lower alkynyl ester (e.g., ethynyl ester, propynyl ester, etc.); lower alkoxy(lower)alkyl ester (e.g., methoxymethyl ester, ethoxymethyl ester, isopropoxymethyl ester, 1-methoxyethyl ester, 1-ethoxyethyl ester, etc.); mono(or di or tri)-aryl(lower)alkyl ester, for example, mono(or di or tri)phenyl(lower)-alkyl ester which may have one or more suitable substituent(s) [e.g., benzyl ester, 4-methoxybenzyl ester, 4-nitrobenzyl ester, phenethyl ester, trityl ester, benzhydryl ester, bis(methoxyphenyl)methyl ester, 3,4-dimethoxybenzyl ester, 4-hydroxy-3,5-di-tert-butylbenzyl ester, etc.]; and aryl ester which may have one or more suitable substituent(s) such as substituted or unsubstituted phenyl ester (e.g., phenyl ester, tolyl ester, tert-butylphenyl ester, xylyl ester, mesityl ester, cumenyl ester, 4-chlorophenyl ester, 4-methoxyphenyl ester, etc.).

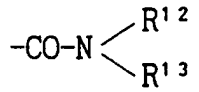
Suitable "trihalomethyl" includes, for example, trifluoromethyl,

trichloromethyl and tribromomethyl, in which preferred one is trifluoromethyl.

Suitable "amino protective group" includes, for example, acyl and conventional protective group such as mono(or di or tri)aryl(lower)-alkyl, for example, mono(or di or tri)phenyl(lower)alkyl (e.g., benzyl, trityl, etc.).

Suitable "acyl" and "acyl moiety" in the terms "acylamino", "diacylamino" and "acylamino(lower)alkyl" include, for example, carbamoyl which may be substituted by suitable substituent(s), aliphatic acyl group and acyl group containing an aromatic ring, which is referred to as aromatic acyl, or a heterocyclic ring, which is referred to as heterocyclic acyl.

Suitable examples of said acyl are illustrated as follows:
"carbamoyl which may be substituted by suitable substituent(s)" includes a group of the formula



wherein R^{12} and R^{13} are the same or different and each is hydrogen, lower alkyl, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, phenyl(lower)-alkyl, pyridyl, pyridyl(lower)alkyl or 3,4-methylenedioxyphenyl; aliphatic acyl such as lower alkanoyl which may be substituted by one to three halogen atoms (e.g., formyl, acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, 2,2-dimethylpropanoyl, hexanoyl, trichloroacetyl, trifluoroacetyl, etc.), lower alkoxycarbonyl (e.g., methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl, tert-pentyloxycarbonyl, etc.), lower alkylsulfonyl (e.g., methylsulfonyl, ethylsulfonyl, etc.), lower alkoxysulfonyl (e.g., methoxysulfonyl, ethoxysulfonyl, etc.), cyclo(lower)alkylcarbonyl (e.g., cyclopentylcarbonyl, cyclohexylcarbonyl, etc.), and the like; aromatic acyl such as aroyl (e.g., benzoyl, toluoyl, naphthoyl, etc.), aryl(lower)alkanoyl [e.g., phenyl(lower)alkanoyl (e.g., phenylacetyl,

phenylpropanoyl, phenylbutanoyl, etc.), naphthyl(lower)alkanoyl (e.g., naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, etc.), etc.], aryl(lower)alkoxycarbonyl [e.g., phenyl(lower)alkoxycarbonyl (e.g., benzyloxycarbonyl, etc.), etc.], aryloxycarbonyl (e.g., phenoxycarbonyl, naphthyloxycarbonyl, etc.), aryloxy(lower)alkanoyl (e.g., phenoxyacetyl, phenoxypropionyl, etc.), arylsulfonyl (e.g., phenylsulfonyl, p-tolylsufonyl, etc.), and the like;
heterocyclic acyl such as indolylcarbonyl (e.g., indolyl-2-ylcarbonyl, etc.), benzofuranylcarbonyl (e.g., benzofuran-2-ylcarbonyl), quinoxalinylcarbonyl, quinolylcarbonyl, pyrrolylcarbonyl, benzimidazolylcarbonyl, benzothienylcarbonyl, benzothiazolylcarbonyl, imidazolylcarbonyl, pyridylcarbonyl, morpholinylcarbonyl (e.g., morpholinocarbonyl) and the like.

"Optionally protected hydroxy" includes hydroxy and protected hydroxy. Suitable examples of "hydroxy protective group" in the term "protected hydroxy" include acyl (e.g., acetyl, trichloroacetyl, etc.), mono(or di or tri)phenyl(lower)alkyl which may have one or more suitable substituent(s) (e.g., benzyl, 4-methoxybenzyl, trityl, etc.), trisubstituted silyl [e.g., tri(lower)alkylsilyl (e.g., trimethylsilyl, tert-butyldimethylsilyl, etc.), etc.], tetrahydropyranyl and the like.

Suitable "protected carboxy" is carboxy group protected by conventional protective group such as lower alkoxycarbonyl [e.g., methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, sec-butoxycarbonyl, isobutoxycarbonyl, tert-butoxycarbonyl, pentyloxycarbonyl, neopentyloxycarbonyl, hexyloxycarbonyl, etc.], optionally substituted phenyl(lower)-alkoxycarbonyl for exemple, mono- or di- or triphenyl(lower)-alkoxycarbonyl which may be substituted by nitro [e.g., benzyloxycarbonyl, 4-nitrobenzyloxycarbonyl, benzhydryloxycarbonyl, trityloxycarbonyl, etc.] and the like.

Suitable "cyclo(lower)alkyl" includes cycloalkyl having 3 to 6

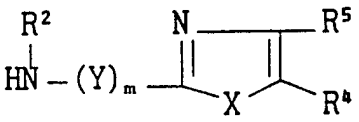
carbon atoms, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, in which more preferred ones are cyclopropyl and cyclobutyl.

The term "morpholinyl" includes 2-morpholinyl, 3-morpholinyl and 4-morpholinyl (i.e. morpholino).

The term "piperidyl" includes 1-piperidyl (i.e. piperidino), 2-piperidyl, 3-piperidyl and 4-piperidyl.

The object compound (I) of the present invention can be prepared by the following processes.

Process (1)



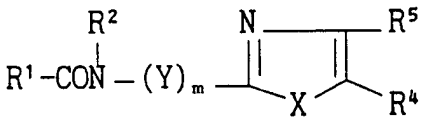
(II)

or its reactive derivative at the amino group, or a salt thereof

R^1-COOH

(III)

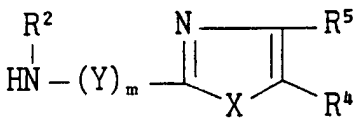
or its reactive derivative at the carboxy group, or a salt thereof



(I)

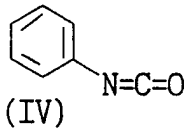
or a salt thereof

Process (2)

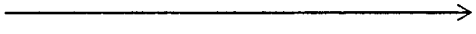


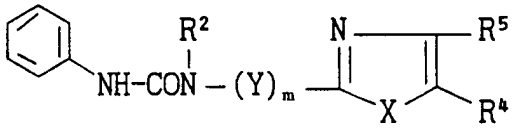
(II)

or a salt thereof



(IV)

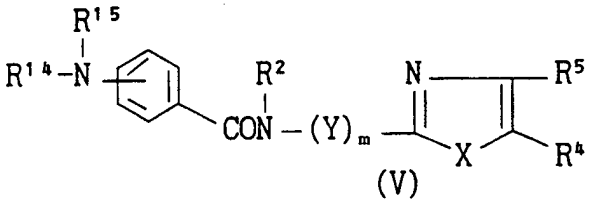




(I)-1

or a salt thereof

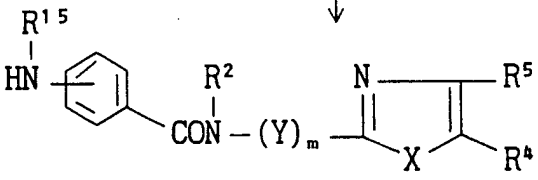
Process (3)



(V)

or a salt thereof

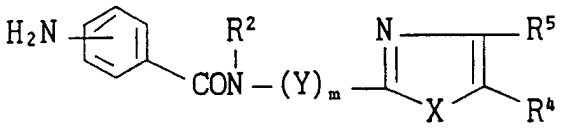
Elimination reaction of the amino protective group



(I)-2

or a salt thereof

Process (4)



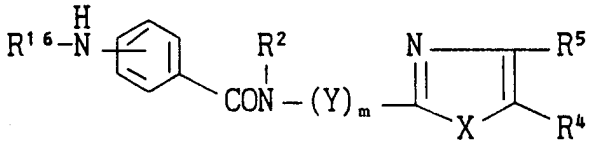
(I)-3

or its reactive derivative
at the amino group,
or a salt thereof

R^{16}-OH

(VI)

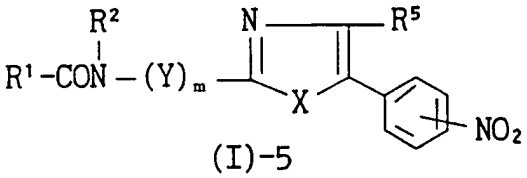
or its reactive derivative
at the carboxy group,
or a salt thereof



(I)-4

or a salt thereof

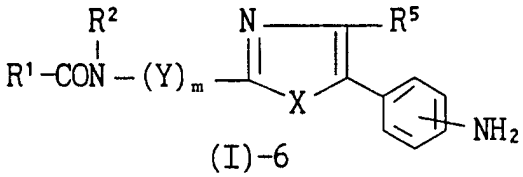
Process (5)



(I)-5

or a salt thereof

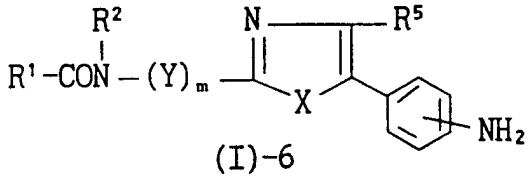
reduction



(I)-6

or a salt thereof

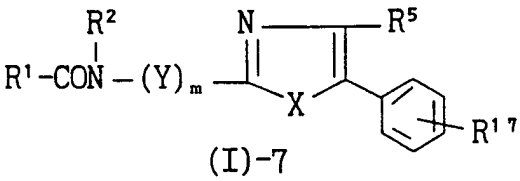
Process (6)



(I)-6

or a salt thereof

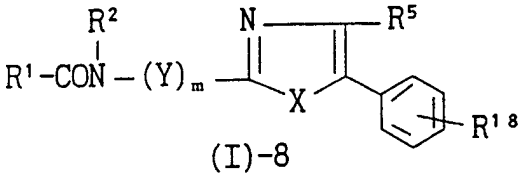
acylation



(I)-7

or a salt thereof

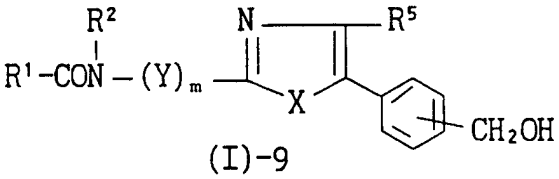
Process (7)



(I)-8

or a salt thereof

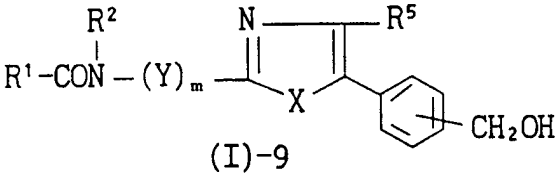
reduction



(I)-9

or a salt thereof

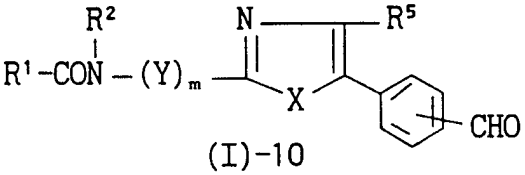
Process (8)



(I)-9

or a salt thereof

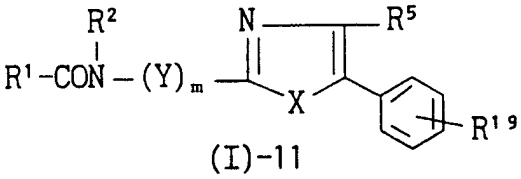
oxidation



(I)-10

or a salt thereof

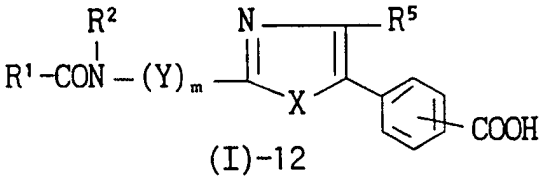
Process (9)



(I)-11

or a salt thereof

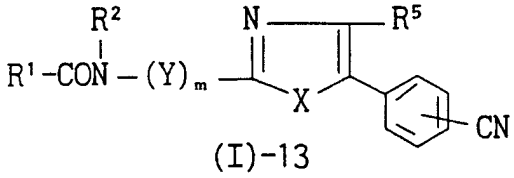
hydrolysis



(I)-12

or a salt thereof

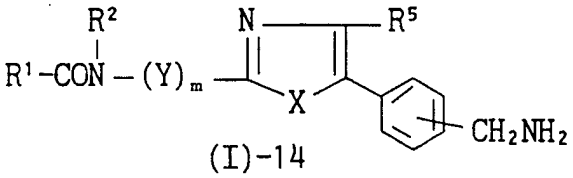
Process (10)



(I)-13

or a salt thereof

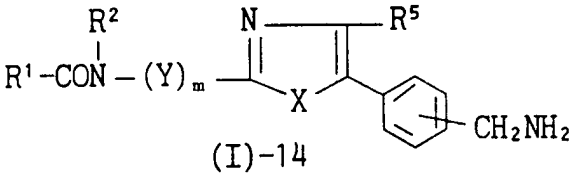
reduction



(I)-14

or a salt thereof

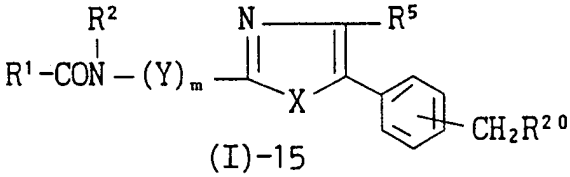
Process (11)



(I)-14

or a salt thereof

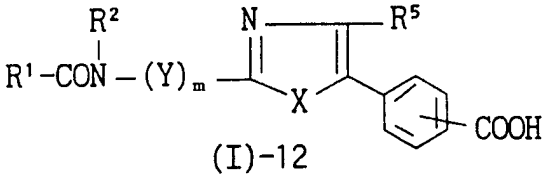
acylation



(I)-15

or a salt thereof

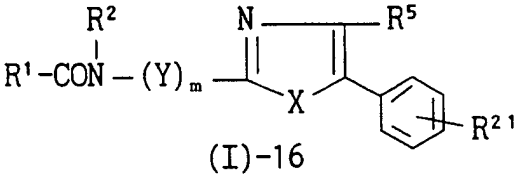
Process (12)



(I)-12

or a salt thereof

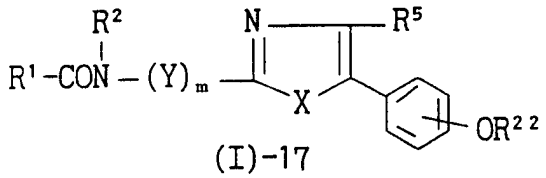
amidation



(I)-16

or a salt thereof

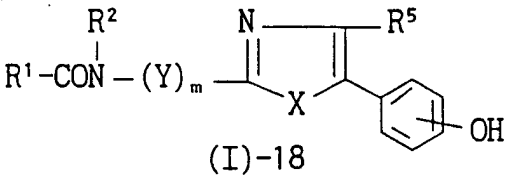
Process (13)



(I)-17

or a salt thereof

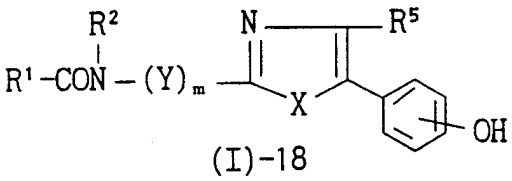
Elimination reaction of the hydroxy protective group



(I)-18

or a salt thereof

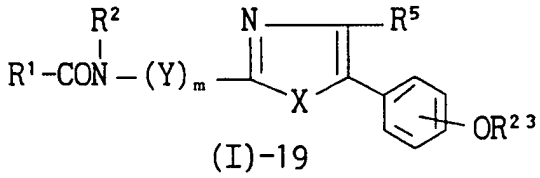
Process (14)



(I)-18

or a salt thereof

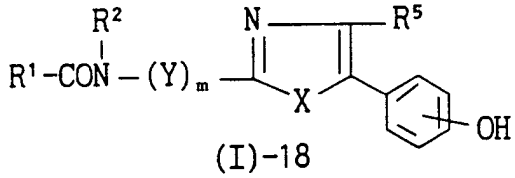
esterification



(I)-19

or a salt thereof

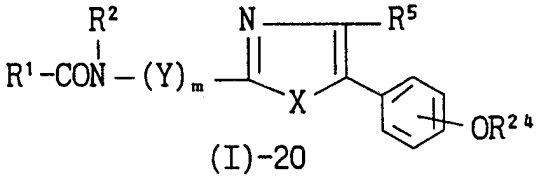
Process (15)



(I)-18

or a salt thereof

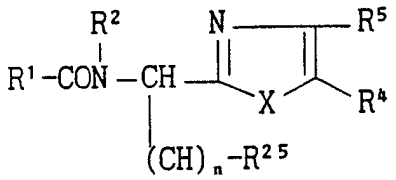
O-alkylation



(I)-20

or a salt thereof

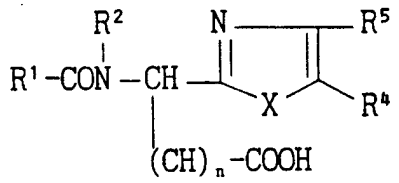
Process (16)



(I)-21

or a salt thereof

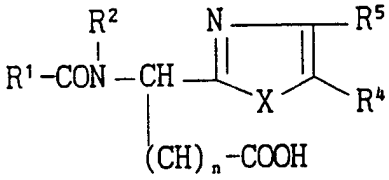
Elimination reaction of the carboxy protective group



(I)-22

or a salt thereof

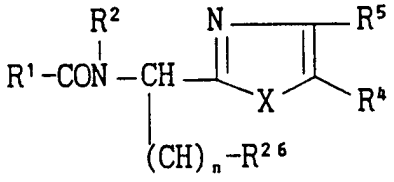
Process (17)



(I)-22

or a salt thereof

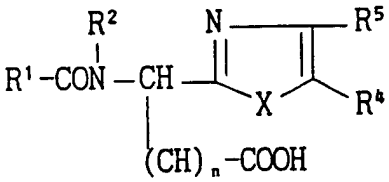
esterification



(I)-23

or a salt thereof

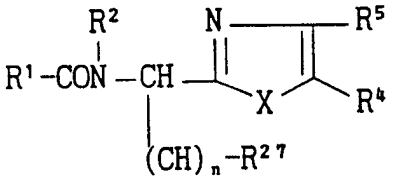
Process (18)



(I)-22

or a salt thereof

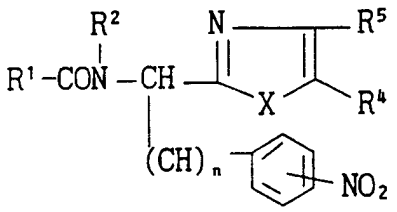
amidation



(I)-24

or a salt thereof

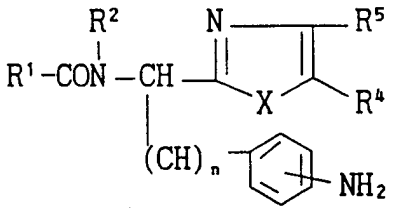
Process (19)



(I)-25

or a salt thereof

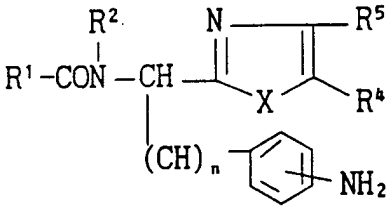
reduction



(I)-26

or a salt thereof

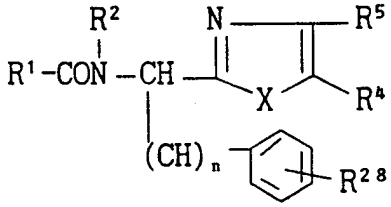
Process (20)



(I)-26

or a salt thereof

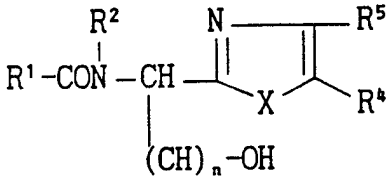
acylation



(I)-27

or a salt thereof

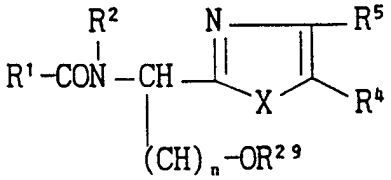
Process (21)



(I)-28

or a salt thereof

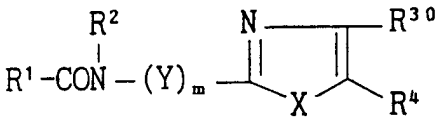
esterification



(I)-29

or a salt thereof

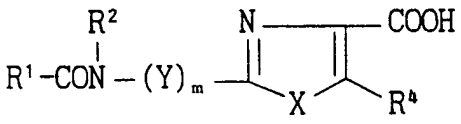
Process (22)



(I)-30

or a salt thereof

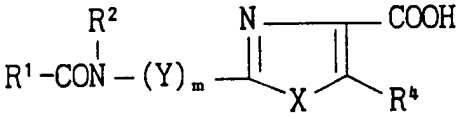
hydrolysis



(I)-31

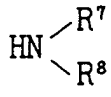
or a salt thereof

Process (23)



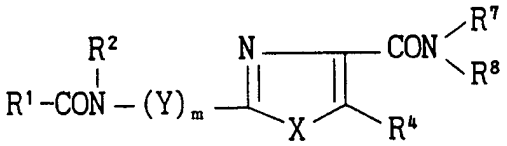
(I)-31

or its reactive derivative at the carboxy group, or a salt thereof



(VII)

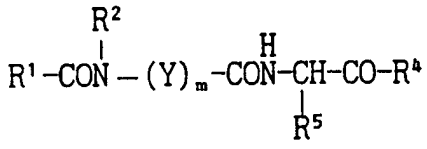
or its reactive derivative at the amino group, or a salt thereof



(I)-32

or a salt thereof

Process (24)

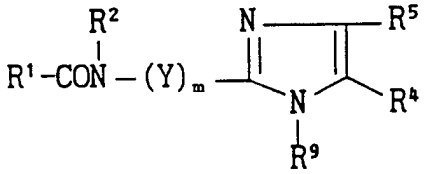


(VIII)

R^9-NH_2

(IX)

acid



(I)-33

wherein R^1, R^2, R^4, R^5, R^7, R^8, R^9, X, Y, m and n are each as

defined above,

R^{14} is amino protective group,

R^{15} is hydrogen or lower alkyl,

R^{16} is acyl,

R^{17} is acylamino or diacylamino,

R^{18} is carboxy or lower alkoxycarbonyl,

R^{19} is esterified carboxy,

R^{20} is acylamino or diacylamino,

R^{21} is carbamoyl which may be substituted by suitable substituent(s),

R^{22} is hydroxy protective group,

R^{23} is acyl,

R^{24} is lower alkyl,

R^{25} is protected carboxy,

R^{26} is esterified carboxy,

R^{27} is carbamoyl which may be substituted by suitable substituent(s),

R^{28} is acylamino or diacylamino,

R^{29} is acyl, and

R^{30} is esterified carboxy.

The starting compounds can be prepared by the method of Preparation mentioned below or by a process known in the art for preparing their structually analogous compounds.

The processes for preparing the object compound are explained in detail in the following.

Process (1)

The compound (I) or a salt thereof can be prepared by reacting the compound (II) or its reactive derivative at the amino group, or a salt thereof with the compound (III) or its reactive derivative at the

carboxy group, or a salt thereof.

Suitable reactive derivative of the compound (II) includes Schiff's base type imino or its tautomeric enamine type isomer formed by the reaction of the compound (II) with a carbonyl compound such as aldehyde, ketone or the like; a silyl derivative formed by the reaction of the compound (II) with a silyl compound such as N,O-bis(trimethylsilyl)acetamide, N-trimethylsilylacetamide or the like; a derivative formed by the reaction of the compound (II) with phosphorus trichloride or phosgene.

Suitable reactive derivative of the compound (III) includes an acid halide, an acid anhydride and an activated ester. The suitable example may be an acid chloride; an acid azide; a mixed acid anhydride with an acid such as substituted phosphoric acid (e.g., dialkylphosphoric acid, phenylphosphoric acid, diphenylphosphoric acid, dibenzylphosphoric acid, halogenated phosphoric acid, etc.), dialkylphosphorous acid, sulfurous acid, thiosulfuric acid, alkanesulfonic acid (e.g., methanesulfonic acid, ethanesulfonic acid, etc.), sulfuric acid, alkylcarbonic acid, aliphatic carboxylic acid (e.g., pivalic acid, pentanoic acid, isopentanoic acid, 2-ethylbutyric acid, trichloroacetic acid, etc.); aromatic carboxylic acid (e.g., benzoic acid, etc.); a symmetrical acid anhydride; an activated amide with imidazole, 4-substituted imidazole, dimethylpyrazole, triazole or tetrazole; an activated ester (e.g., cyanomethyl ester, methoxymethyl ester, dimethyliminomethyl [$(CH_3)_2N^+=CH-$] ester, vinyl ester, propargyl ester, p-nitrophenyl ester, 2,4-dinitrophenyl ester, trichlorophenyl ester, pentachlorophenyl ester, mesylphenyl ester, phenylazophenyl ester, phenyl thioester, p-nitrophenyl thioester, p-cresyl thioester, carboxymethyl thioester, pyranyl ester, pyridyl ester, piperidyl ester, 8-quinolyl thioester, etc.); or an ester with an N-hydroxy compound (e.g., N,N-dimethylhydroxylamine, 1-hydroxy-2-(1H)-pyridone, N-hydroxysuccinimide, N-hydroxybenzotriazole, N-hydroxyphthalimide, 1-hydroxy-6-chloro-1H-benzotriazole, etc.).

These reactive derivatives can optionally be selected from them according to the kind of the compound (III) to be used.

The reaction is usually carried out in a conventional solvent such as water, acetone, dioxane, acetonitrile, chloroform, methylene chloride, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvents which do not adversely affect the reaction, or the mixture thereof.

When the compound (III) is used in free acid form or its salt form in the reaction, the reaction is preferably carried out in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide; N-cyclohexyl-N'-morpholinoethylcarbodiimide; N-cyclohexyl-N'-(4-diethylaminocyclohexyl)carbodiimide; N,N'-diisopropylcarbodiimide; N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide; N,N-carbonyl-bis-(2-methylimidazole); pentamethylene-ketene-N-cyclohexylimine; diphenylketene-N-cyclohexylimine; ethoxyacetylene; 1-alkoxy-1-chloroethylene; trialkyl phosphite; isopropyl polyphosphate; phosphorus oxychloride (phosphoryl chloride); phosphorus trichloride; thionyl chloride; oxalyl chloride; triphenylphosphine; 2-ethyl-7-hydroxybenzisoxazolium salt; 2-ethyl-5-(m-sulfophenyl)isoxazolium hydroxide intramolecular salt; 1-(p-chlorobenzenesulfonyloxy)-6-chloro-1H-benzotriazole; so-called Vilsmeier reagent prepared by the reaction of N,N-dimethylformamide with thionyl chloride, phosgene, phosphorus oxychloride, etc.; or the like.

The reaction may also be carried out in the presence of an organic or inorganic base such as an alkali metal bicarbonate, tri(lower)alkylamine, pyridine, N-(lower)alkylmorpholine, N,N-di(lower)alkylbenzylamine, or the like.

The reaction temperature is not critical, and the reaction is usually carried out under cooling to heating.

Process (2)

The compound (I)-1 or a salt thereof can be prepared by reacting the compound (II) or a salt thereof with the compound (IV).

The reaction can be carried out in the same manner as in or a manner similar to Example 27.

Process (3)

The compound (I)-2 or a salt thereof can be prepared by subjecting the compound (V) or a salt thereof to elimination reaction of the amino protective group.

Suitable method of this elimination reaction includes conventional one such as hydrolysis, reduction and the like.

(i) For hydrolysis :

The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid.

Suitable base includes an inorganic base and an organic base such as an alkali metal [e.g., sodium, potassium, etc.], an alkaline earth metal [e.g., magnesium, calcium, etc.], the hydroxide or carbonate or hydrogencarbonate thereof, trialkylamine [e.g., trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]non-5-one, or the like.

Suitable acid includes an organic acid [e.g., formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], and an inorganic acid [e.g., hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, hydrogen bromide, etc.].

The elimination using Lewis acid such as trihaloacetic acid [e.g., trichloroacetic acid, trifluoroacetic acid, etc.], or the like is preferably carried out in the presence of cation trapping agents [e.g., anisole, phenol, etc.]. This reaction is usually carried out without solvent.

The reaction may be carried out in a conventional solvent such as water, alcohol (e.g., methanol, ethanol, isopropyl alcohol, etc.), tetrahydrofuran, dioxane, toluene, methylene chloride, ethylene

dichloride, chloroform, N,N-dimethylformamide, N,N-dimethylacetamide or any other organic solvents which do not adversely affect the reaction, or a mixture thereof.

The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

(ii) For reduction :

Reduction is carried out in a conventional manner, including chemical reduction and catalytic reduction.

Suitable reducing reagent to be used in chemical reduction are hydrides (e.g., hydrogen iodide, hydrogen sulfide, lithium aluminum hydride, sodium borohydride, sodium cyanoborohydride, etc.), or a combination of a metal (e.g., tin, zinc, iron, etc.) or metallic compound (e.g., chromium chloride, chromium acetate, etc.) and an organic acid or inorganic acid (e.g., formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.).

Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalysts (e.g., platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.), palladium catalysts (e.g., spongy palladium, palladium black, palladium oxide, palladium on carbon, palladium hydroxide on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.), nickel catalysts (e.g., reduced nickel, nickel oxide, Raney nickel, etc.), cobalt catalysts (e.g., reduced cobalt, Raney cobalt, etc.), iron catalysts (e.g., reduced iron, Raney iron, Ullman iron, etc.), and the like.

The reduction is usually carried out in a conventional solvent such as water, alcohol (e.g., methanol, ethanol, isopropyl alcohol, etc.), tetrahydrofuran, dioxane, toluene, methylene chloride, ethylene dichloride, chloroform, N,N-dimethylformamide, N,N-dimethylacetamide or any other organic solvents which do not adversely affect the reaction, or a mixture thereof.

Additionally, in case that the above-mentioned acids to be used in chemical reduction are in a liquid state, they can also be used as a solvent.

The reaction temperature of this reduction is not critical and the reaction is usually carried out under cooling to warming.

Process (4)

The compound (I)-4 or a salt thereof can be prepared by reacting the compound (I)-3 or its reactive derivative at the amino group, or a salt thereof with the compound (VI) or its reactive derivative at the carboxy group, or a salt thereof.

This reaction can be carried out in a similar manner to the reaction in the aforementioned Process (1), and therefore the reagents to be used and the reaction conditions (e.g., solvent, reaction temperature, etc.) can be referred to those of the Process (1).

Process (5)

The compound (I)-6 or a salt thereof can be prepared by subjecting the compound (I)-5 or a salt thereof to reduction.

The reduction can be carried out in the same manner as in or a manner similar to Example 60.

Process (6)

The compound (I)-7 or a salt thereof can be prepared by subjecting the compound (I)-6 or a salt thereof to acylation.

The acylation can be carried out in the same manner as in or a manner similar to Example 61.

Process (7)

The compound (I)-9 or a salt thereof can be prepared by subjecting the compound (I)-8 or a salt thereof to reduction.

The reduction can be carried out in the same manner as in or a manner similar to Example 111.

Process (8)

The compound (I)-10 or a salt thereof can be prepared by subjecting the compound (I)-9 or a salt thereof to oxidation.

The oxidation can be carried out in the same manner as in or a manner similar to Example 112.

Process (9)

The compound (I)-12 or a salt thereof can be prepared by subjecting the compound (I)-11 or a salt thereof to hydrolysis.

The hydrolysis can be carried out in the same manner as in or a manner similar to Example 113.

Process (10)

The compound (I)-14 or a salt thereof can be prepared by subjecting the compound (I)-13 or a salt thereof to reduction.

The reduction can be carried out in the same manner as in or a manner similar to Example 123.

Process (11)

The compound (I)-15 or a salt thereof can be prepared by subjecting the compound (I)-14 or a salt thereof to acylation.

The acylation can be carried out in the same manner as in or a manner similar to Example 124.

Process (12)

The compound (I)-16 or a salt thereof can be prepared by subjecting the compound (I)-12 or a salt thereof to amidation.

The amidation can be carried out in the same manner as in or a manner similar to Example 127.

Process (13)

The compound (I)-18 or a salt thereof can be prepared by subjecting the compound (I)-17 or a salt thereof to elimination reaction of the hydroxy protective group.

This reaction can be carried out in a similar manner to the reaction in the aforementioned Process (3), and therefore the reagents to be used and the reaction conditions (e.g., solvent, reaction temperature, etc.) can be referred to those of the Process (3).

Process (14)

The compound (I)-19 or a salt thereof can be prepared by subjecting the compound (I)-18 or a salt thereof to esterification.

The esterification can be carried out in the same manner as in or a manner similar to Example 133.

Process (15)

The compound (I)-20 or a salt thereof can be prepared by subjecting the compound (I)-18 or a salt thereof to O-alkylation.

The O-alkylation can be carried out in the same manner as in or a manner similar to Example 135.

Process (16)

The compound (I)-22 or a salt thereof can be prepared by subjecting the compound (I)-21 or a salt thereof to elimination reaction of the carboxy protective group.

This reaction can be carried out in a similar manner to the reaction in the aforementioned Process (3), and therefore the reagents to be used and the reaction conditions (e.g., solvent, reaction temperature, etc.) can be referred to those of the Process (3).

Process (17)

The compound (I)-23 or a salt thereof can be prepared by subjecting the compound (I)-22 or a salt thereof to esterification.

The esterification can be carried out in the same manner as in or a manner similar to Example 74.

Process (18)

The compound (I)-24 or a salt thereof can be prepared by subjecting the compound (I)-22 or a salt thereof to amidation.

The amidation can be carried out in the same manner as in or a manner similar to Example 95.

Process (19)

The compound (I)-26 or a salt thereof can be prepared by subjecting the compound (I)-25 or a salt thereof to reduction.

The reduction can be carried out in the same manner as in or a manner similar to Example 119.

Process (20)

The compound (I)-27 or a salt thereof can be prepared by subjecting the compound (I)-26 or a salt thereof to acylation.

The acylation can be carried out in the same manner as in or a manner similar to Example 120.

Process (21)

The compound (I)-29 or a salt thereof can be prepared by subjecting the compound (I)-28 or a salt thereof to esterification.

The esterification can be carried out in the same manner as in or a manner similar to Example 138.

Process (22)

The compound (I)-31 or a salt thereof can be prepared by subjecting the compound (I)-30 or a salt thereof to hydrolysis.

The hydrolysis can be carried out in the same manner as in or a manner similar to Example 168.

Process (23)

The compound (I)-32 or a salt thereof can be prepared by reacting the compound (I)-31 or its reactive derivative at the carboxy group, or a salt thereof with the compound (VII) or its reactive derivative at the amino group, or a salt thereof.

This reaction can be carried out in a similar manner to the reaction in the aforementioned Process (1), and therefore the reagents to be used and the reaction conditions (e.g., solvent, reaction temperature, etc.) can be referred to those of the Process (1).

Process (24)

The compound (I)-33 can be prepared by reacting the compound (VIII) with the compound (IX) in the presence of an acid.

This reaction can be carried out in the same manner as in or a manner similar to Example 178.

Suitable salts of the starting compounds and their reactive derivatives in Process (1) can be referred to the ones as exemplified for the compound (I).

The compounds obtained by the above process can be isolated and purified by a conventional method such as pulverization, recrystallization, column chromatography, reprecipitation, or the like.

It is to be noted that the compound (I) and the other compounds may include one or more stereoisomer(s) such as optical isomer(s) and geometrical isomer(s) due to asymmetric carbon atom(s) and double

bond(s), and all of such isomers and mixtures thereof are included within the scope of this invention.

The object compounds (I) and pharmaceutically acceptable salts thereof include solvates [e.g., enclosure compounds (e.g., hydrate, etc.)].

The object compounds (I) and pharmaceutically acceptable salts thereof possess a strong inhibitory activity on the production of nitric oxide (NO).

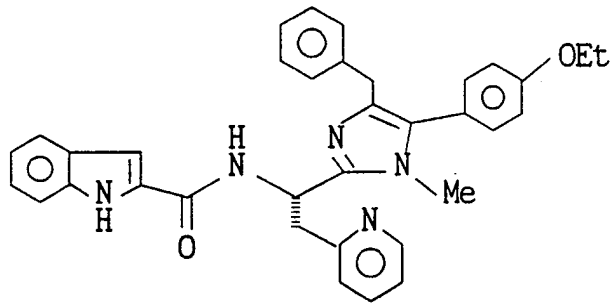
Accordingly, the object compounds (I) and pharmaceutically acceptable salts thereof are expected to possess a nitric oxide synthase (NOS)-inhibitory activity or a NOS-production inhibitory activity.

Accordingly, they are useful for prevention and/or treatment of NO-mediated diseases such as adult respiratory distress syndrome, cardiovascular ischemia, myocarditis, heart failure, synovitis, shock (e.g., septic shock, etc.), diabetes (e.g., insulin-dependent diabetes mellitus, etc.), diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, glomerulonephritis, peptic ulcer, inflammatory bowel disease (e.g., ulcerative colitis, chronic colitis, etc.), cerebral infarction, cerebral ischemia, cerebral hemorrhage, migraine, rheumatoid arthritis, gout, neuritis, postherpetic neuralgia, osteoarthritis, osteoporosis, systemic lupus erythematosus, rejection by organ transplantation, asthma, metastasis, Alzheimer's disease, arthritis, CNS disorders, dermatitis, hepatitis, liver cirrhosis, multiple sclerosis, pancreatitis, atherosclerosis, and the like.

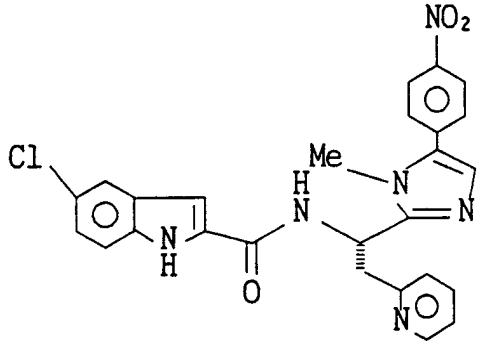
In order to illustrate the usefulness of the object compound (I), the pharmacological test result of the representative compound of the compound (I) is shown in the following.

Test Compounds :

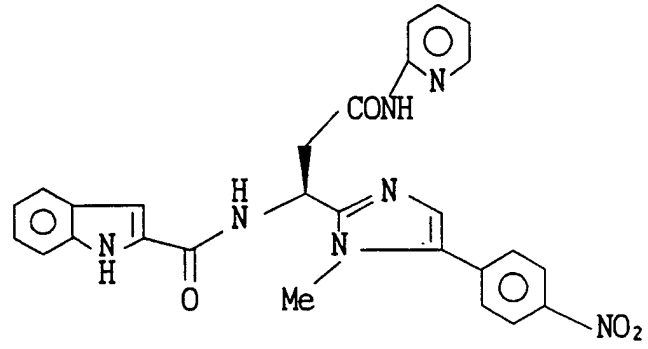
(a)



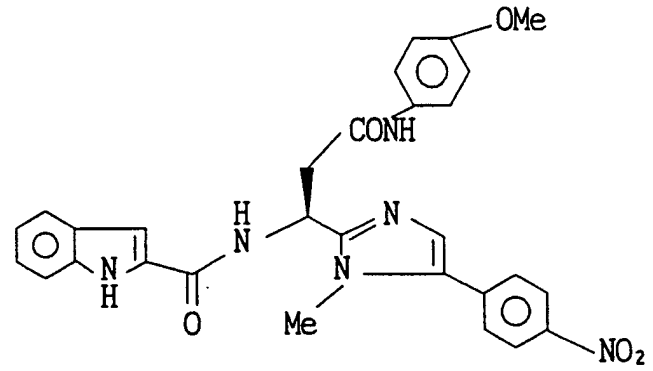
(b)

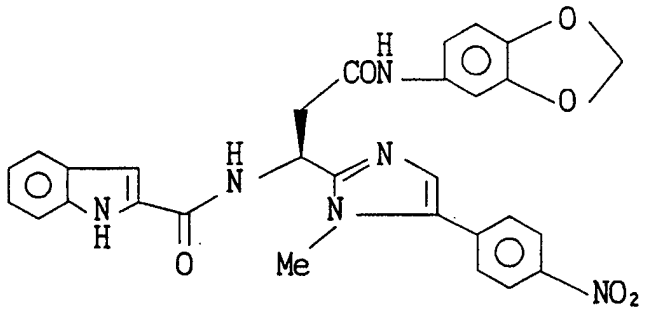


(c)



(d)



(e) 

Test : Assay for inhibitory activity on the production of nitric oxide

The murine macrophage cell line RAW264.7 (American Type Culture Collection, No. TIB71) was used in this study. RAW264.7 cells were grown on F75 plastic culture flasks at 37°C, 5% in Dulbecco's modified Eagle's medium (DMEM) supplemented with L-glutamine, penicillin, streptomycin and 10% heat-inactivated fetal bovine serum. They were removed from culture flasks by rubber cell scraper and were centrifuged and resuspended in DMEM without phenol red. They were plated in 96-well microtiter plates (10^5 cells per well) and allowed to adhere over 2 hours. The test samples were added and the cells were preincubated for 1 hour. Thereafter the cells were activated with both of lipopolysaccharide (LPS) (1 μg/ml) and interferon γ (INF γ) (3 u/ml) for 18-24 hours. An equal volume of Griess reagent (1% sulfanilamide/0.1% N-naphthylethylenediamine dihydrochloride/2.5% H_3PO_4) was added and the cells were incubated at room temperature for 10 minutes. The absorbance was read at 570 nm using microplate reader and NO_2^- was measured using $NaNO_2$ as a standard.

Test result :

Test compound (10^{-5}M)	Inhibition (%)
(a)	100
(b)	100
(c)	100
(d)	100
(e)	100

For therapeutic administration, the object compound (I) of the present invention and pharmaceutically acceptable salts thereof are used in the form of a conventional pharmaceutical preparation in admixture with a conventional pharmaceutically acceptable carrier such as an organic or inorganic solid or liquid excipient which is suitable for oral, parenteral or external administration. The pharmaceutical preparation may be compounded in a solid form such as granule, capsule, tablet, dragee, suppository or ointment, or in a liquid form such as solution, suspension or emulsion for injection, intravenous drip, ingestion, eye drop, etc. If needed, there may be included in the above preparation auxiliary substance such as stabilizing agent, wetting or emulsifying agent, buffer or any other commonly used additives.

The effective ingredient may usually be administered in a unit dose of 0.001 mg/kg to 500 mg/kg, preferably 0.01 mg/kg to 10 mg/kg, 1 to 4 times a day. However, the above dosage may be increased or decreased according to age, body weight and conditions of the patient or administering method.

The preferred embodiments of the amide compounds of the present invention represented by the general formula (I) are as follows.

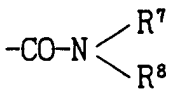
R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro, benzofuranyl, phenyl which may have one or two

suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl, pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is phenyl or pyridyl, each of which has suitable substituent(s) selected from the group consisting of trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl, morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy, or 3,4-methylenedioxyphenyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

$$-CH=CH-CH=CH-$$

Y is a group of the formula



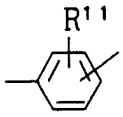
in which R^3 is hydrogen or a group of the formula

$$-(CH_2)_n-R^6$$

in which R^6 is optionally protected hydroxy, acyl, carboxy,

acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and
n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

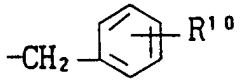
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy; or a pharmaceutically acceptable salt thereof.

Another preferred embodiments of the amide compounds of the present invention represented by the general formula (I) are as follows.

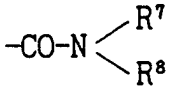
R^1 is indolyl which has a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy,

and nitro, phenyl which may have one or two suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl, pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen or quinolyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

$$-CH=CH-CH=CH-$$

Y is a group of the formula



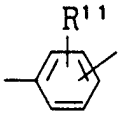
in which R^3 is hydrogen or a group of the formula

$$-(CH_2)_n-R^6$$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino,

diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and
n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

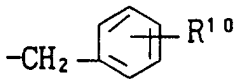
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a pharmaceutically acceptable salt thereof.

Another preferred embodiments of the amide compounds of the present invention represented by the general formula (I) are as follows.

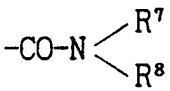
R^1 is indolyl or benzofuranyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen or quinolyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl,

optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

-CH=CH-CH=CH-

Y is a group of the formula

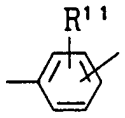


in which R^3 is a group of the formula

$-(CH_2)_n-R^6$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, phenyl which has a suitable substituent selected from the group consisting of amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

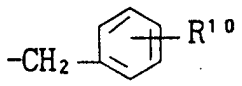
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a pharmaceutically acceptable salt thereof.

The most preferred embodiments of the amide compounds of the present invention represented by the general formula (I) are as follows.

R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro or benzofuranyl;

R^2 is hydrogen;

R^4 is phenyl which may have suitable substituent(s) selected from the group consisting of trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl, morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy;

R^5 is hydrogen;

Y is a group of the formula



in which R^3 is hydrogen or a group of the formula

$-(CH_2)_n-R^6$

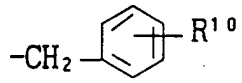
in which R^6 is pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, and

n is an integer of 0 to 3;

m is 0 or 1; and

X is NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a pharmaceutically acceptable salt thereof.

The following Preparations and Examples are given for the purpose of illustrating the present invention in detail.

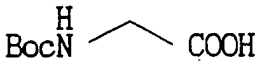
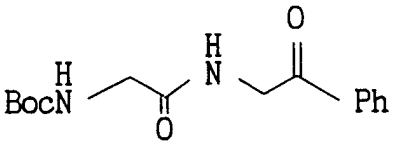
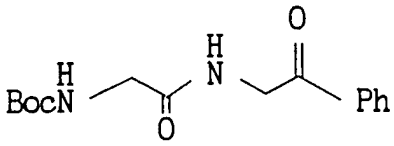
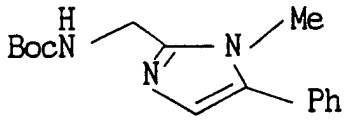
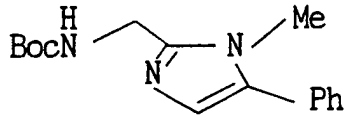
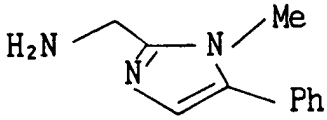
In the following Examples and Preparations, there are employed the other abbreviations in addition to the abbreviations adopted by the IUPAC-IUB (Commission on Biological Nomenclature).

The abbreviations used are as follows.

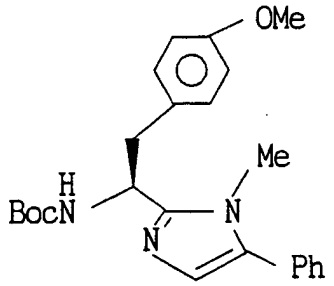
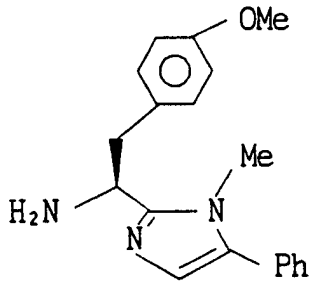
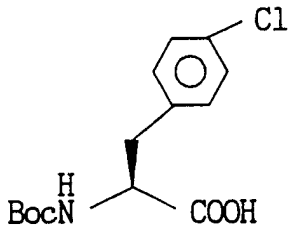
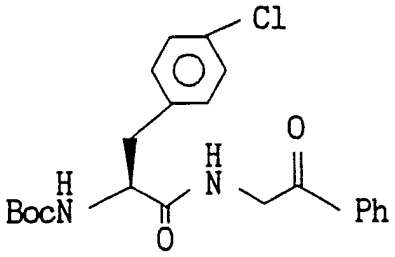
Boc : tert-butoxycarbonyl
Me : methyl
Et : ethyl
Pr : propyl
i-Pr : isopropyl
Bu : butyl
Ph : phenyl
Ts : p-toluenesulfonyl
Ac : acetyl
Bn : benzyl
Cbz : benzlyoxycarbonyl
Tf : trifluoromethanesulfonyl

The starting compounds used and the object compounds obtained in the following Preparations and Examples are given in the Tables as below, in which the formulae of the starting compounds are in the upper and the formulae of the object compounds are in the lower, respectively.

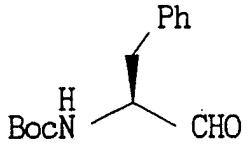
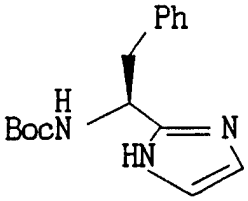
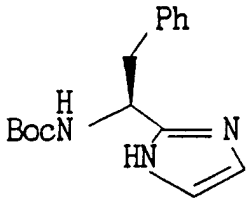
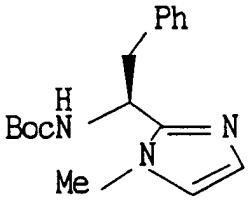
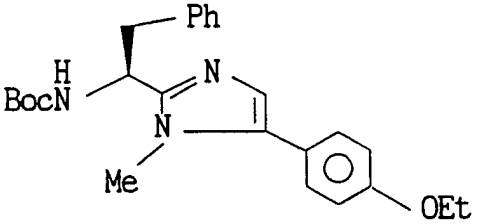
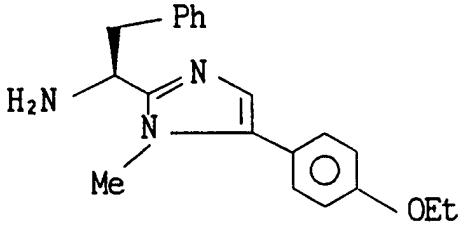
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Preparation No.	Formula
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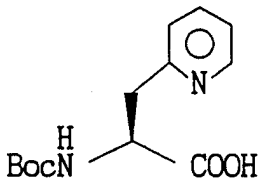
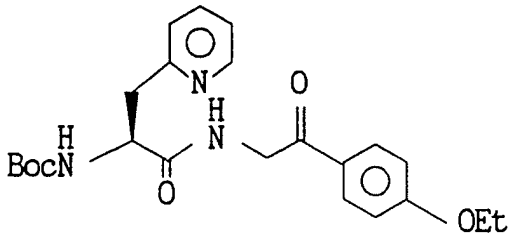
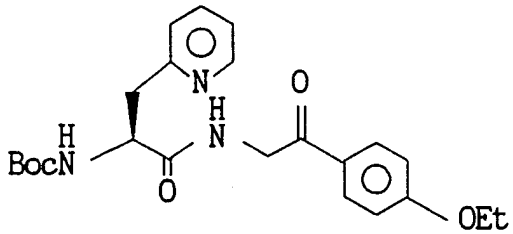
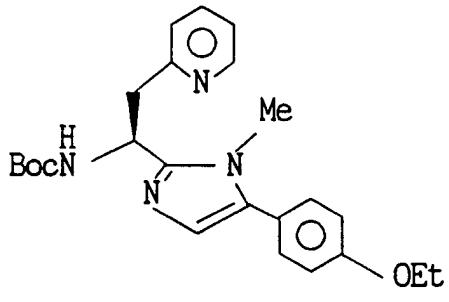
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Preparation No.	Formula
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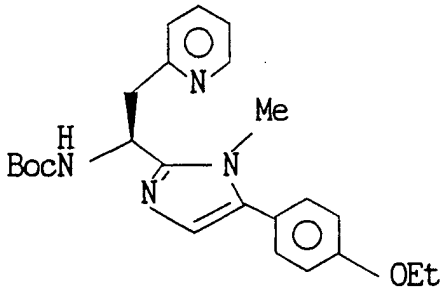
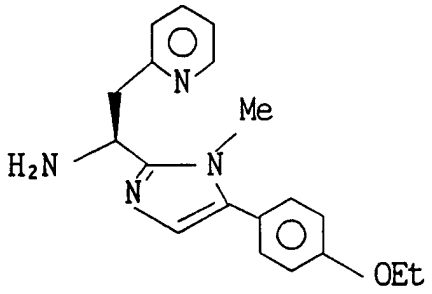
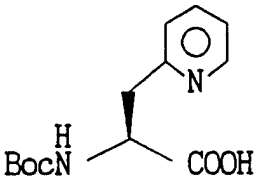
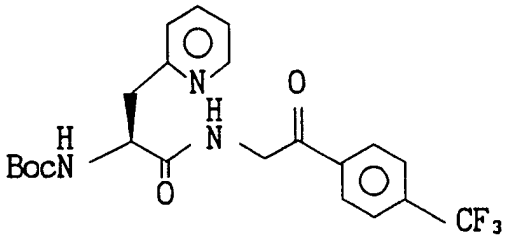
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Preparation No.	Formula
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8	
	

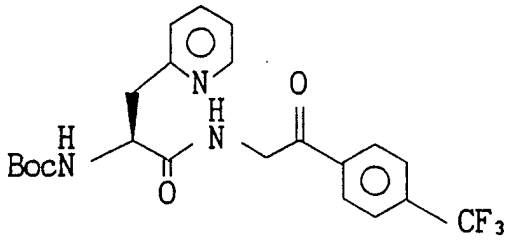
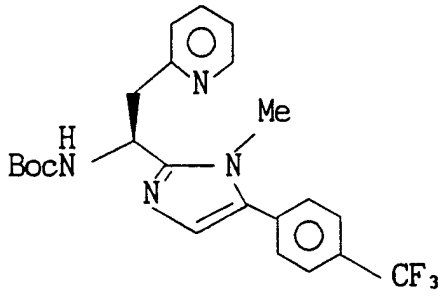
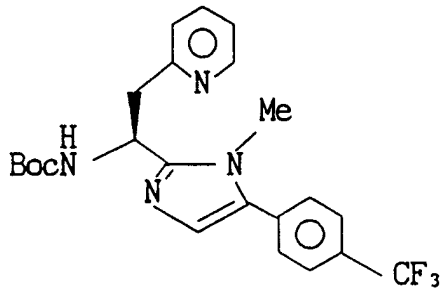
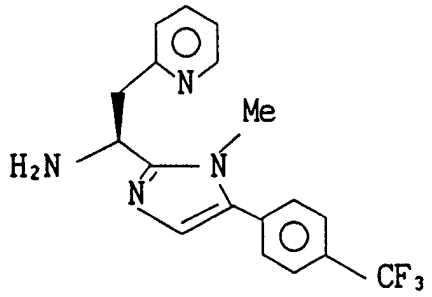
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Preparation No.	Formula
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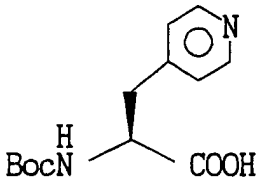
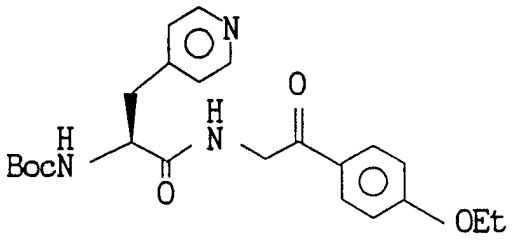
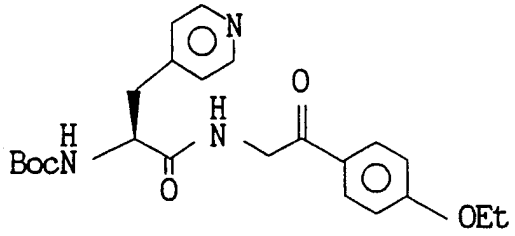
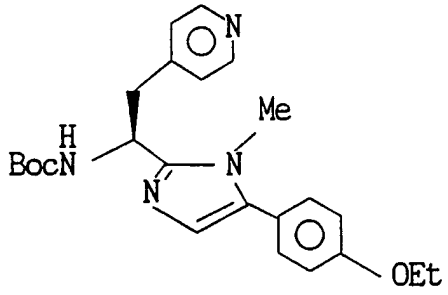
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Preparation No.	Formula
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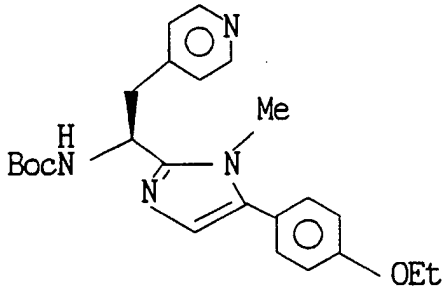
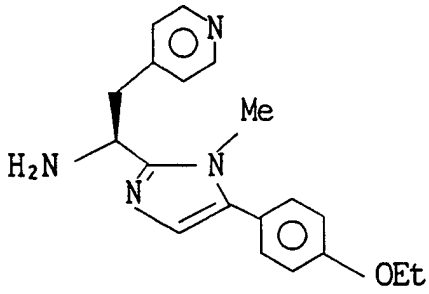
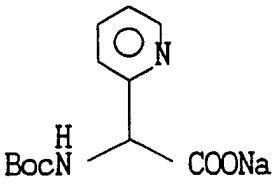
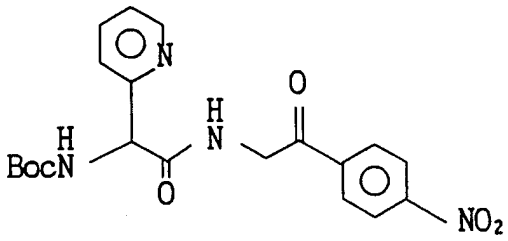
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Preparation No.	Formula
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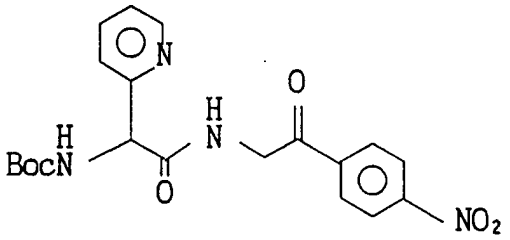
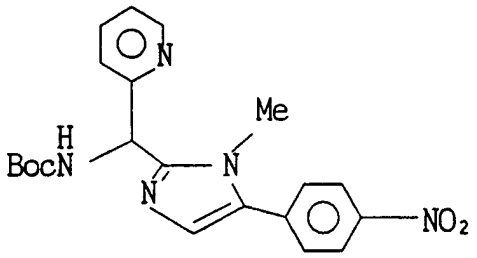
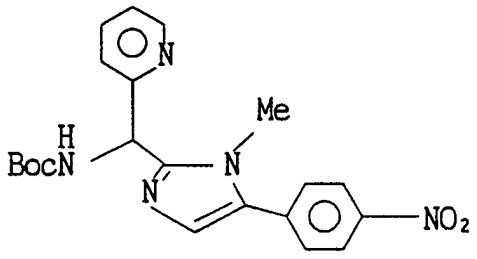
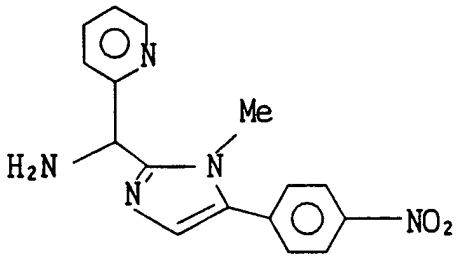
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Preparation No.	Formula
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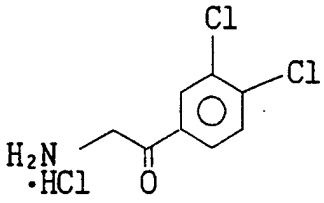
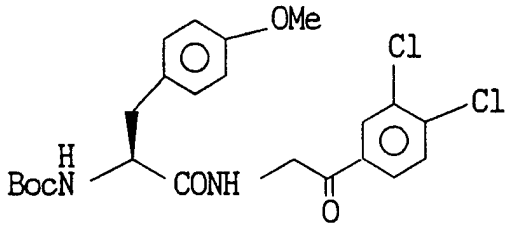
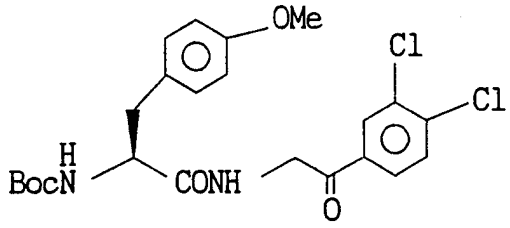
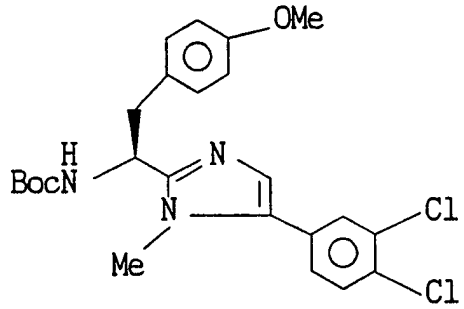
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Preparation No.	Formula
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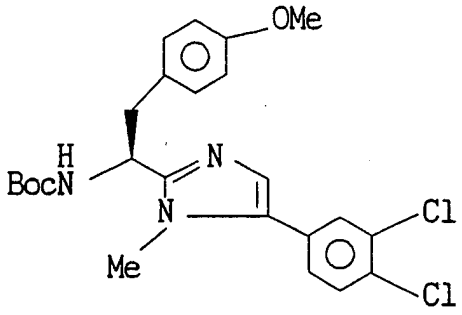
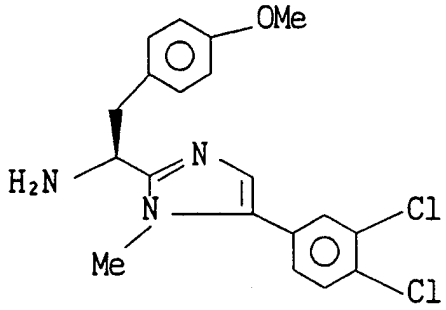
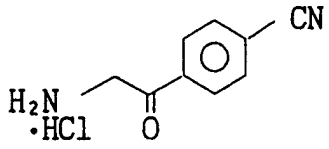
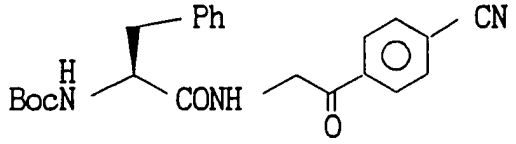
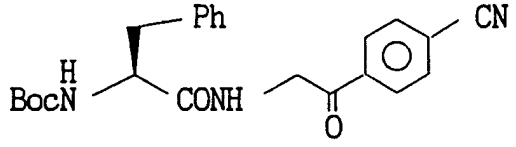
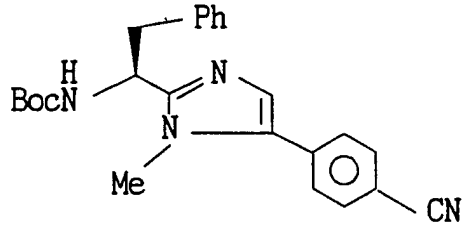
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Preparation No.	Formula
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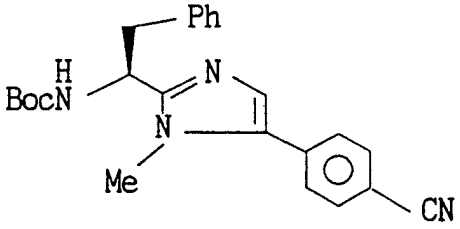
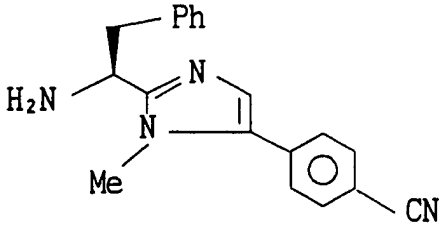
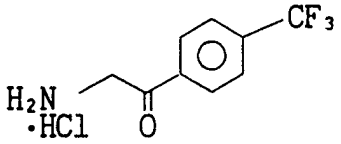
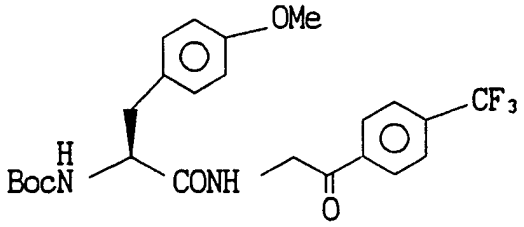
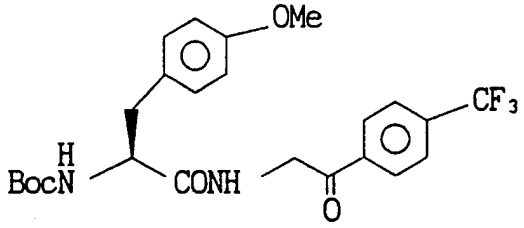
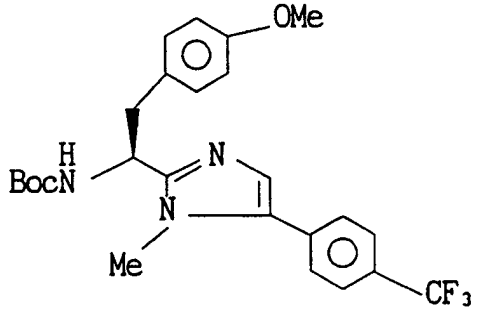
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Preparation No.	Formula
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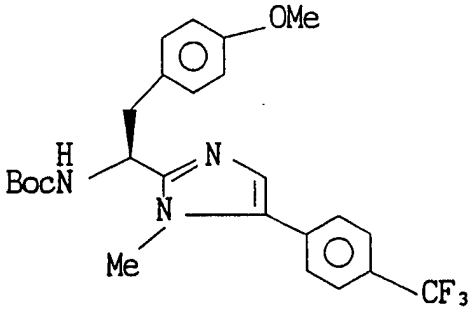
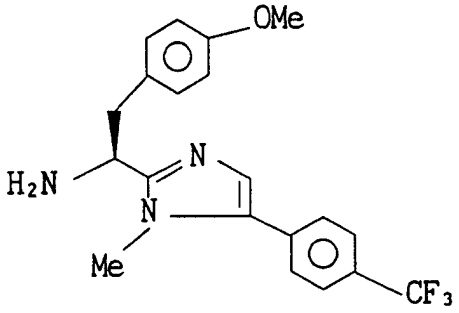
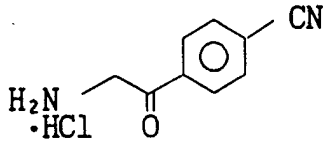
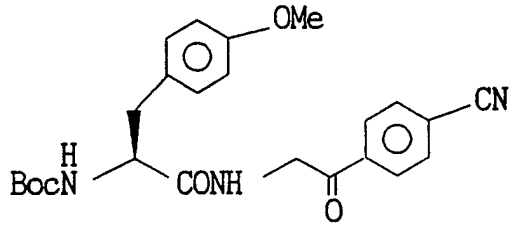
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Preparation No.	Formula
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24	
	
25	
	

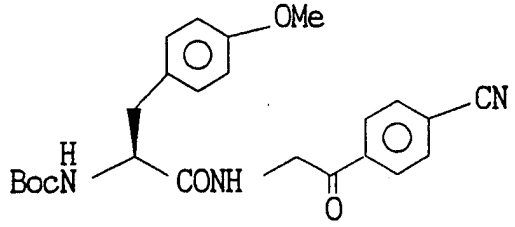
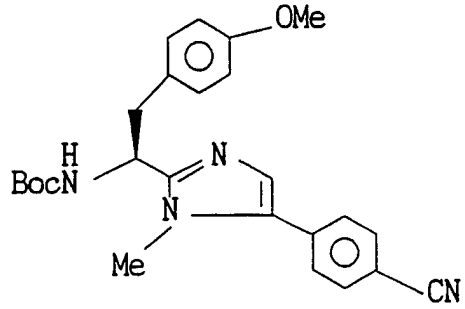
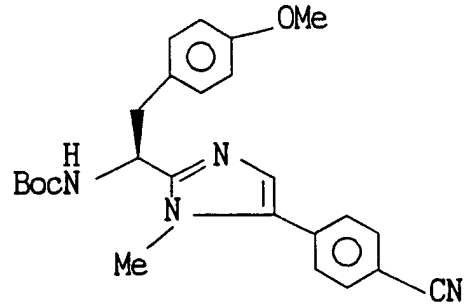
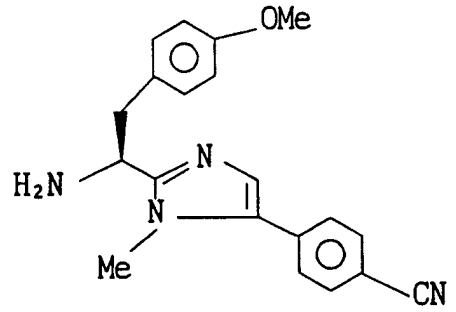
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Preparation No.	Formula
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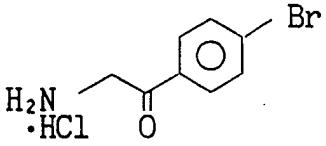
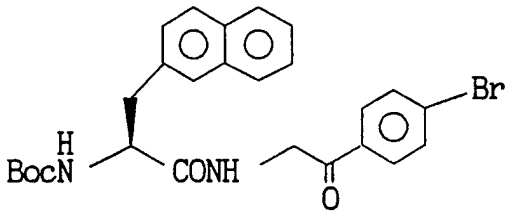
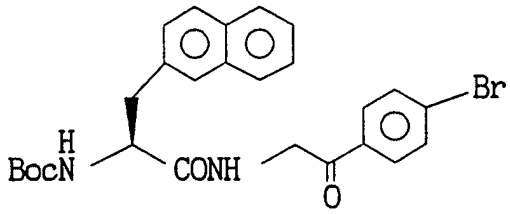
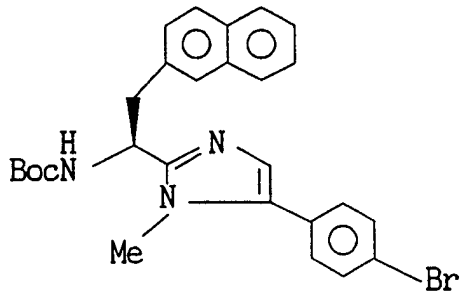
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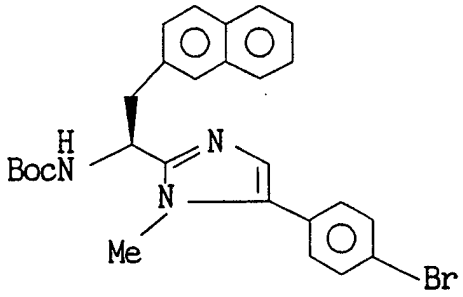
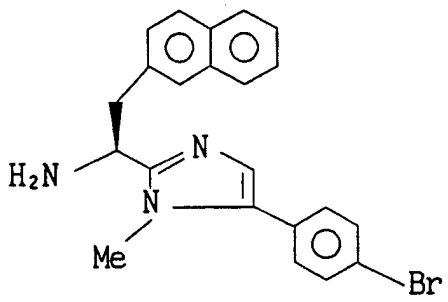
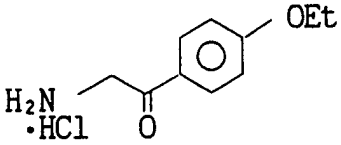
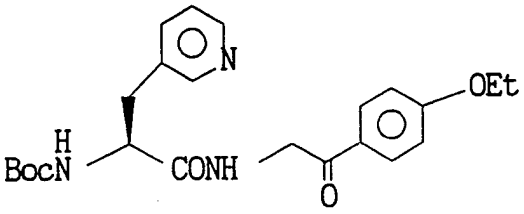
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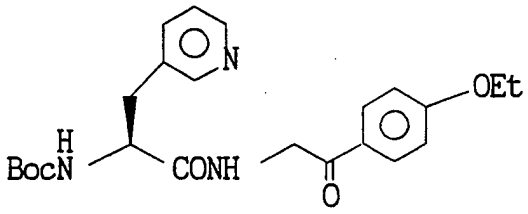
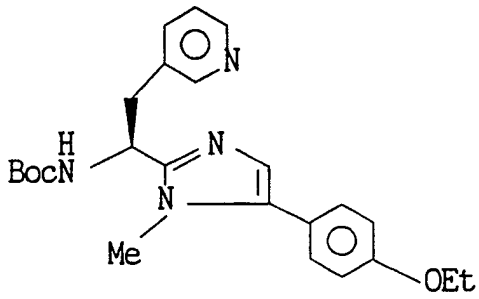
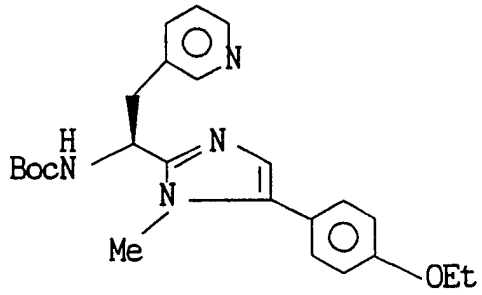
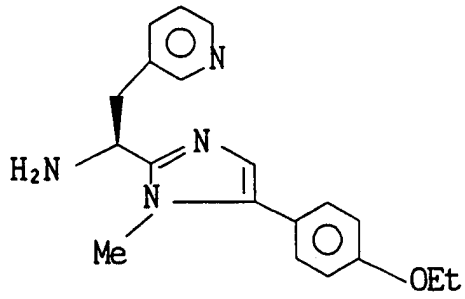
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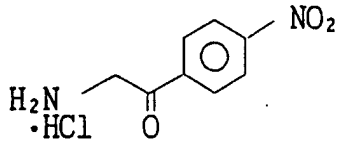
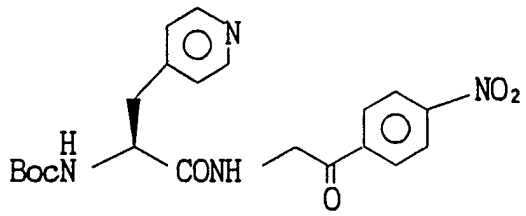
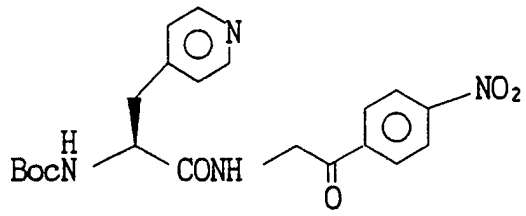
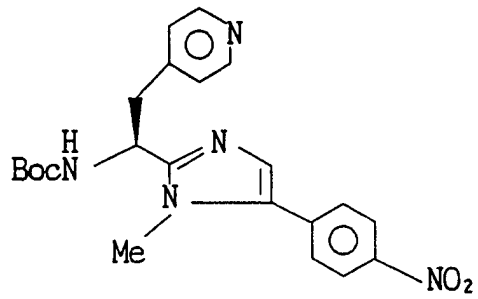
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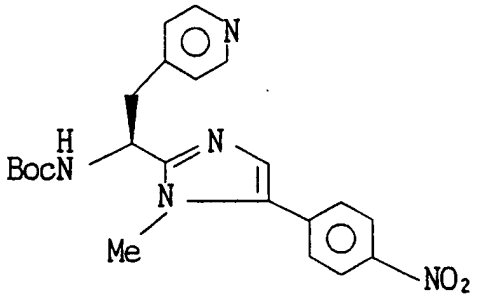
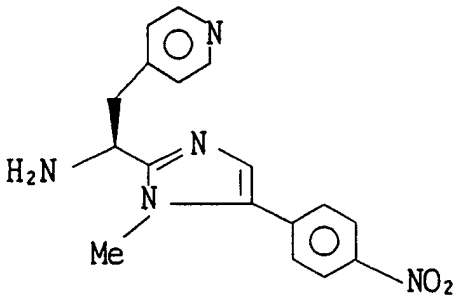
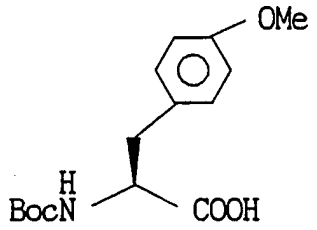
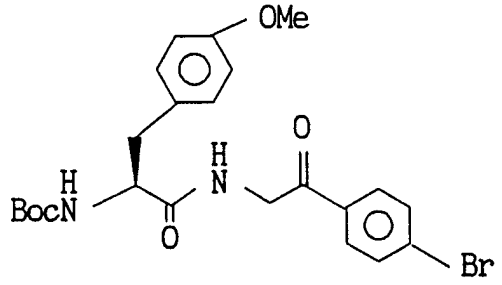
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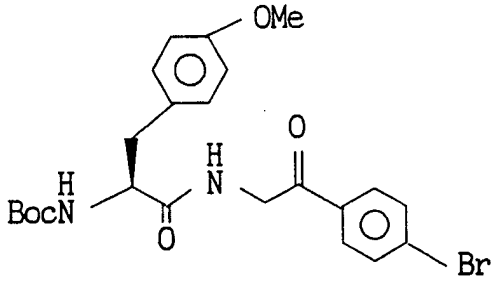
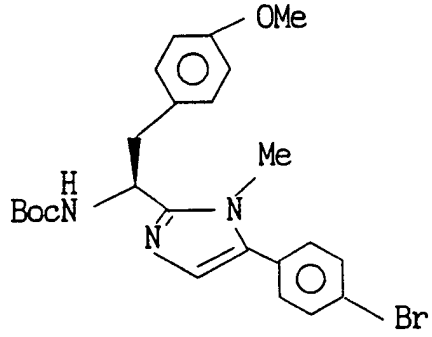
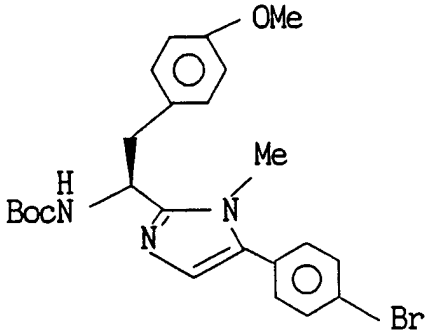
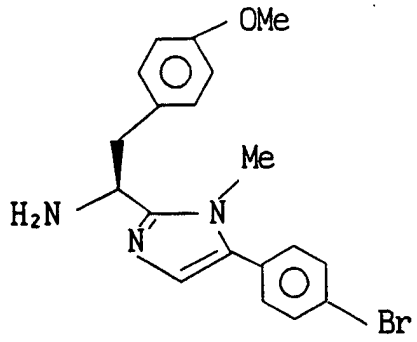
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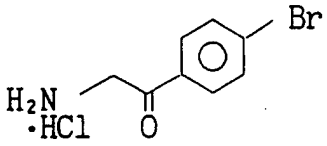
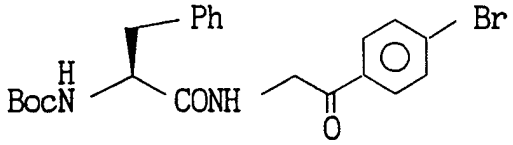
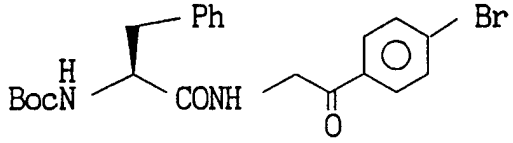
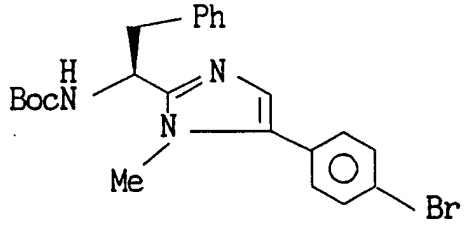
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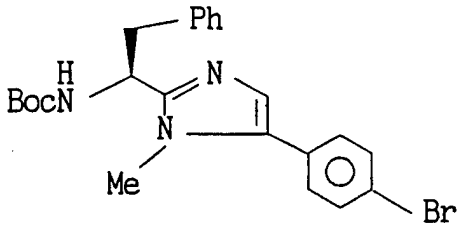
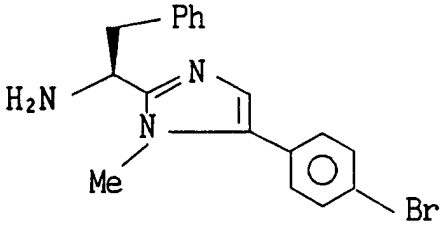
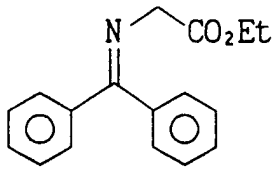
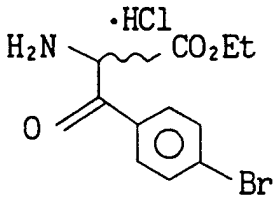
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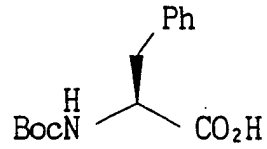
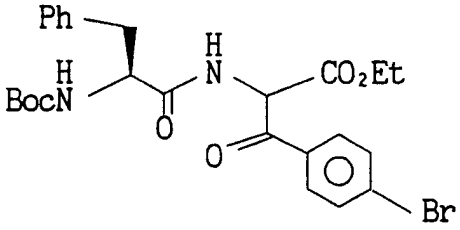
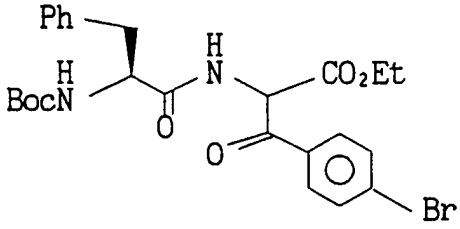
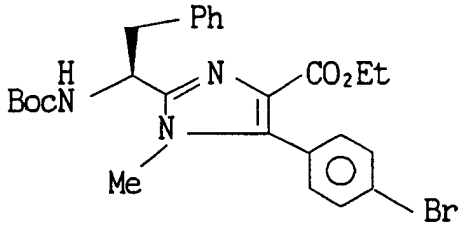
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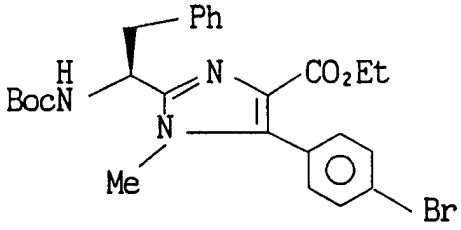
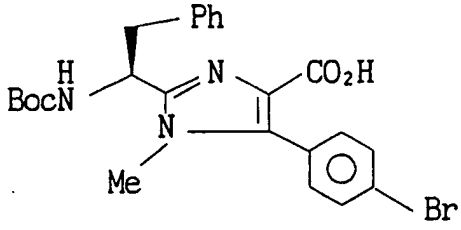
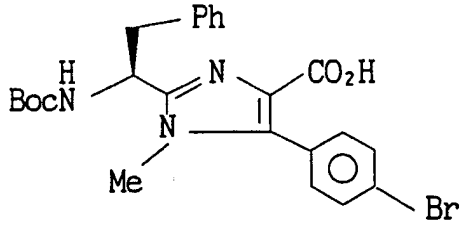
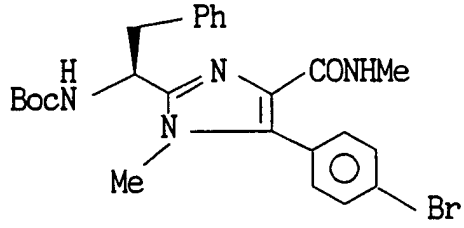
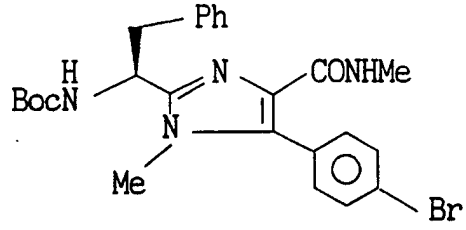
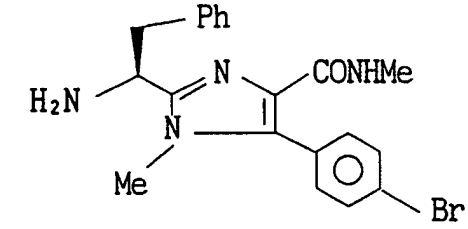
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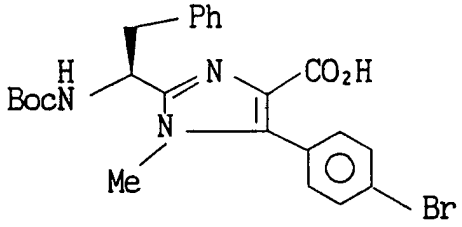
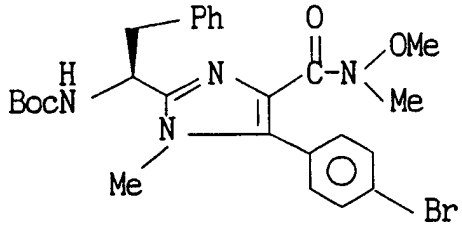
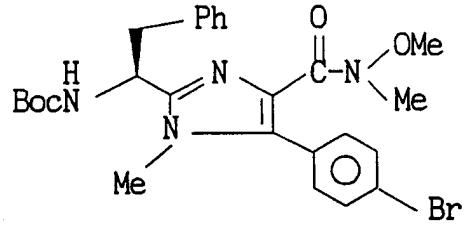
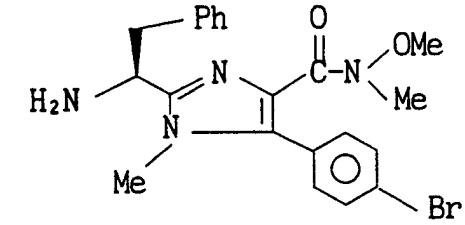
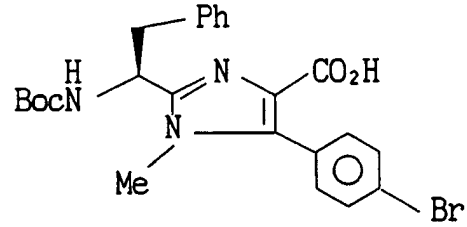
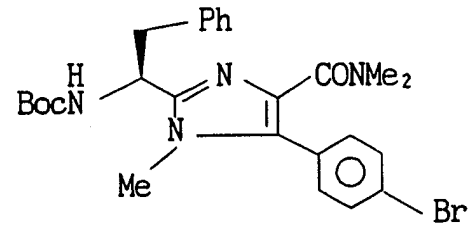
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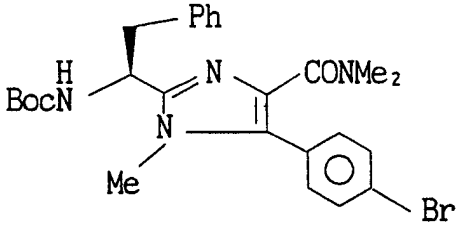
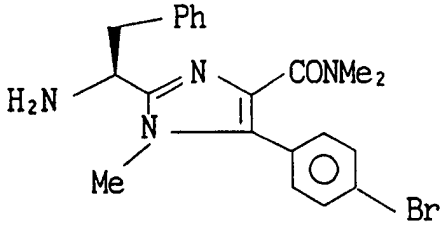
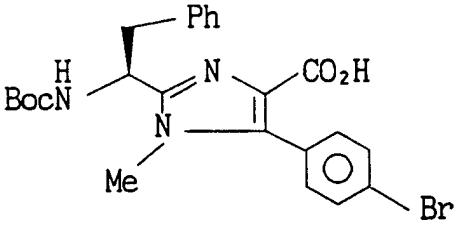
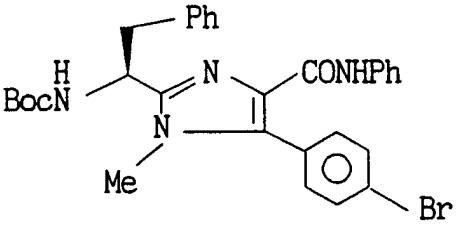
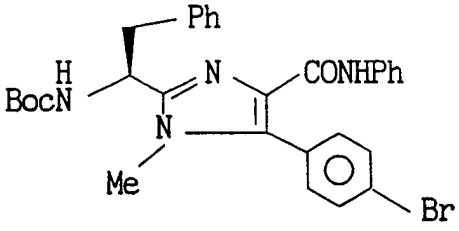
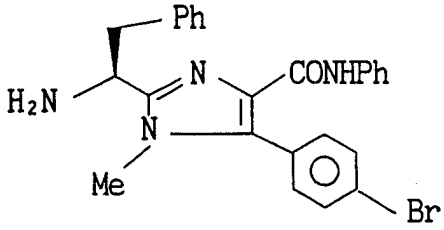
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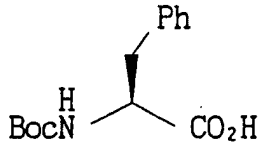
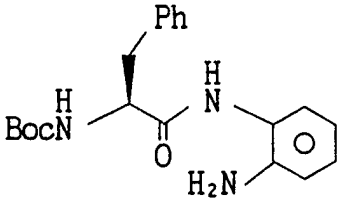
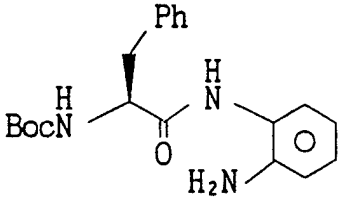
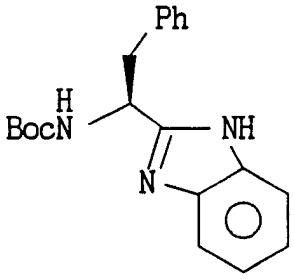
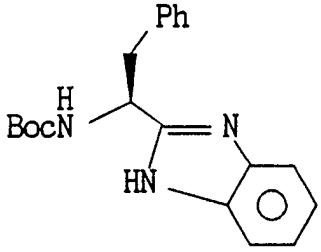
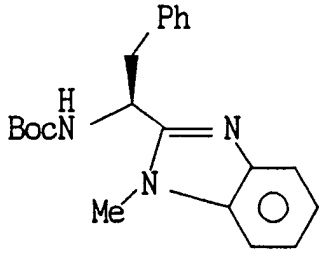
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Preparation No.	Formula
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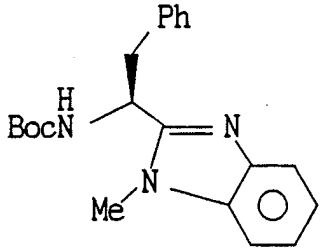
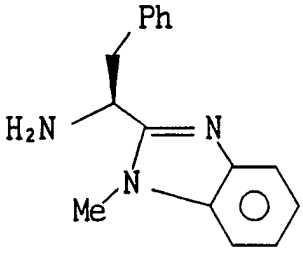
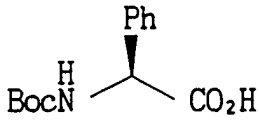
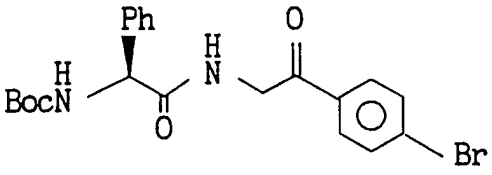
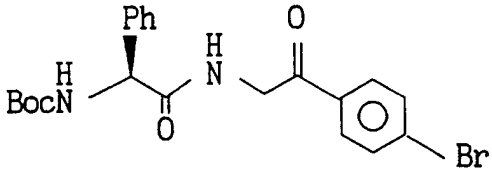
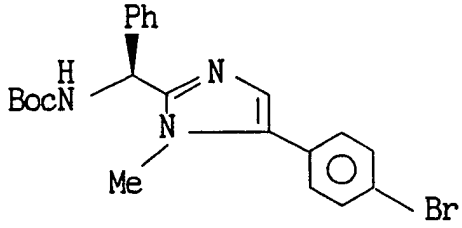
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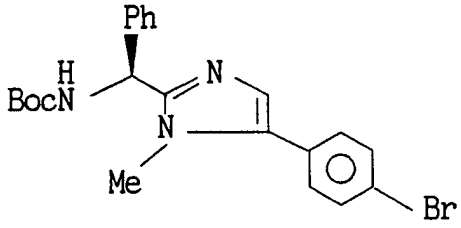
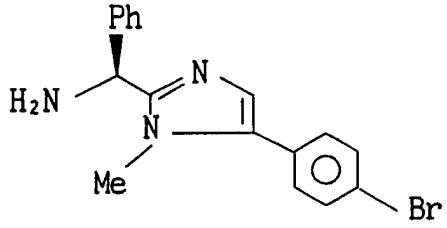
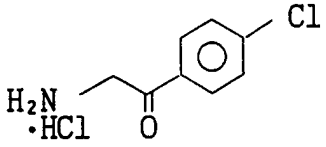
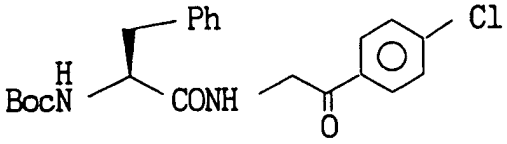
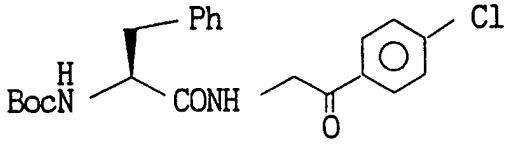
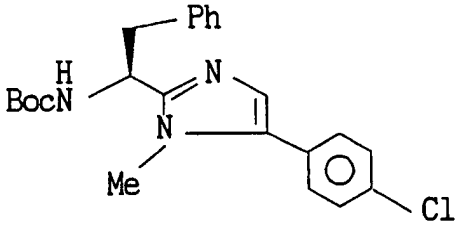
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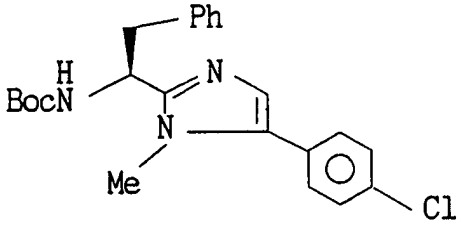
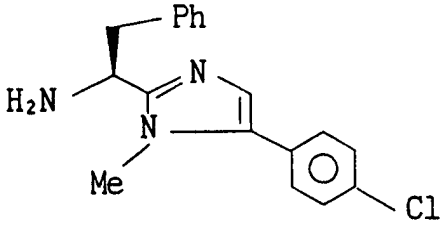
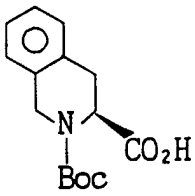
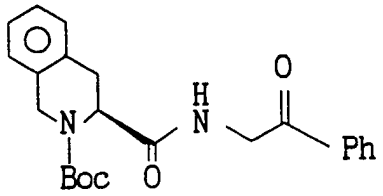
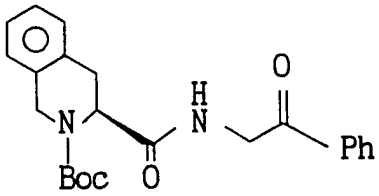
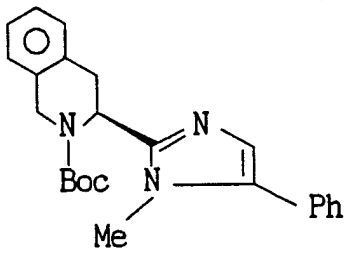
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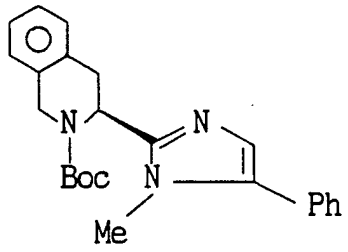
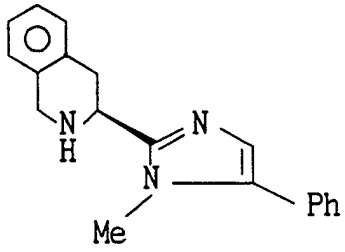
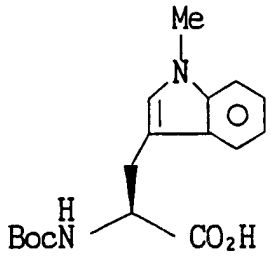
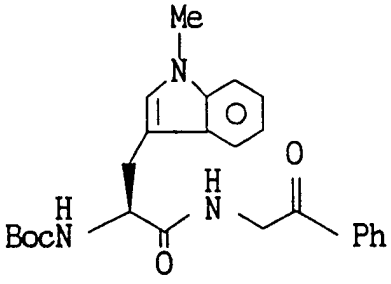
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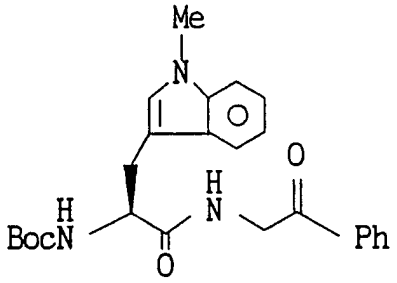
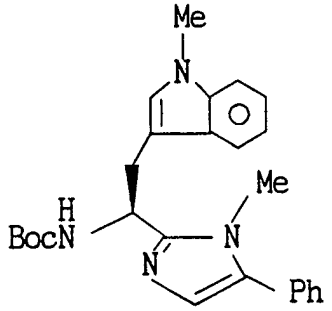
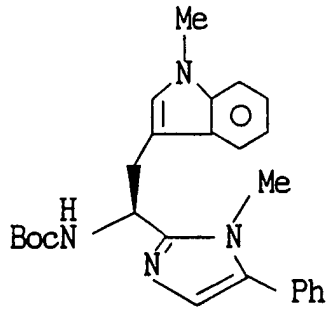
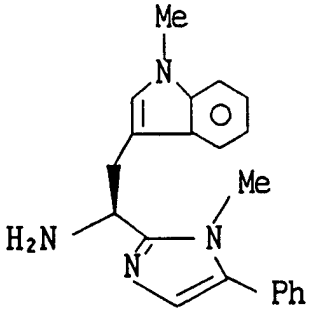
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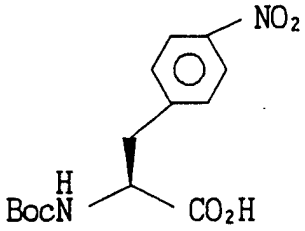
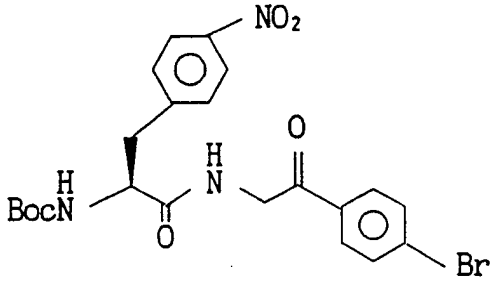
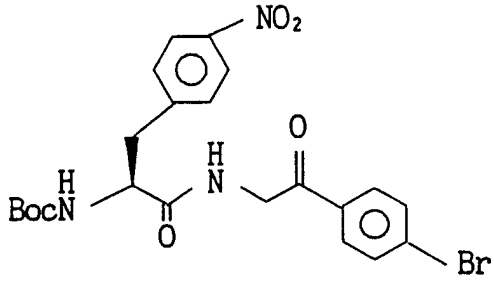
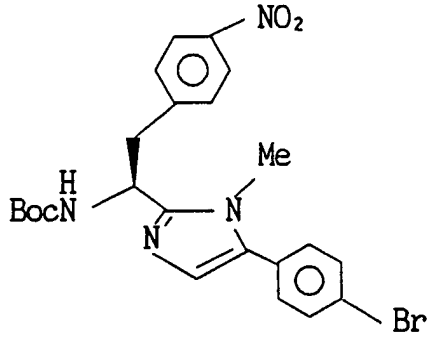
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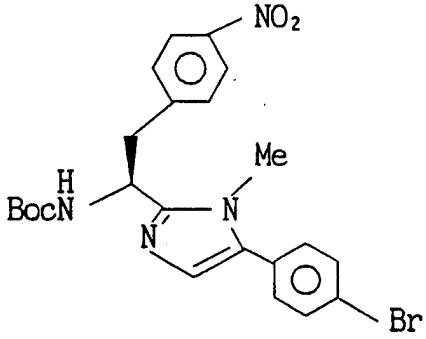
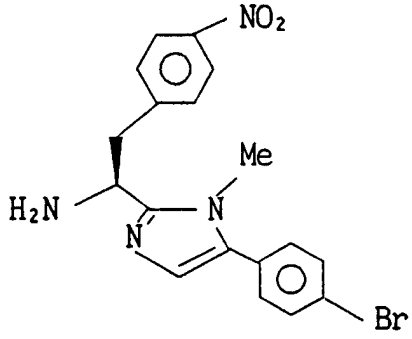
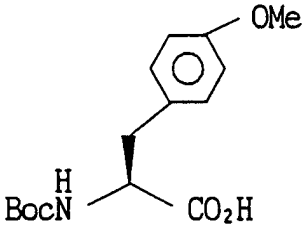
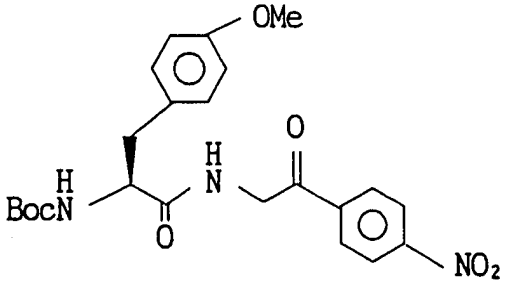
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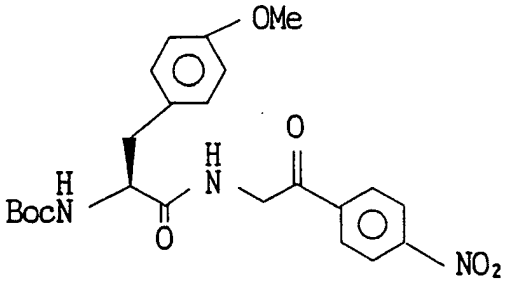
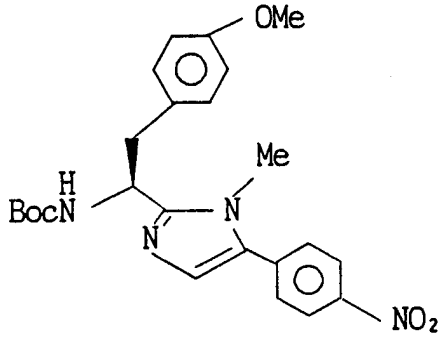
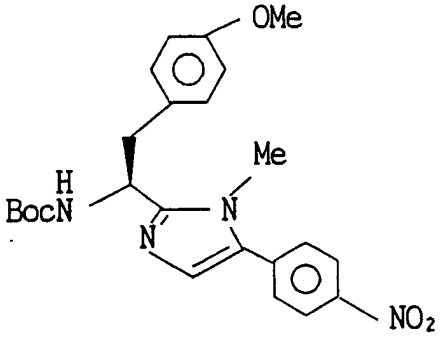
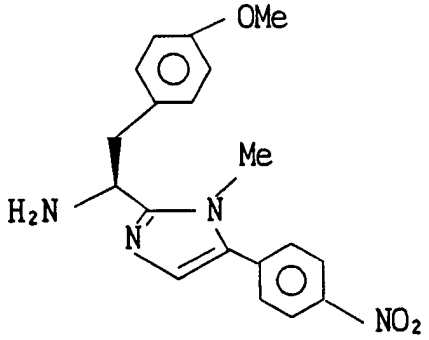
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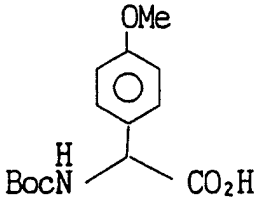
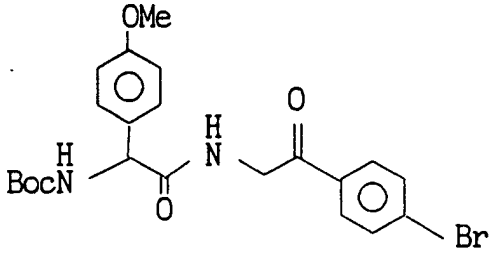
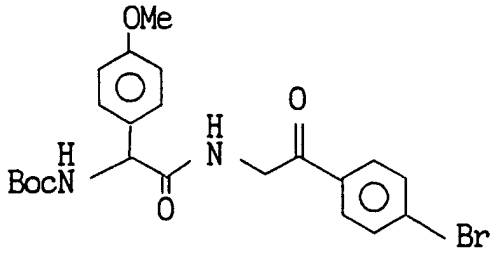
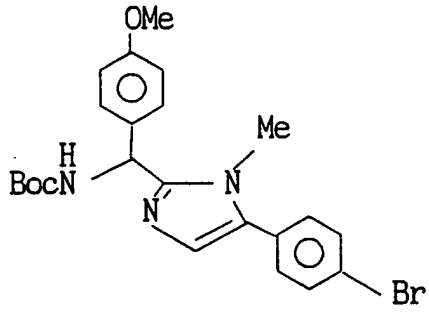
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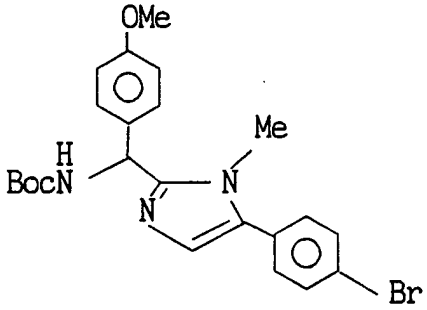
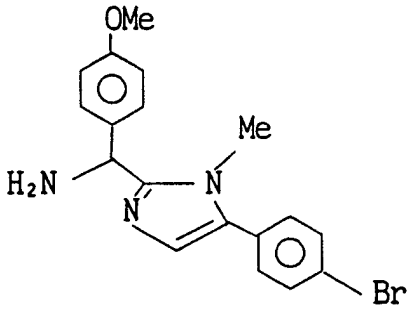
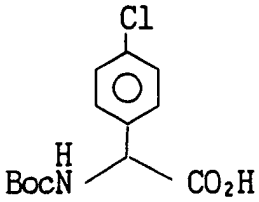
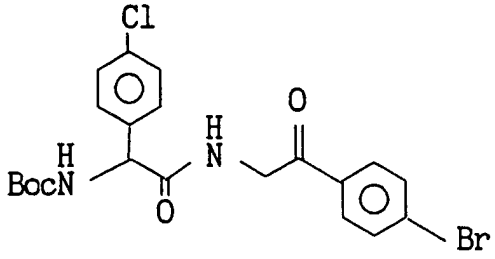
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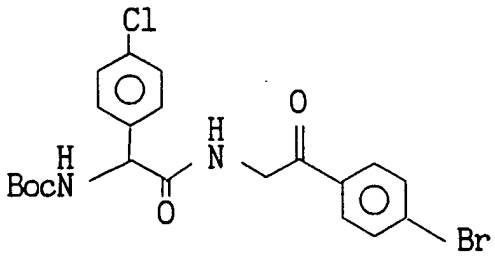
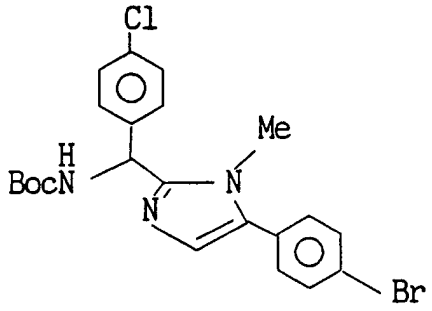
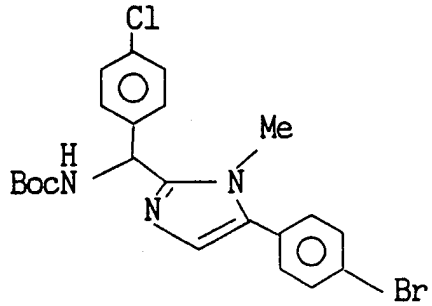
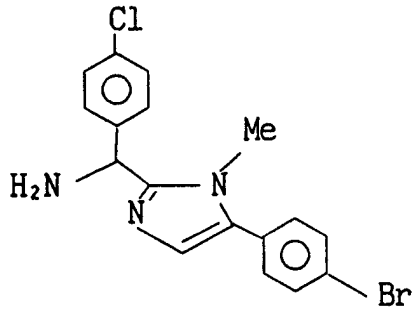
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Preparation No.	Formula
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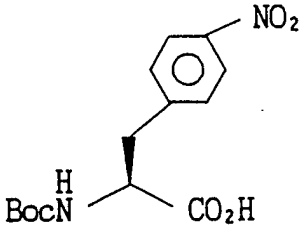
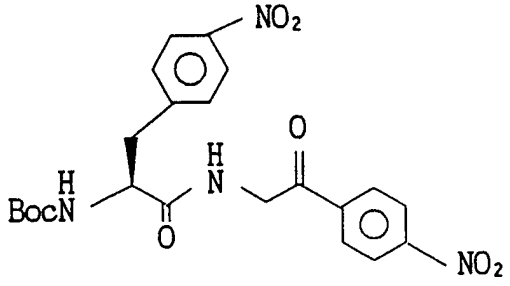
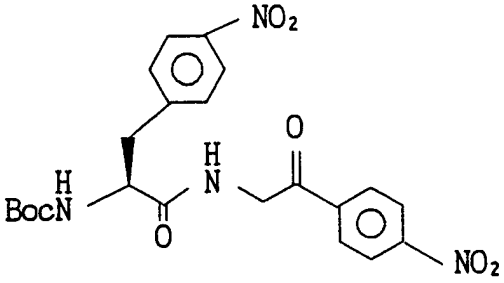
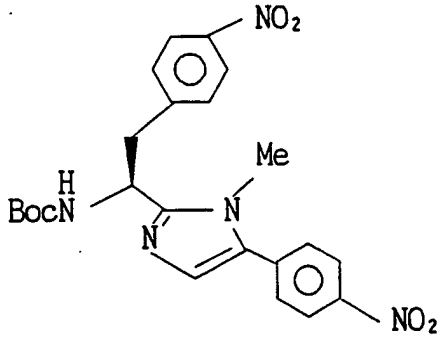
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Preparation No.	Formula
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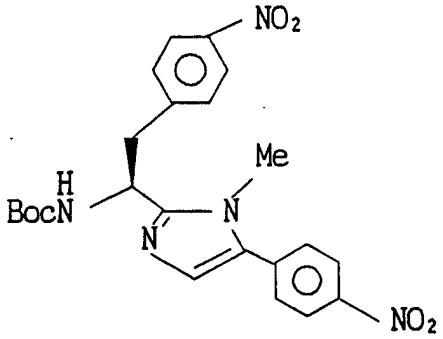
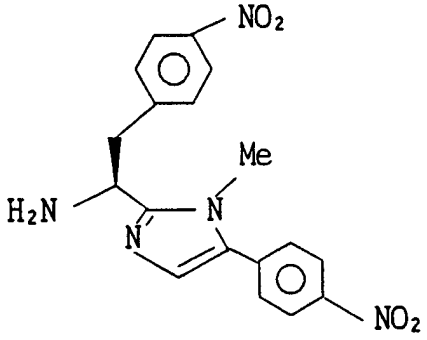
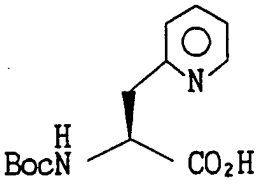
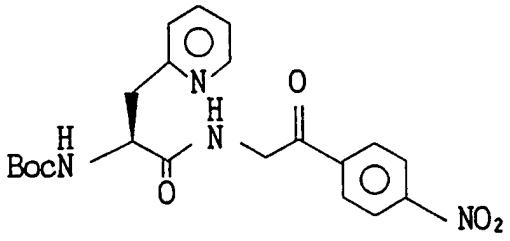
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Preparation No.	Formula
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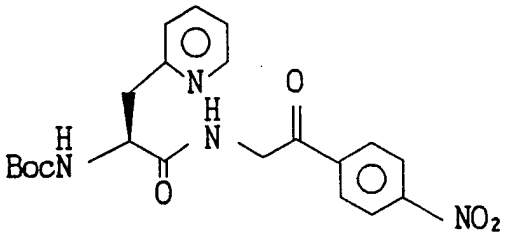
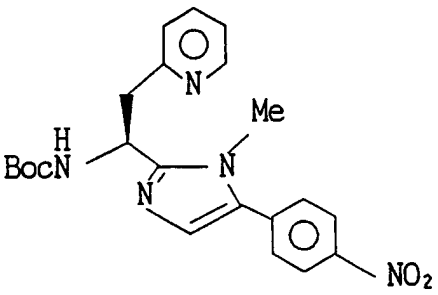
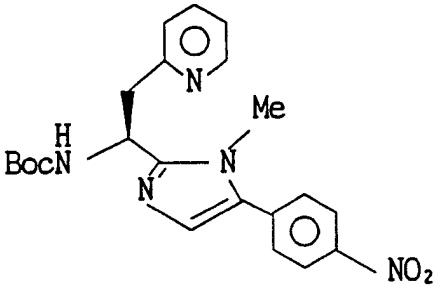
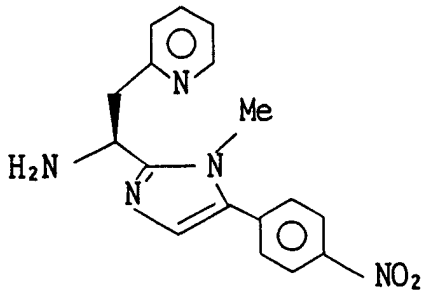
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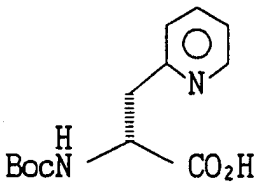
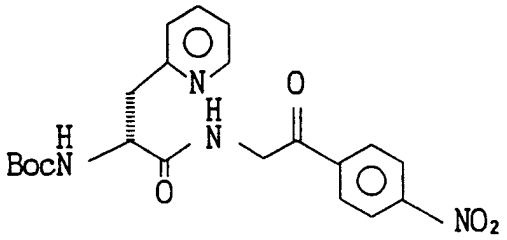
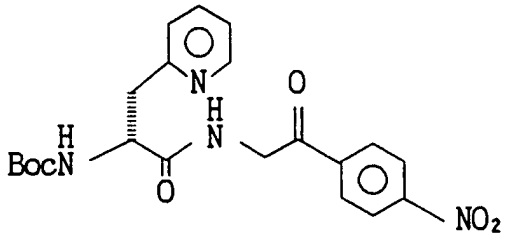
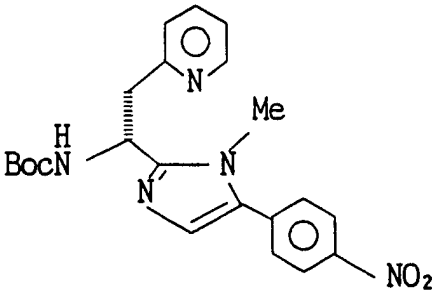
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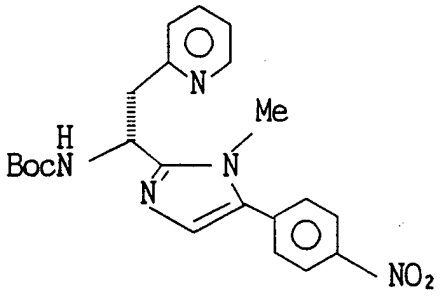
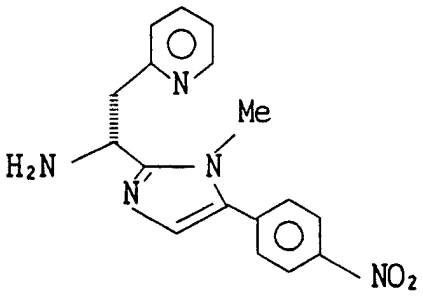
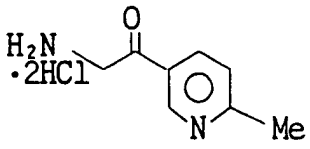
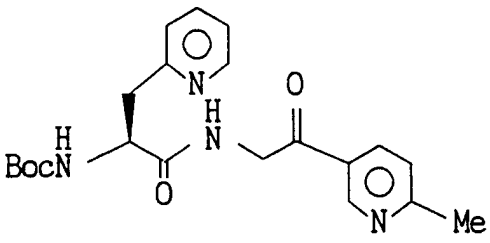
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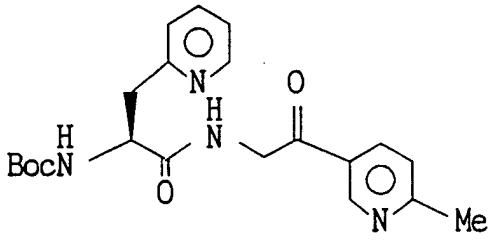
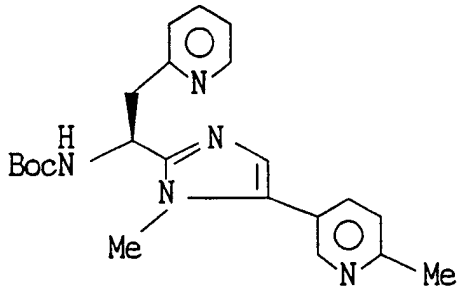
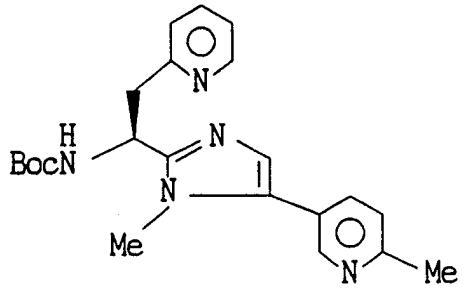
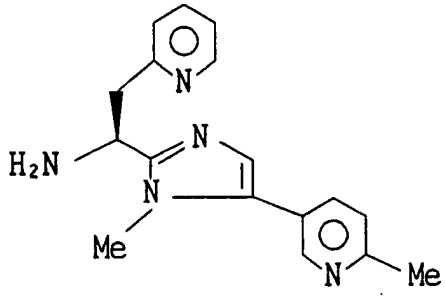
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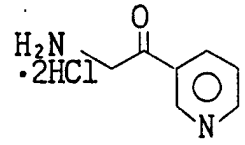
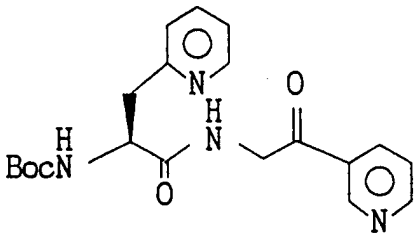
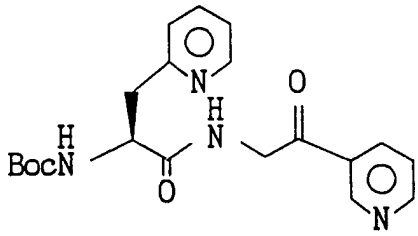
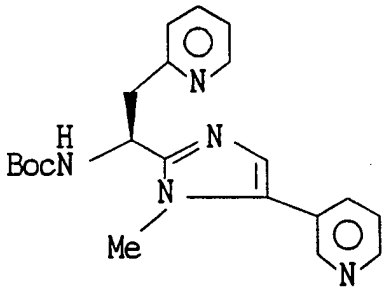
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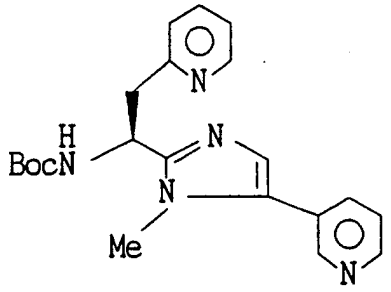
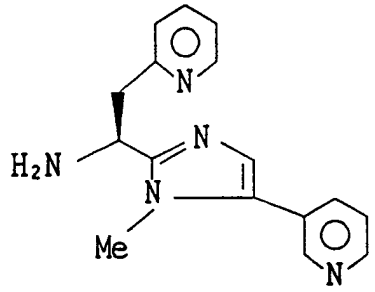
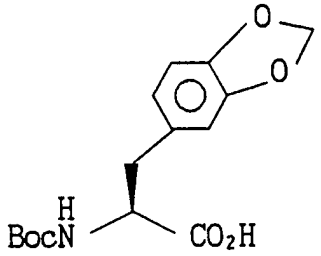
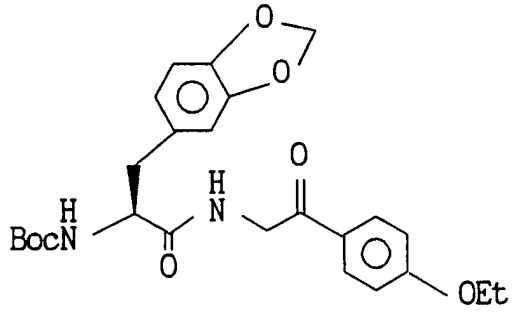
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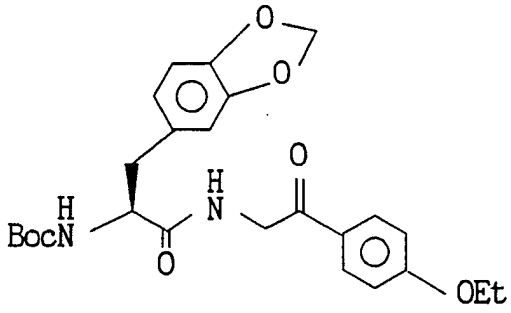
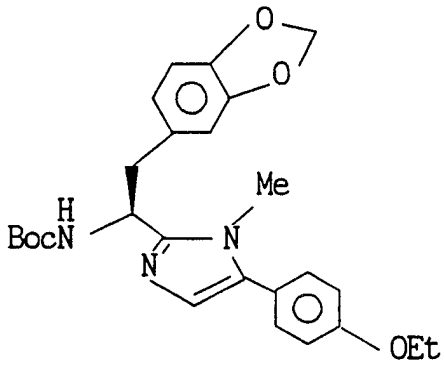
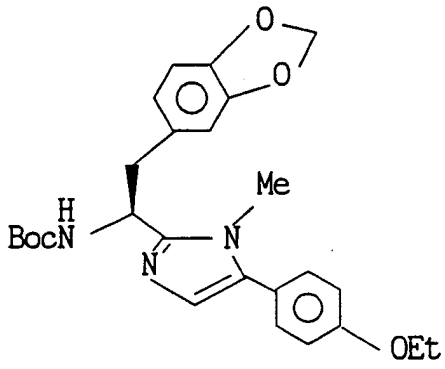
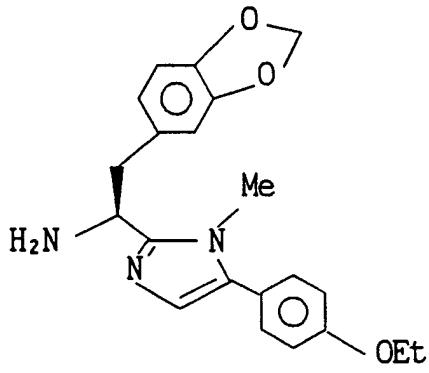
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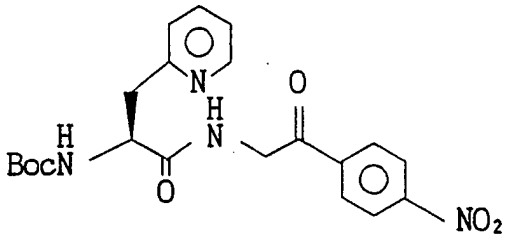
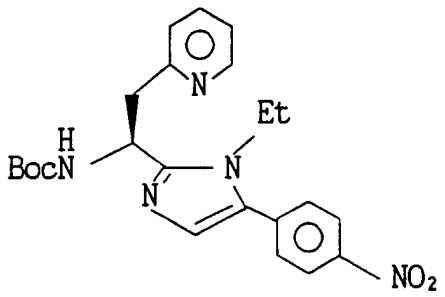
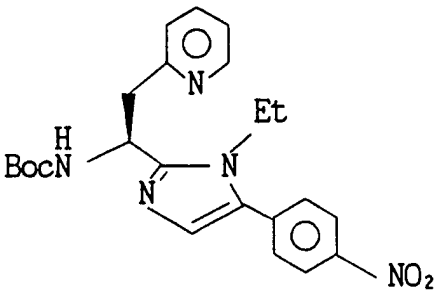
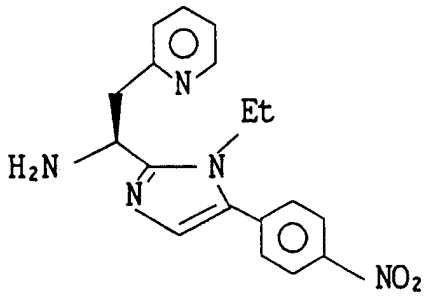
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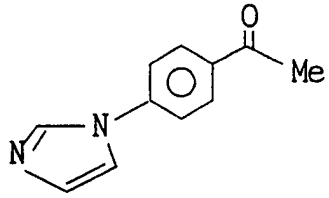
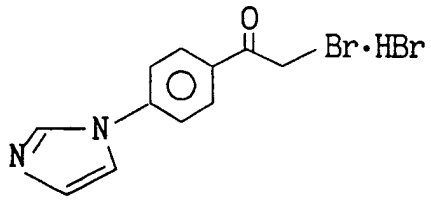
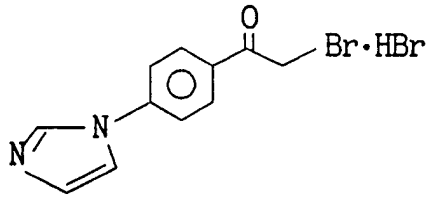
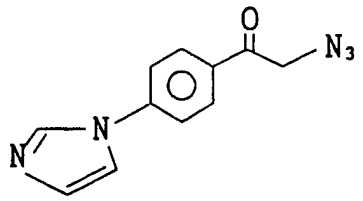
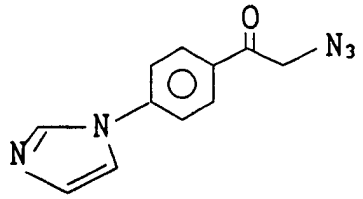
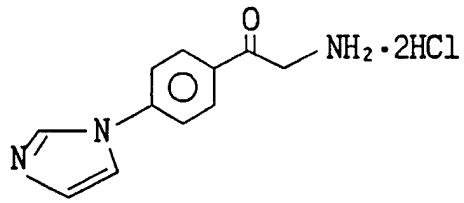
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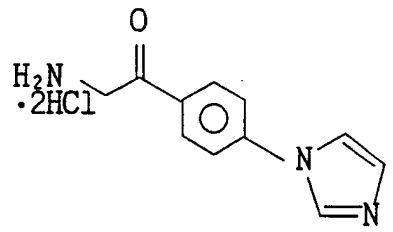
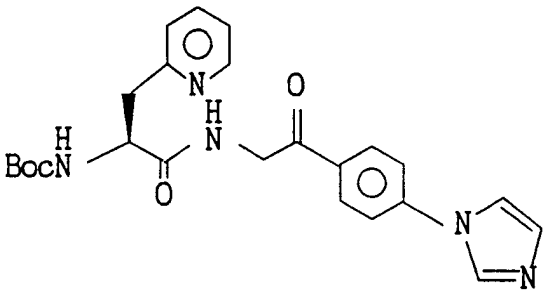
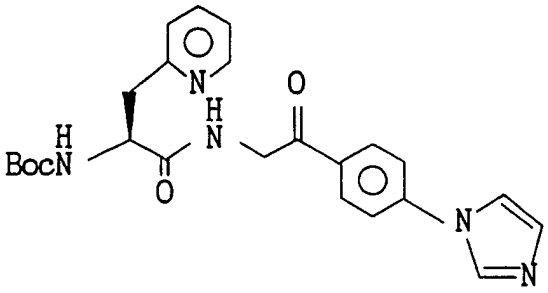
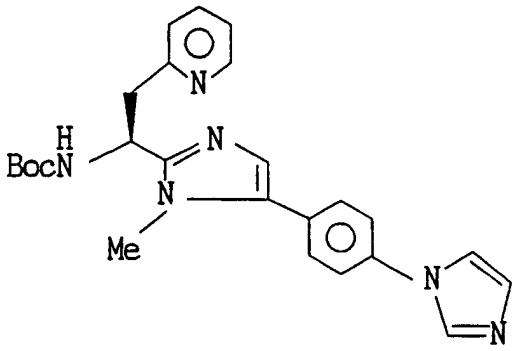
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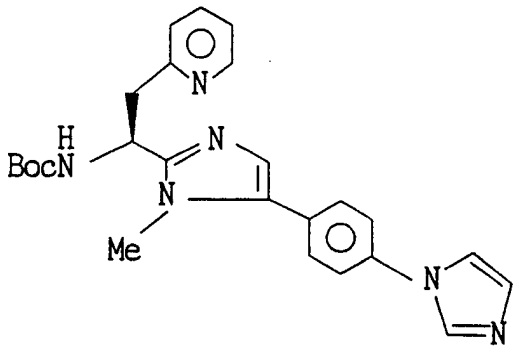
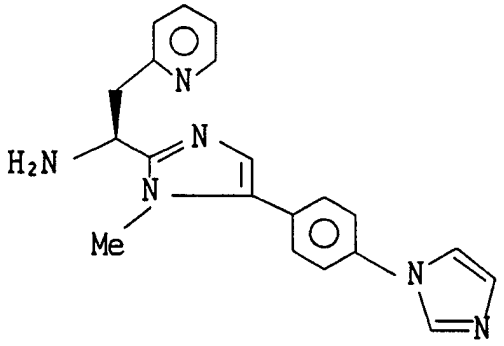
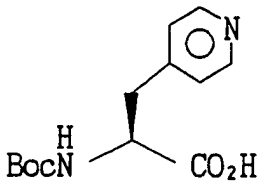
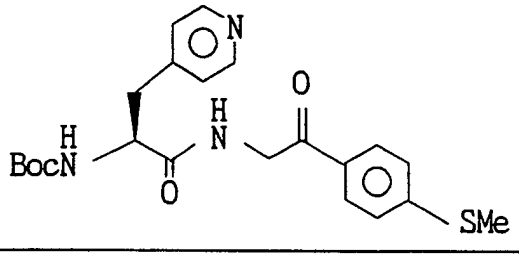
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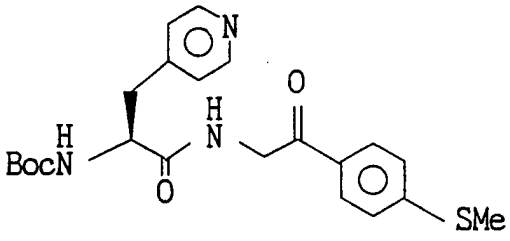
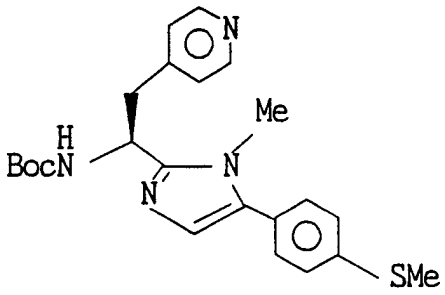
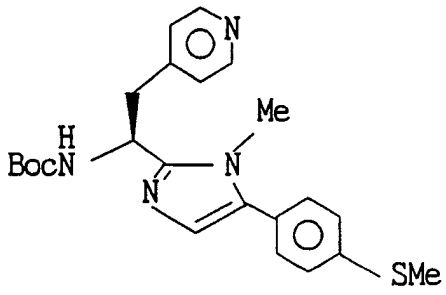
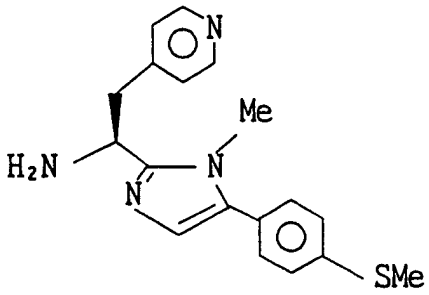
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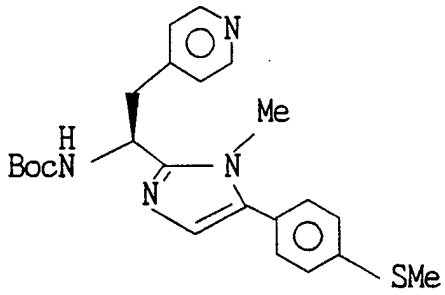
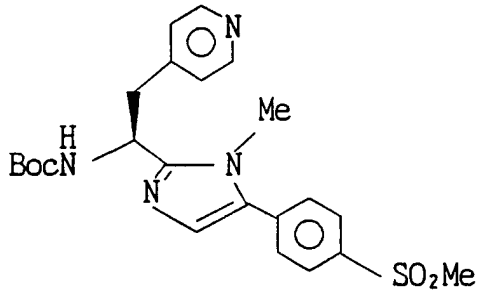
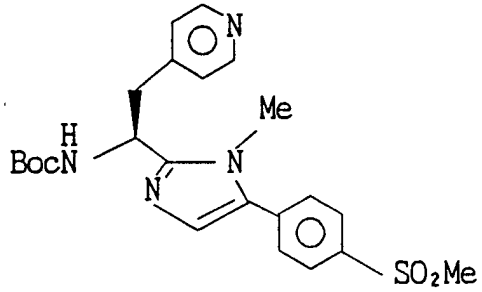
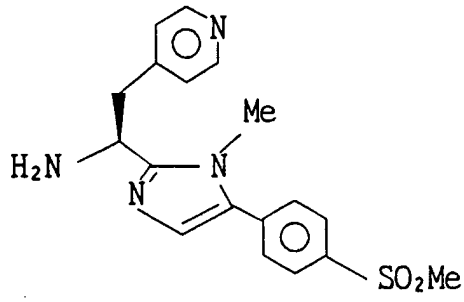
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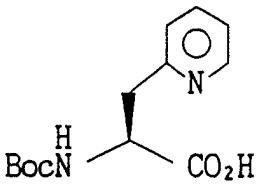
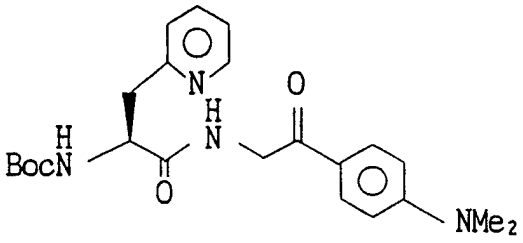
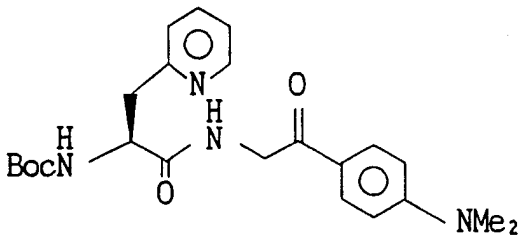
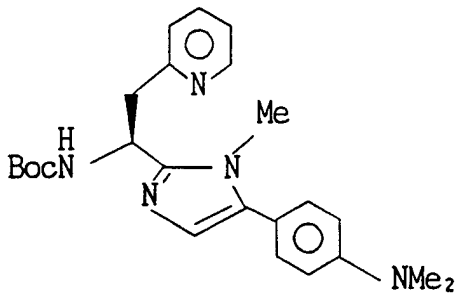
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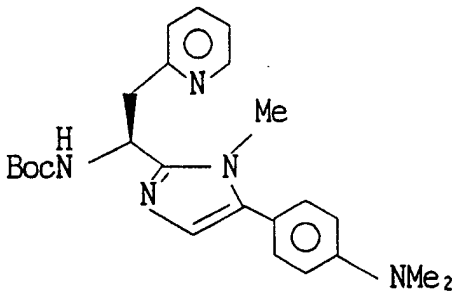
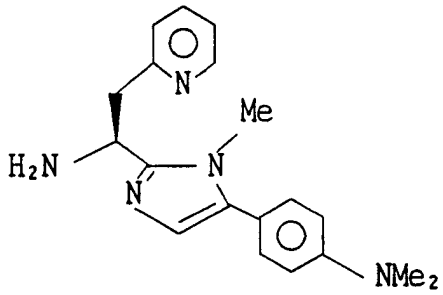
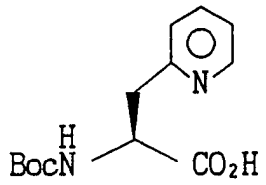
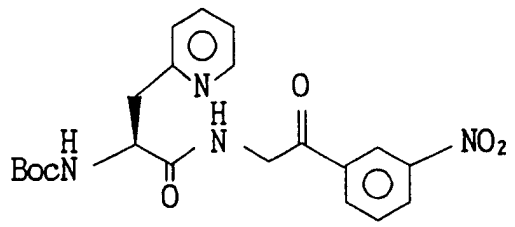
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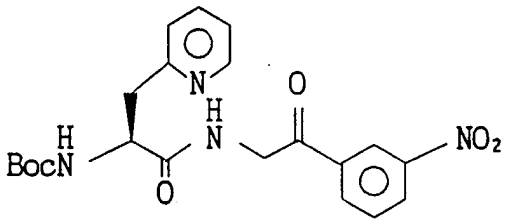
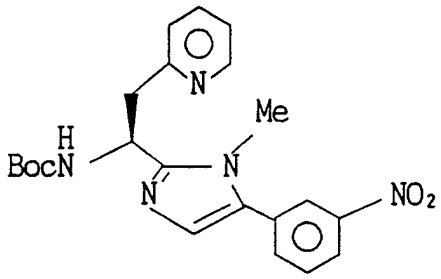
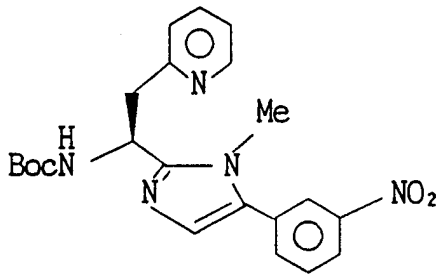
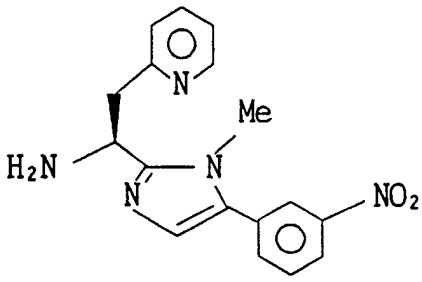
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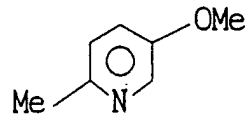
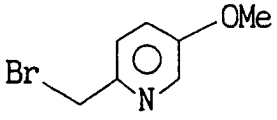
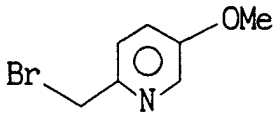
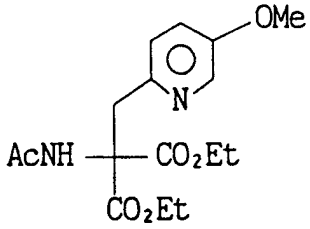
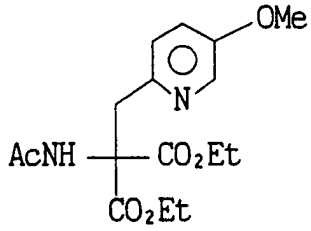
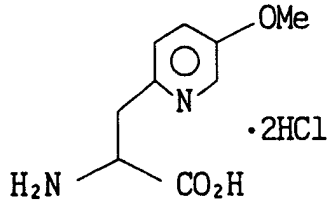
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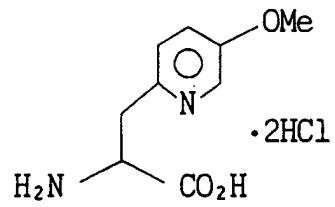
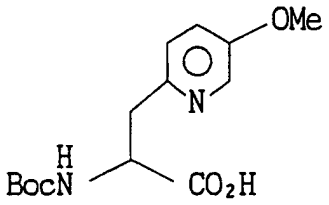
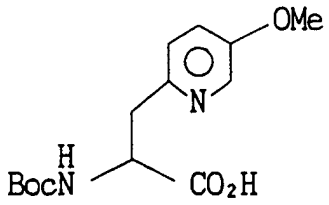
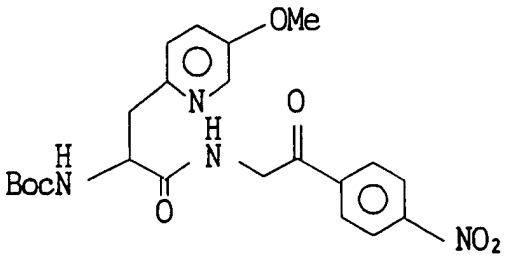
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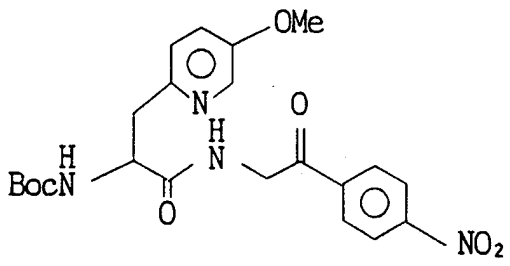
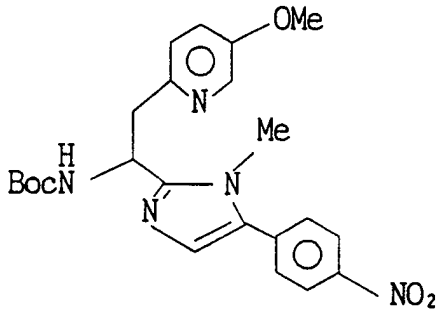
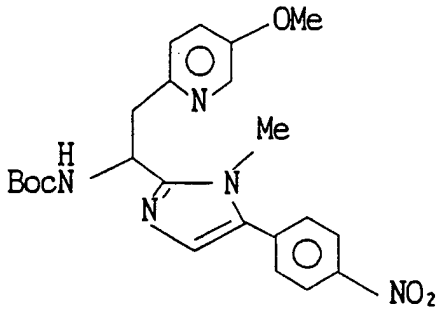
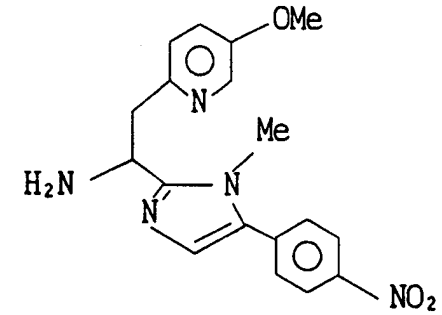
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Preparation No.	Formula
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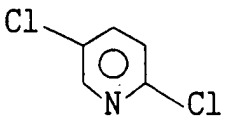
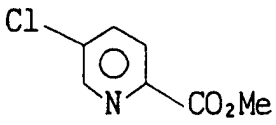
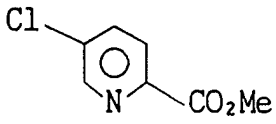
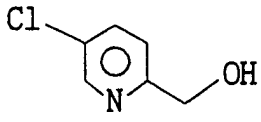
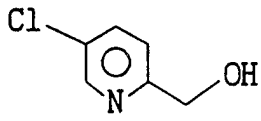
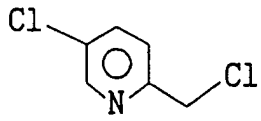
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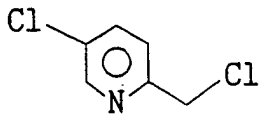
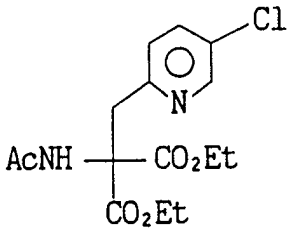
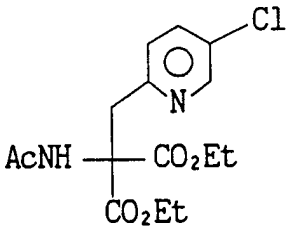
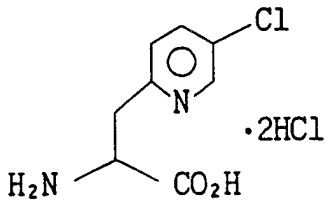
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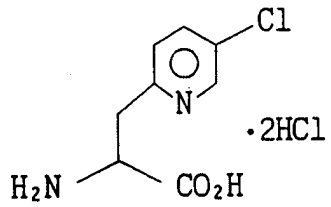
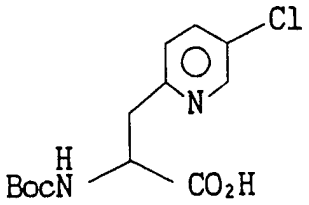
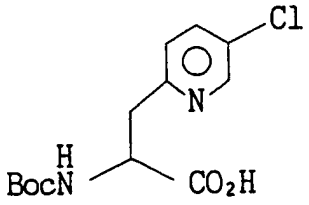
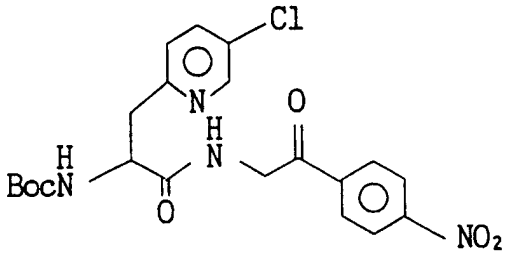
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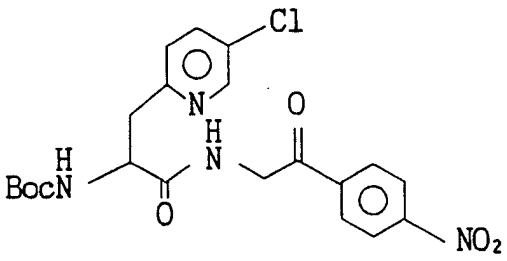
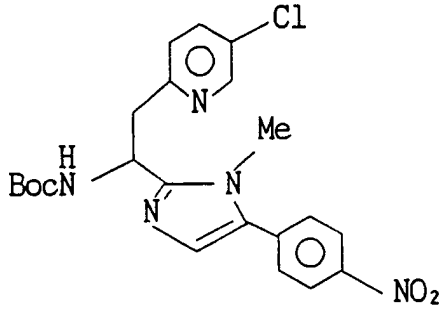
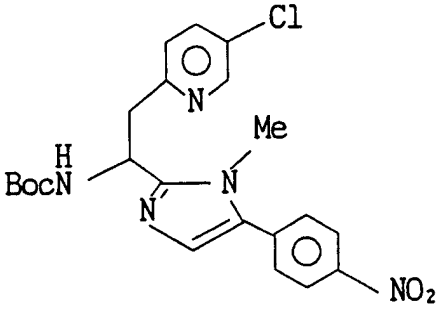
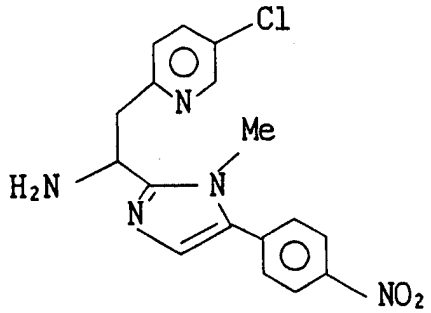
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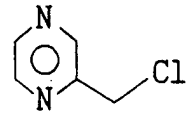
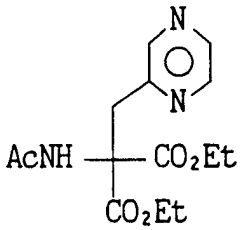
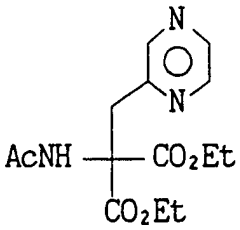
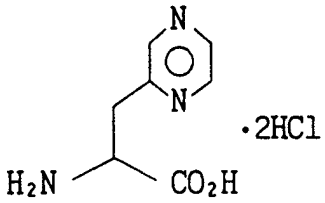
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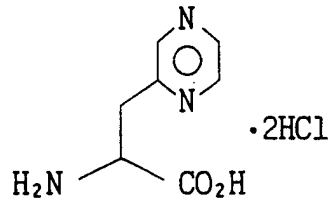
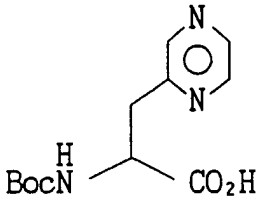
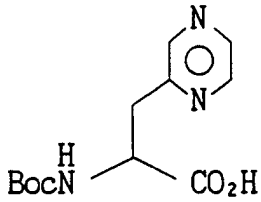
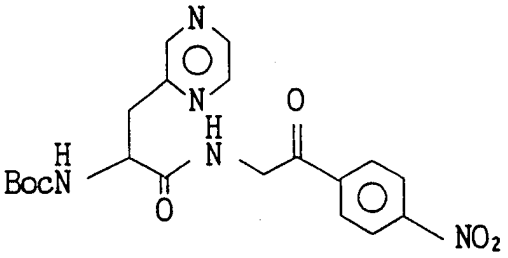
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Preparation No.	Formula
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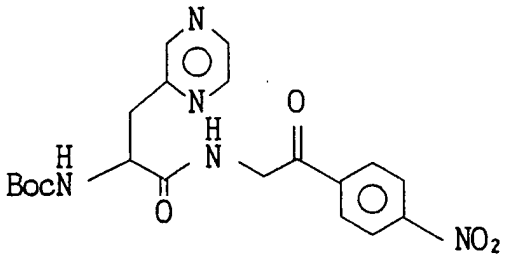
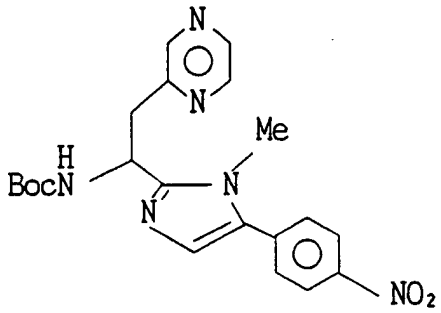
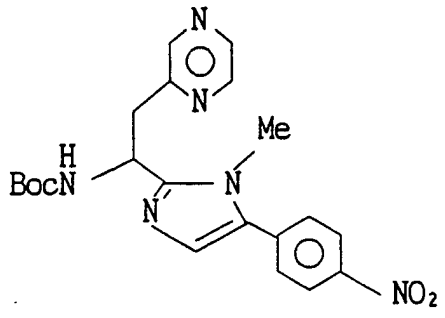
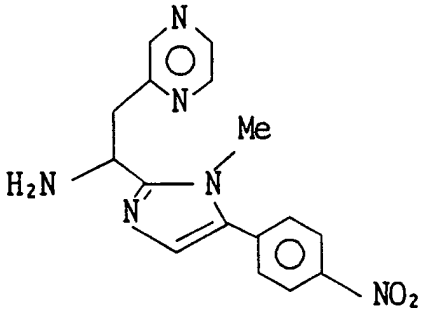
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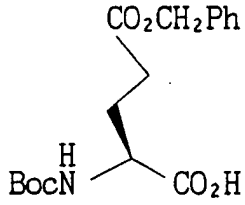
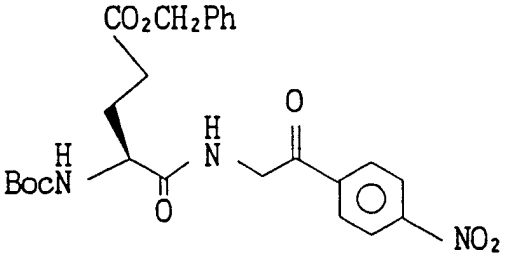
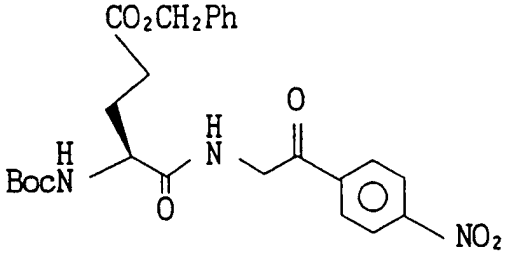
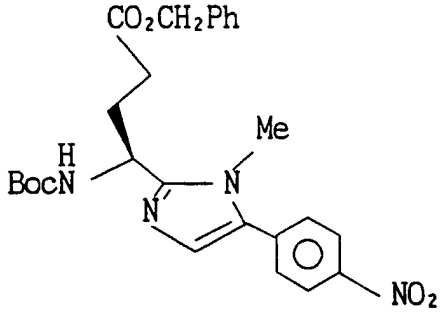
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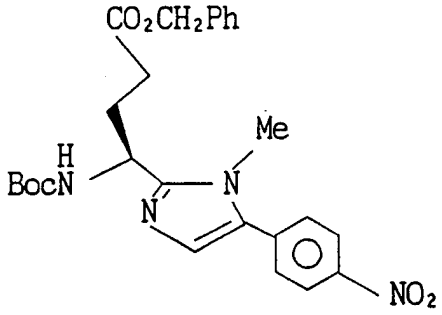
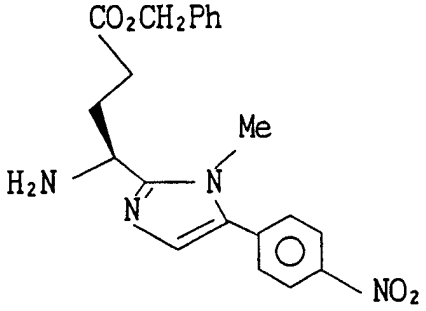
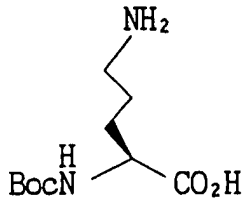
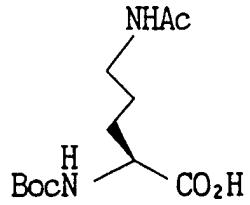
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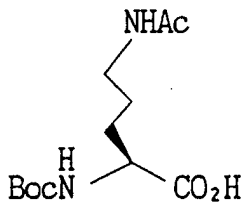
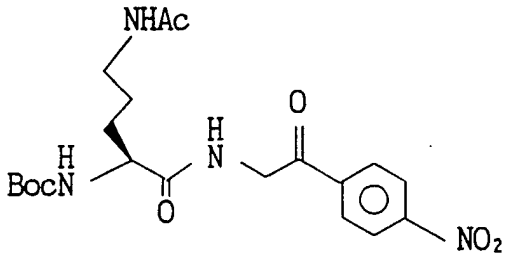
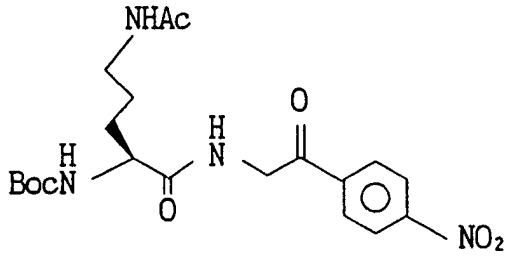
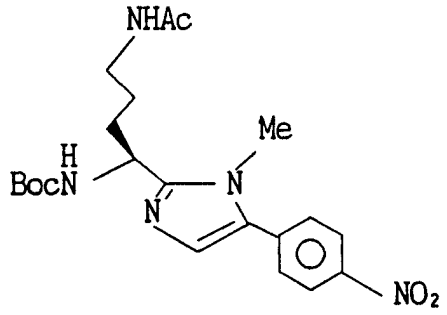
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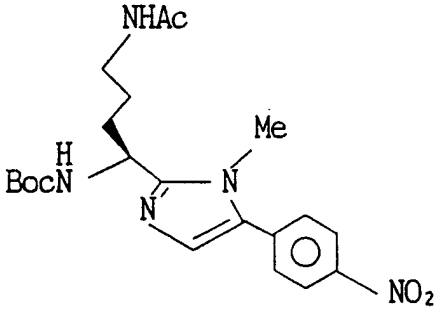
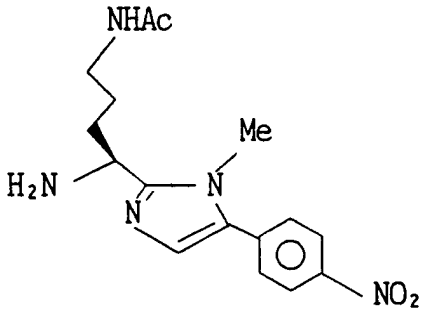
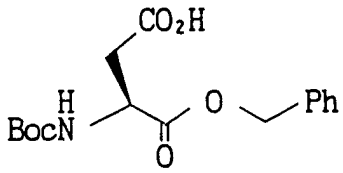
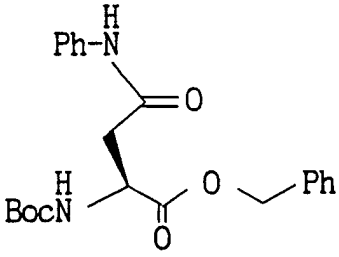
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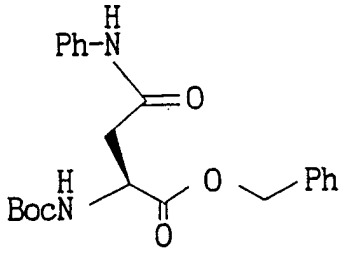
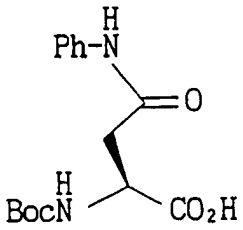
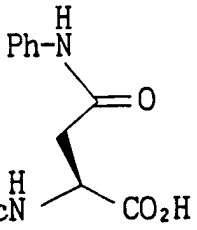
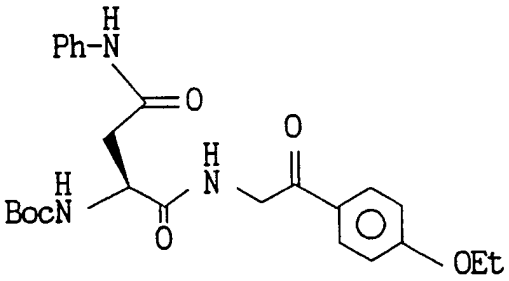
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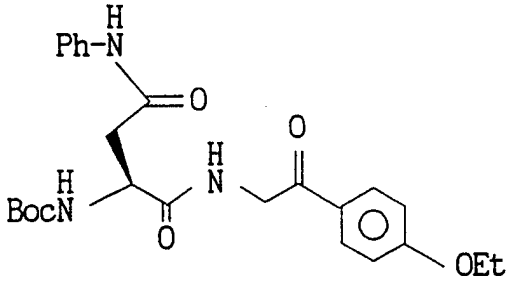
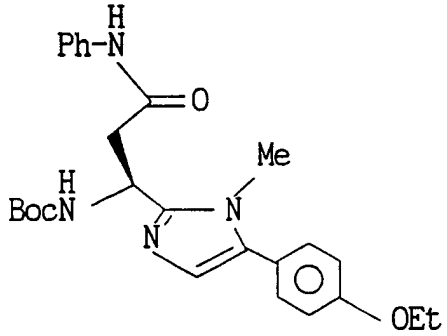
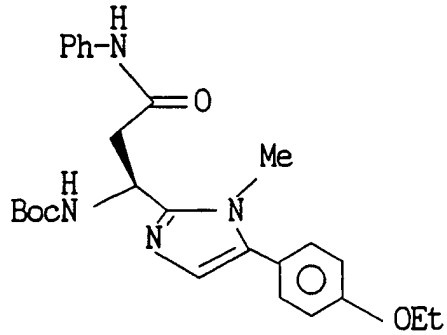
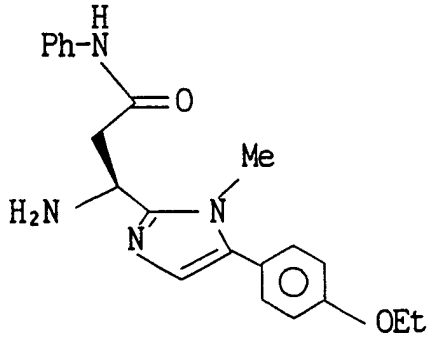
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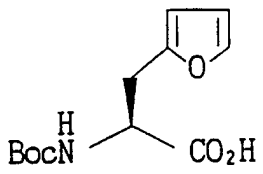
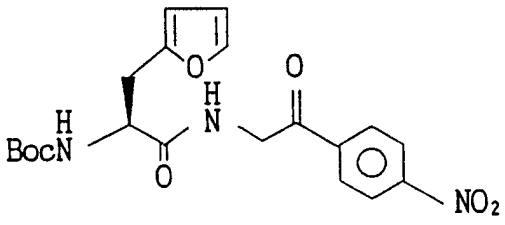
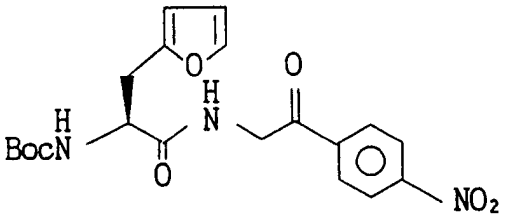
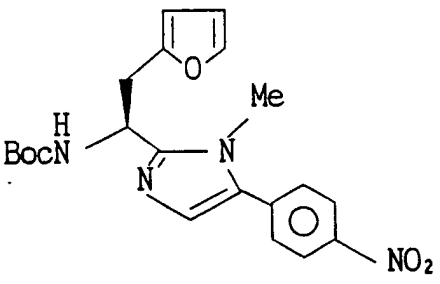
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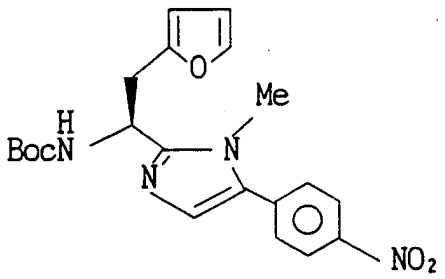
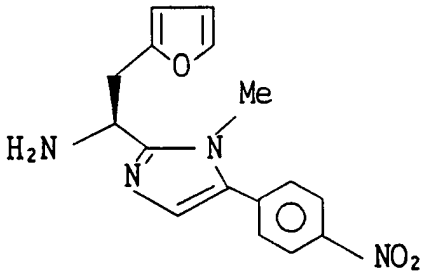
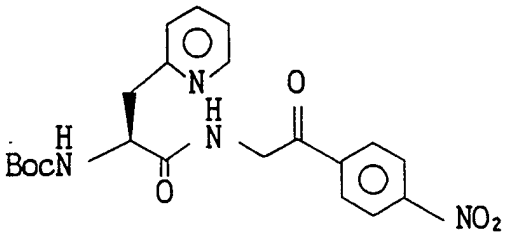
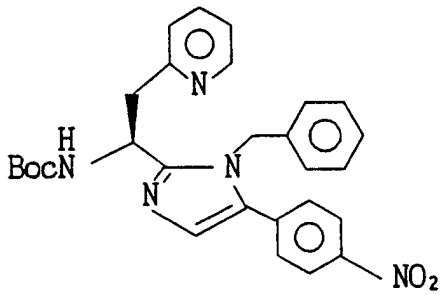
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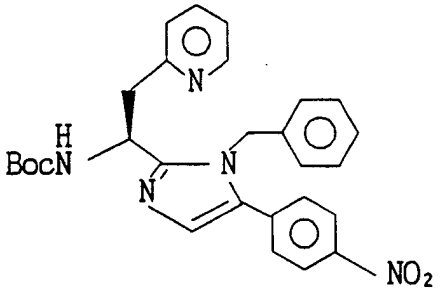
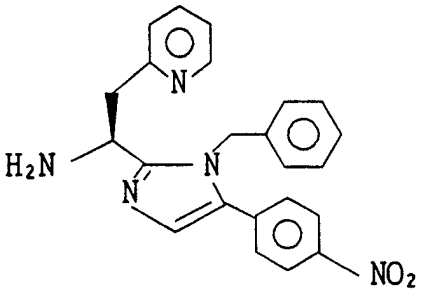
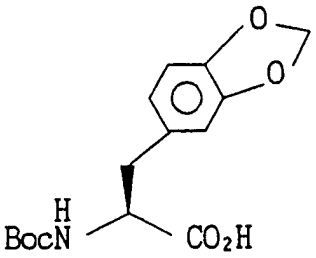
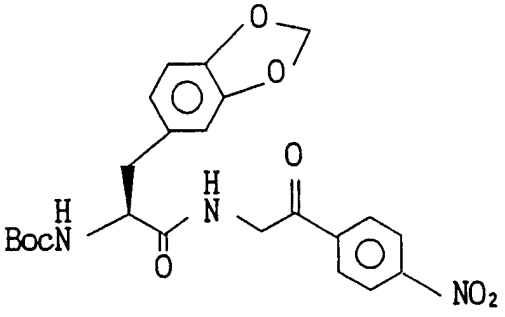
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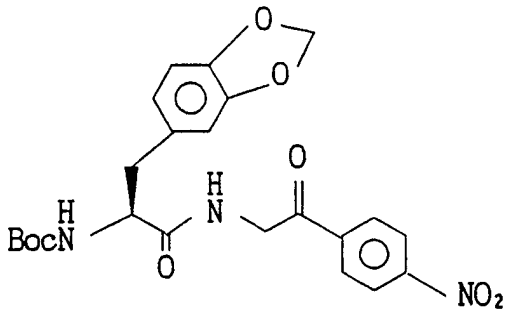
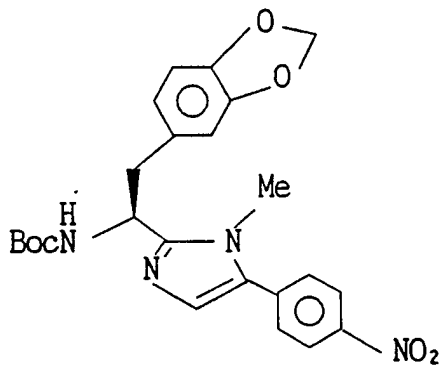
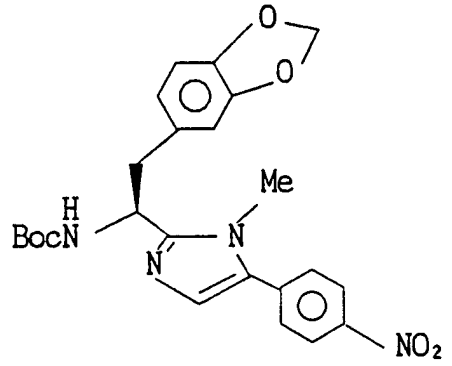
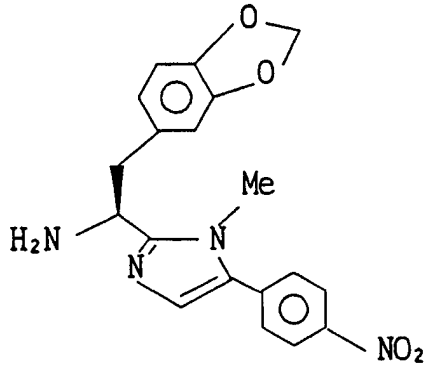
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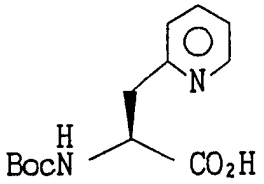
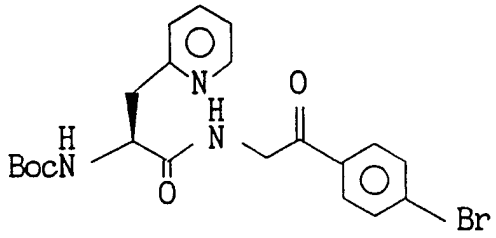
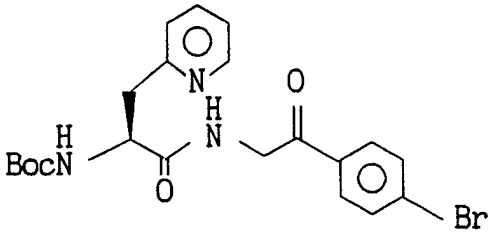
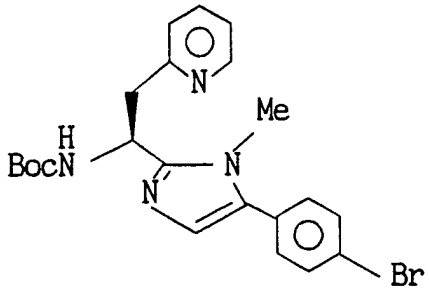
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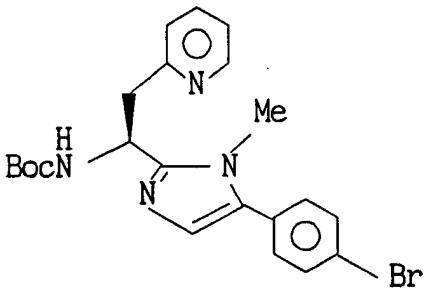
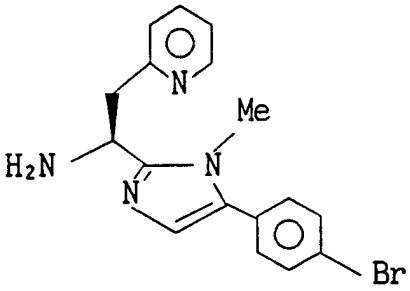
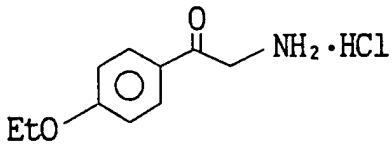
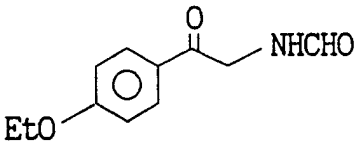
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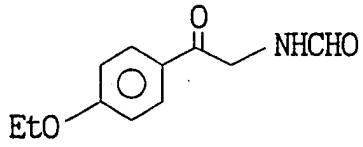
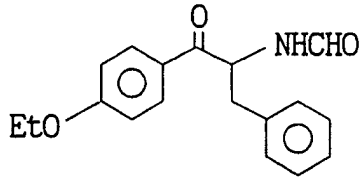
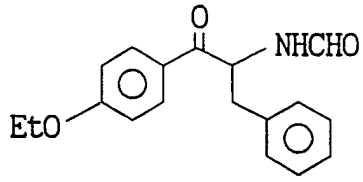
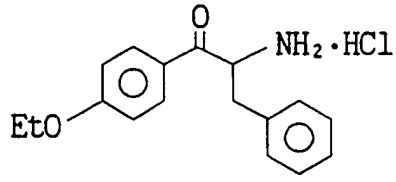
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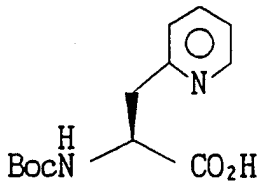
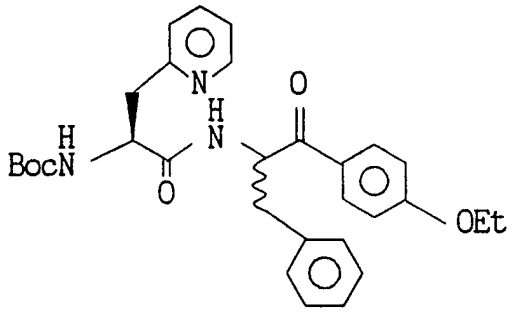
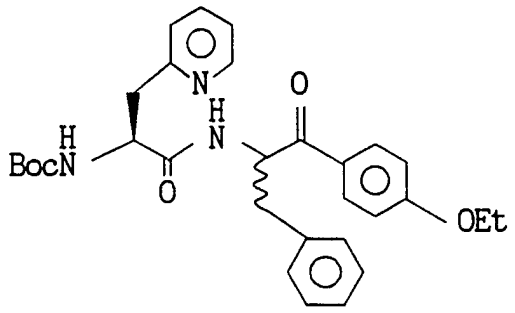
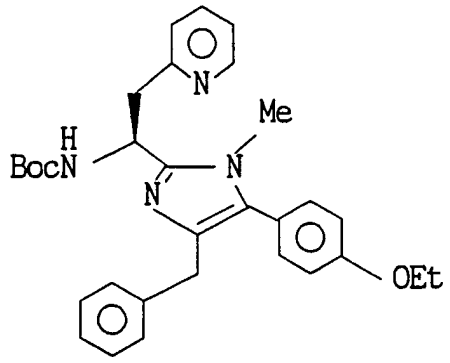
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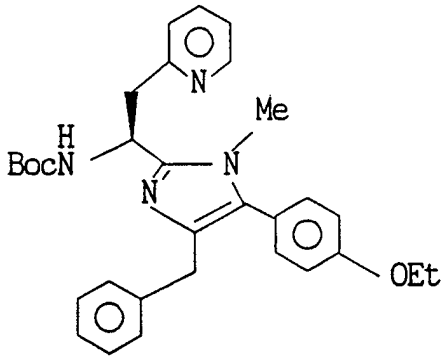
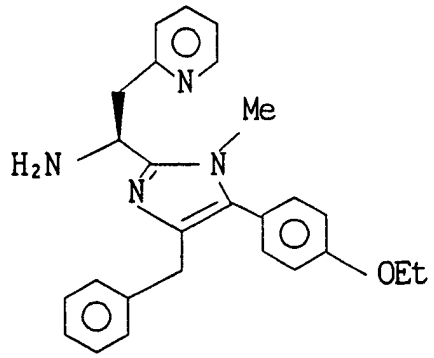
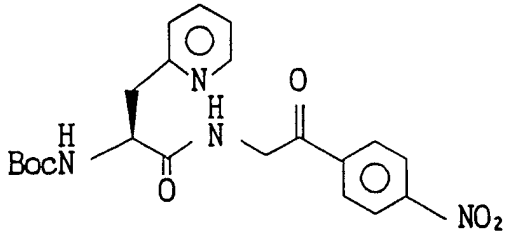
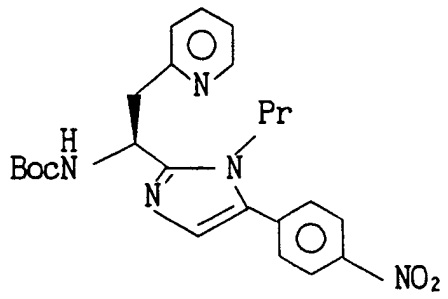
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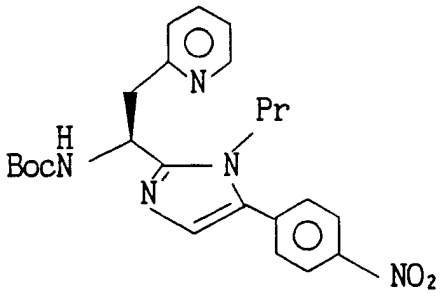
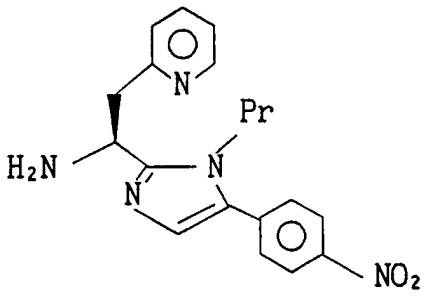
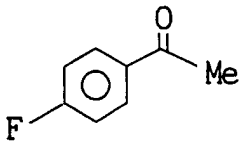
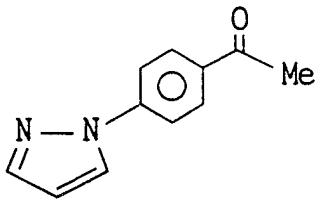
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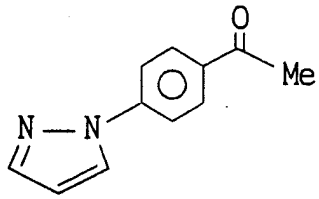
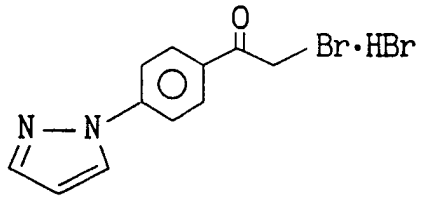
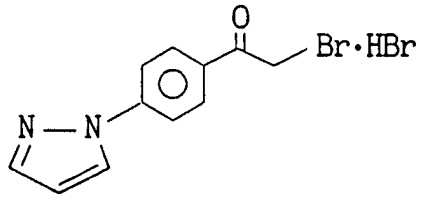
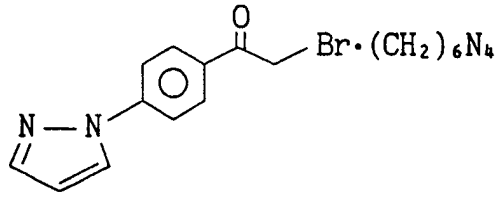
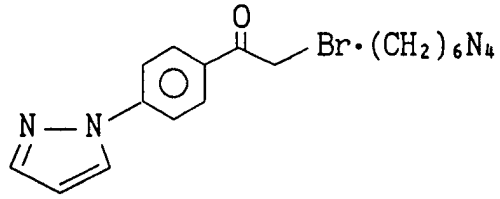
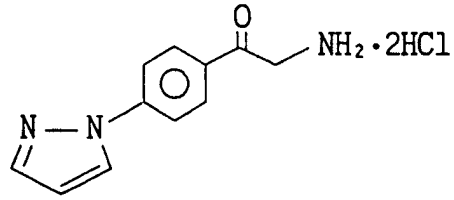
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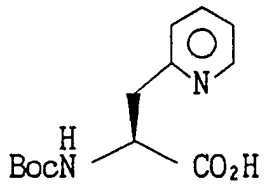
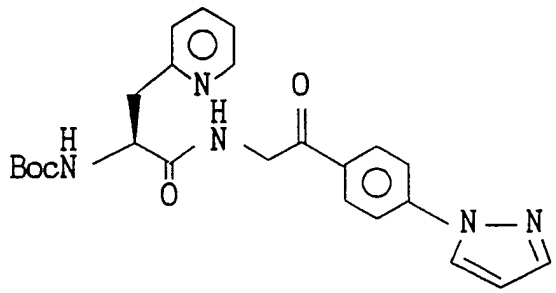
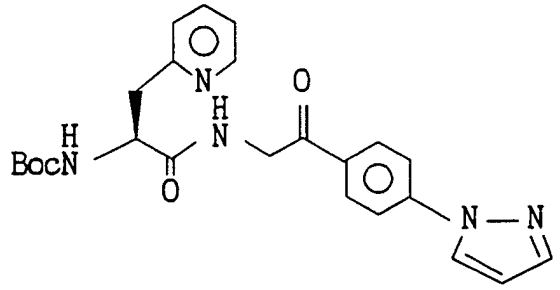
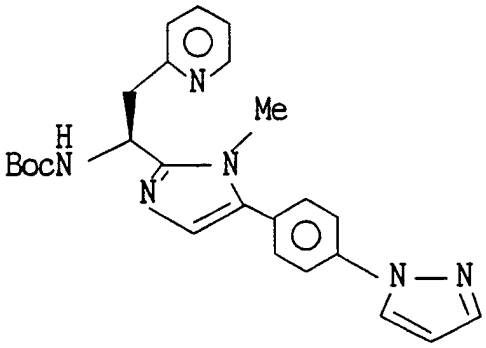
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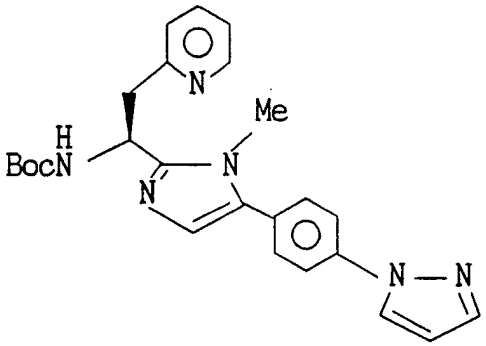
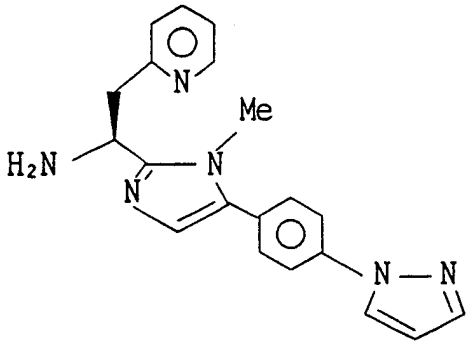
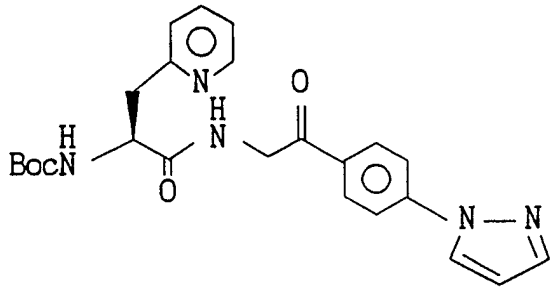
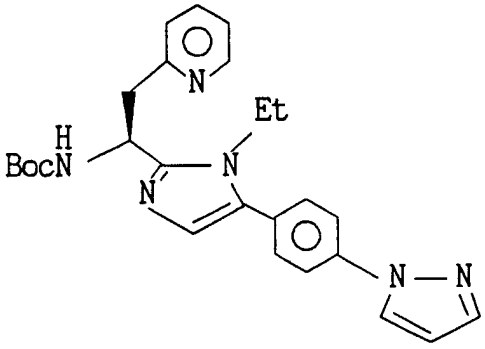
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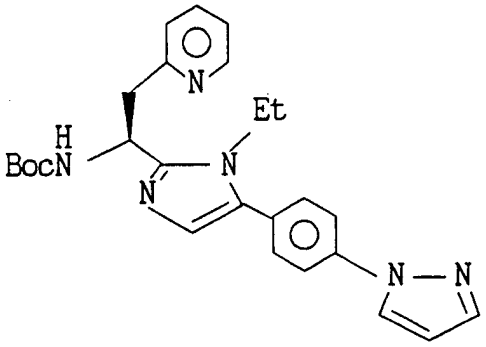
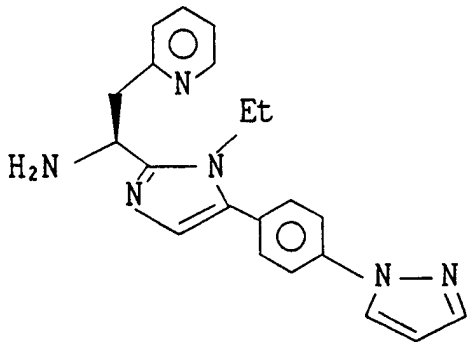
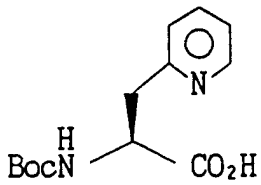
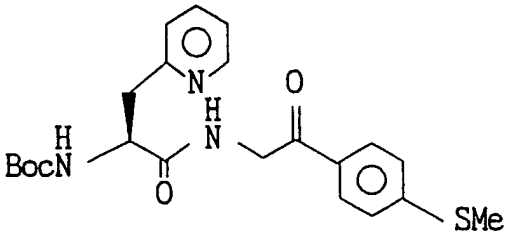
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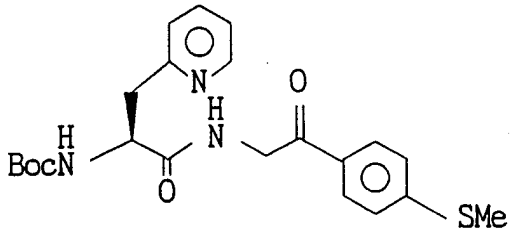
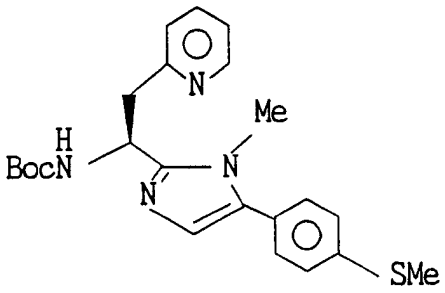
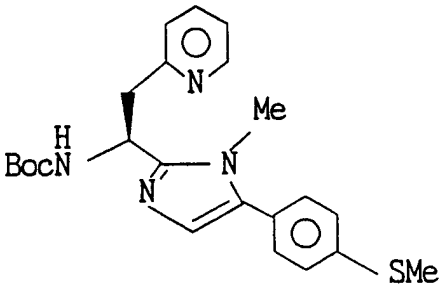
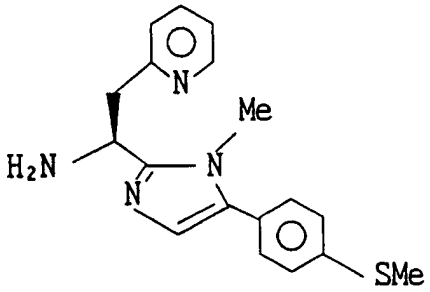
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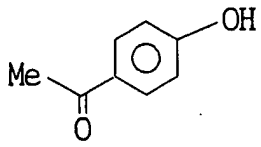
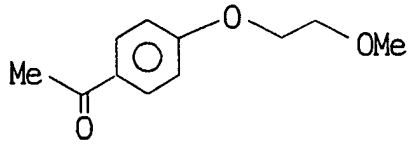
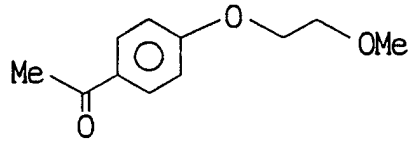
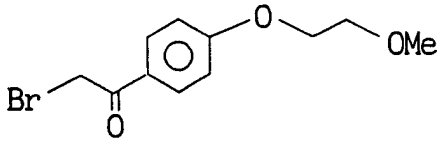
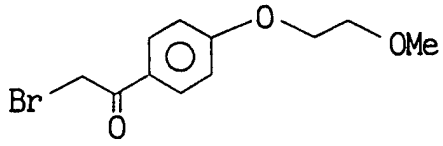
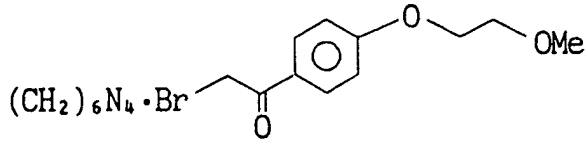
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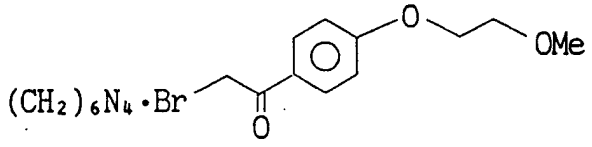
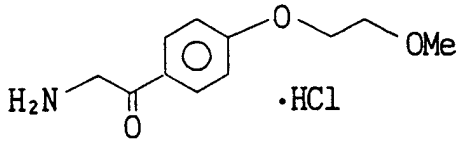
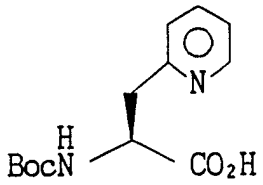
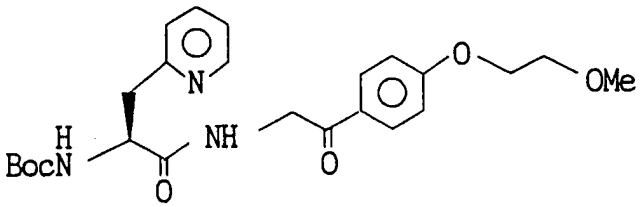
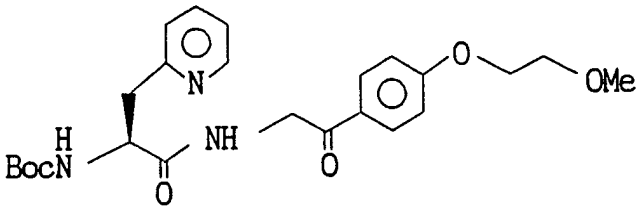
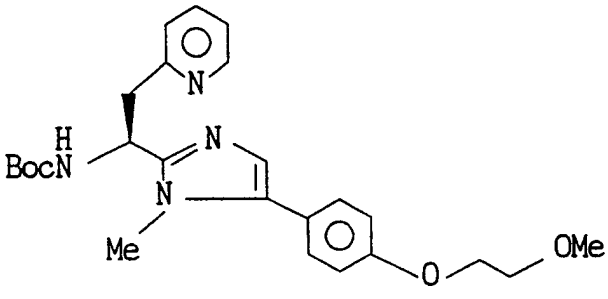
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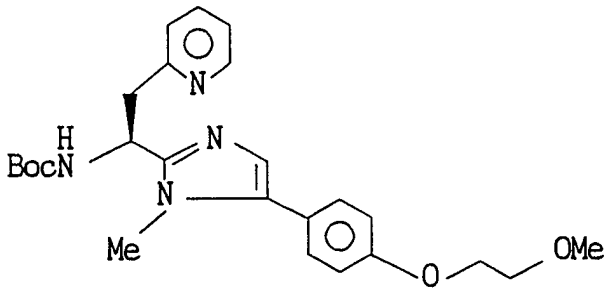
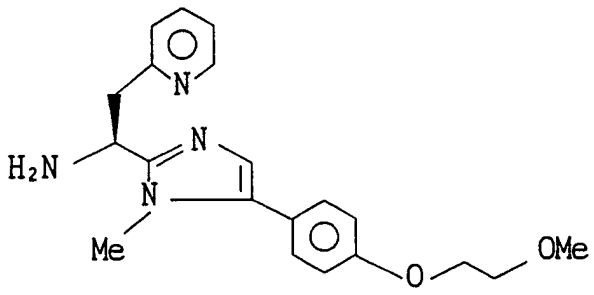
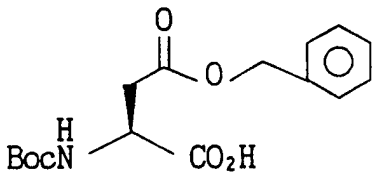
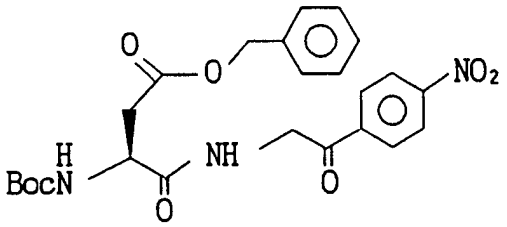
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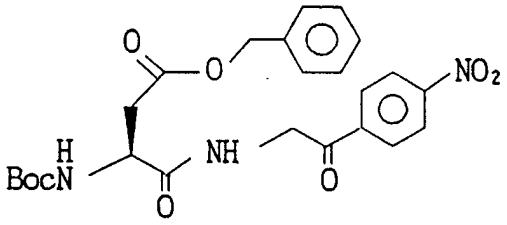
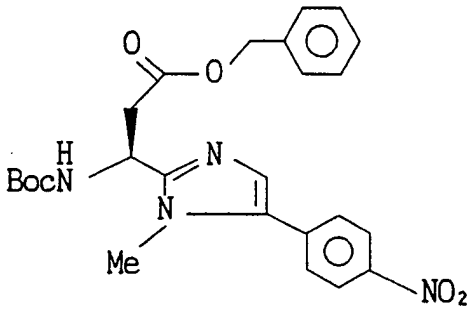
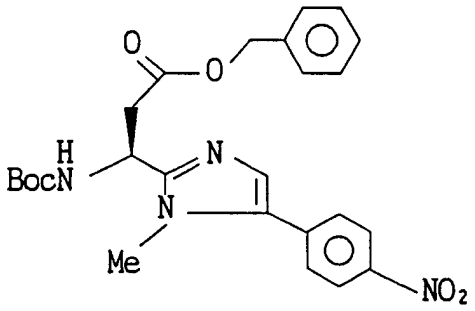
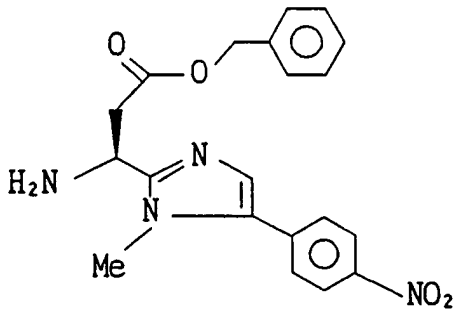
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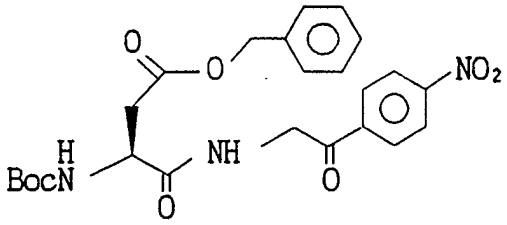
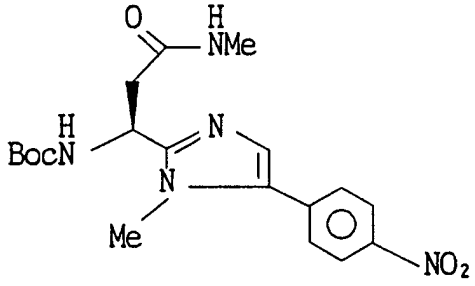
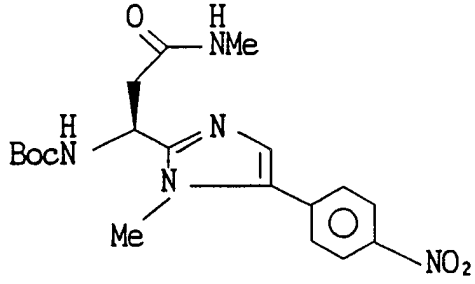
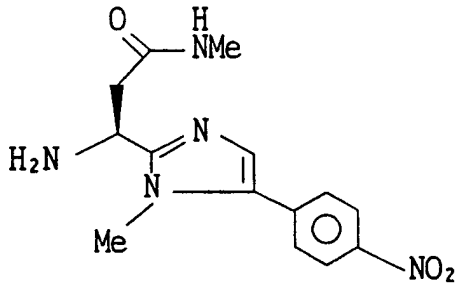
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Preparation No.	Formula
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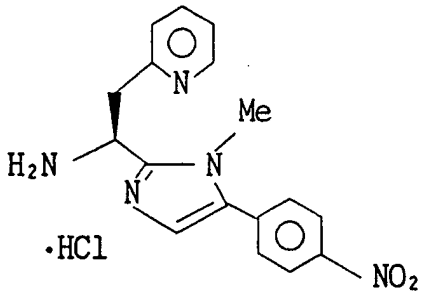
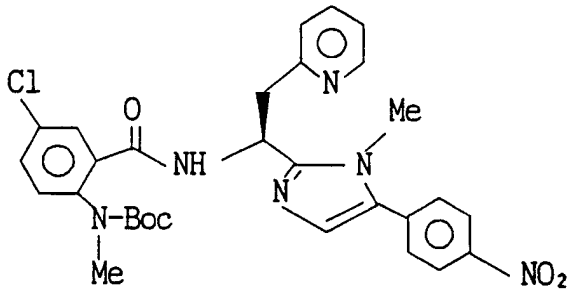
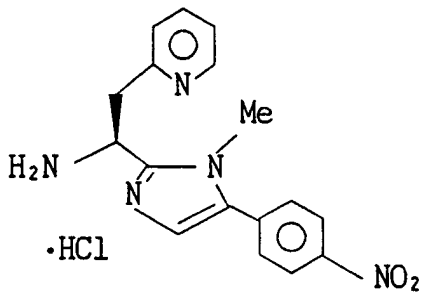
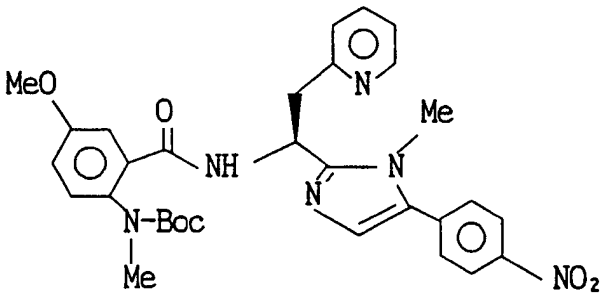
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Preparation No.	Formula
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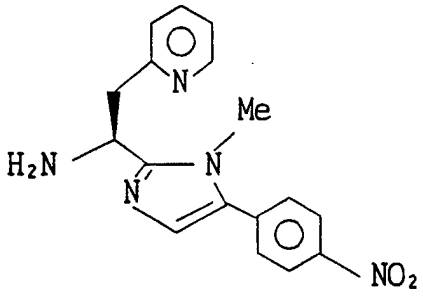
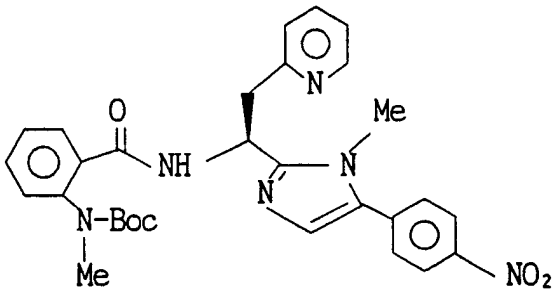
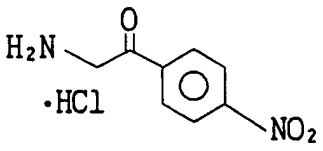
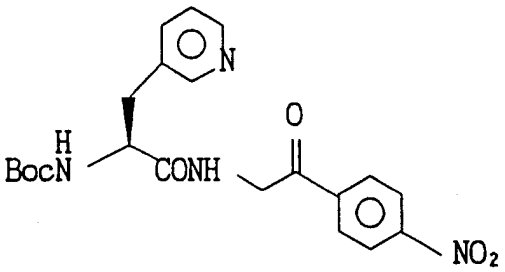
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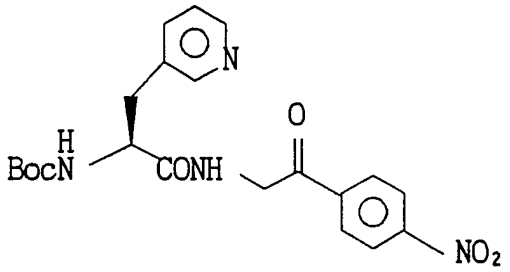
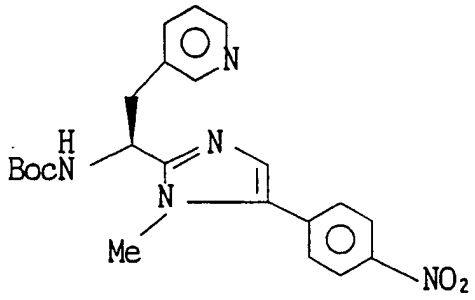
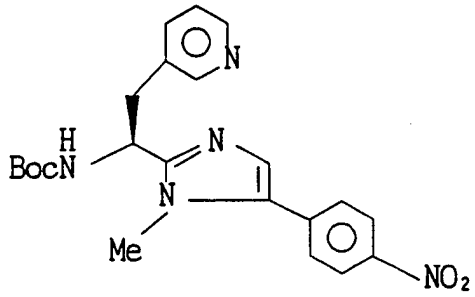
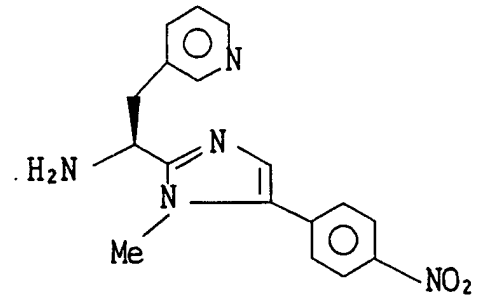
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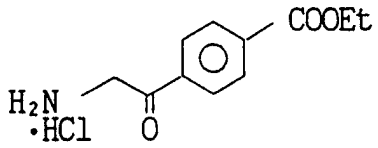
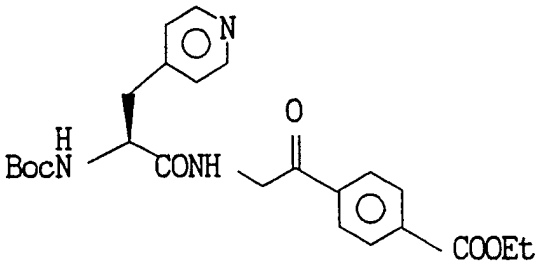
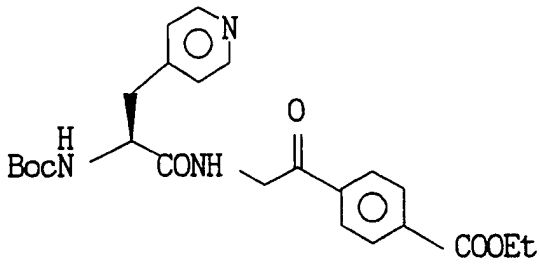
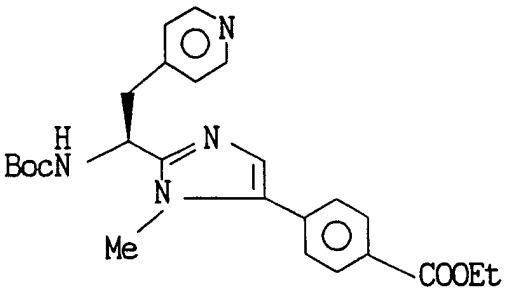
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Preparation No.	Formula
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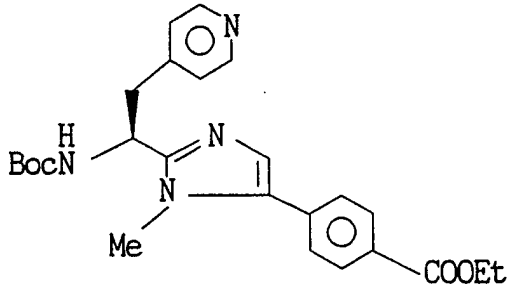
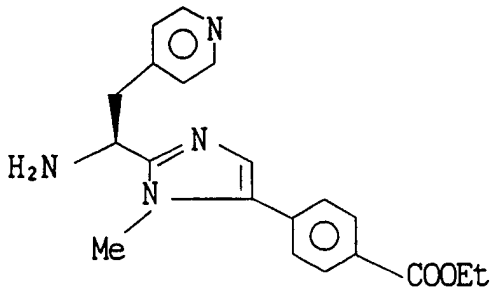
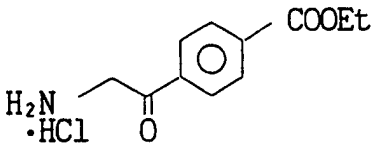
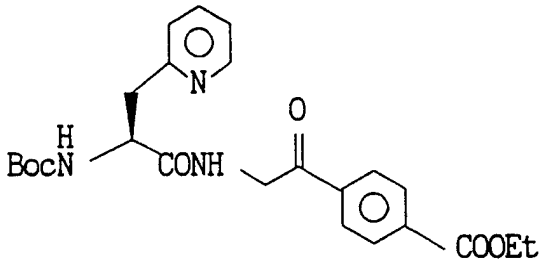
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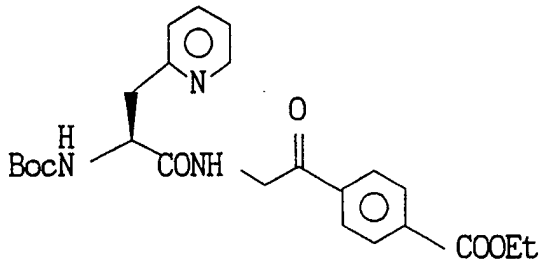
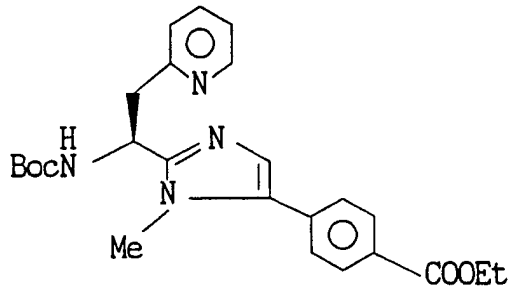
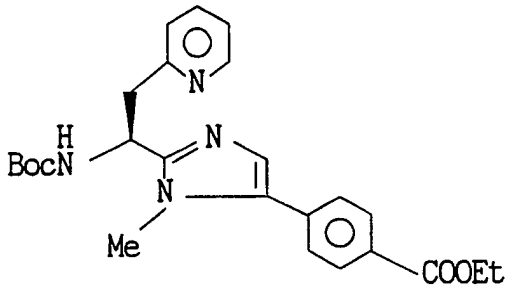
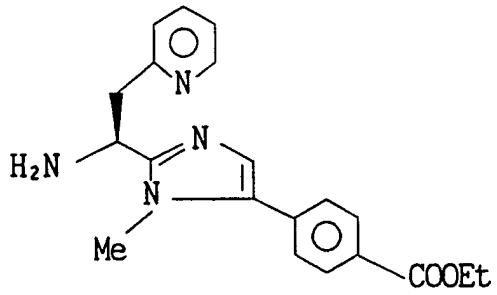
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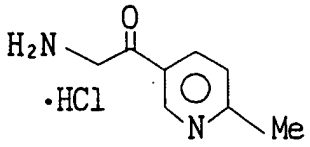
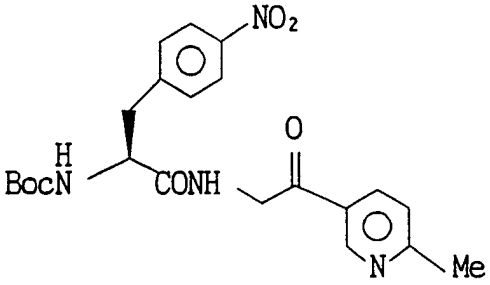
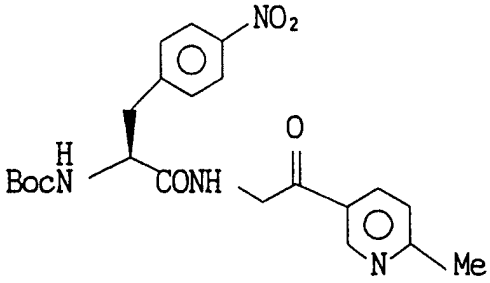
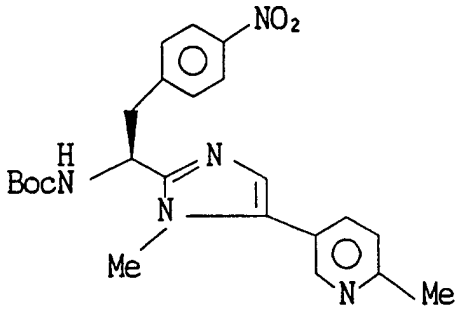
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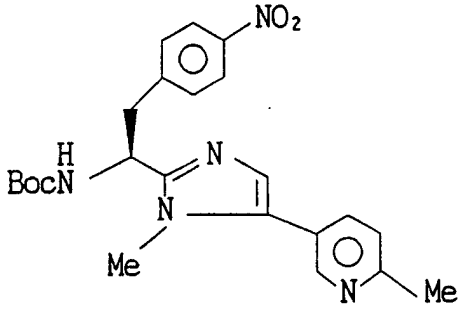
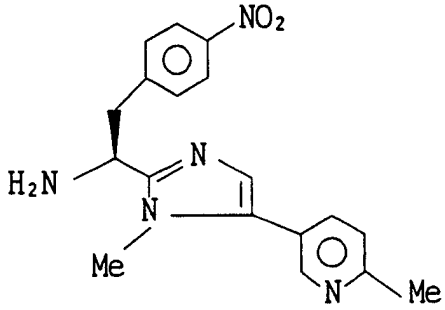
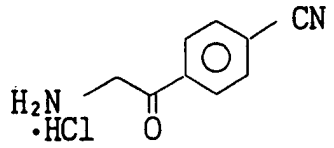
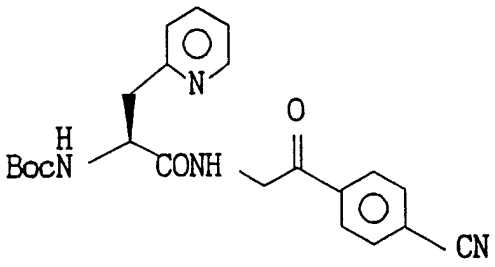
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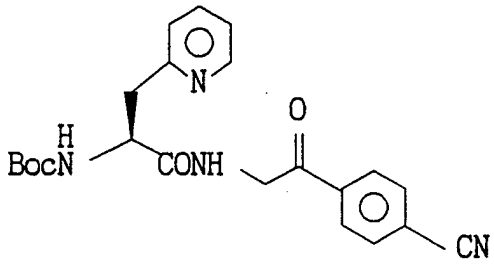
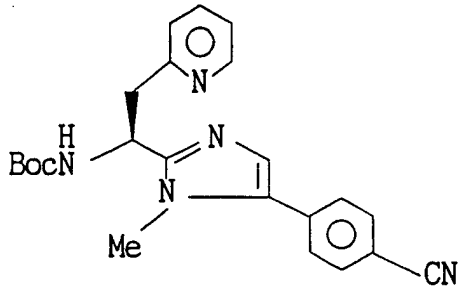
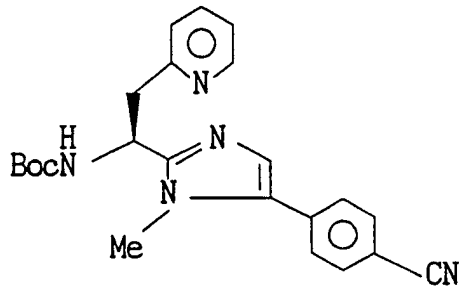
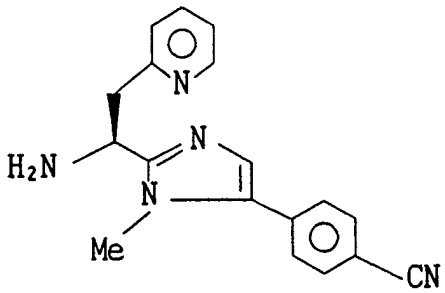
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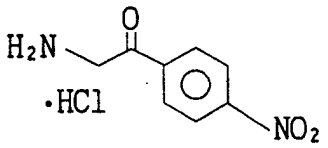
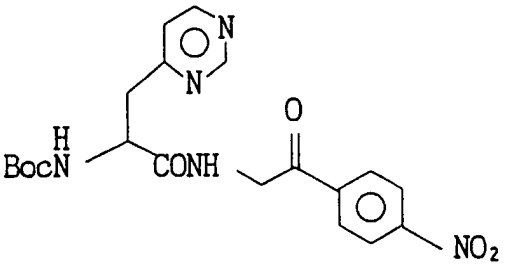
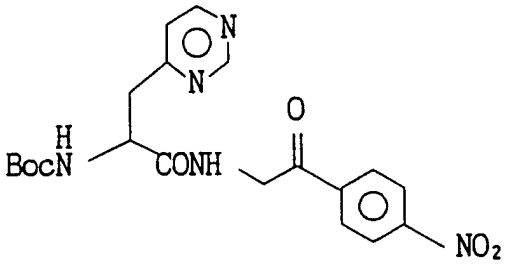
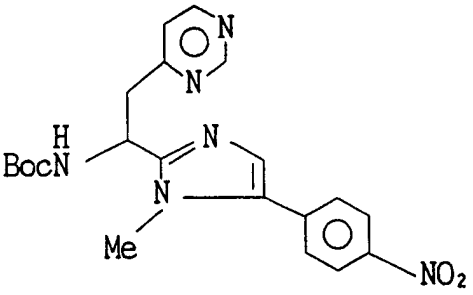
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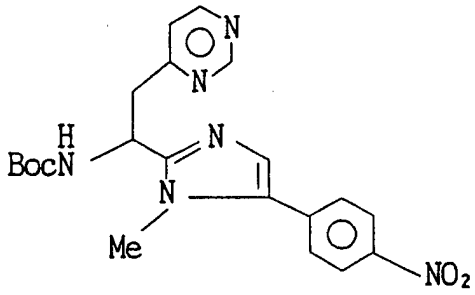
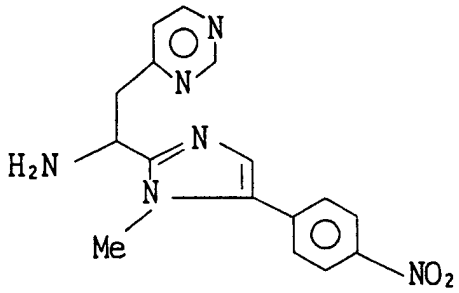
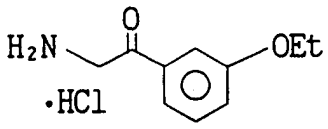
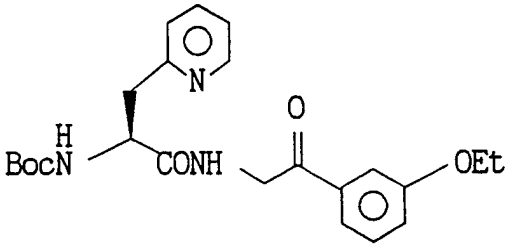
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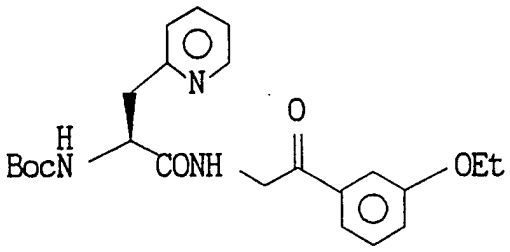
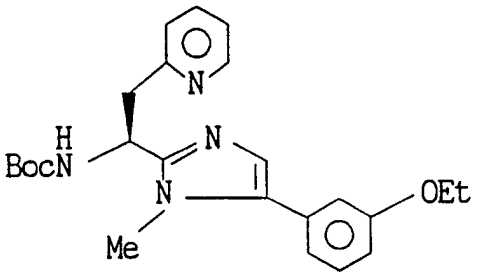
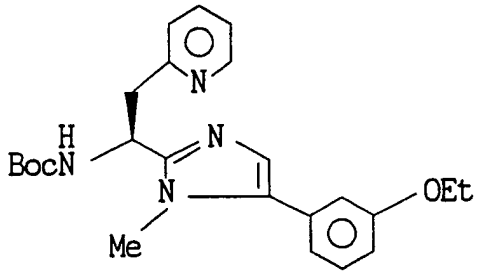
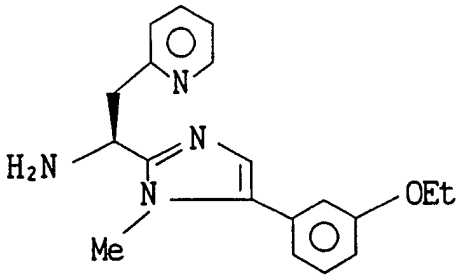
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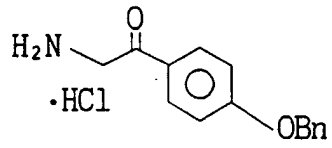
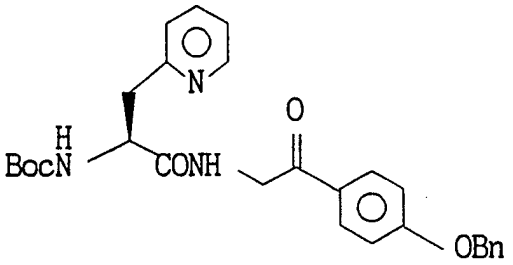
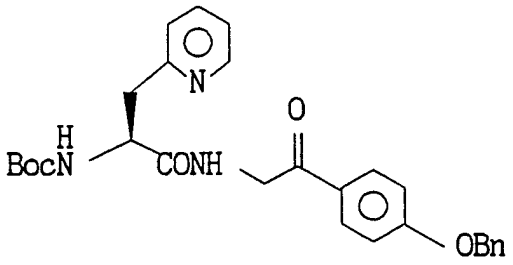
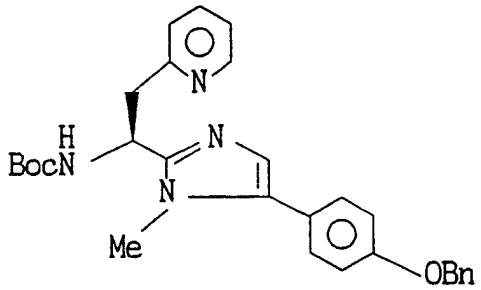
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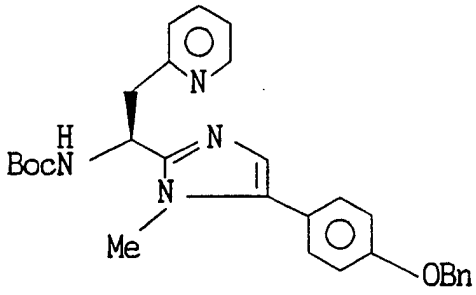
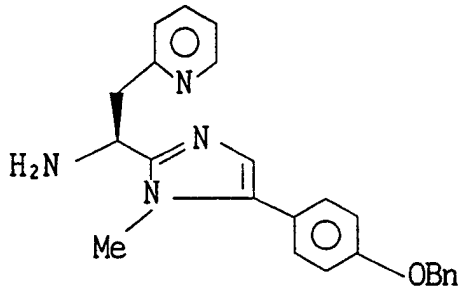
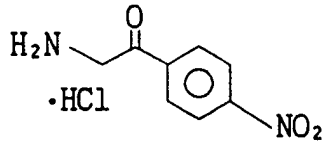
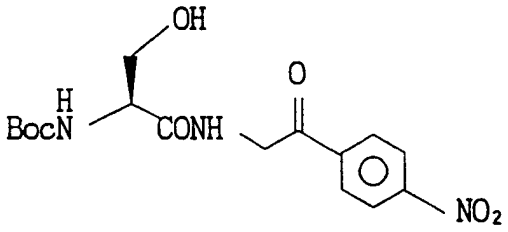
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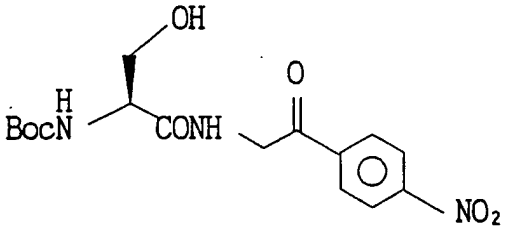
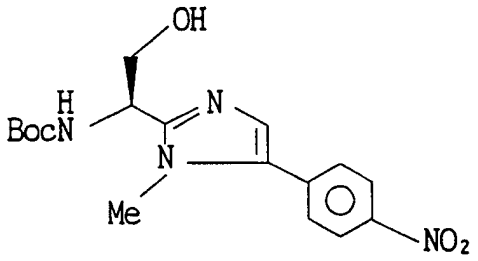
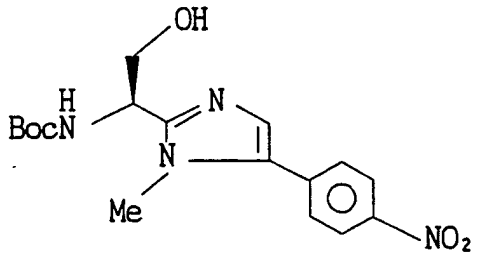
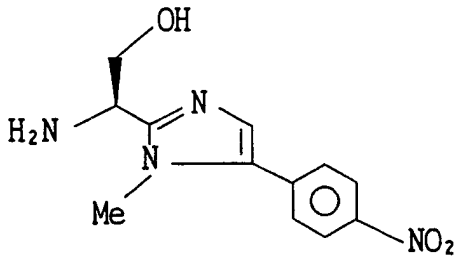
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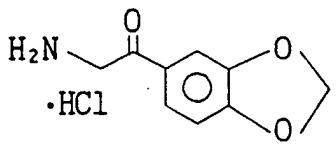
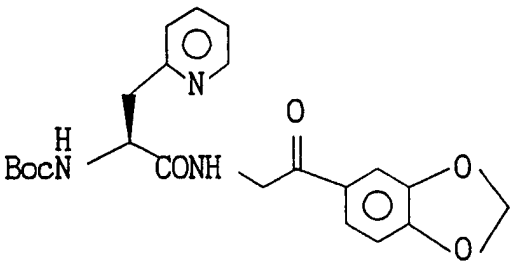
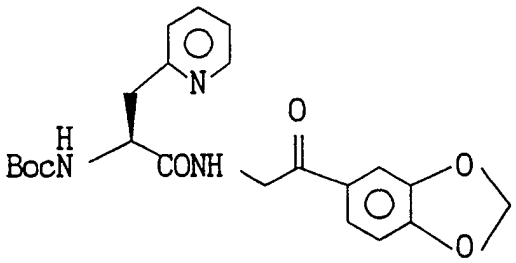
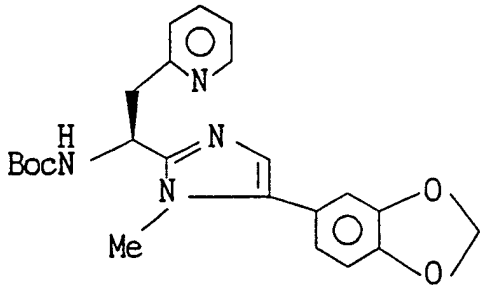
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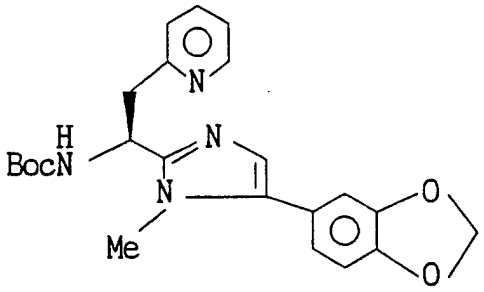
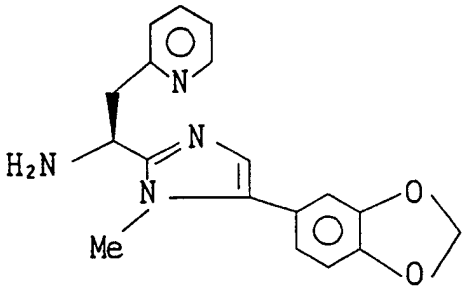
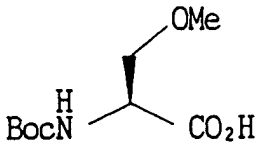
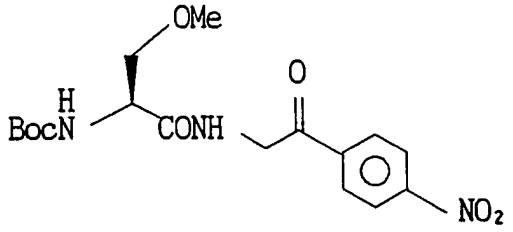
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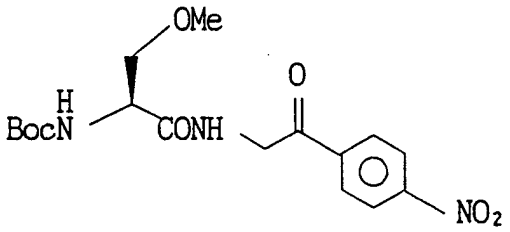
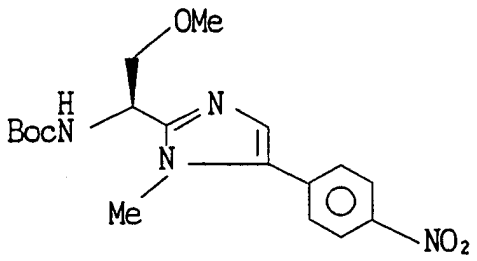
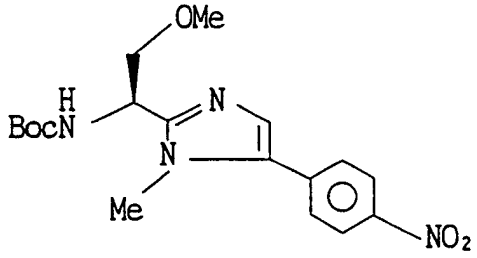
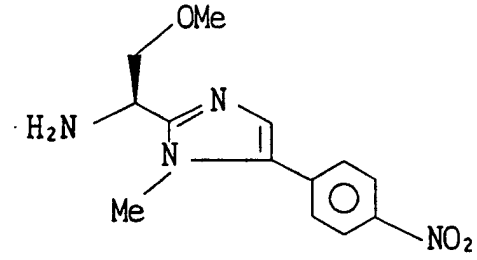
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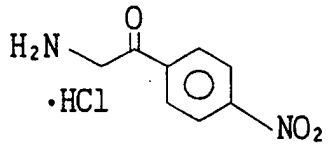
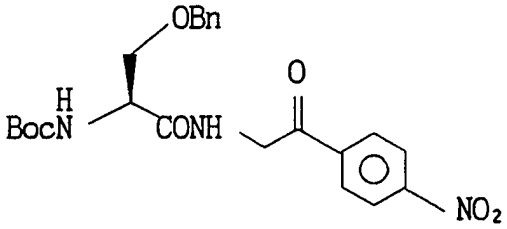
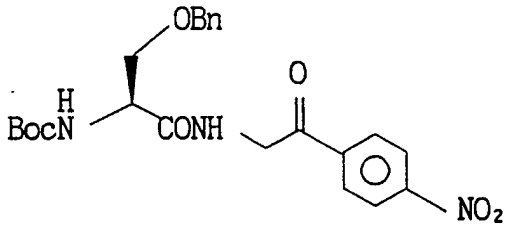
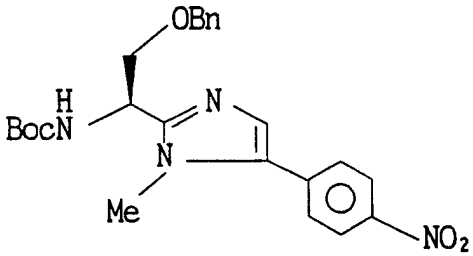
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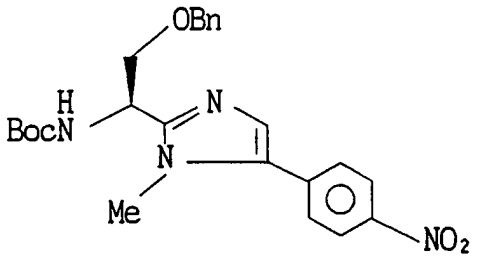
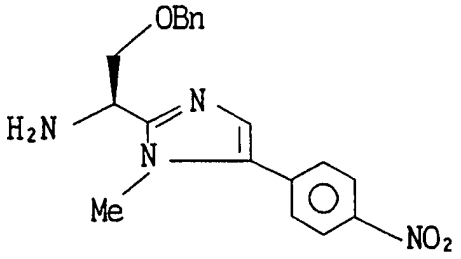
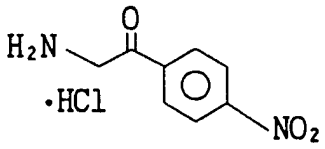
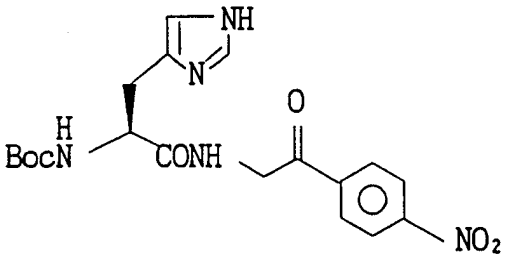
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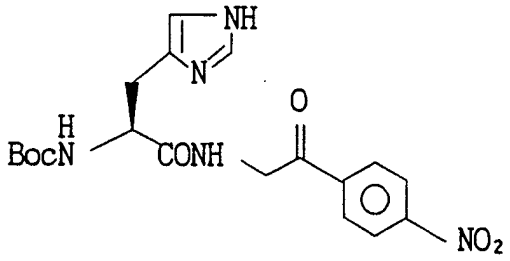
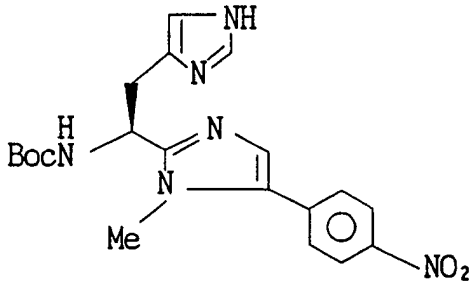
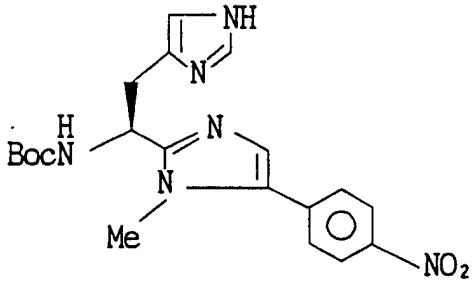
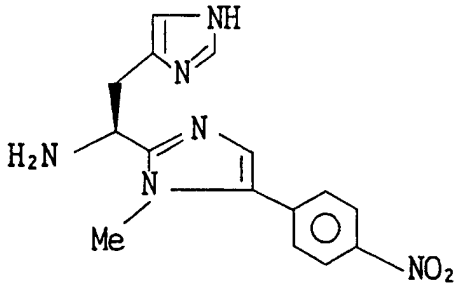
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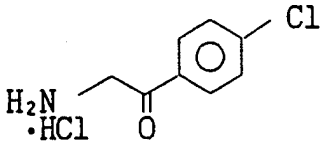
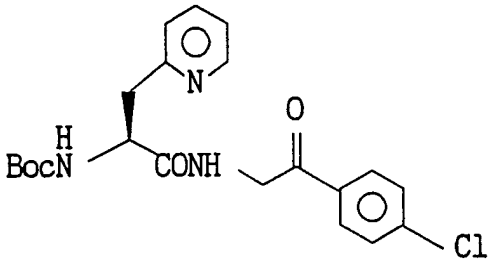
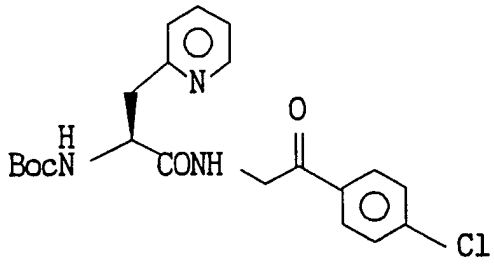
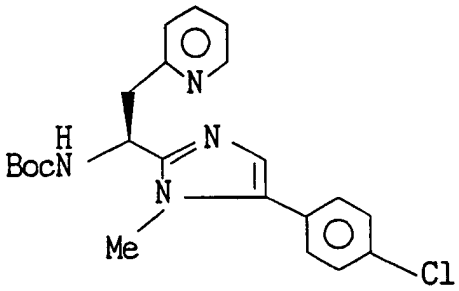
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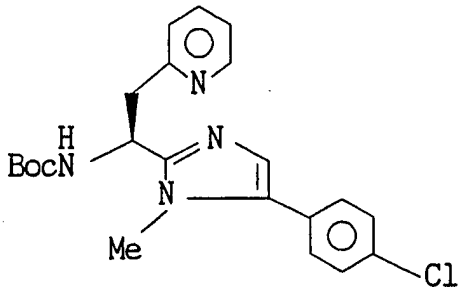
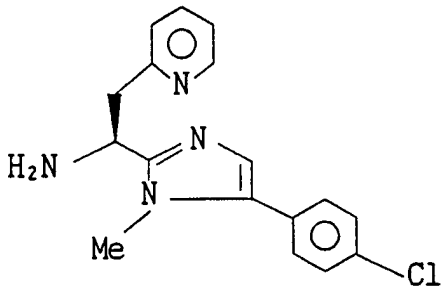
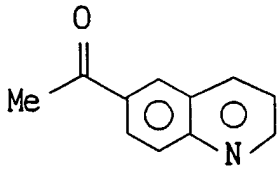
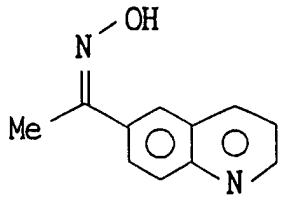
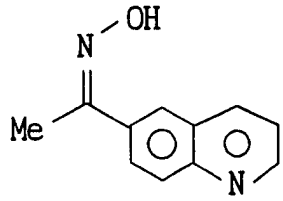
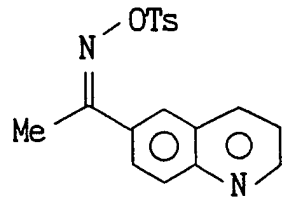
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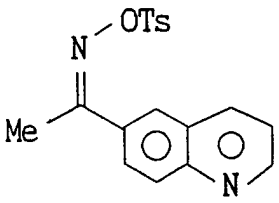
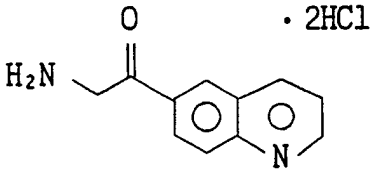
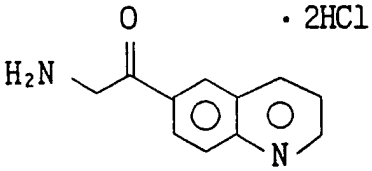
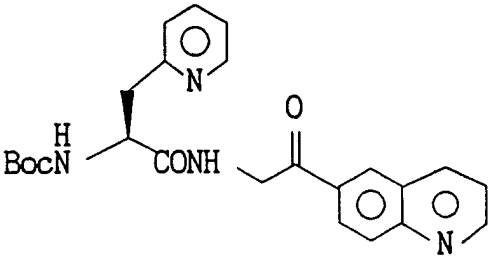
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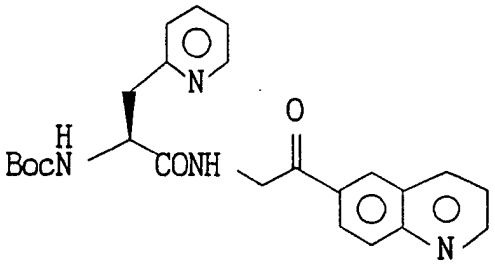
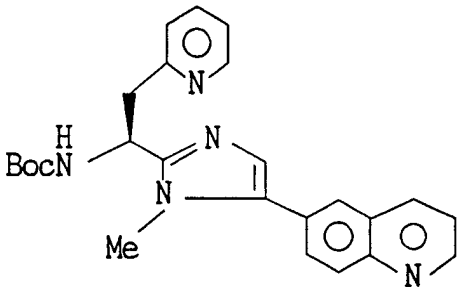
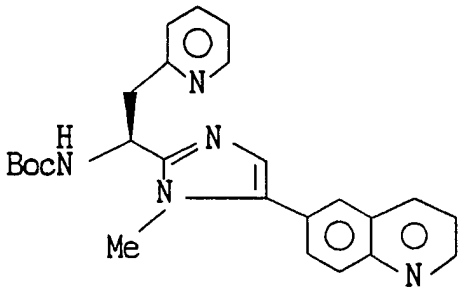
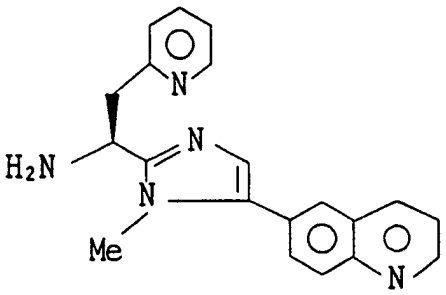
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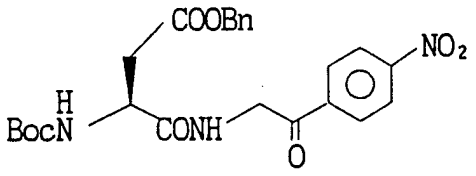
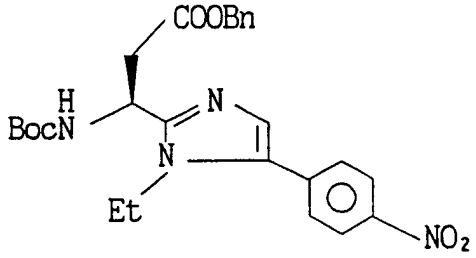
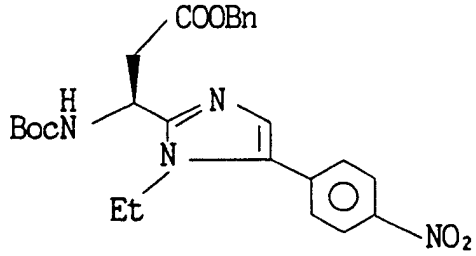
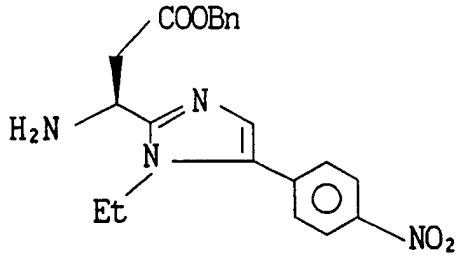
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Preparation No.	Formula
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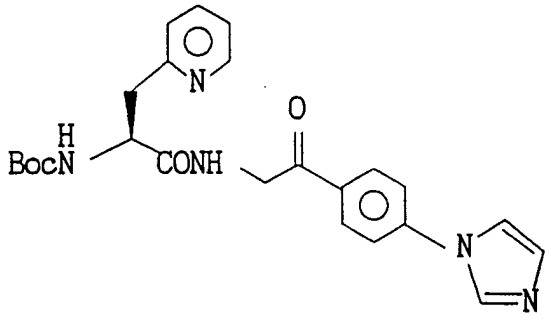
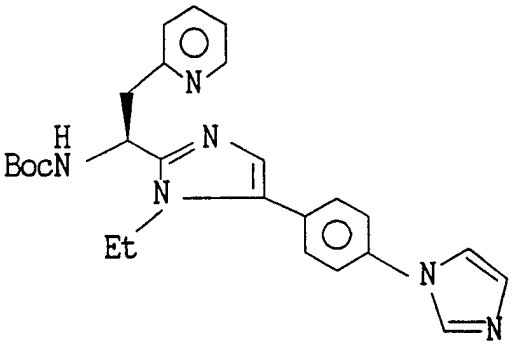
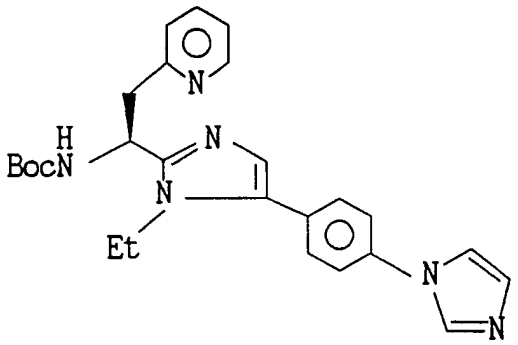
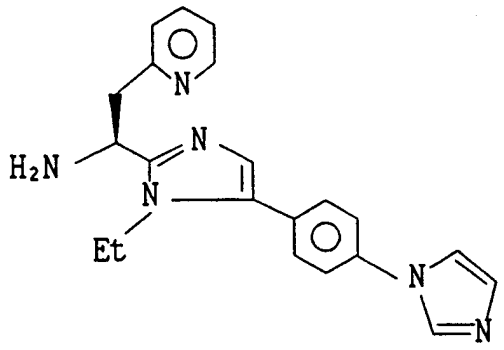
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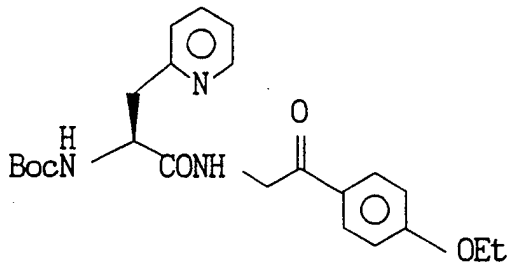
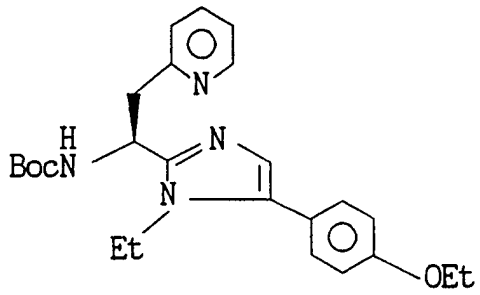
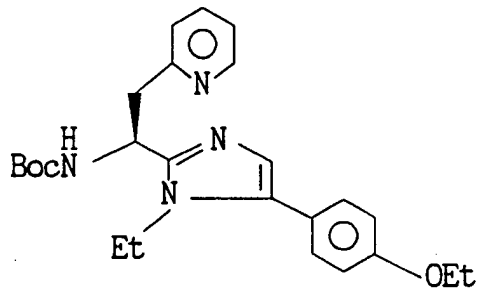
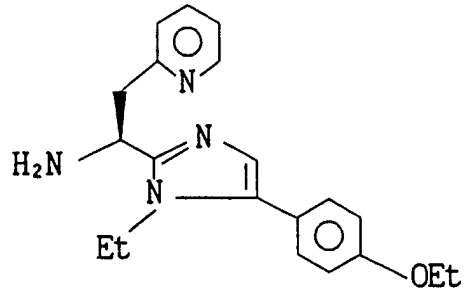
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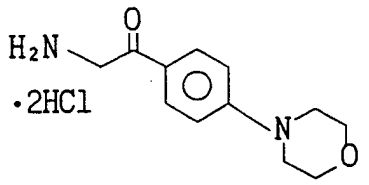
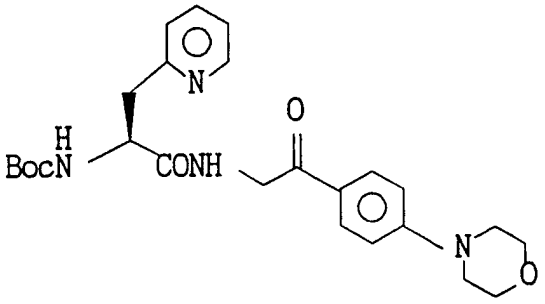
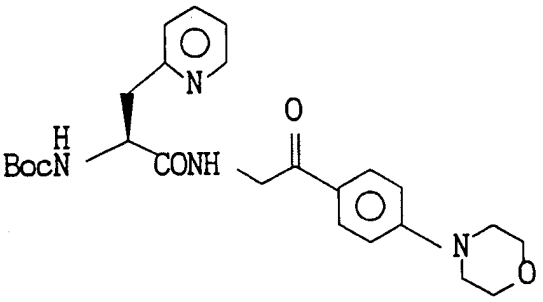
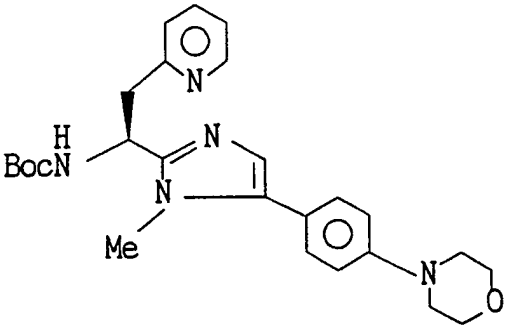
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Preparation No.	Formula
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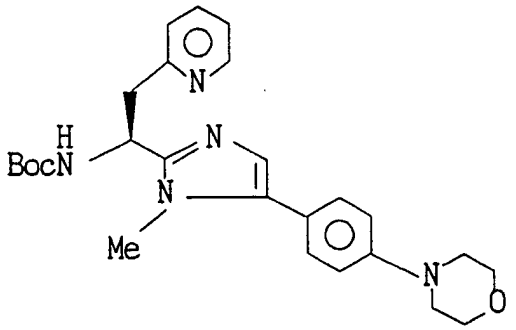
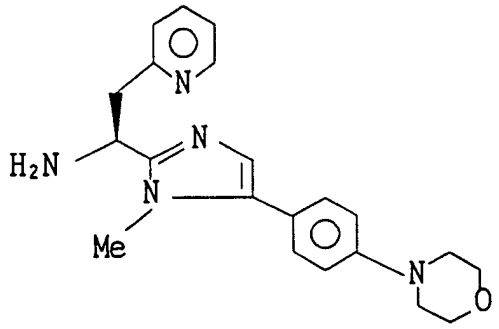
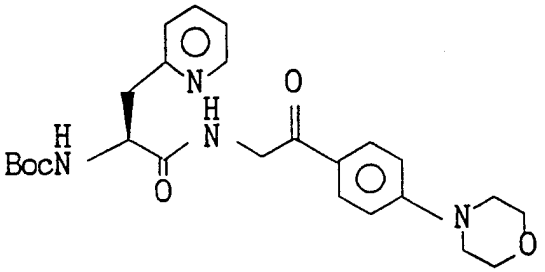
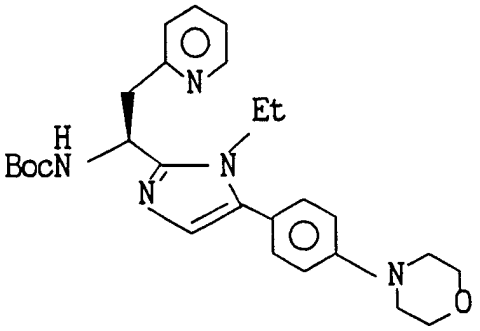
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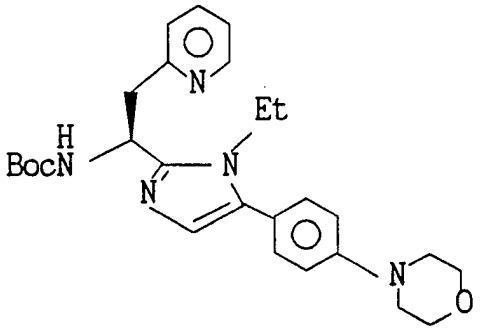
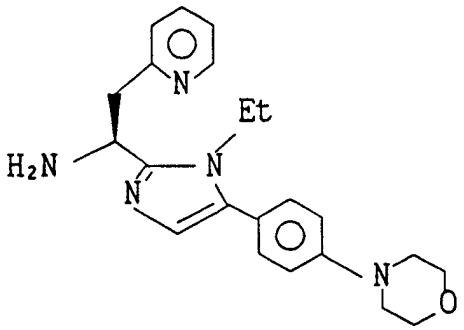
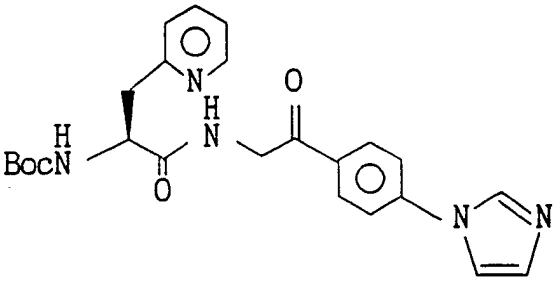
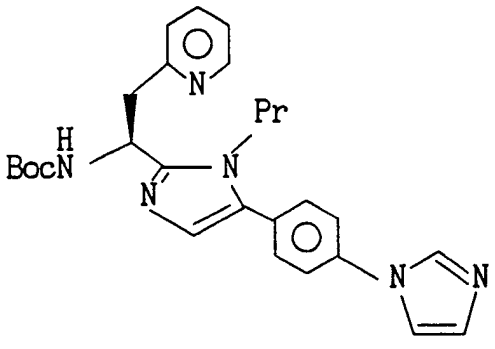
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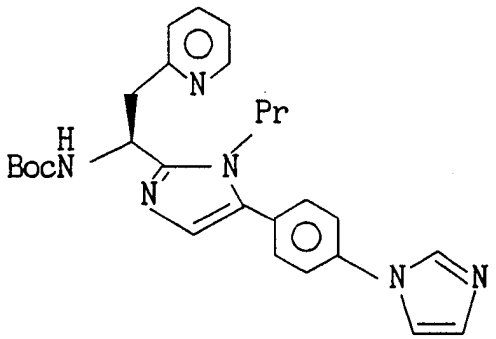
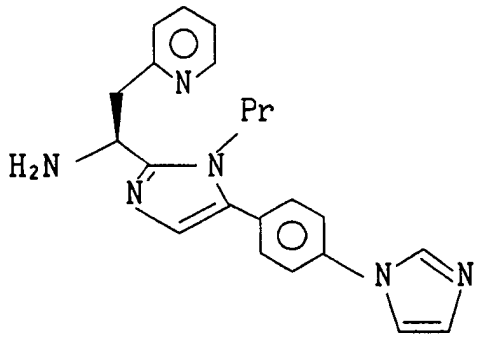
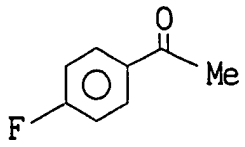
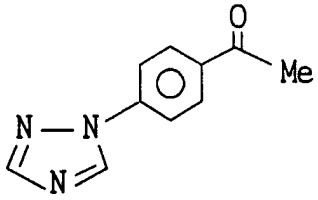
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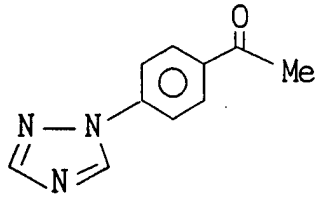
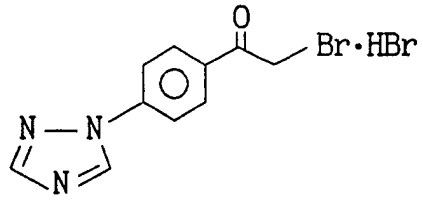
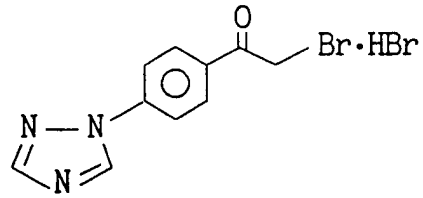
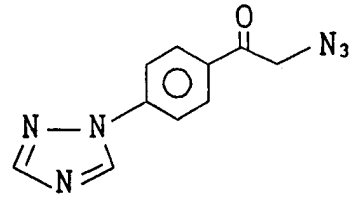
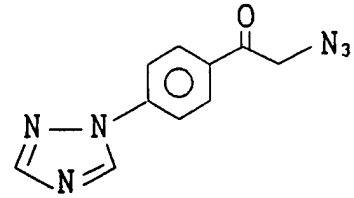
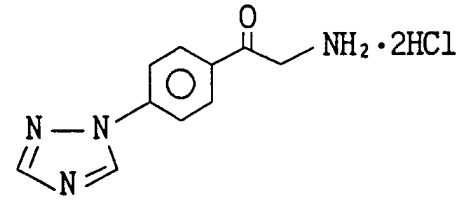
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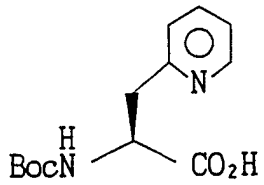
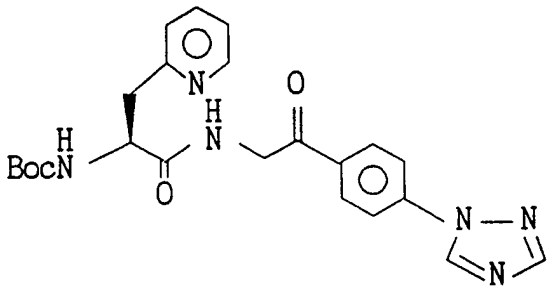
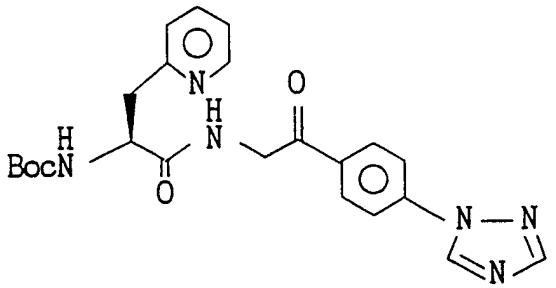
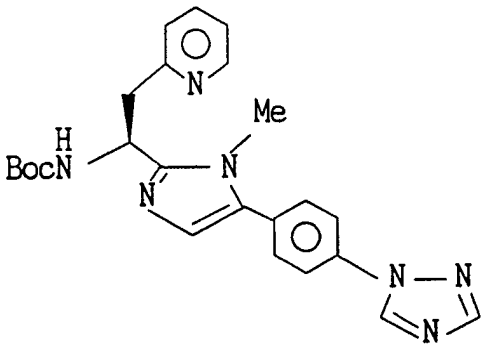
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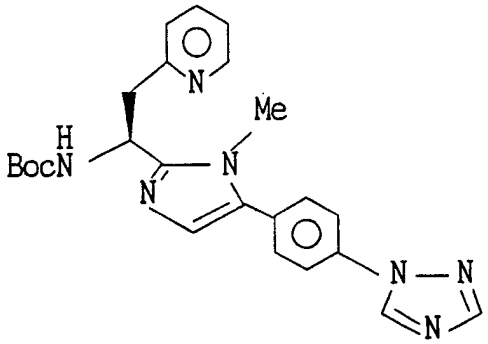
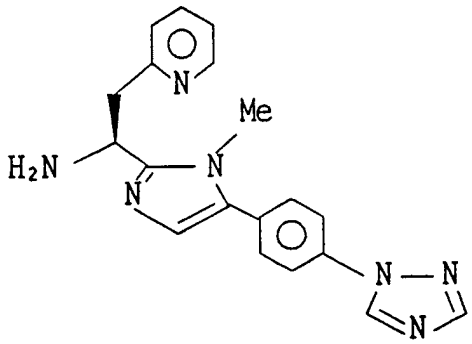
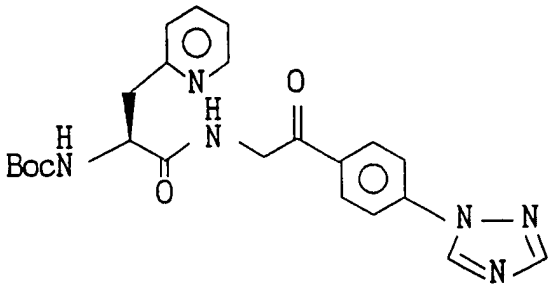
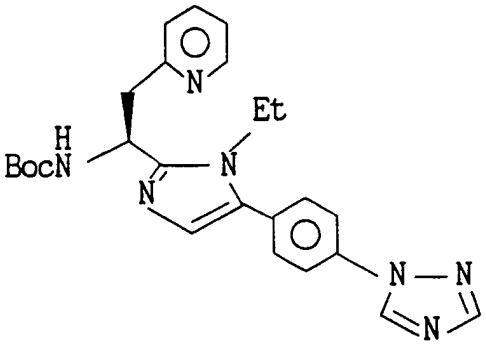
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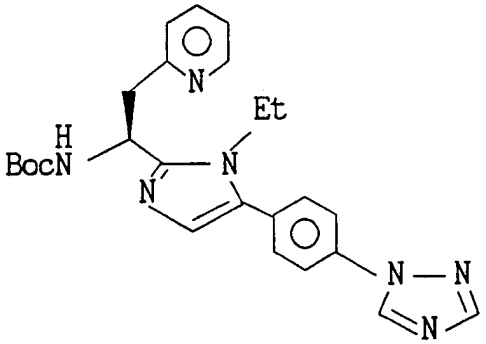
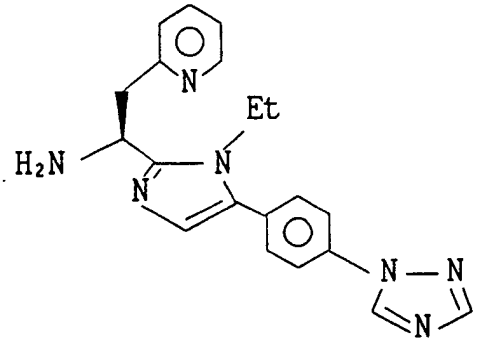
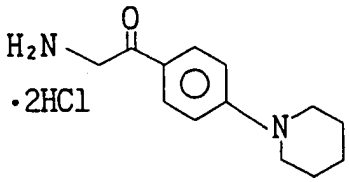
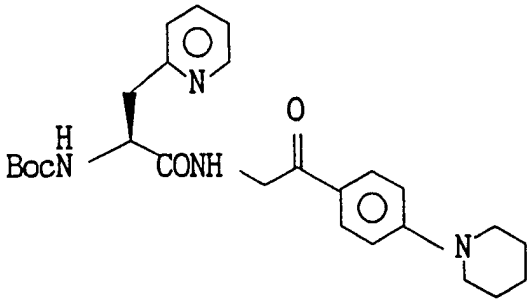
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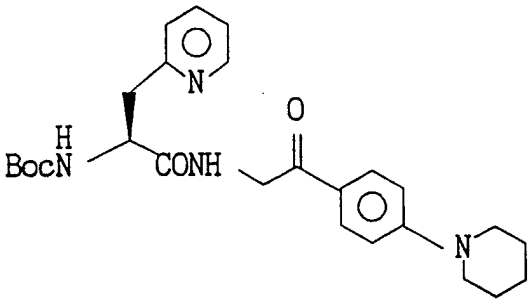
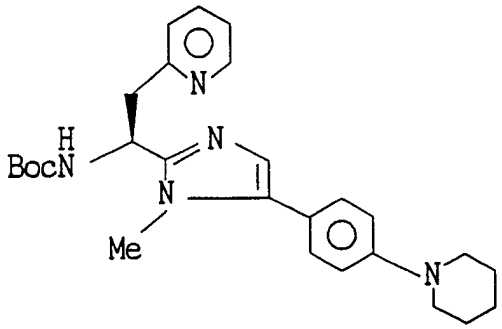
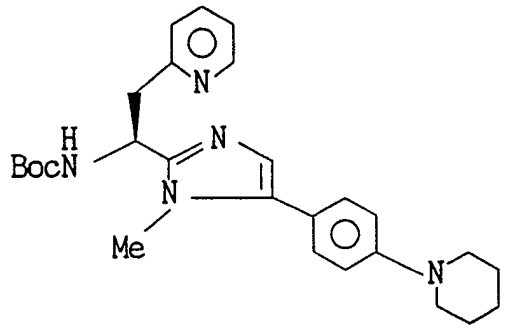
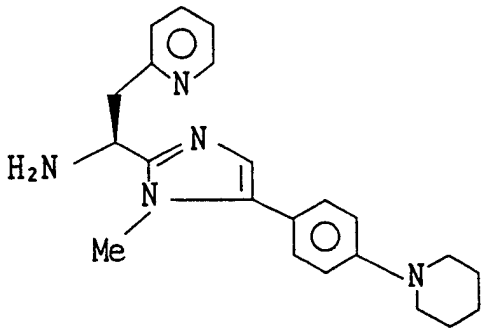
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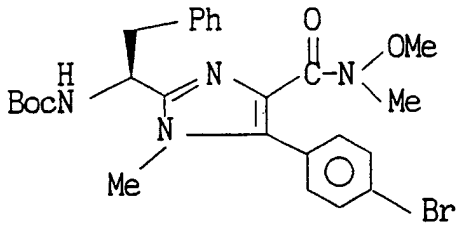
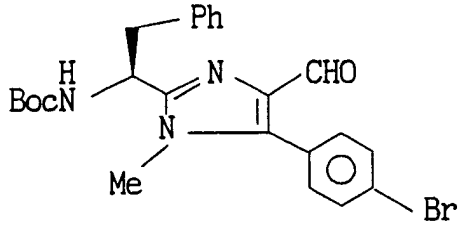
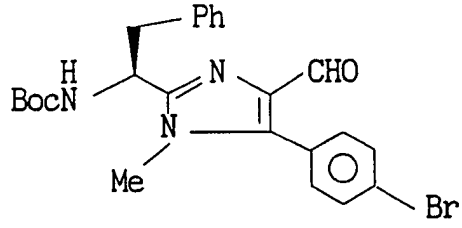
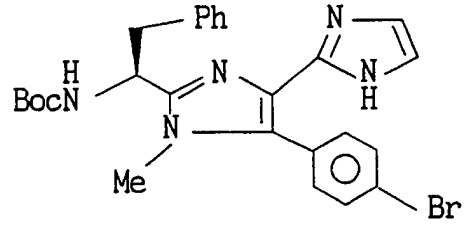
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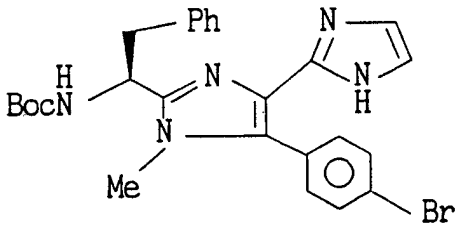
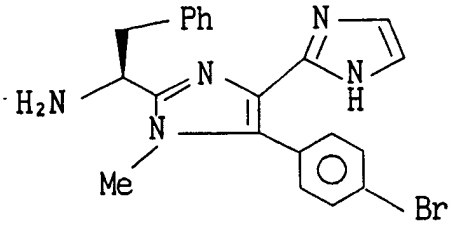
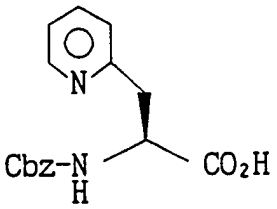
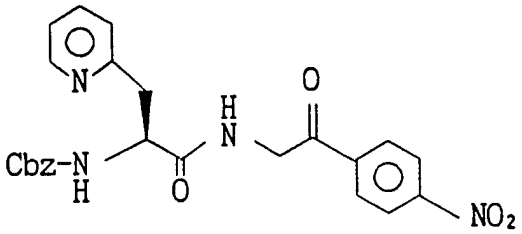
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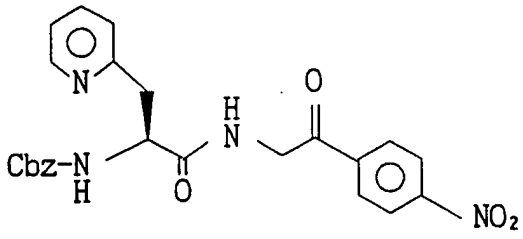
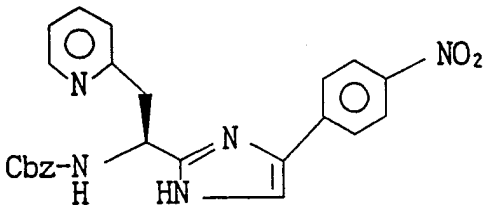
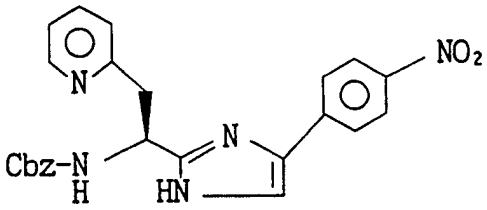
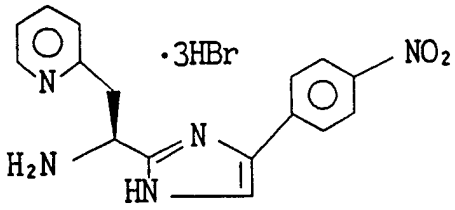
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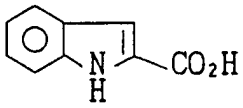
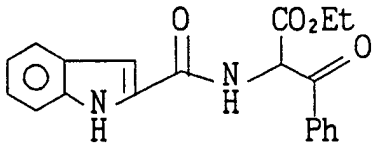
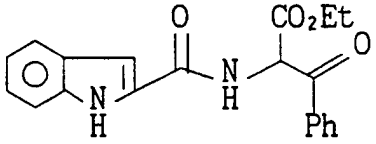
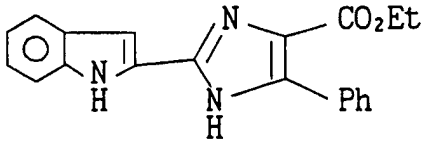
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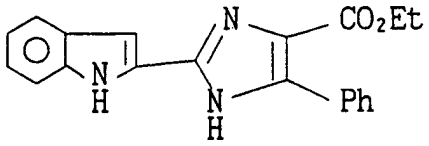
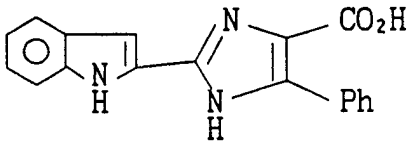
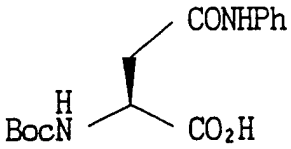
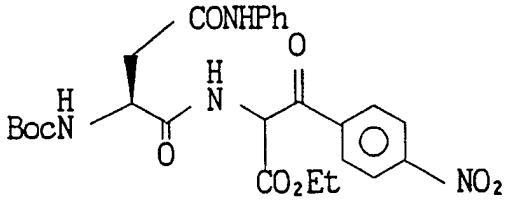
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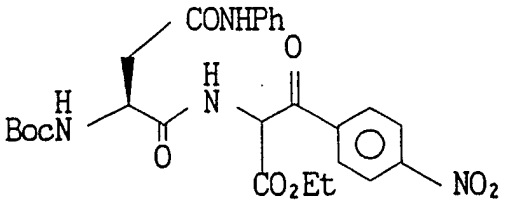
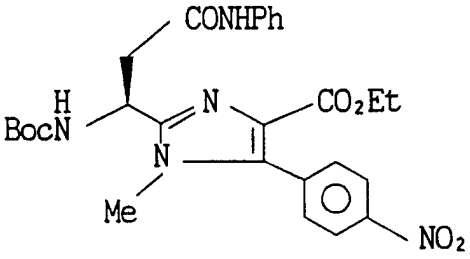
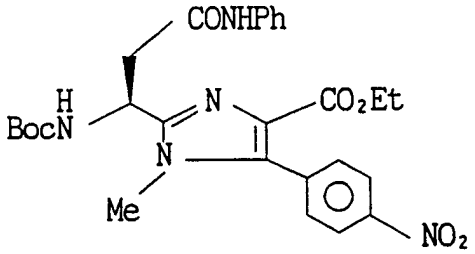
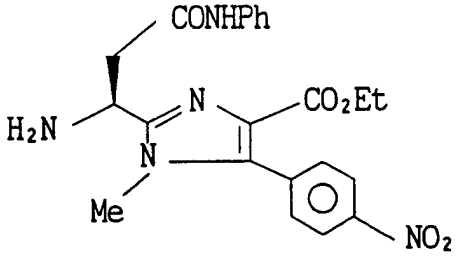
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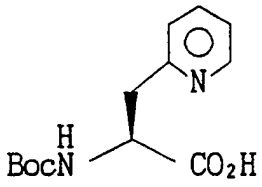
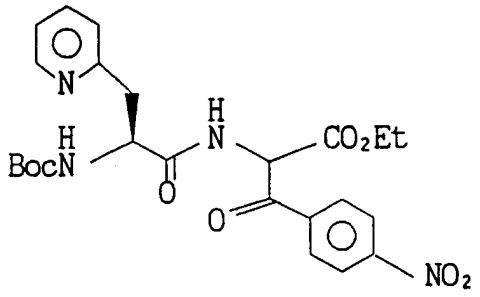
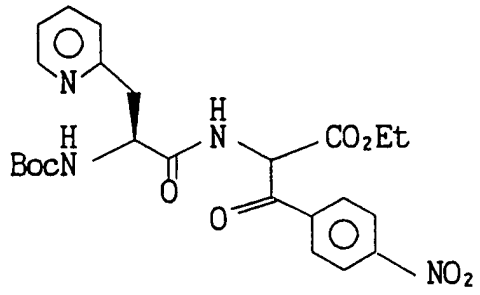
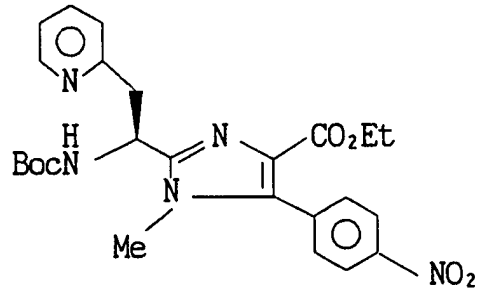
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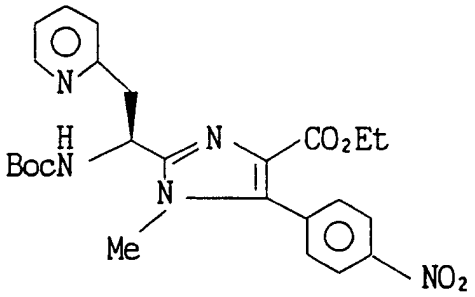
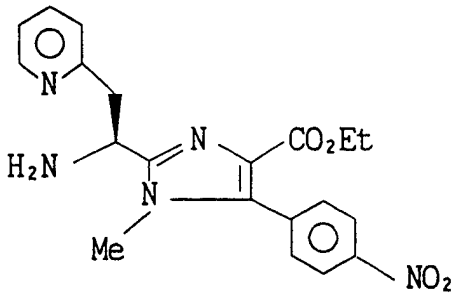
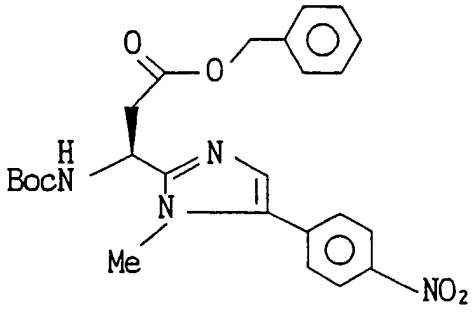
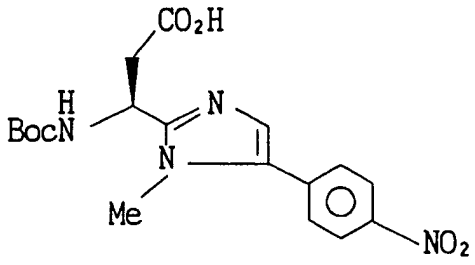
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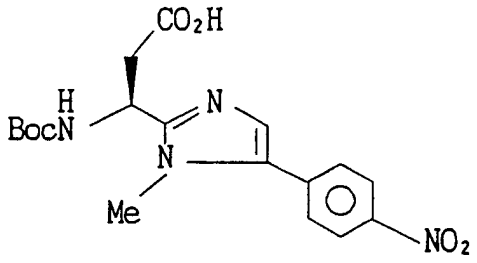
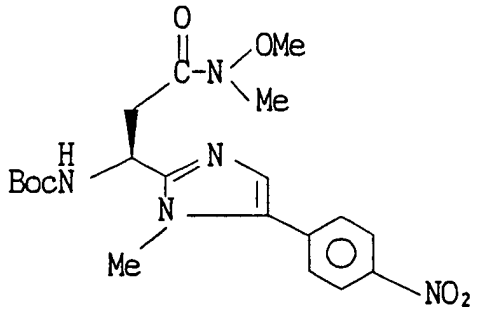
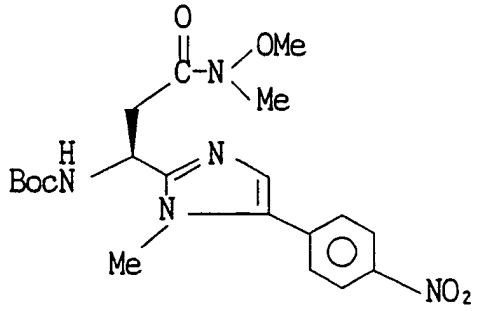
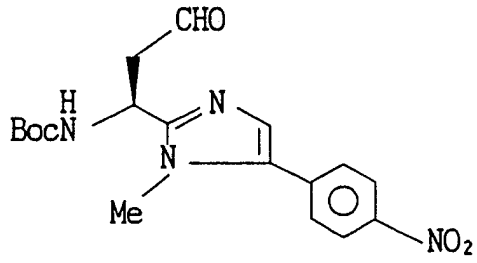
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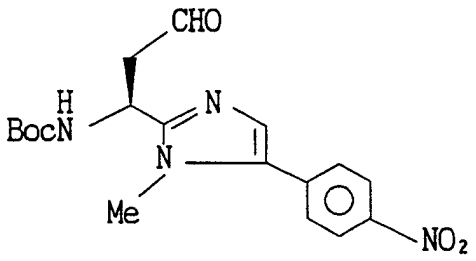
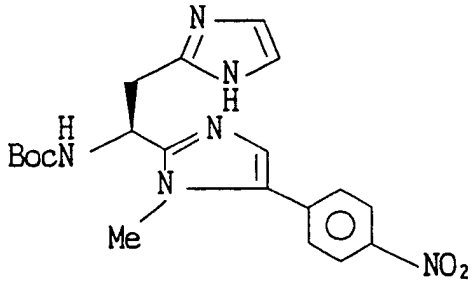
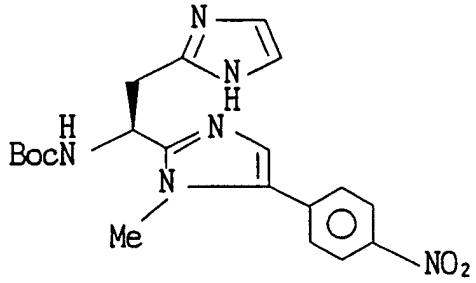
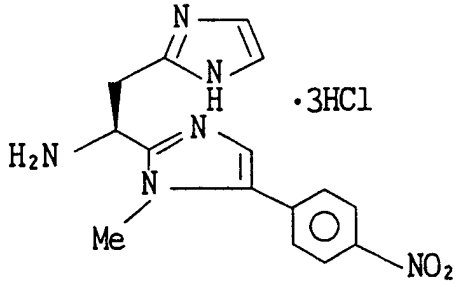
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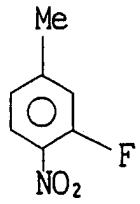
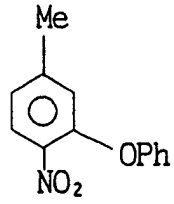
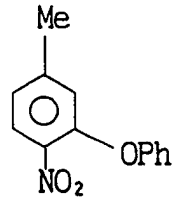
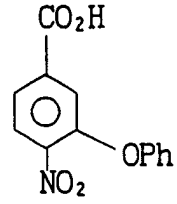
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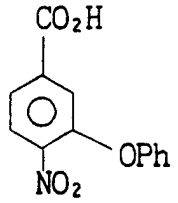
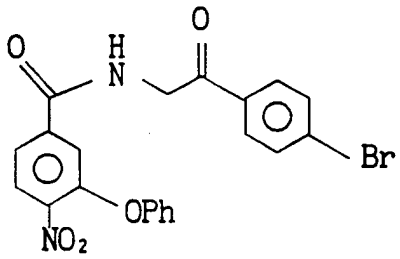
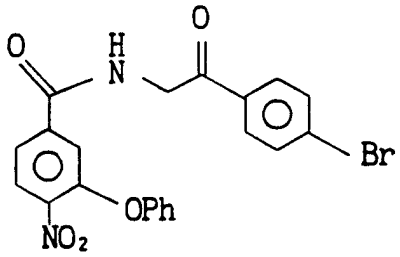
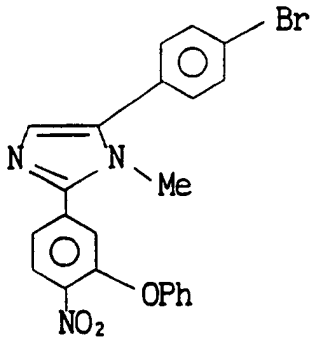
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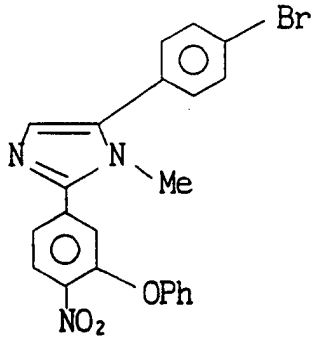
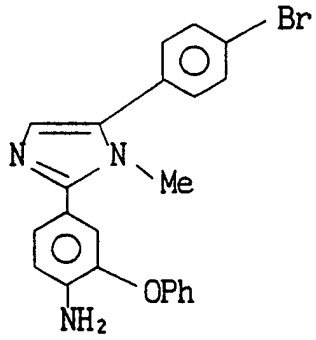
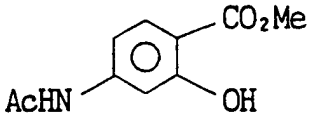
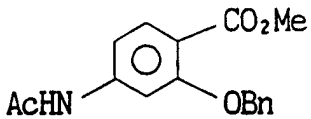
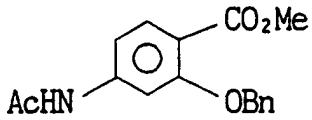
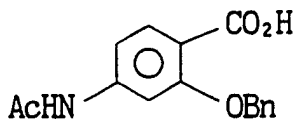
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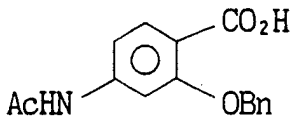
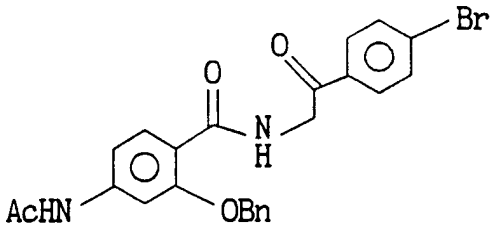
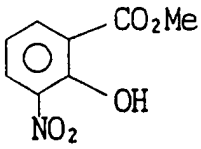
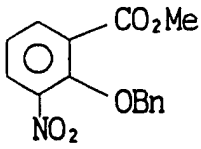
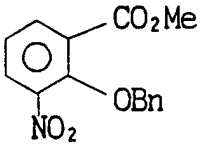
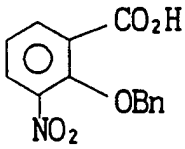
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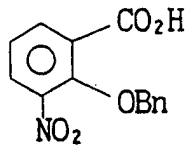
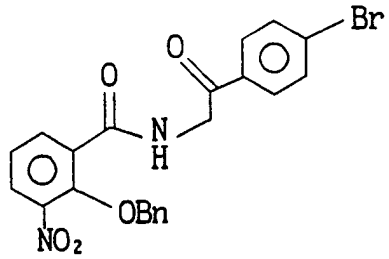
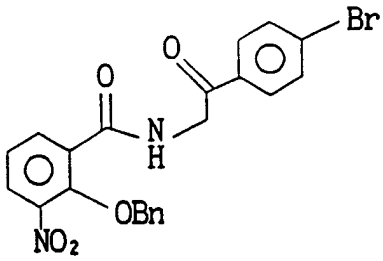
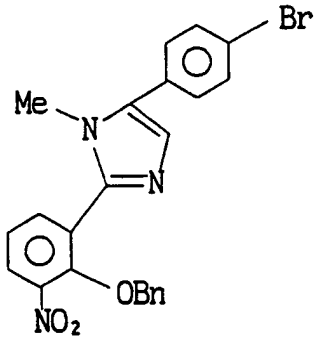
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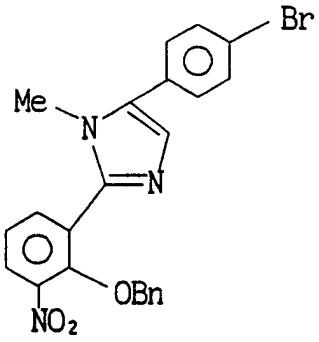
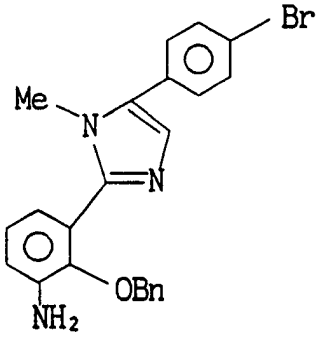
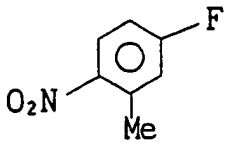
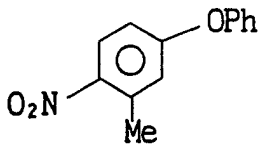
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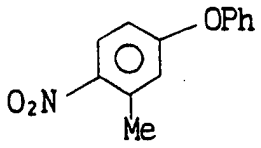
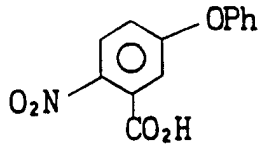
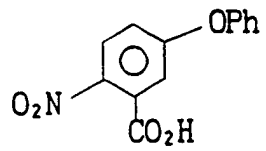
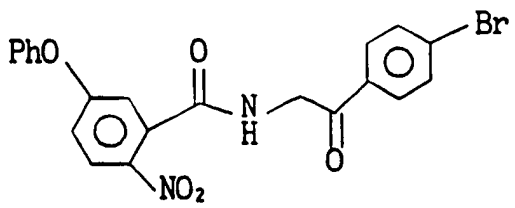
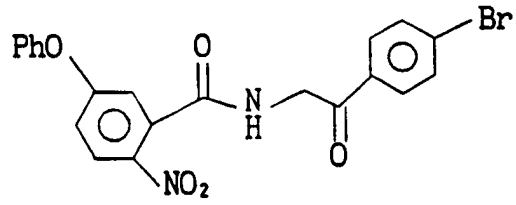
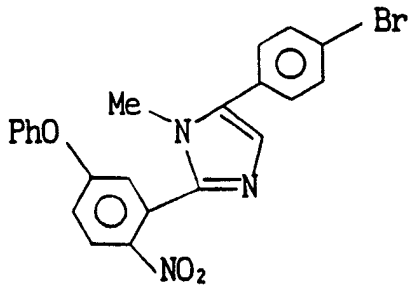
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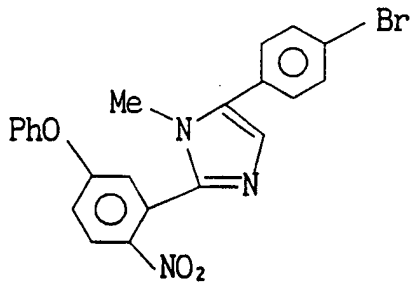
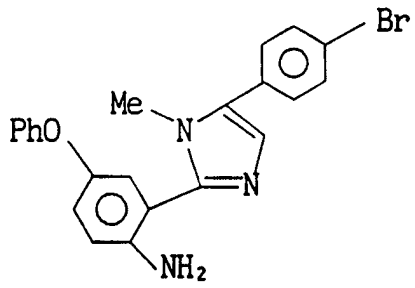
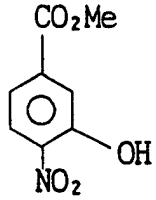
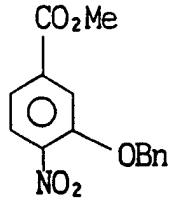
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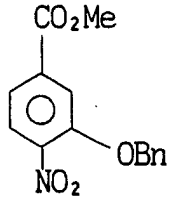
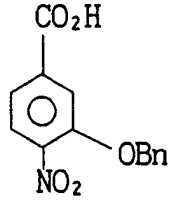
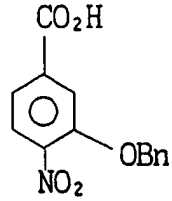
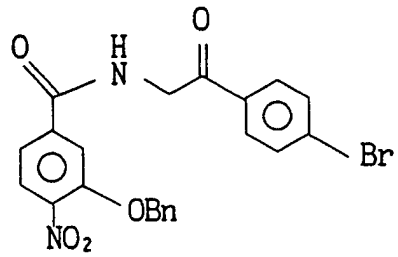
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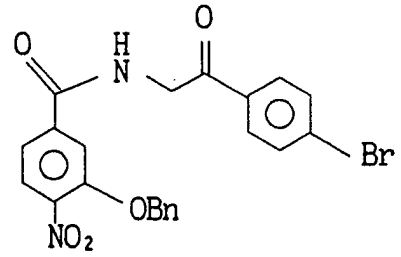
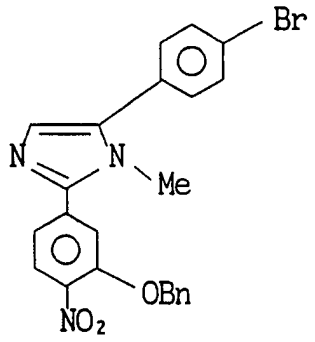
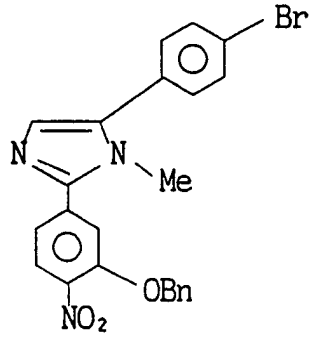
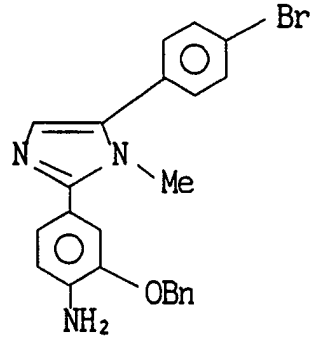
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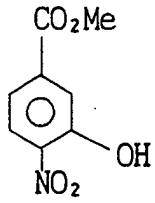
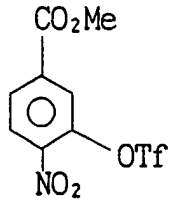
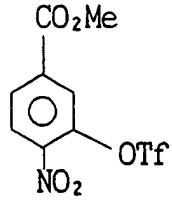
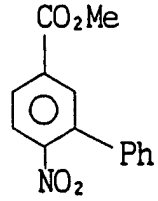
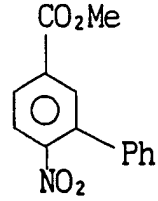
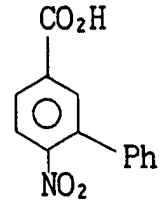
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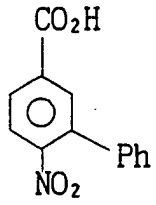
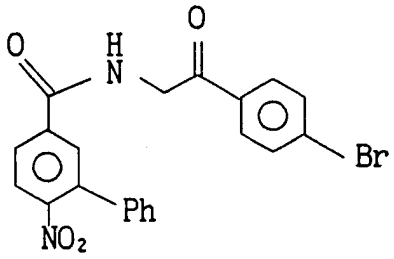
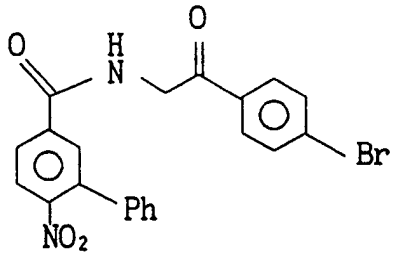
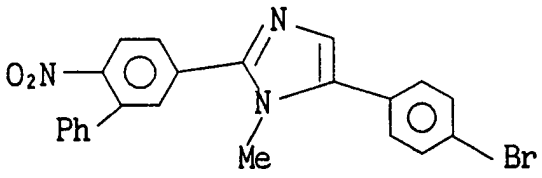
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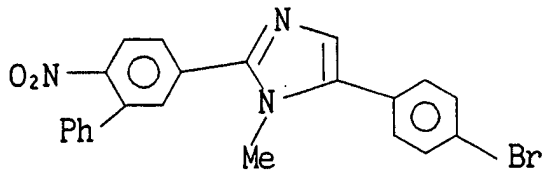
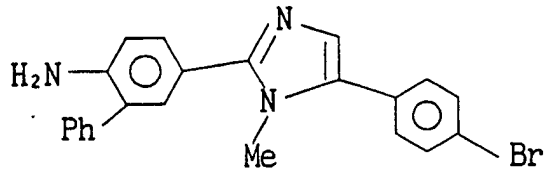
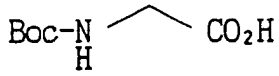
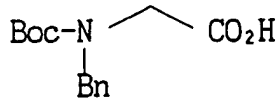
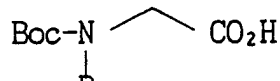
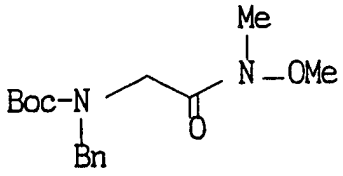
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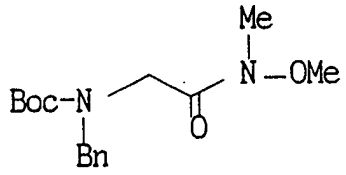
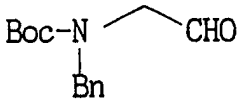
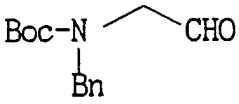
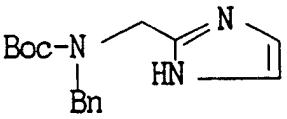
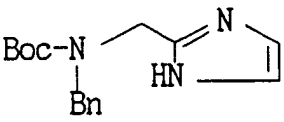
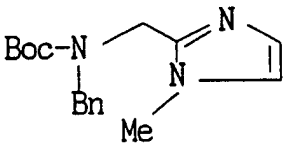
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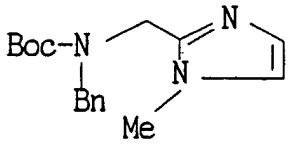
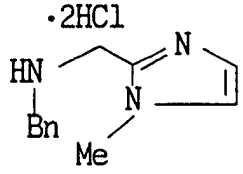
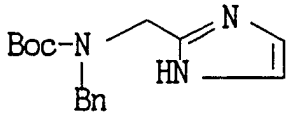
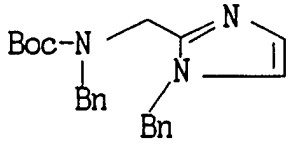
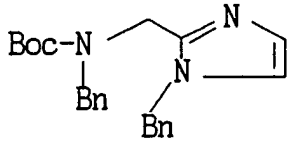
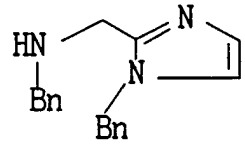
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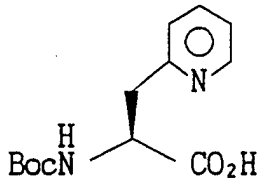
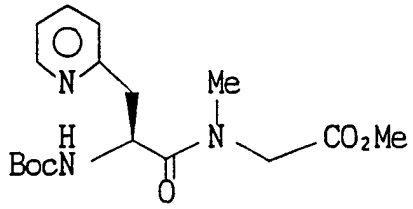
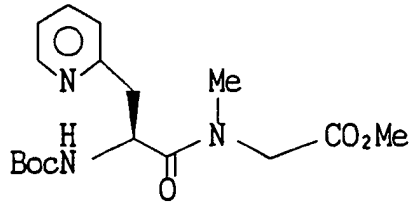
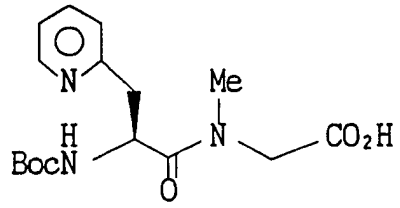
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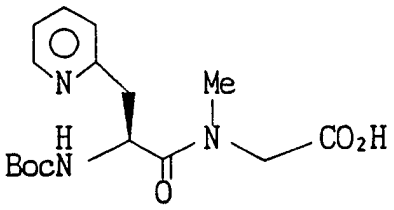
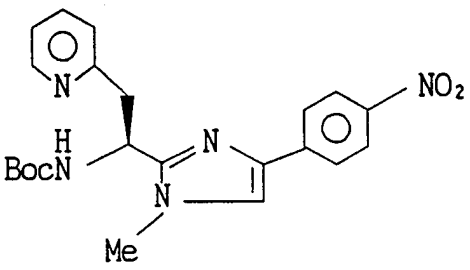
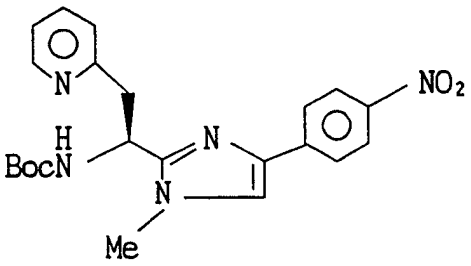
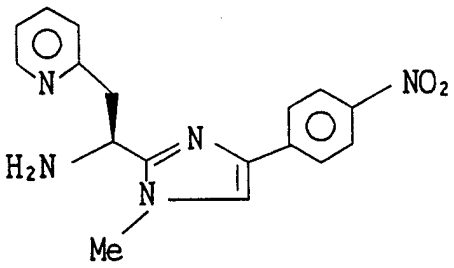
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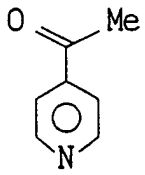
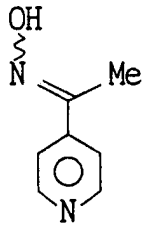
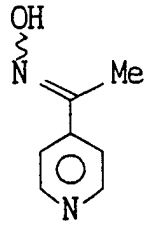
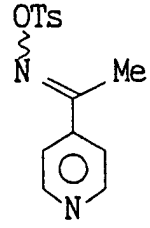
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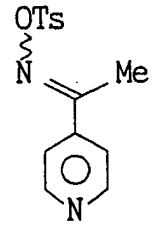
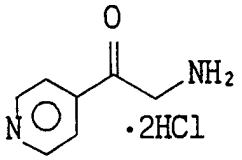
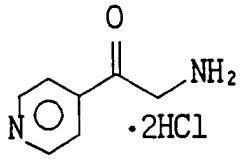
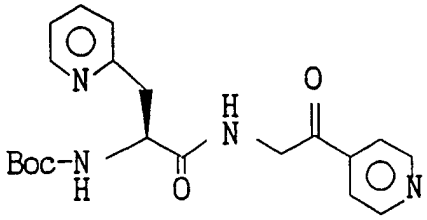
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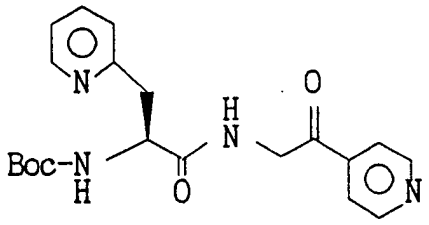
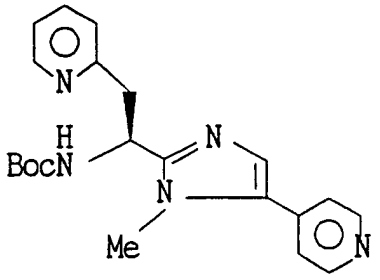
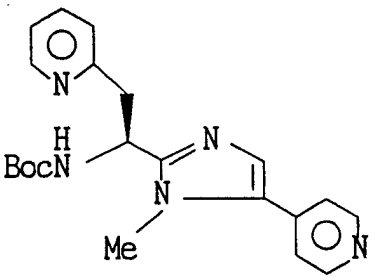
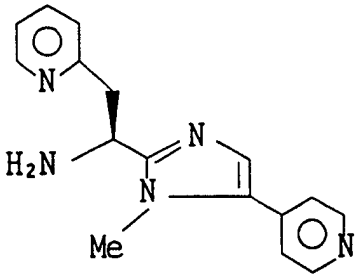
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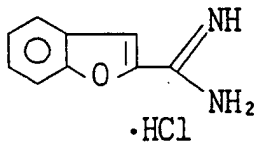
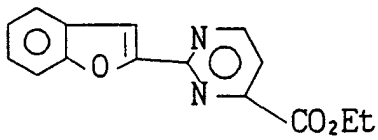
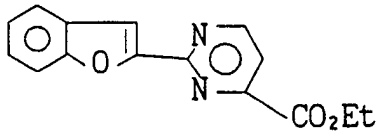
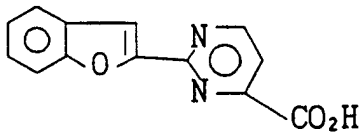
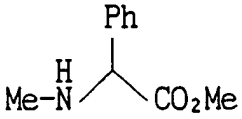
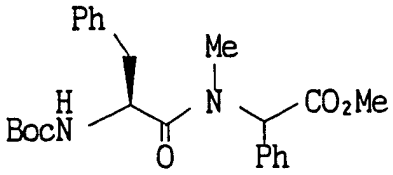
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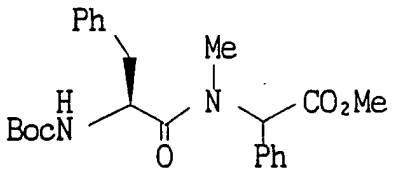
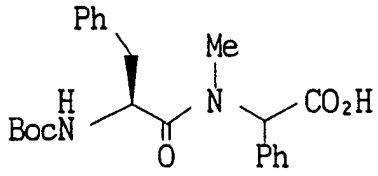
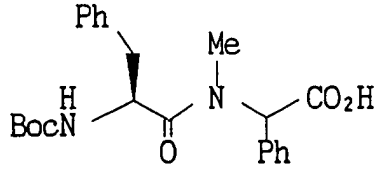
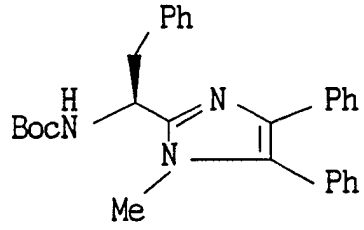
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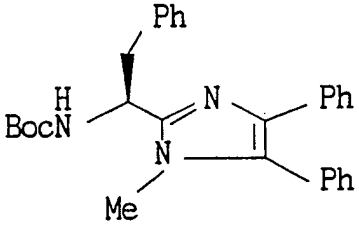
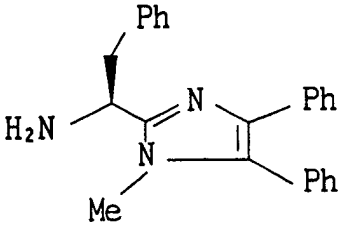
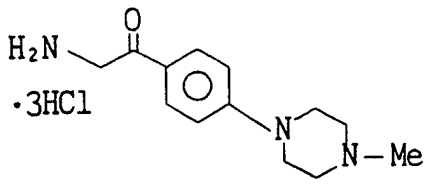
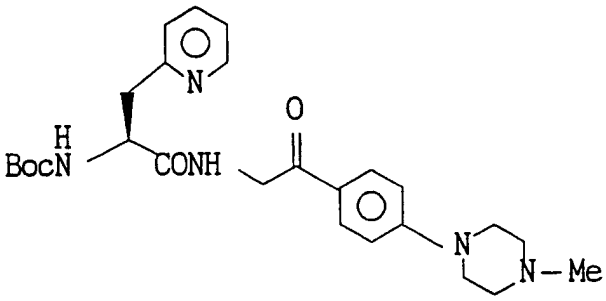
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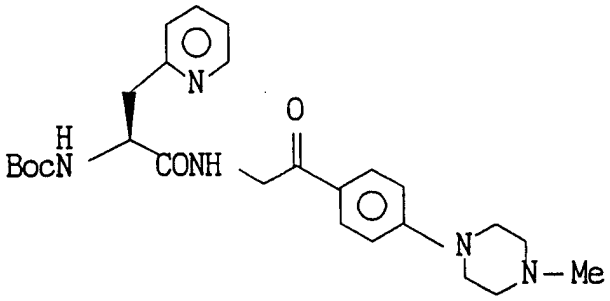
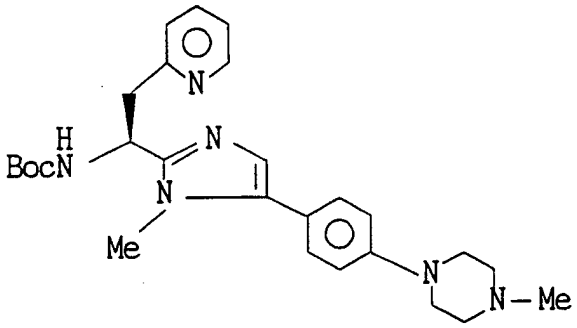
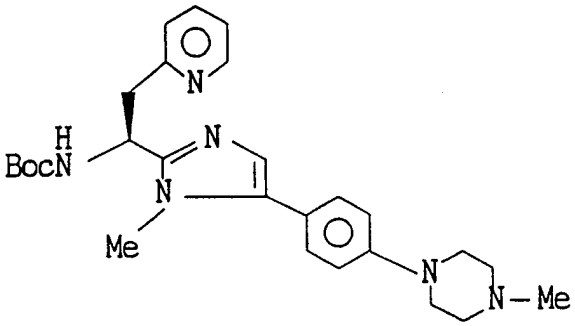
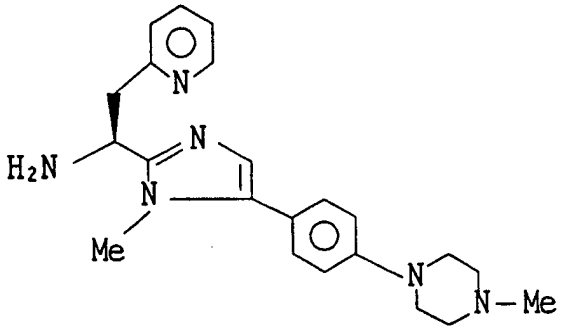
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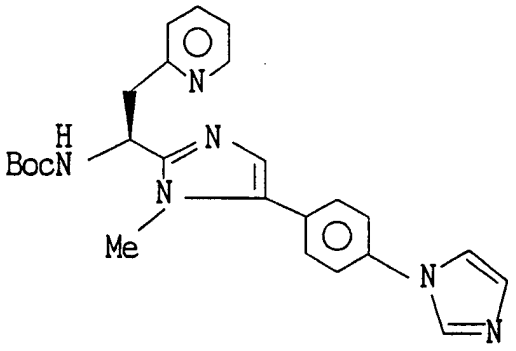
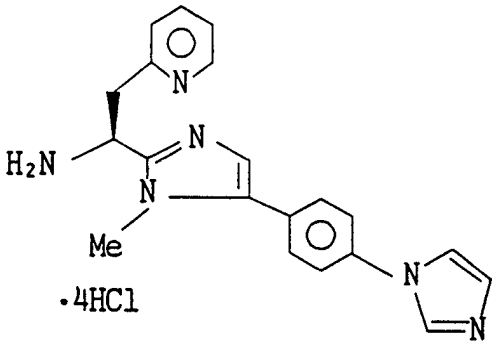
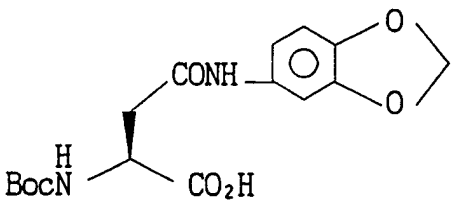
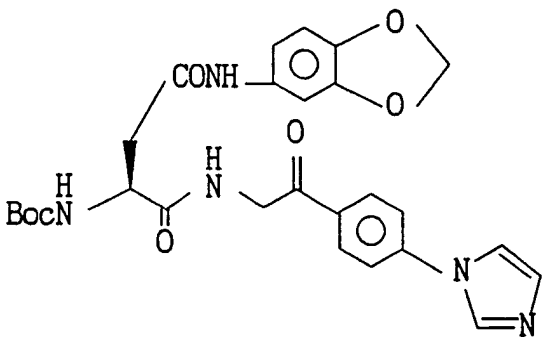
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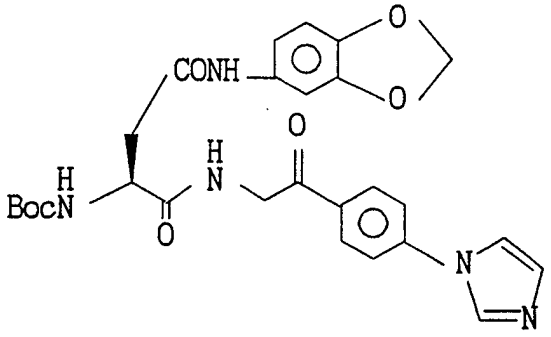
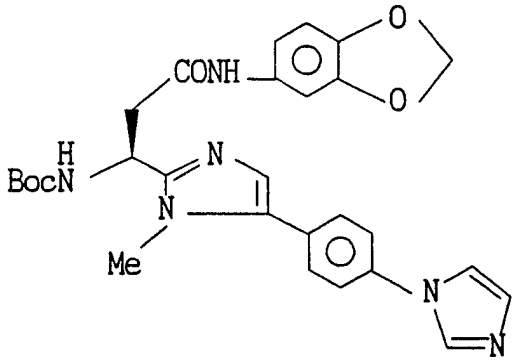
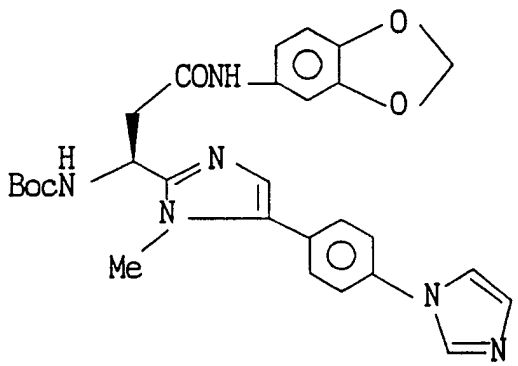
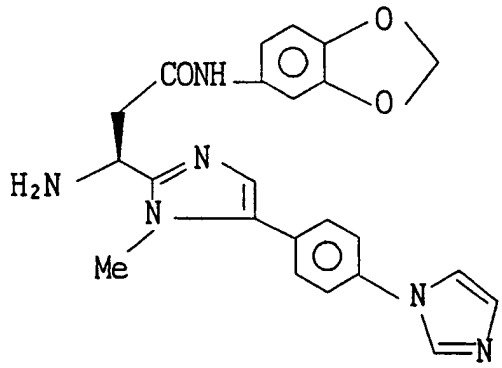
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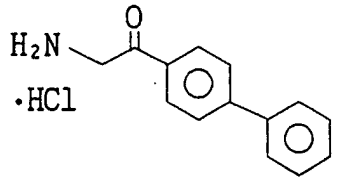
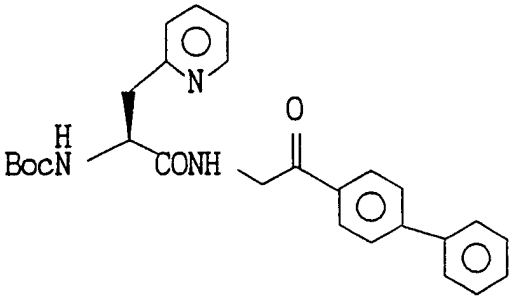
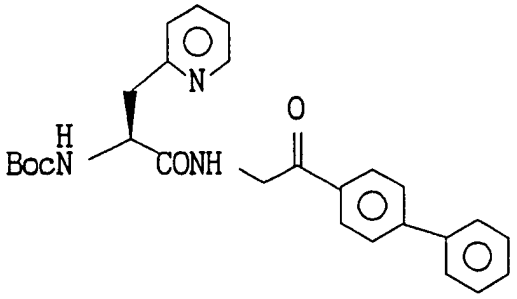
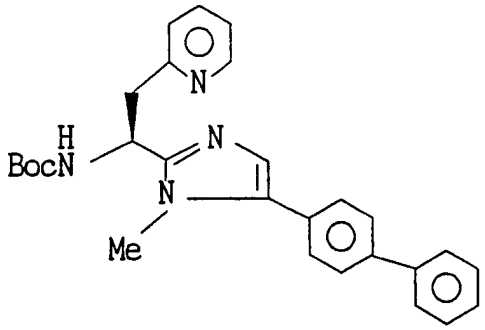
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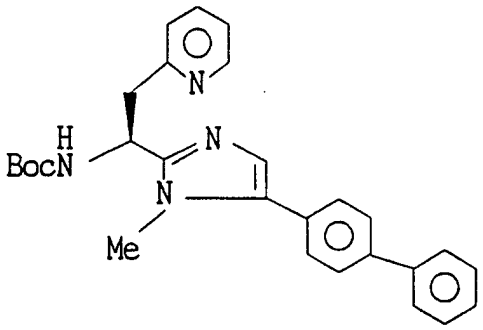
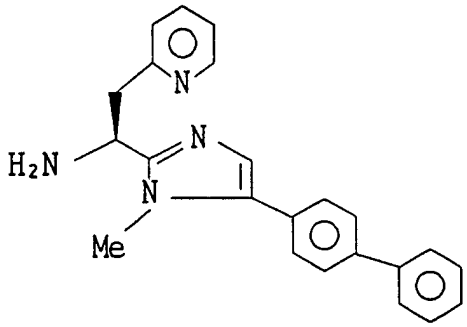
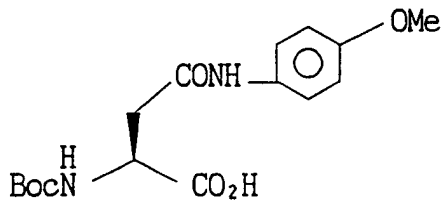
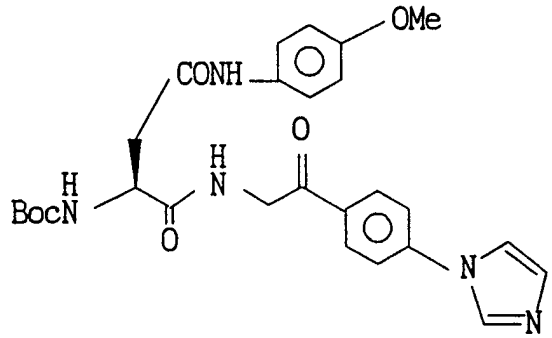
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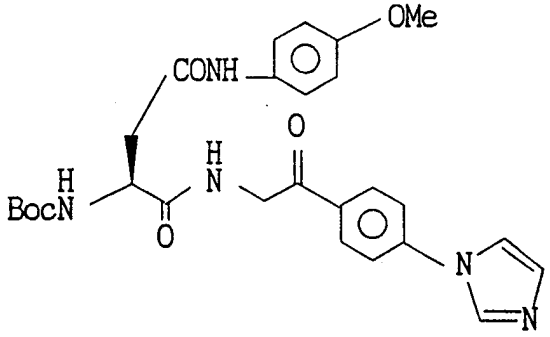
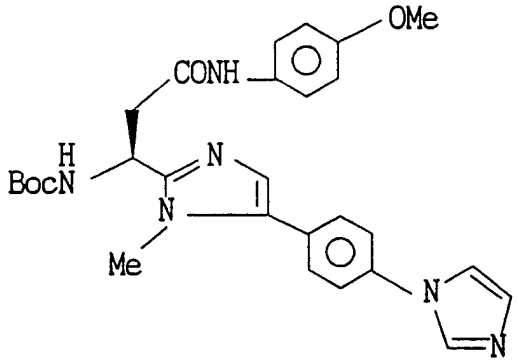
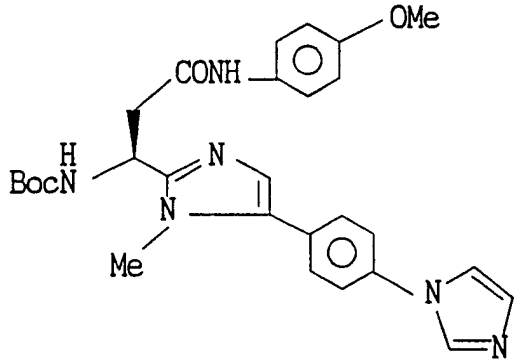
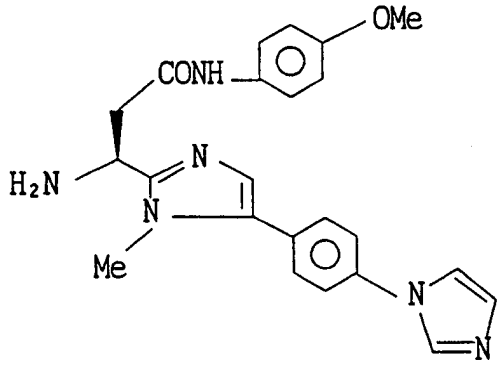
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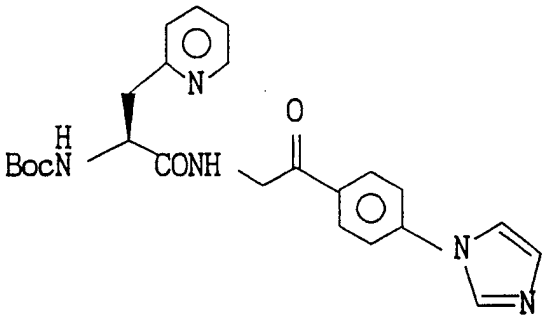
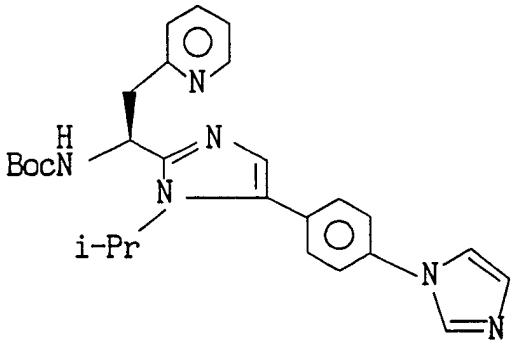
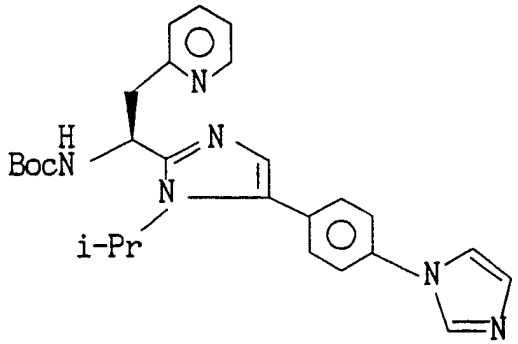
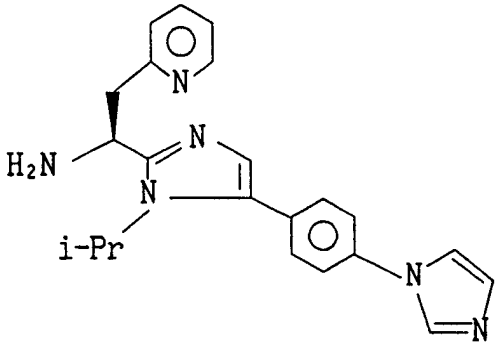
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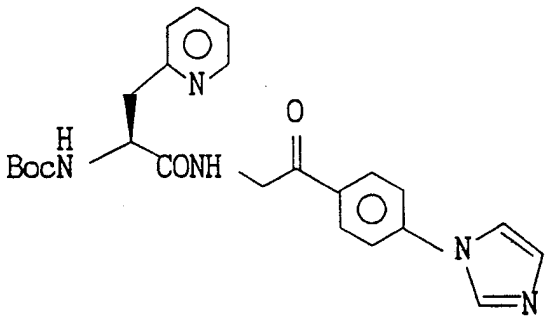
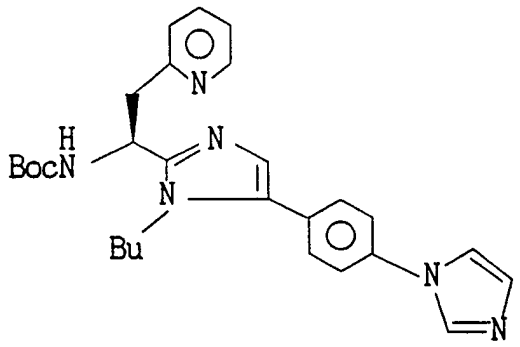
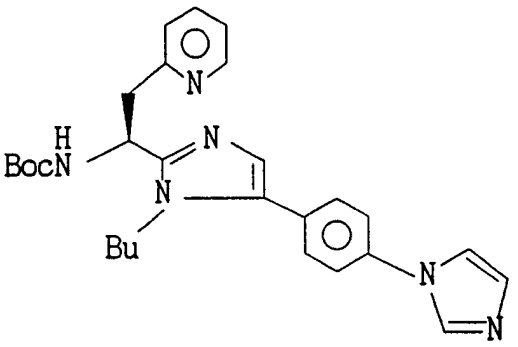
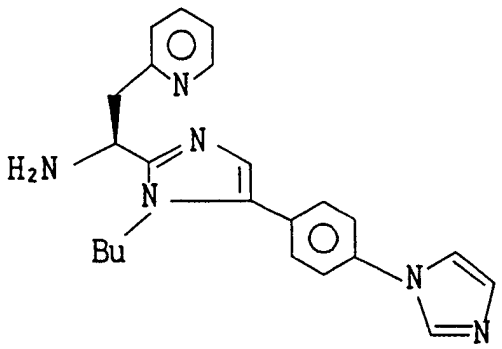
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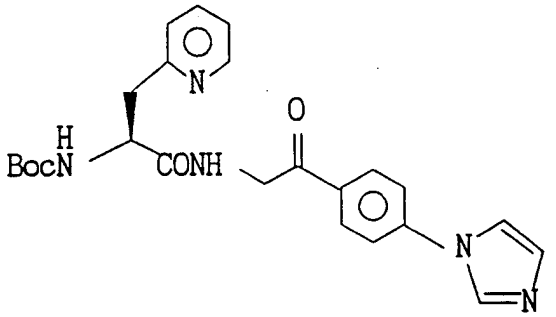
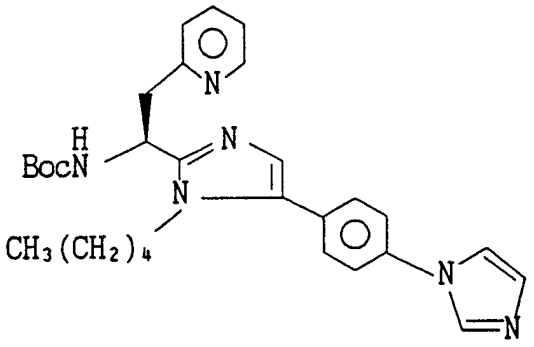
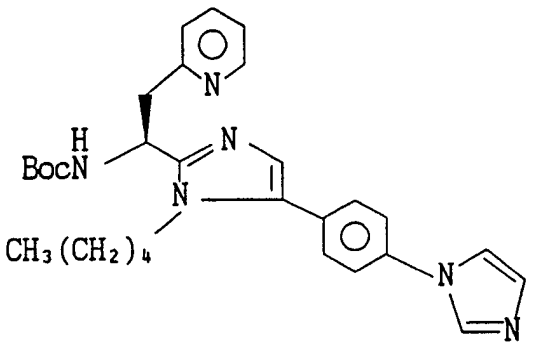
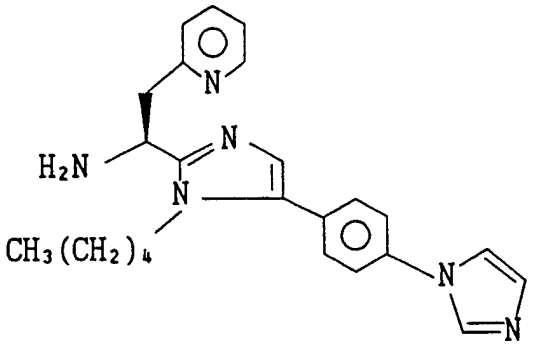
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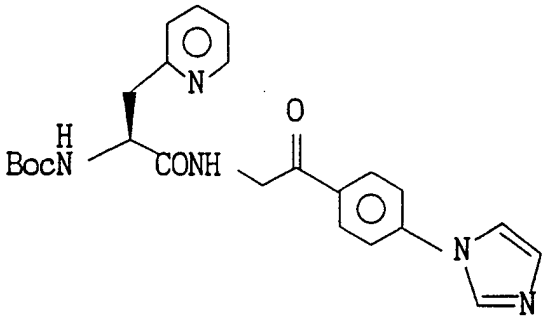
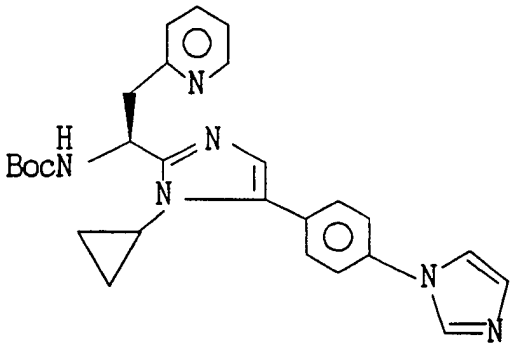
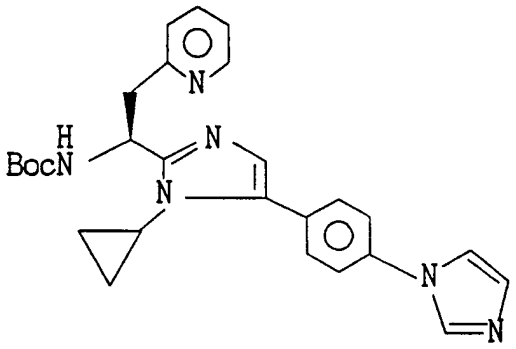
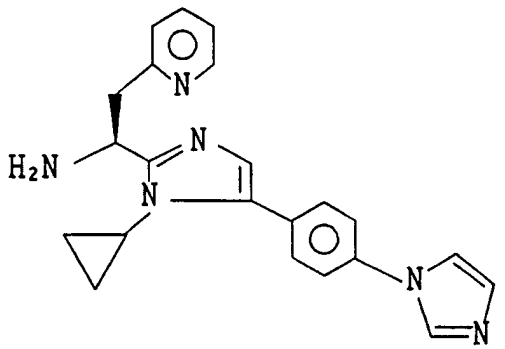
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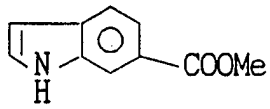
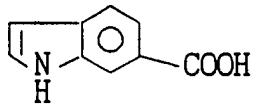
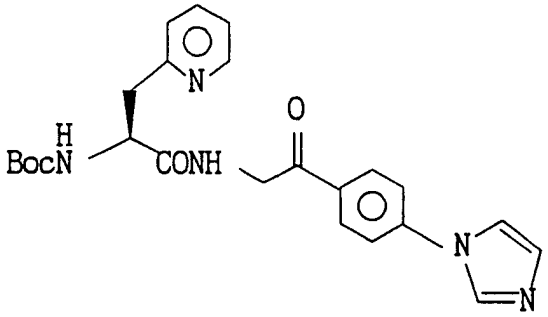
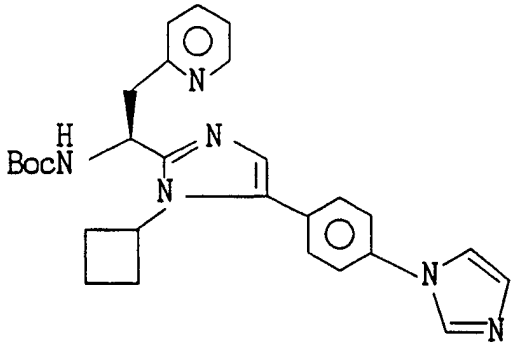
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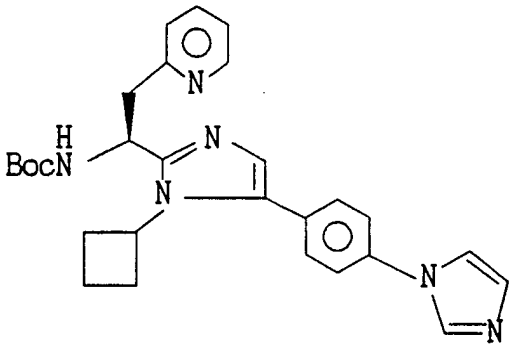
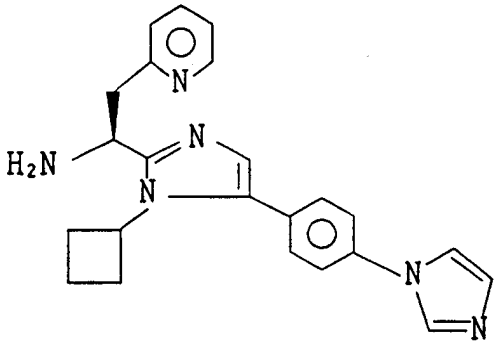
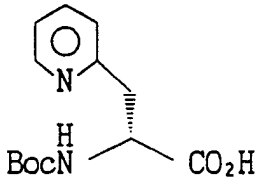
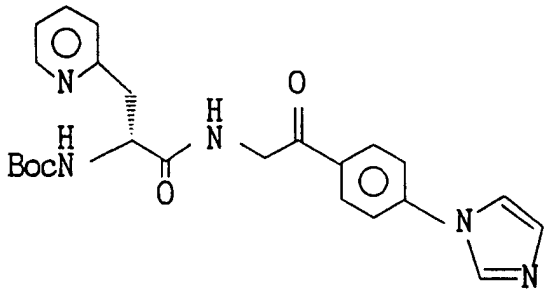
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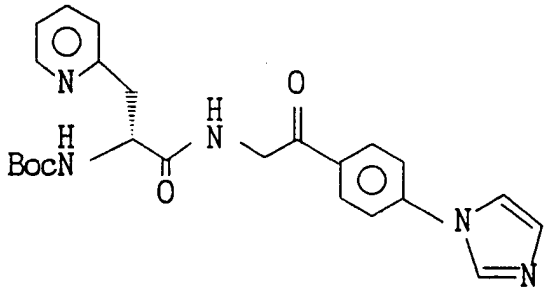
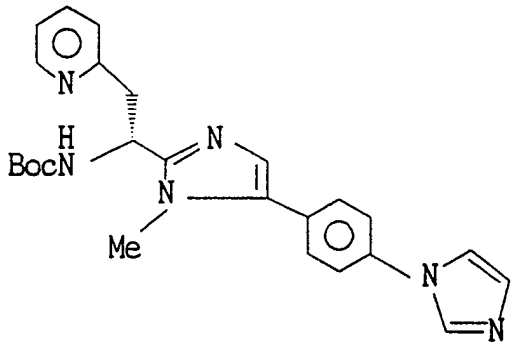
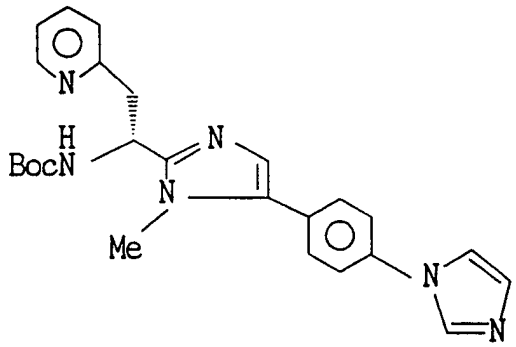
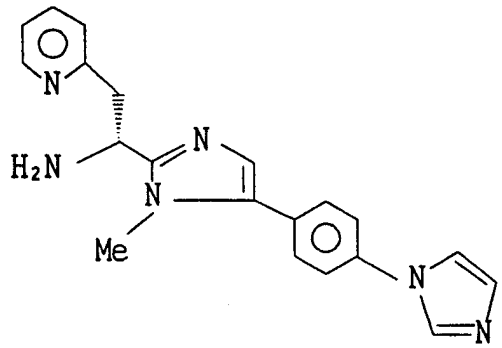
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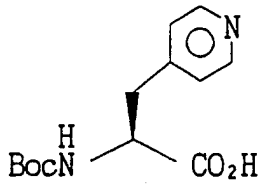
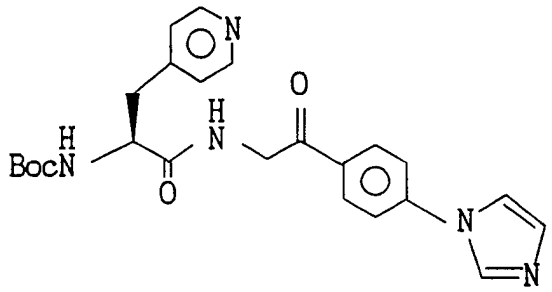
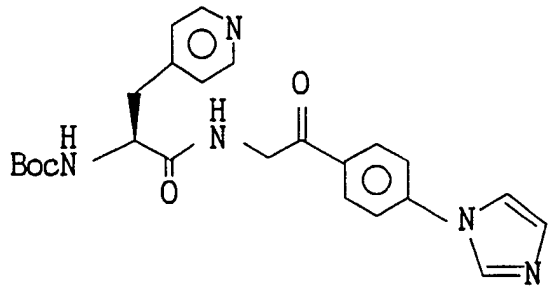
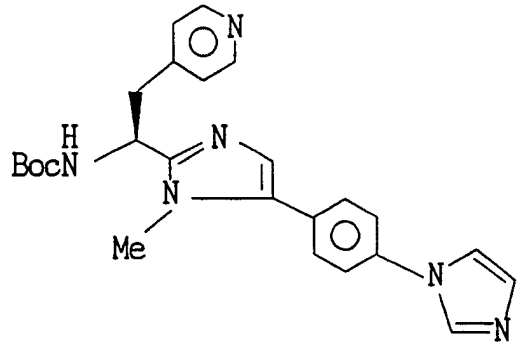
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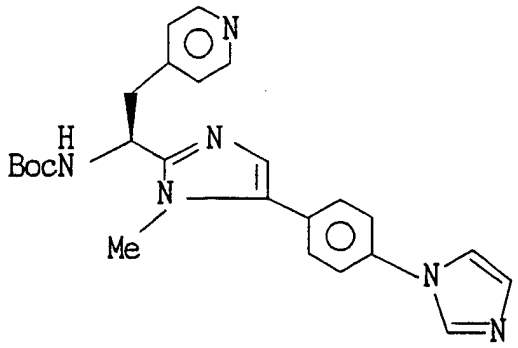
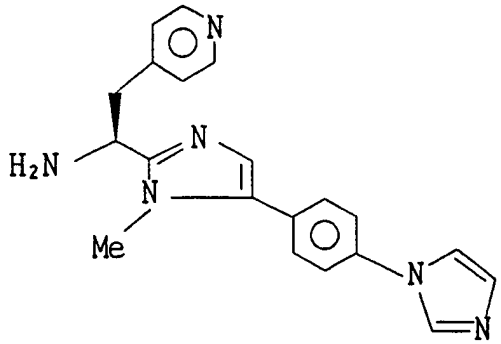
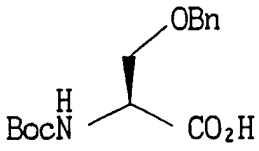
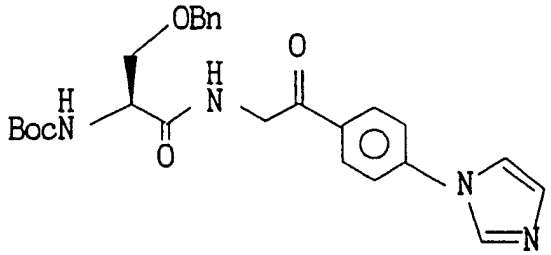
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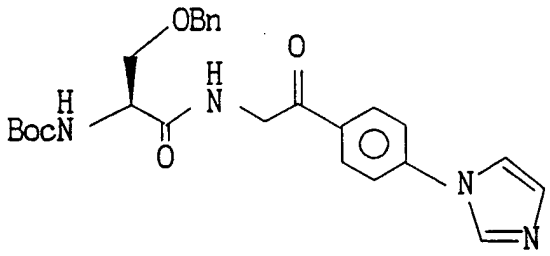
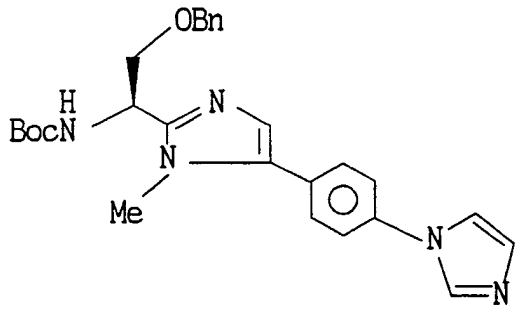
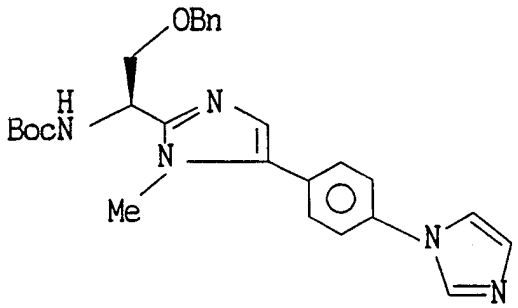
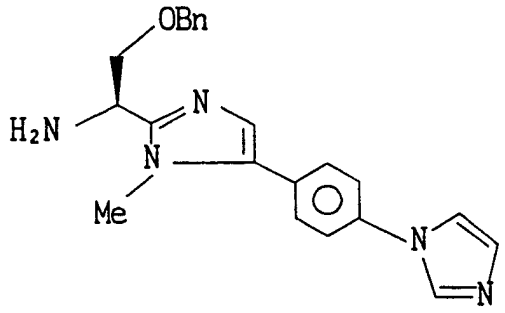
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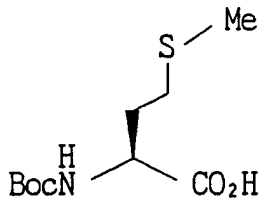
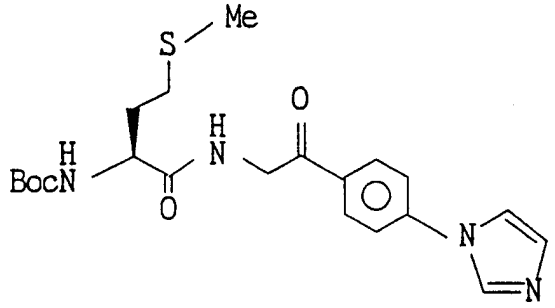
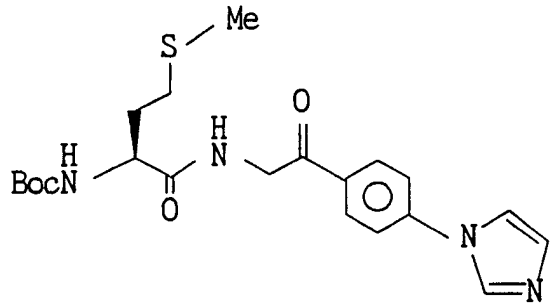
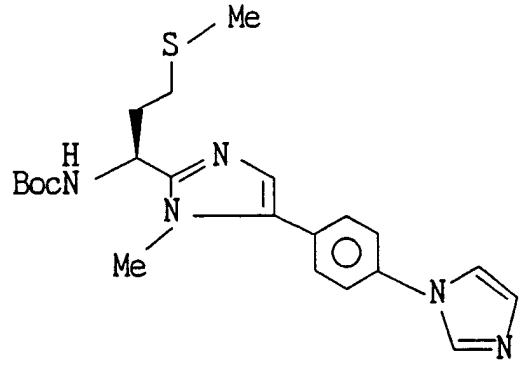
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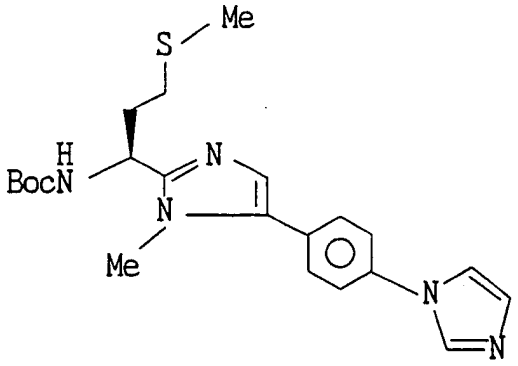
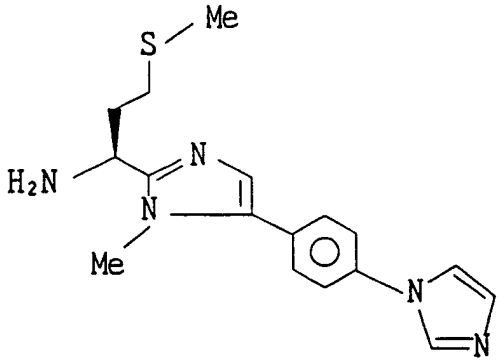
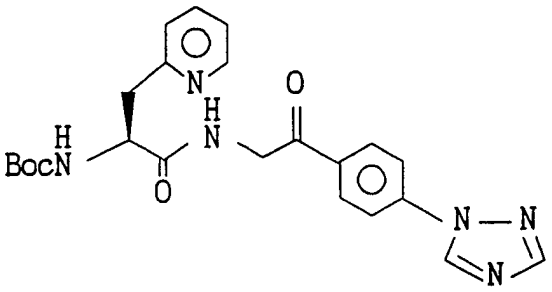
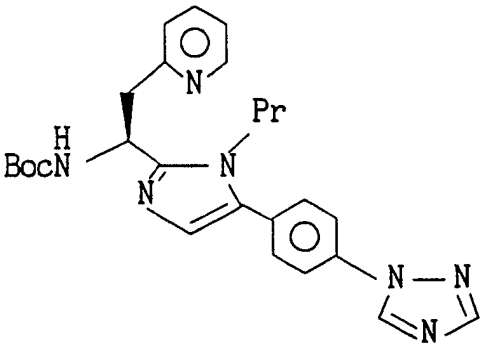
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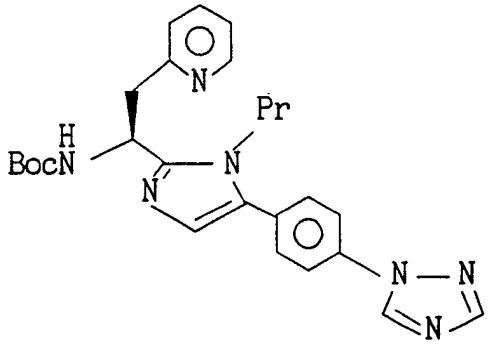
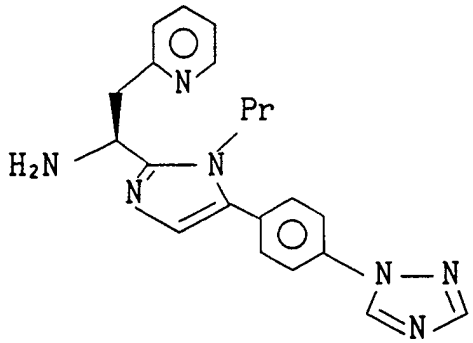
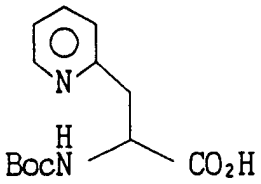
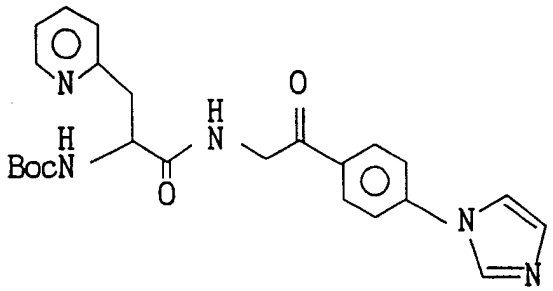
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Preparation No.	Formula
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385	
	

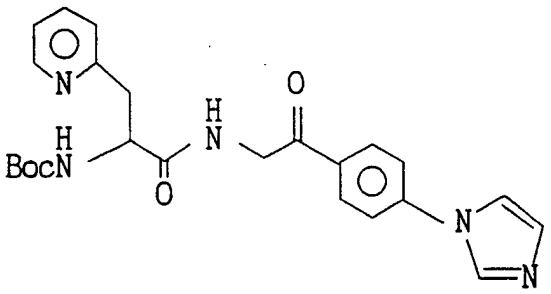
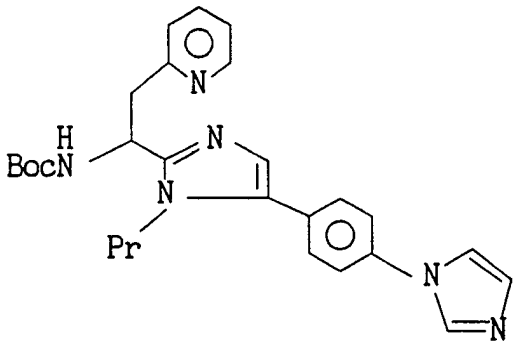
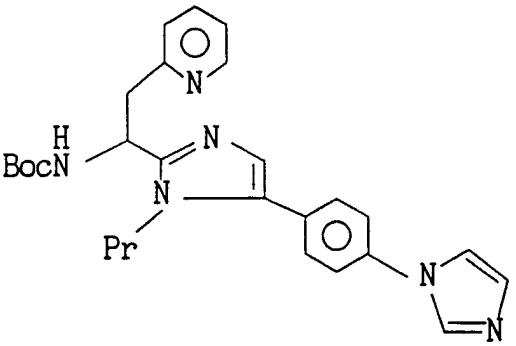
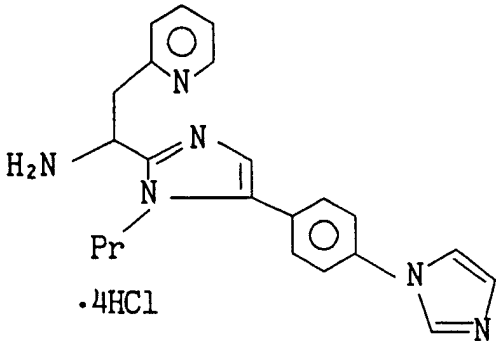
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Preparation No.	Formula
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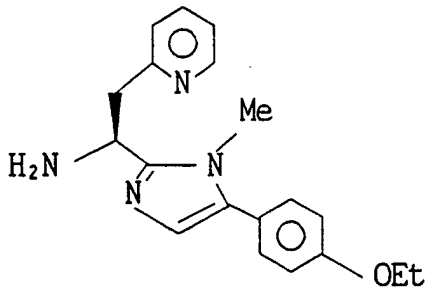
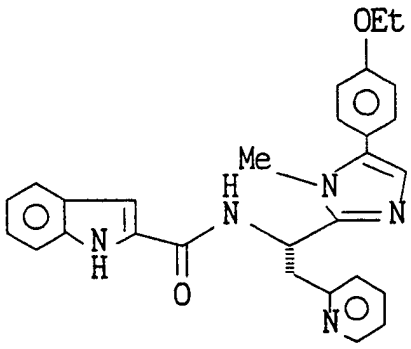
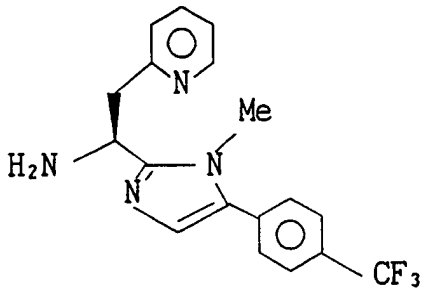
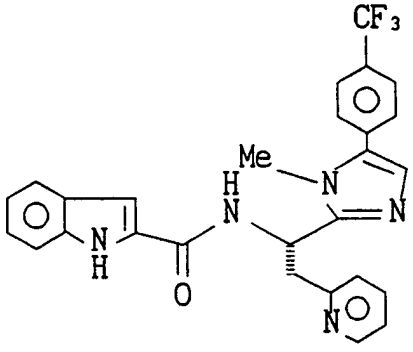
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Preparation No.	Formula
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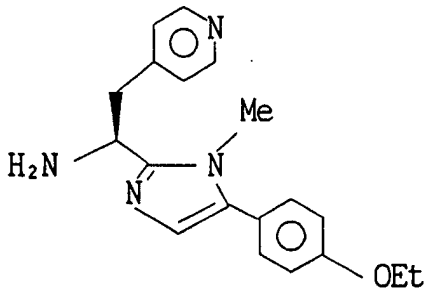
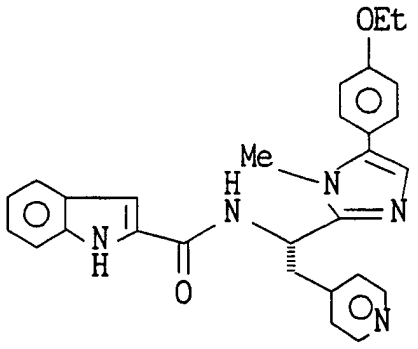
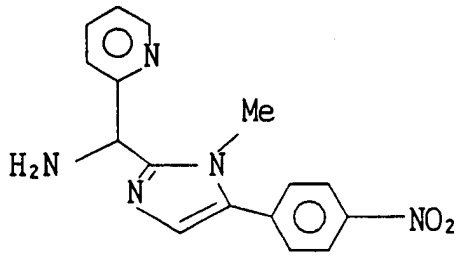
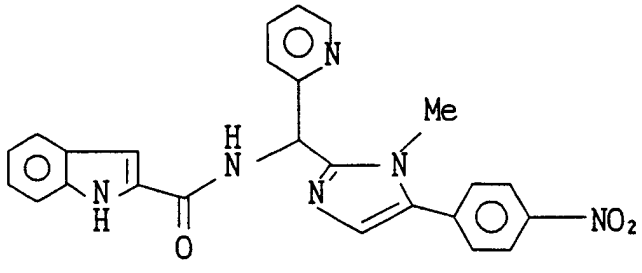
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Preparation No.	Formula
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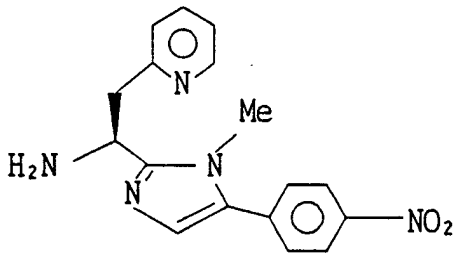
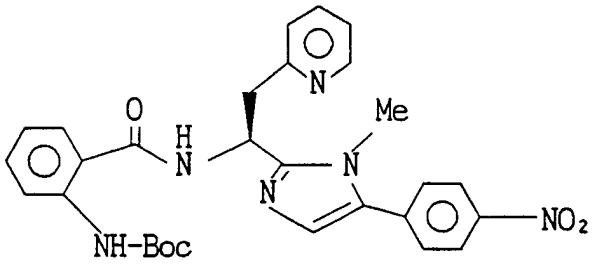
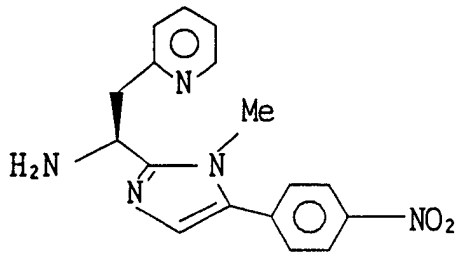
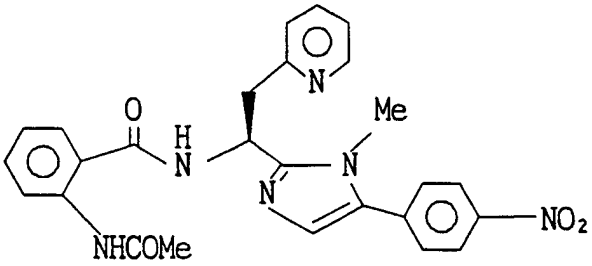
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Example No.	Formula
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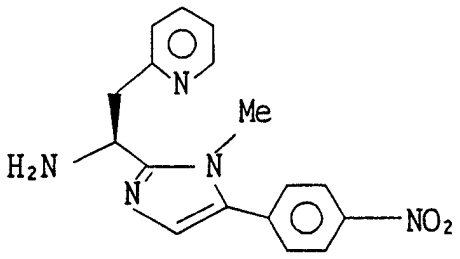
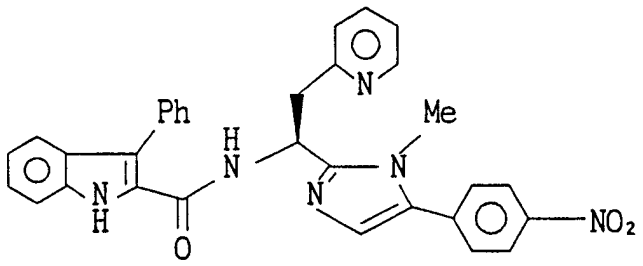
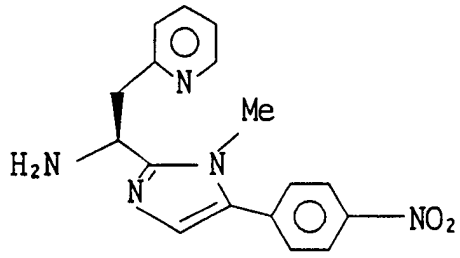
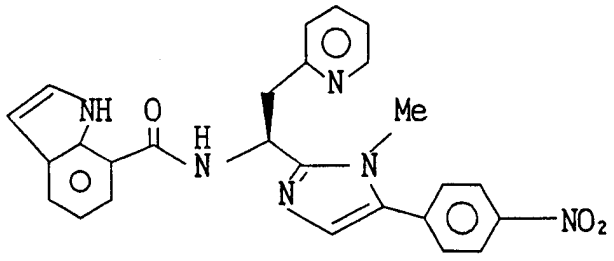
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Example No.	Formula
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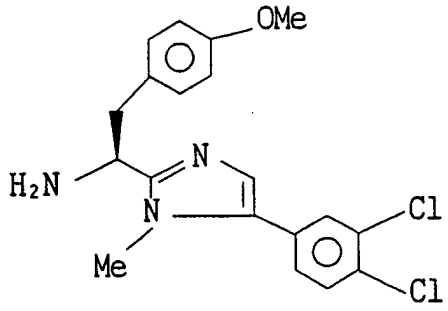
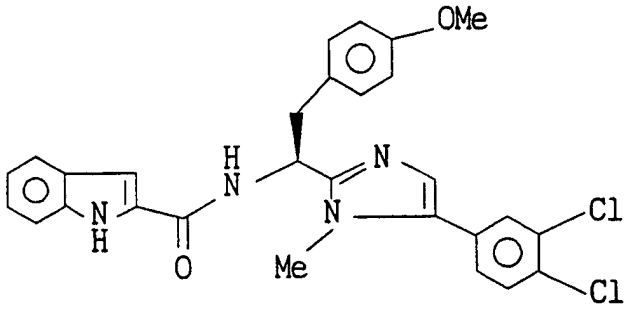
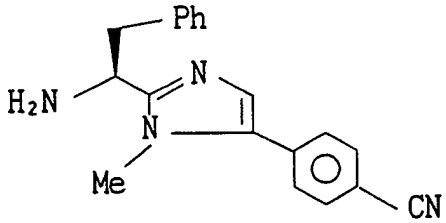
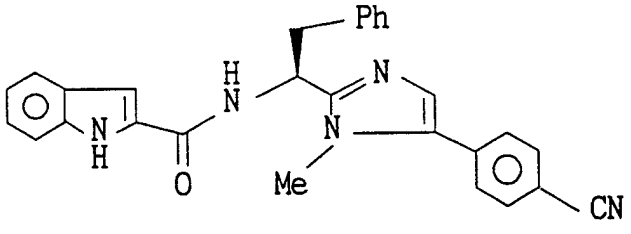
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Example No.	Formula
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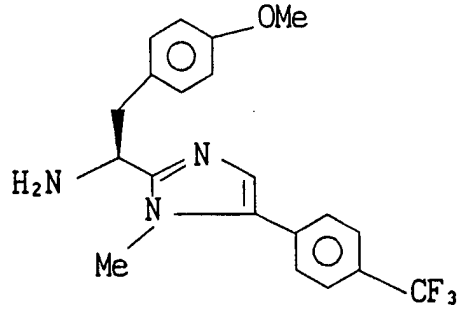
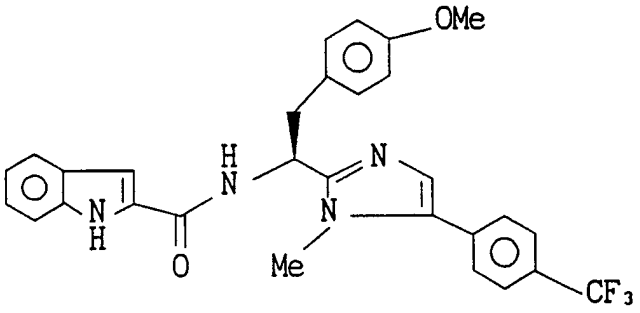
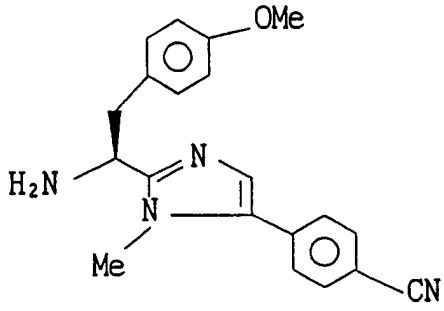
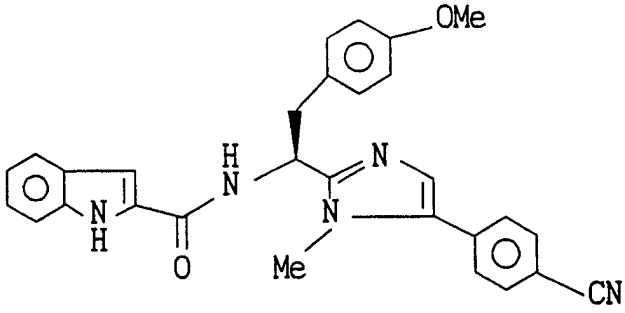
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Example No.	Formula
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8	
	

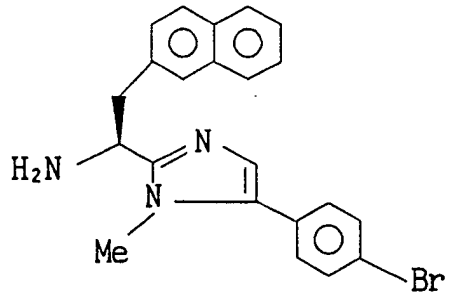
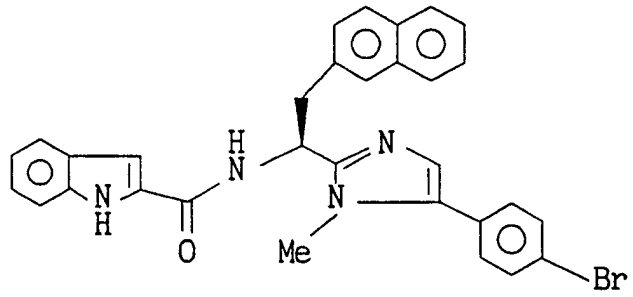
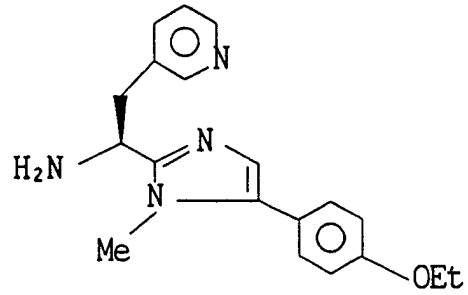
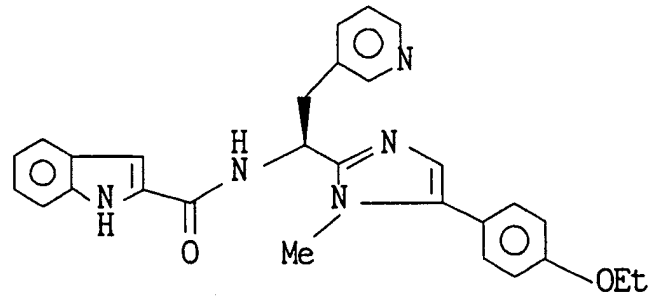
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Example No.	Formula
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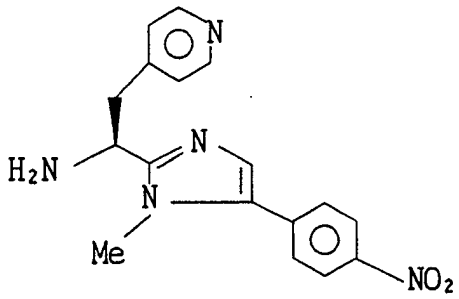
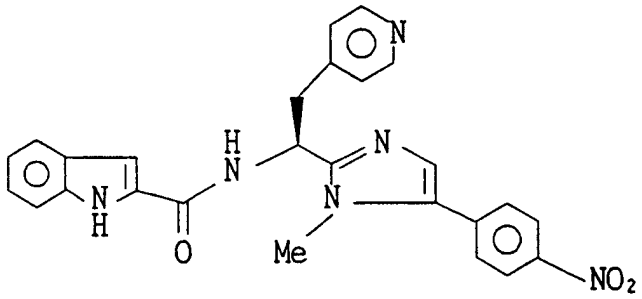
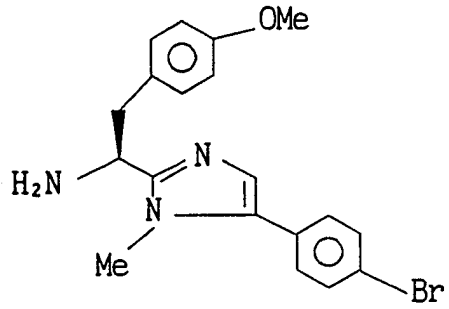
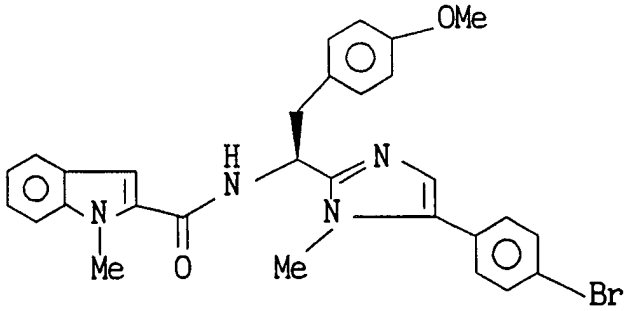
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Example No.	Formula
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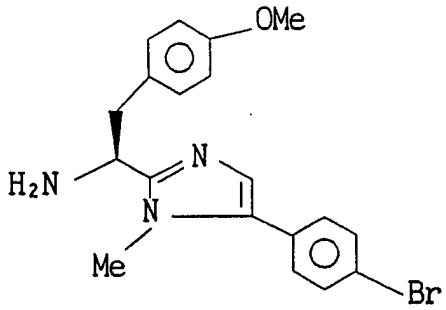
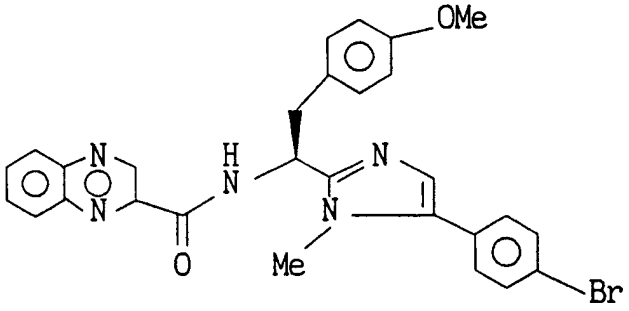
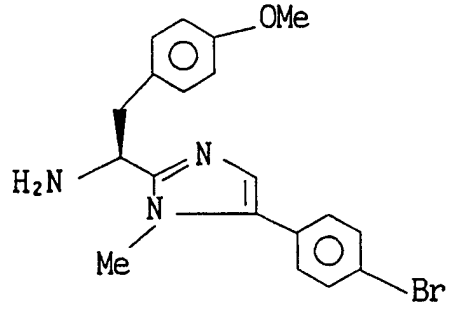
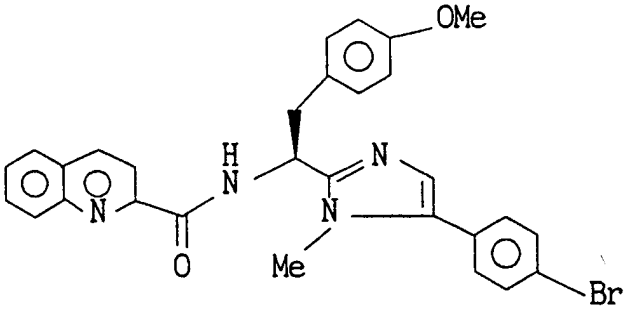
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Example No.	Formula
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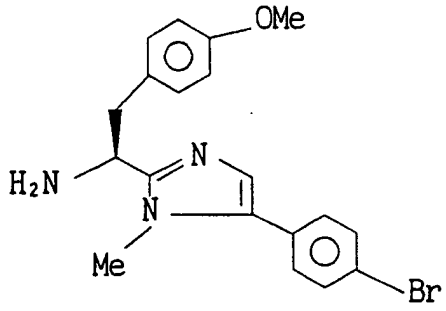
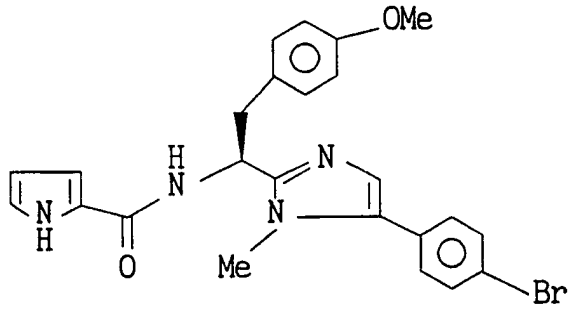
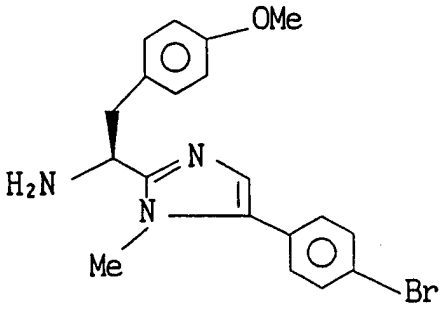
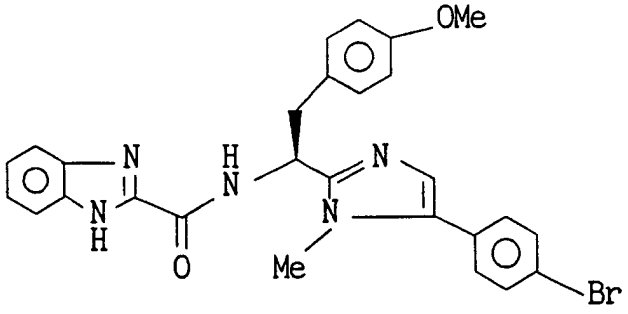
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Example No.	Formula
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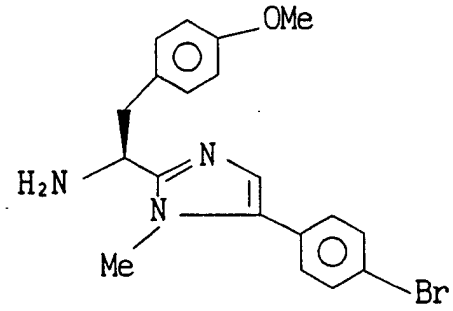
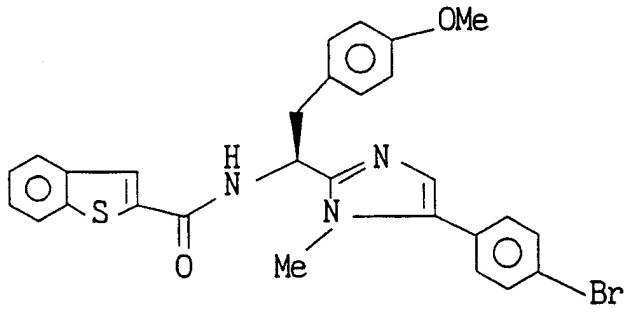
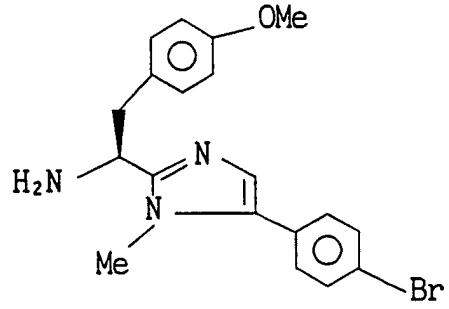
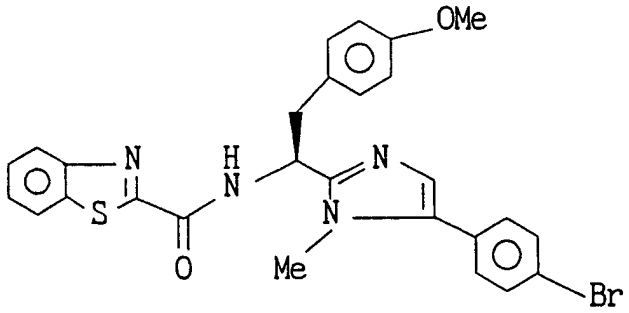
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Example No.	Formula
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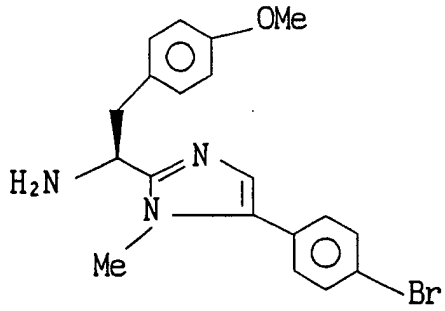
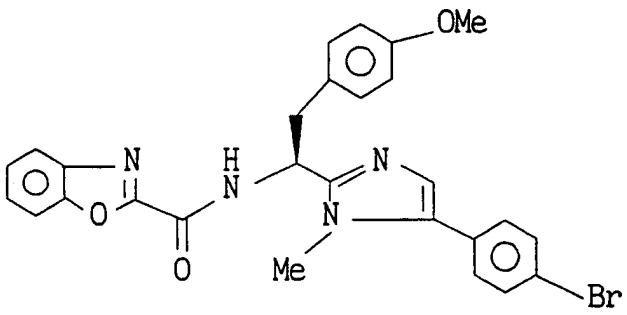
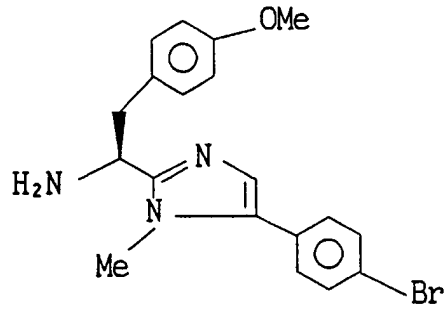
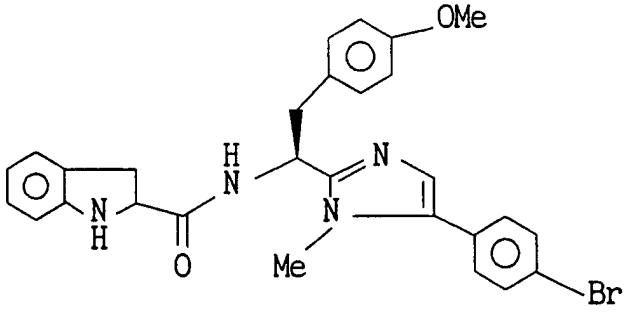
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Example No.	Formula
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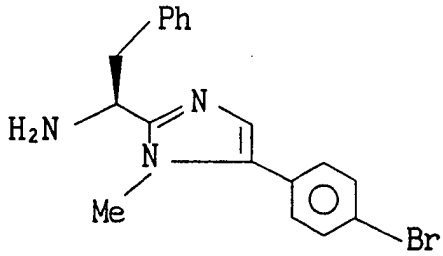
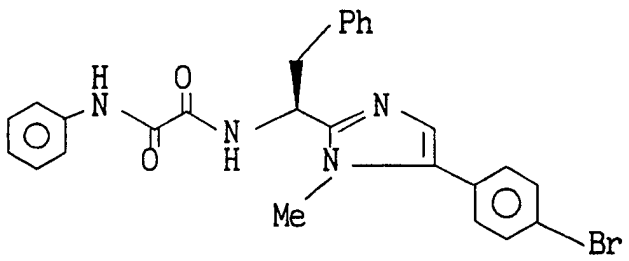
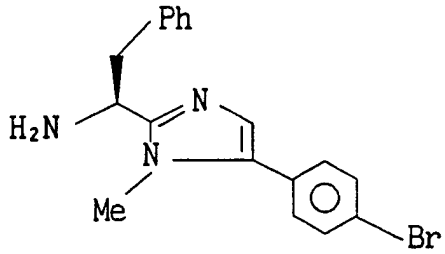
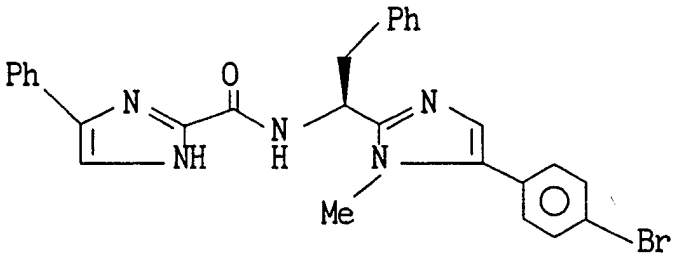
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Example No.	Formula
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22	
	

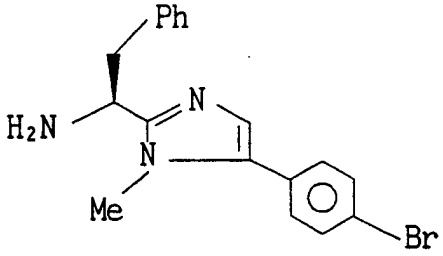
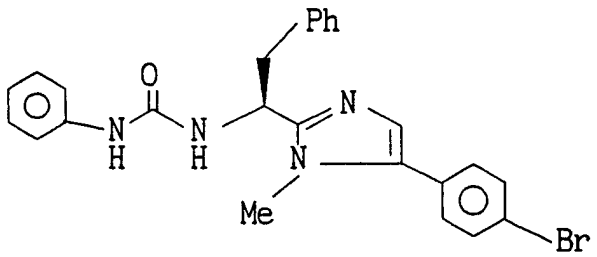
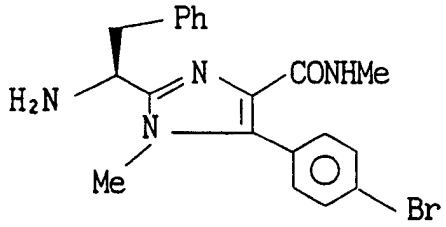
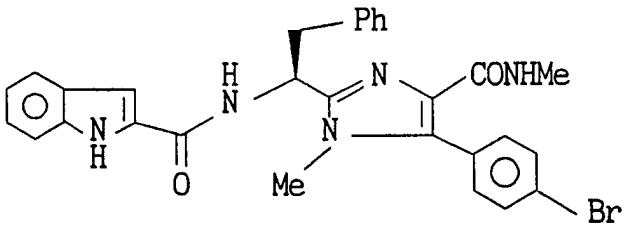
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Example No.	Formula
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24	
	

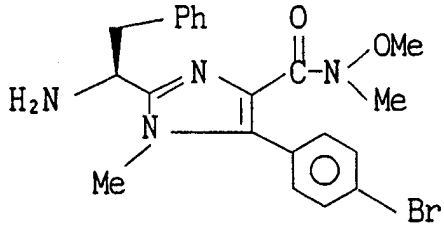
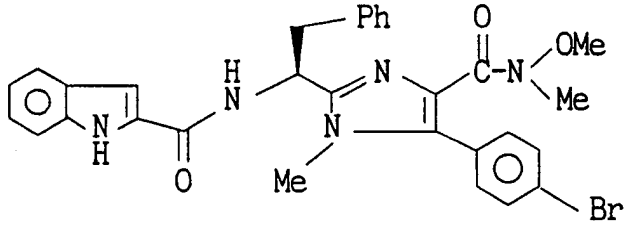
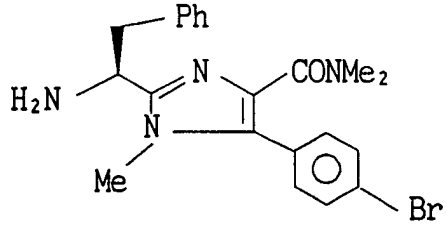
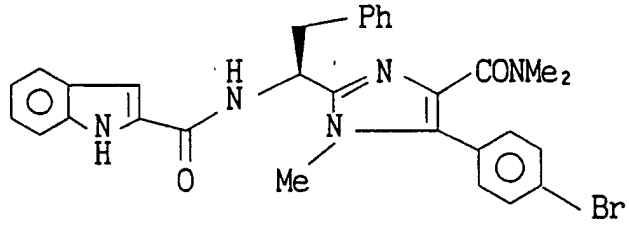
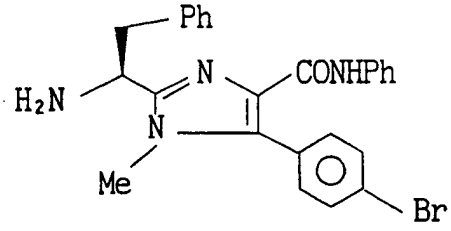
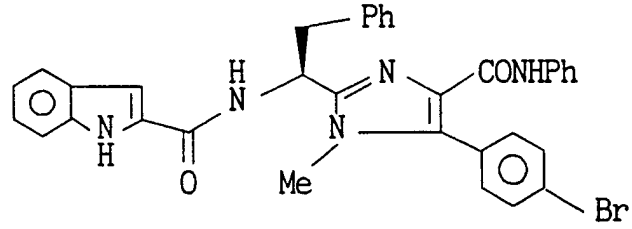
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Example No.	Formula
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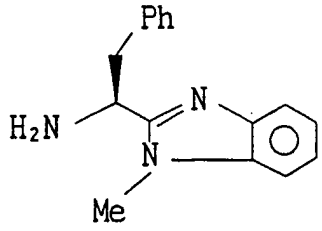
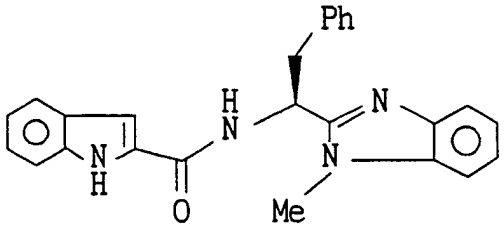
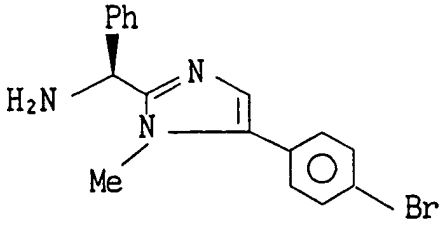
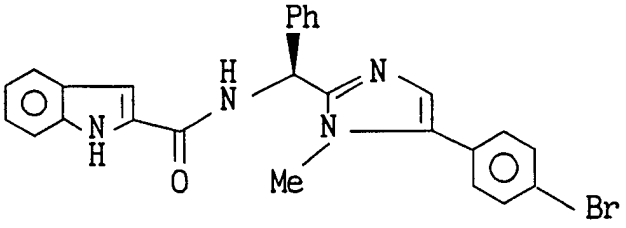
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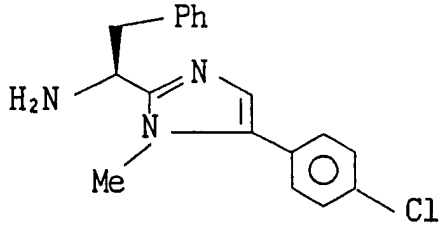
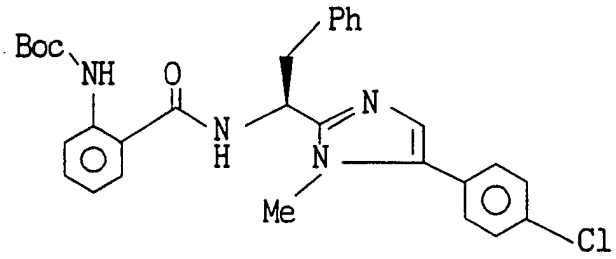
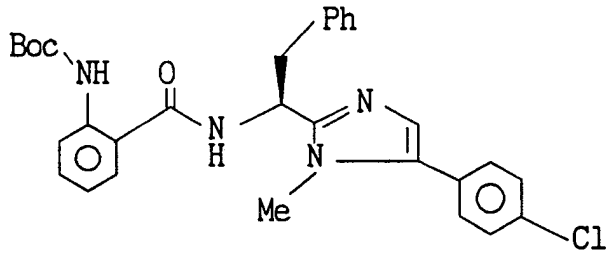
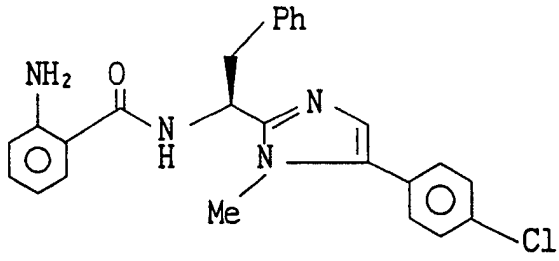
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Example No.	Formula
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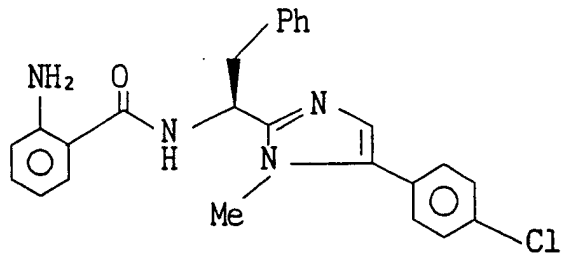
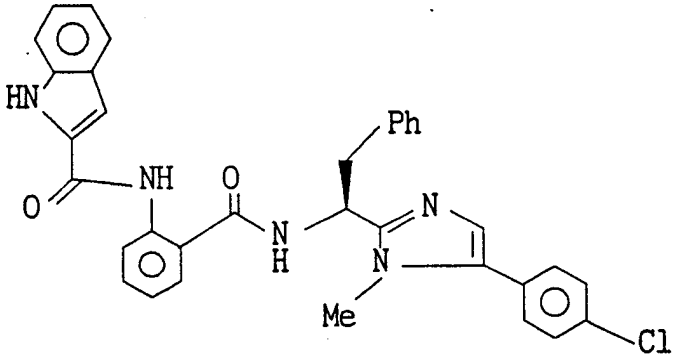
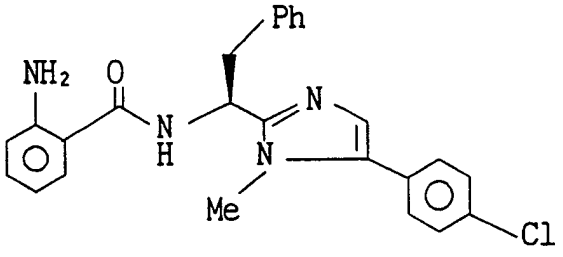
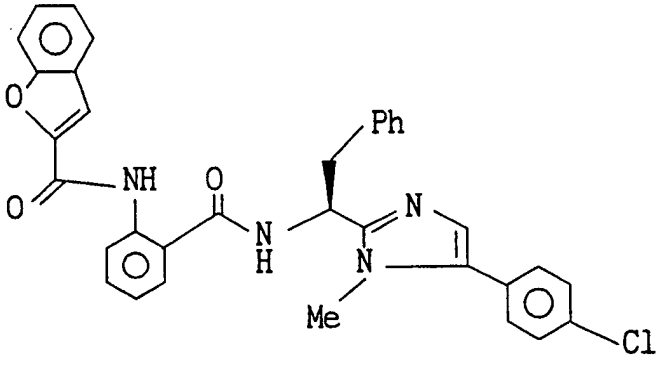
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Example No.	Formula
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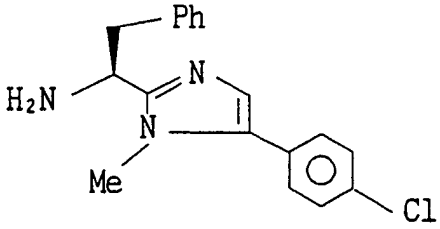
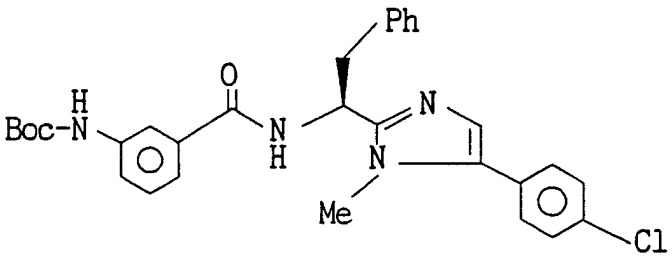
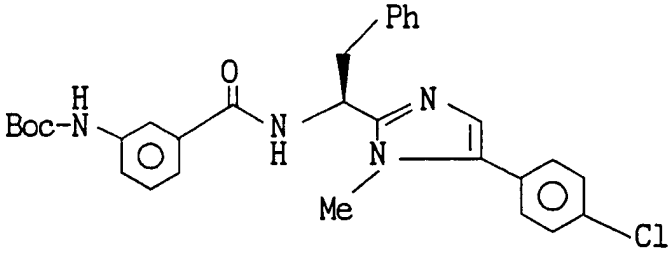
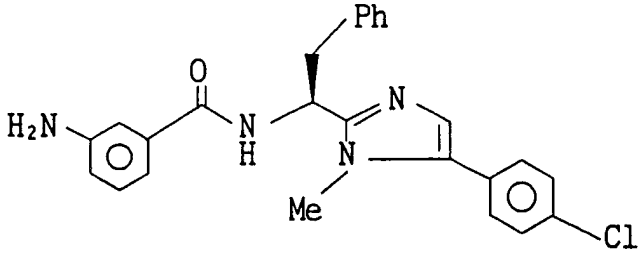
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Example No.	Formula
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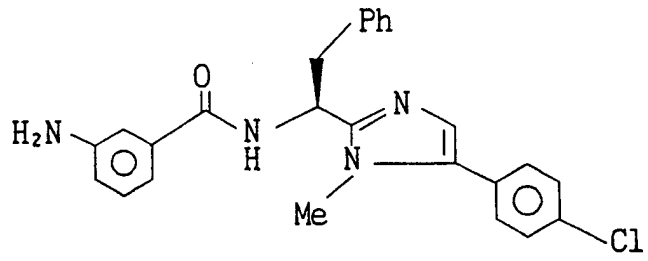
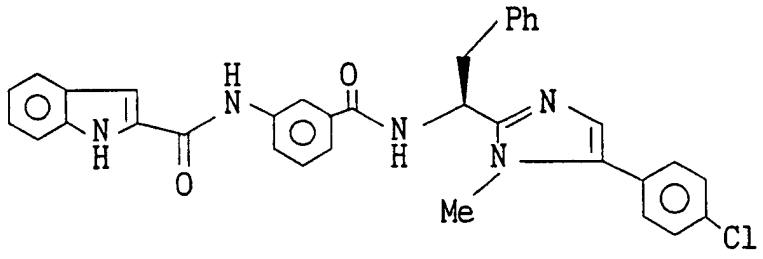
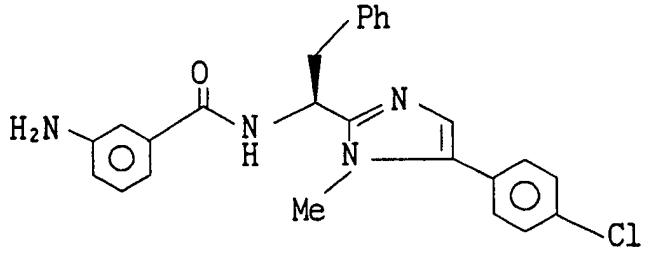
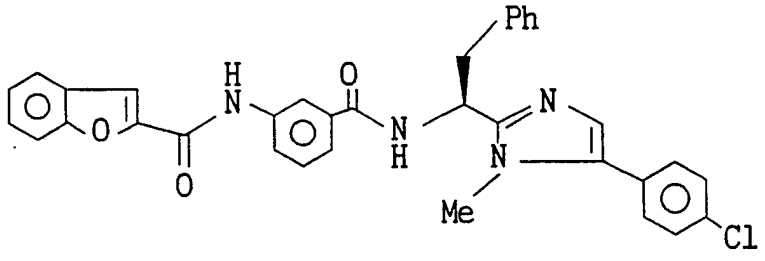
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Example No.	Formula
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37	
	

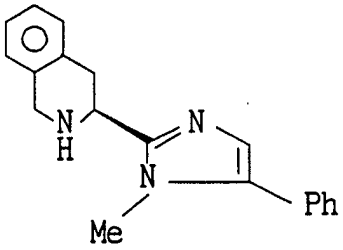
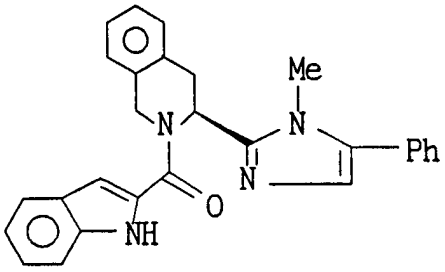
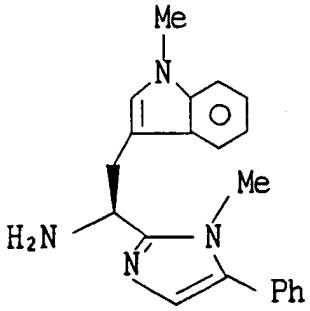
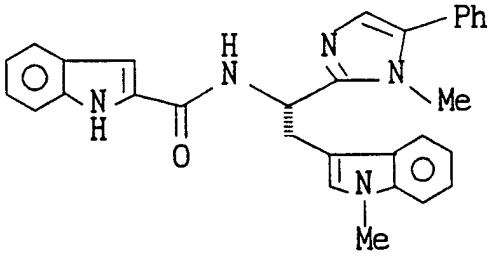
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Example No.	Formula
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39	
	

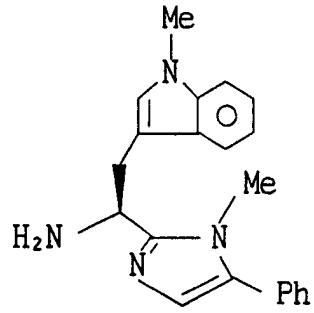
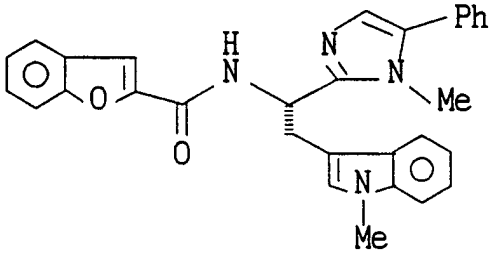
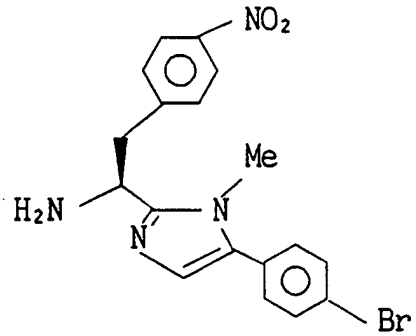
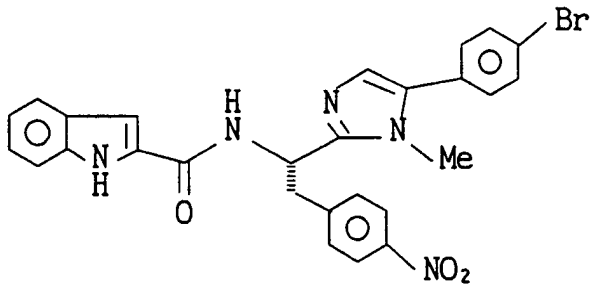
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Example No.	Formula
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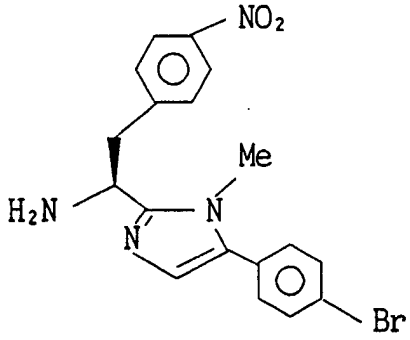
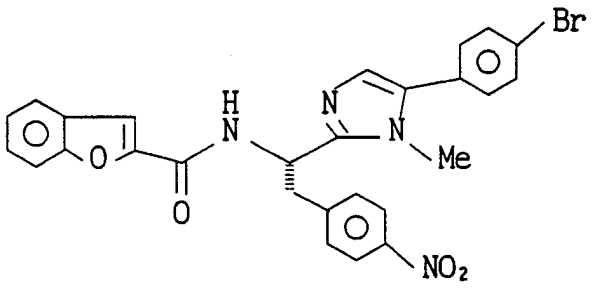
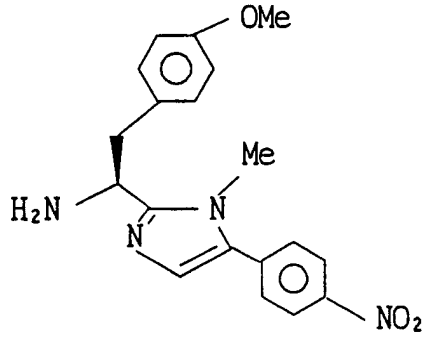
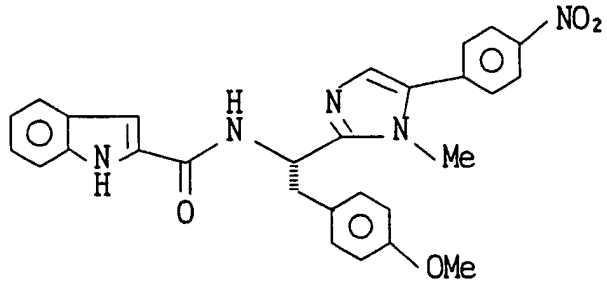
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Example No.	Formula
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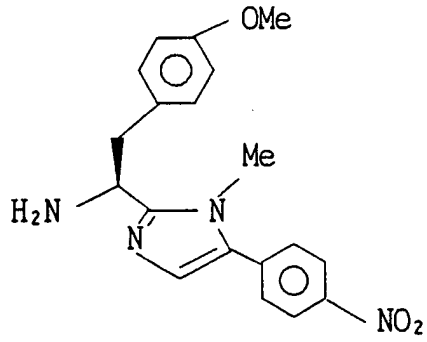
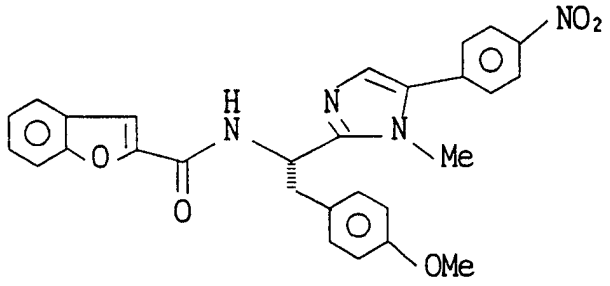
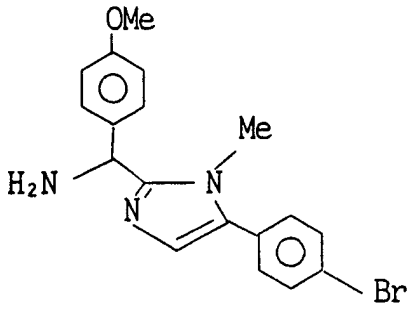
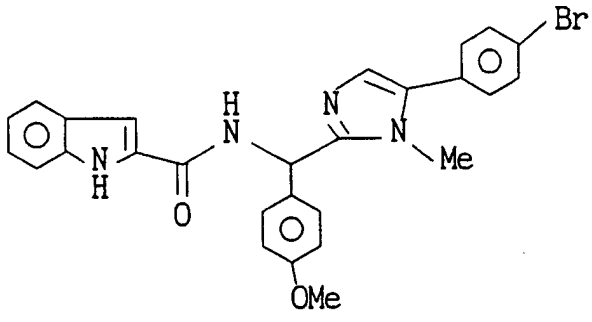
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Example No.	Formula
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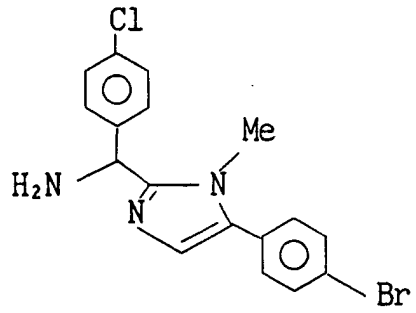
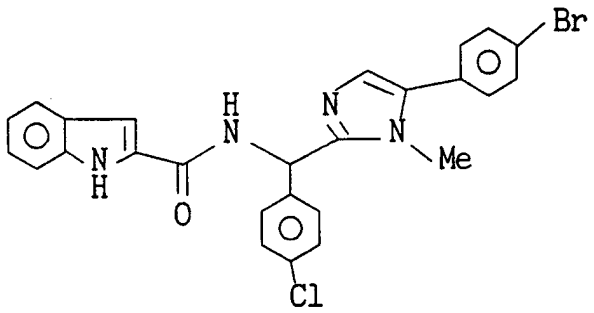
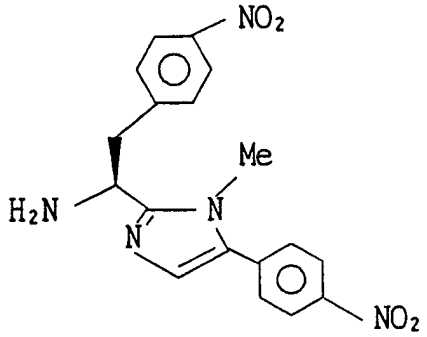
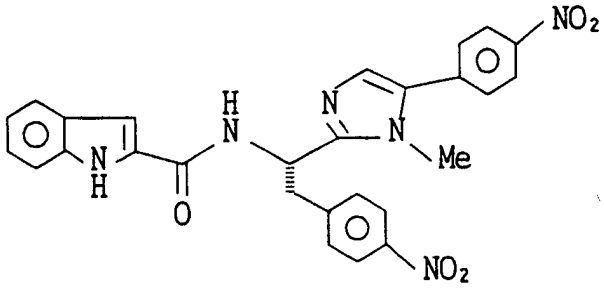
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Example No.	Formula
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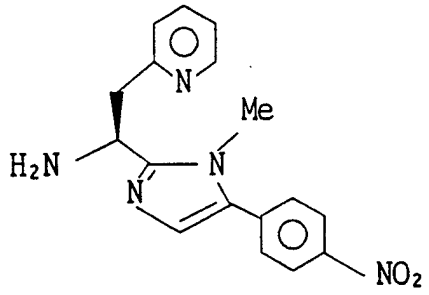
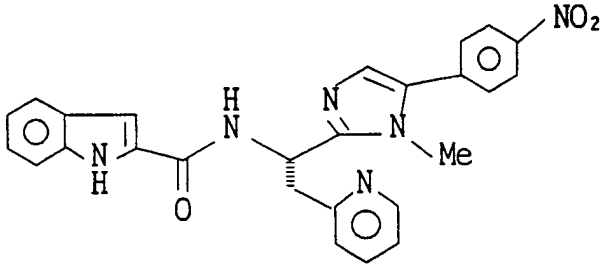
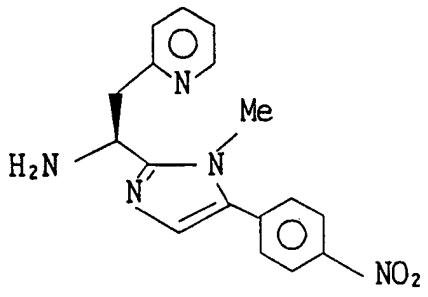
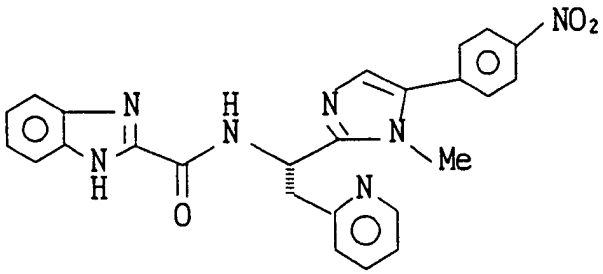
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Example No.	Formula
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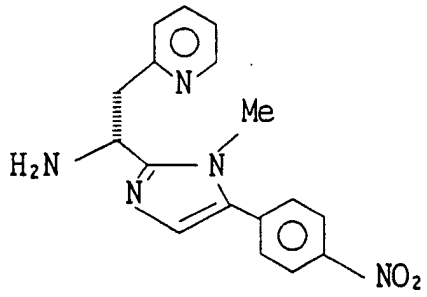
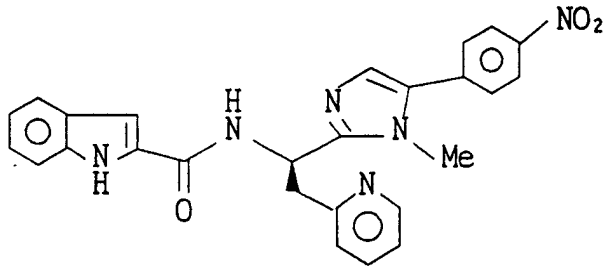
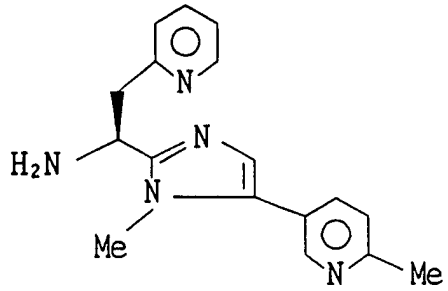
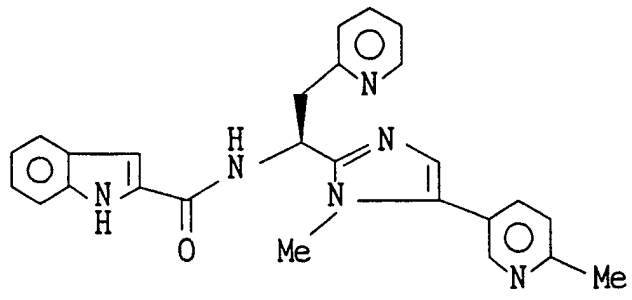
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Example No.	Formula
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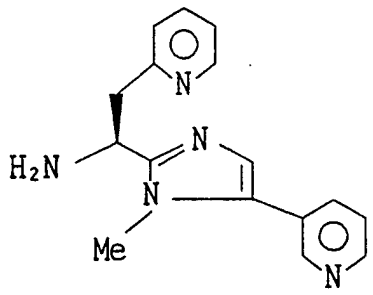
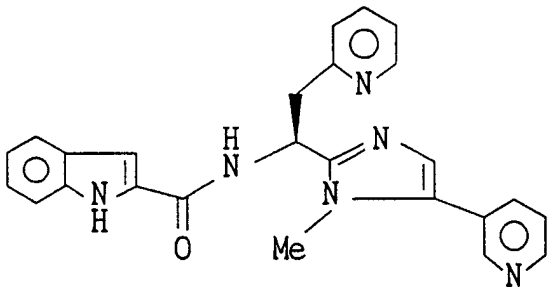
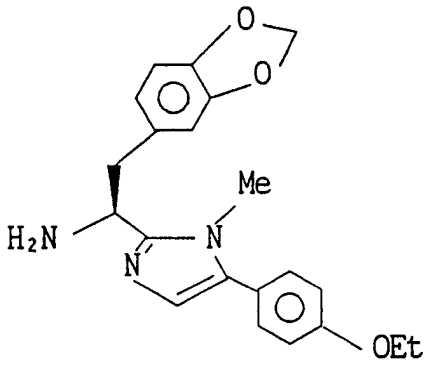
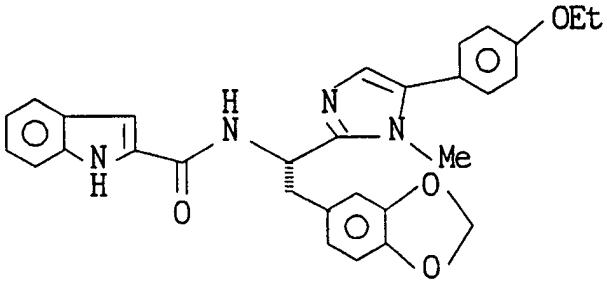
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Example No.	Formula
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53	
	

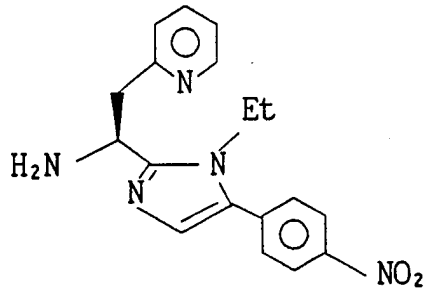
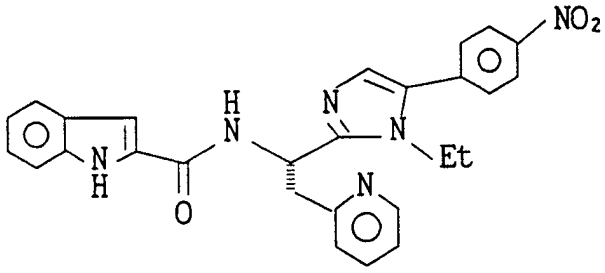
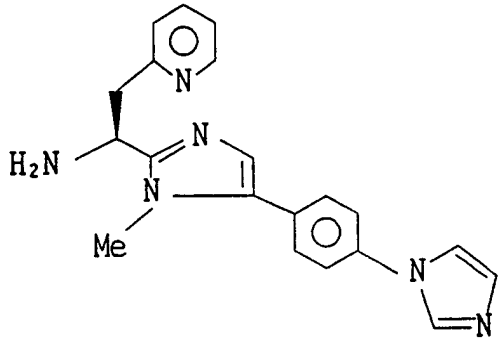
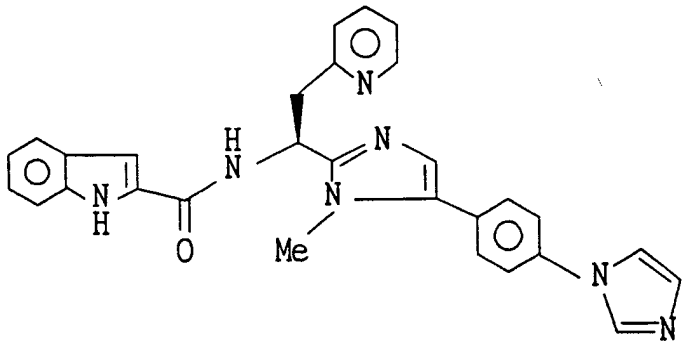
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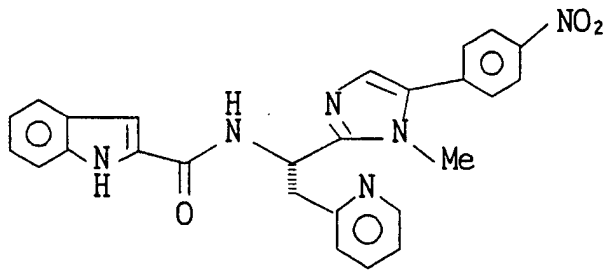
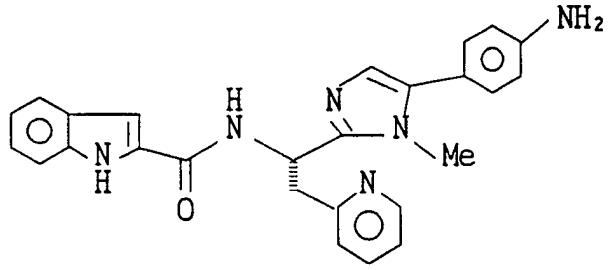
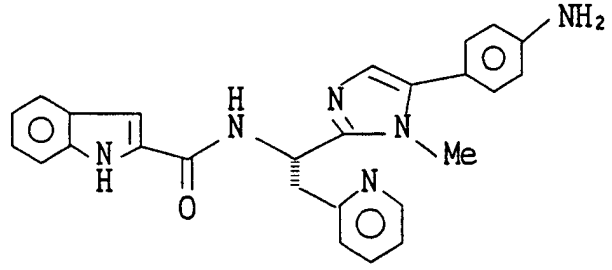
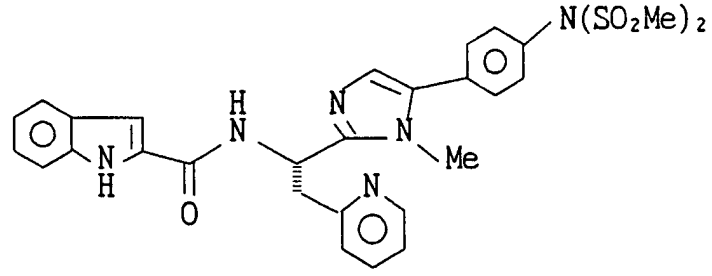
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Example No.	Formula
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57	
	

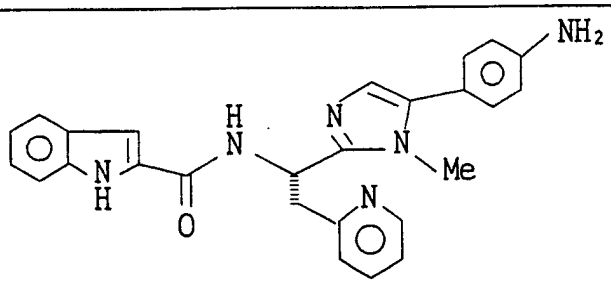
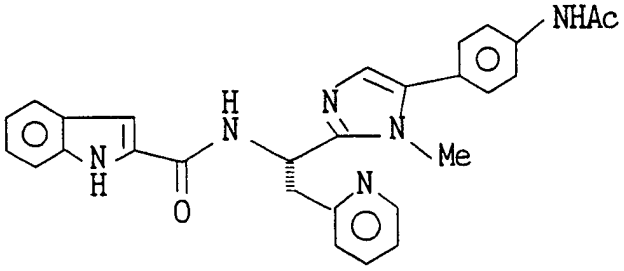
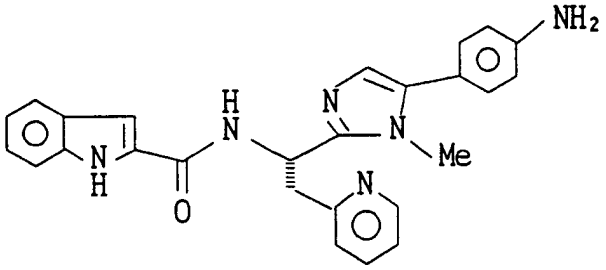
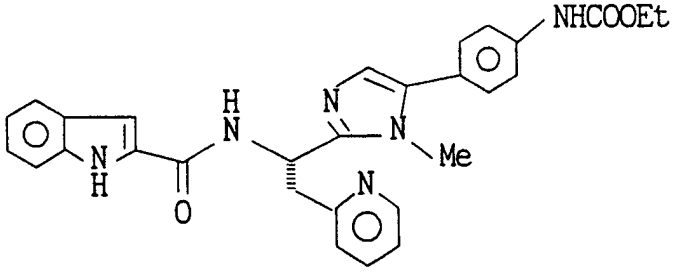
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Example No.	Formula
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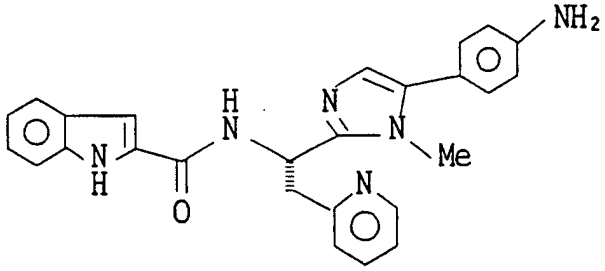
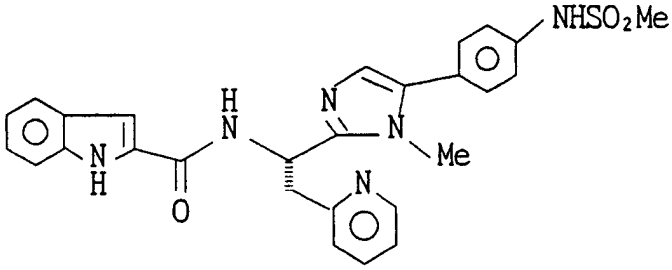
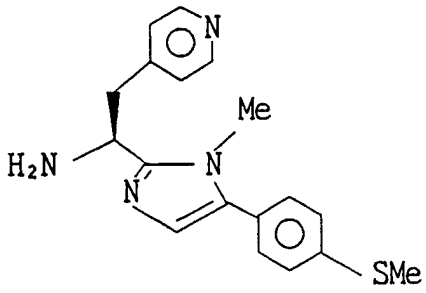
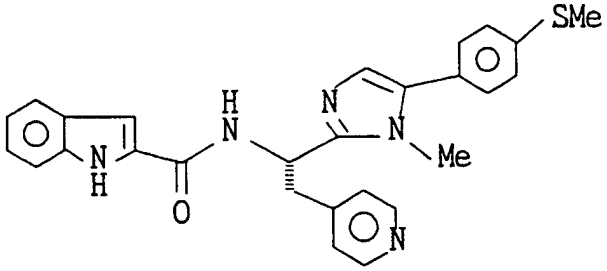
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Example No.	Formula
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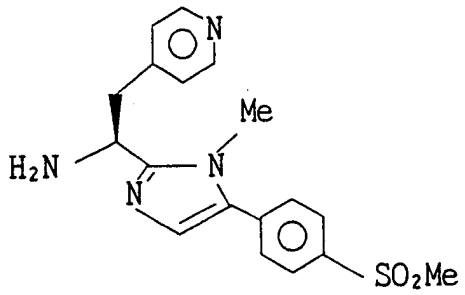
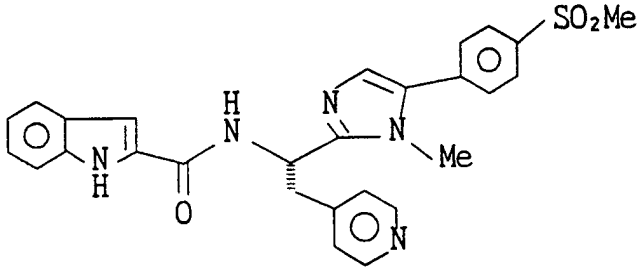
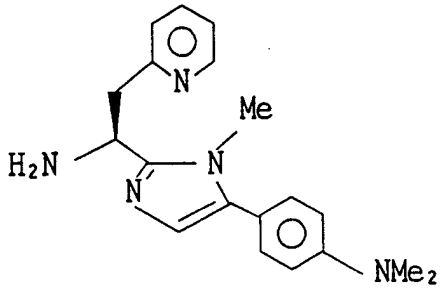
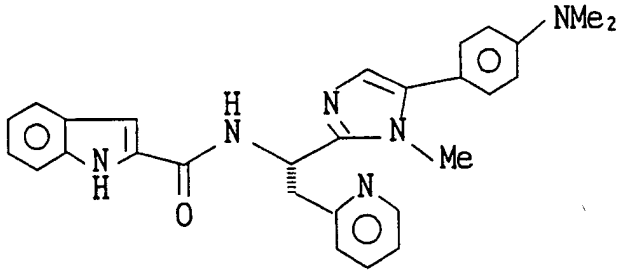
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Example No.	Formula
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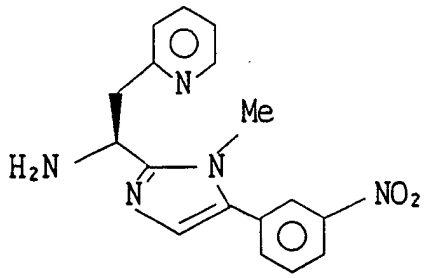
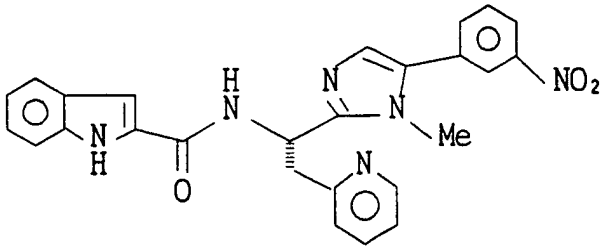
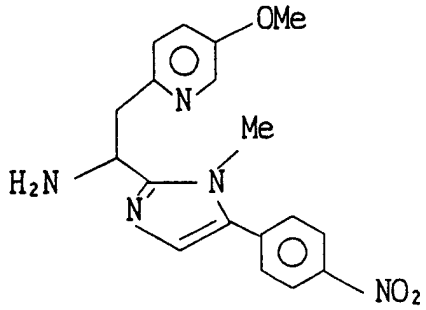
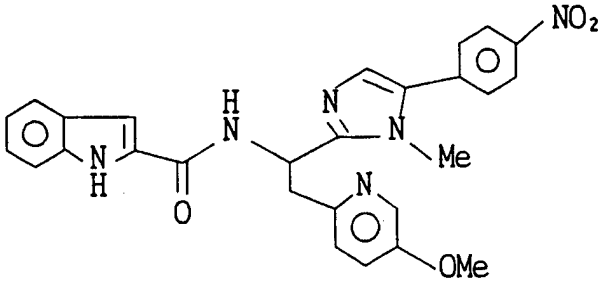
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Example No.	Formula
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65	
	

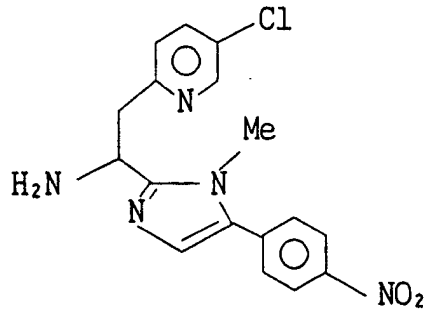
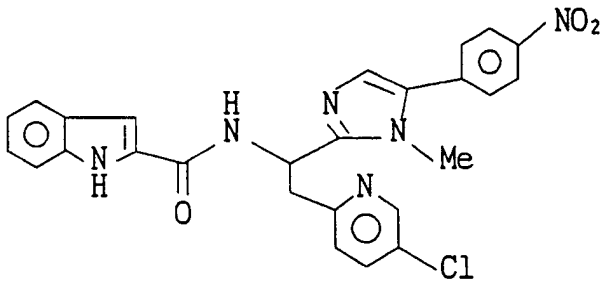
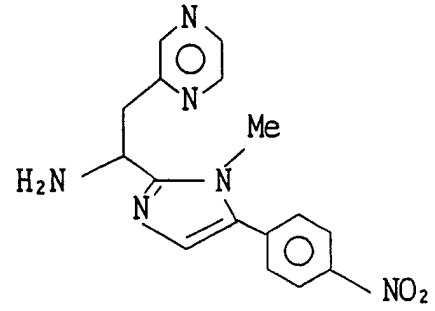
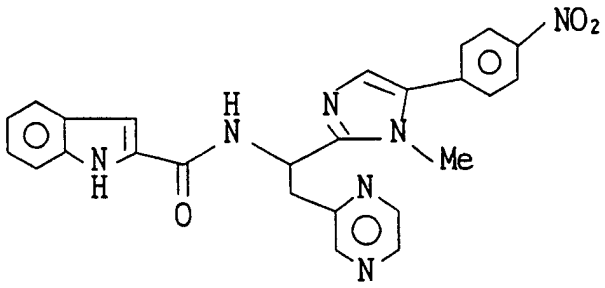
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Example No.	Formula
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67	
	

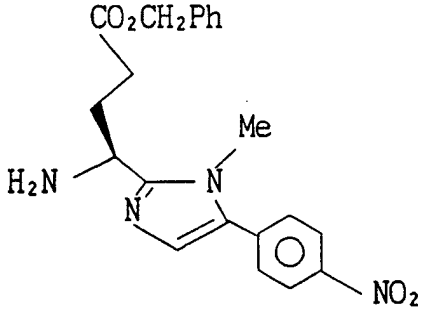
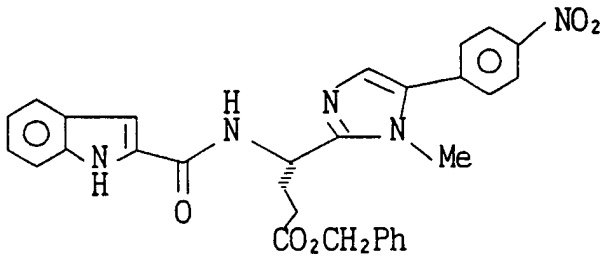
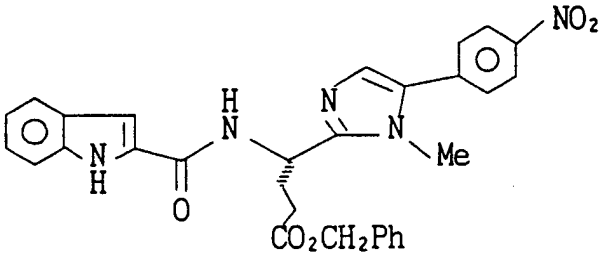
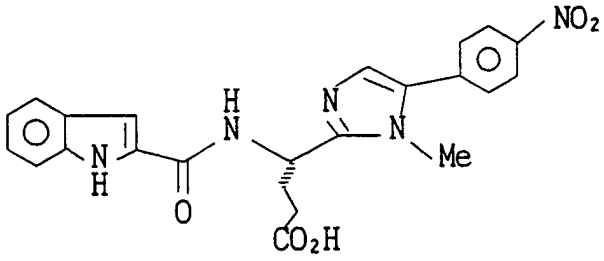
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Example No.	Formula
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69	
	

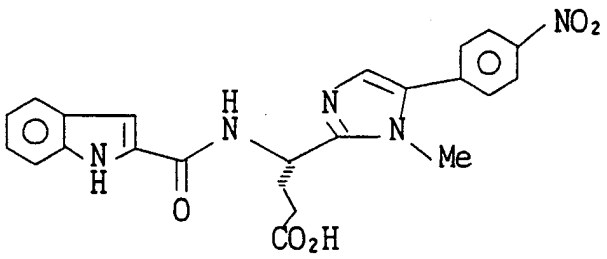
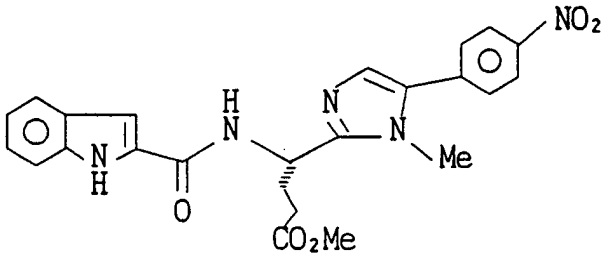
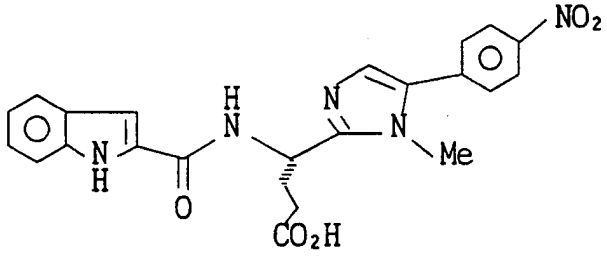
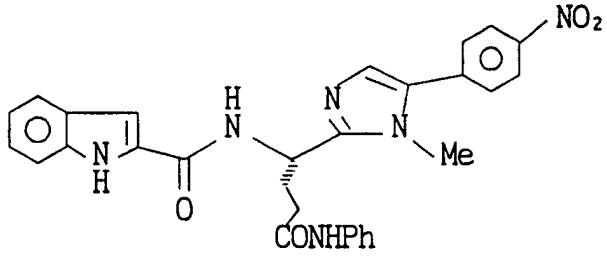
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Example No.	Formula
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71	
	

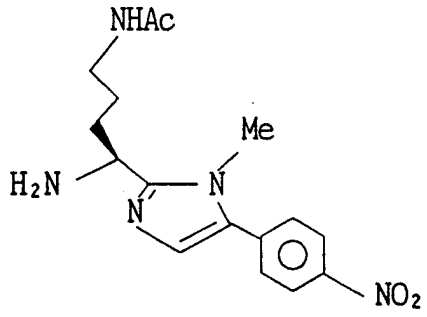
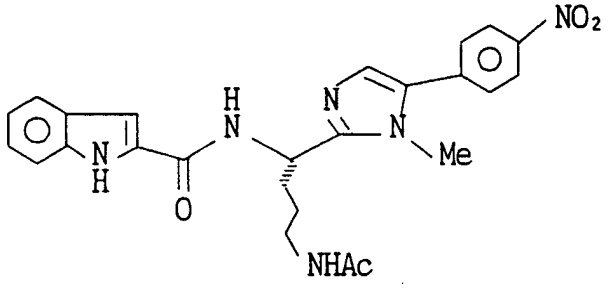
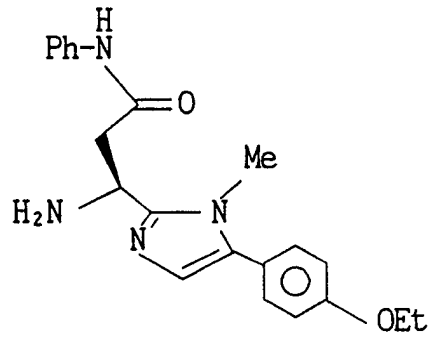
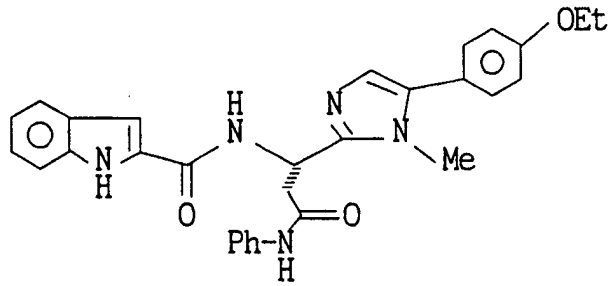
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Example No.	Formula
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73	
	

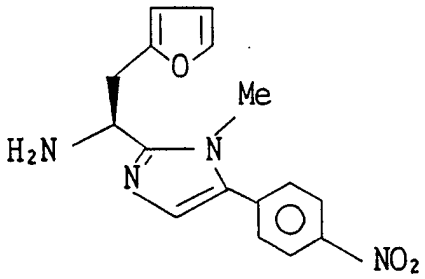
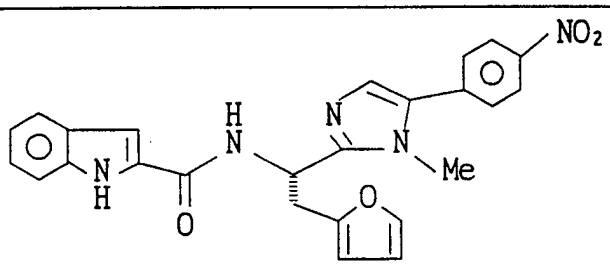
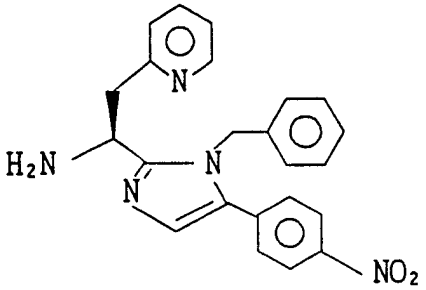
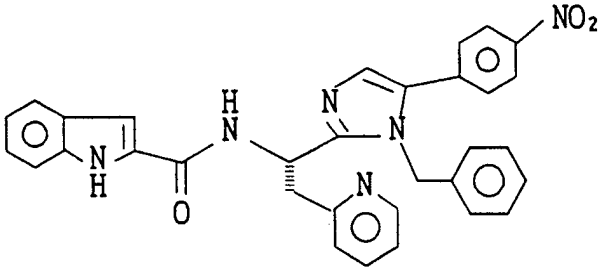
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Example No.	Formula
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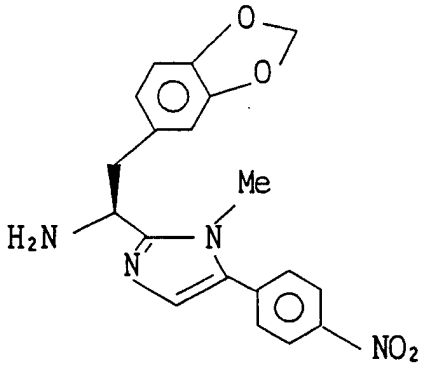
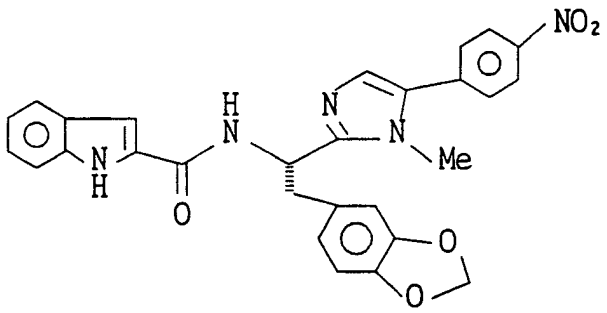
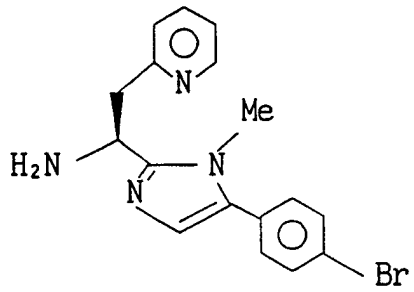
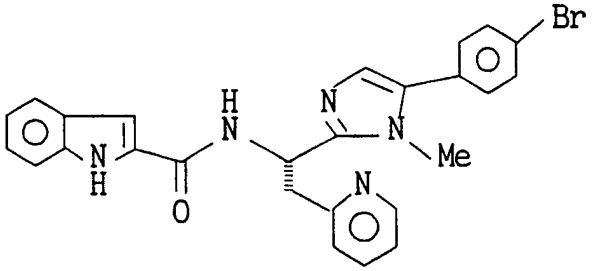
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Example No.	Formula
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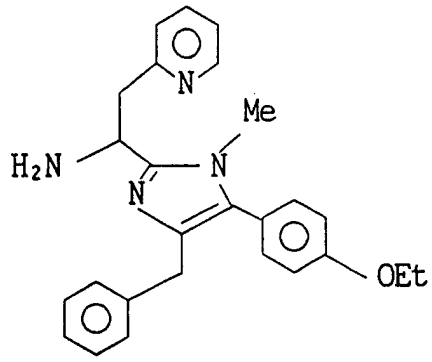
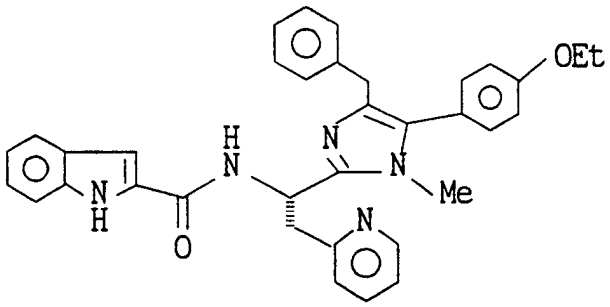
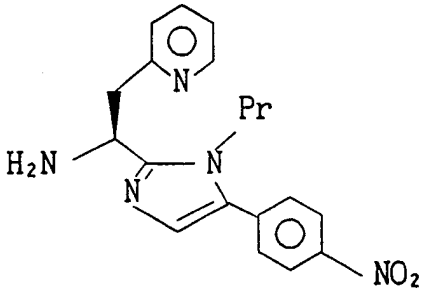
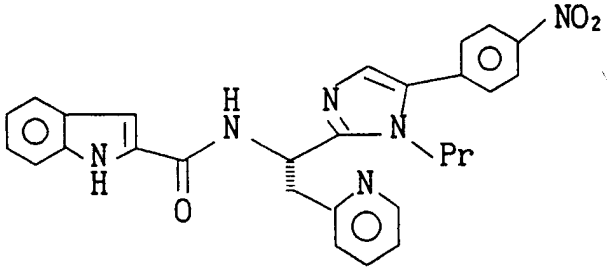
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Example No.	Formula
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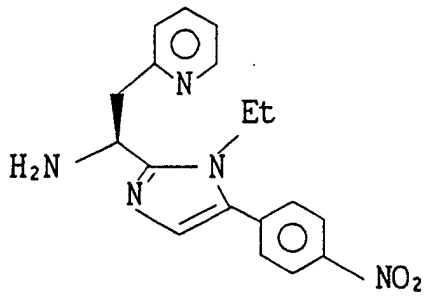
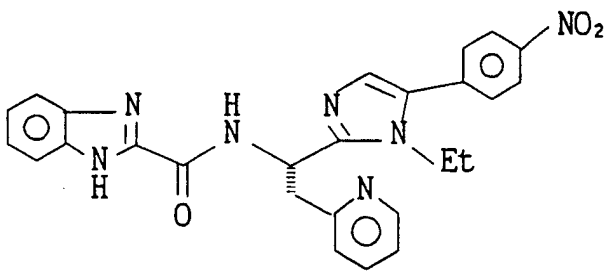
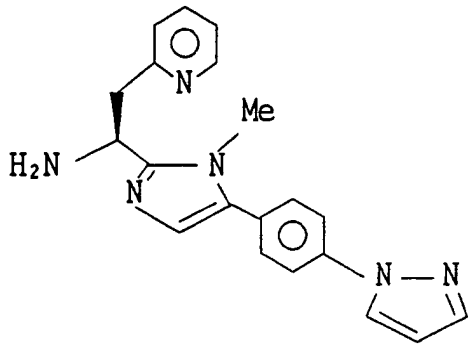
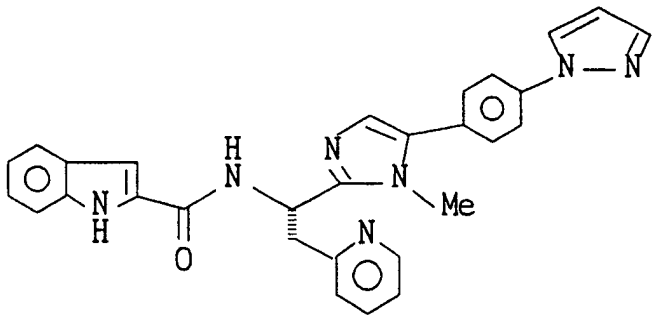
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Example No.	Formula
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81	
	

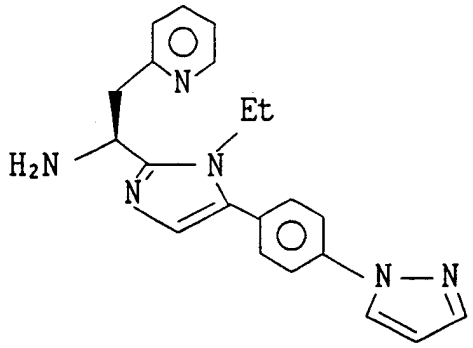
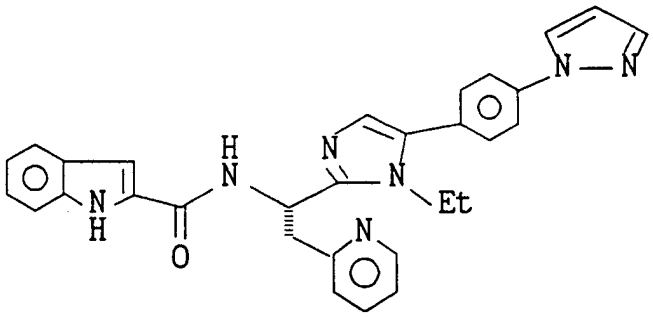
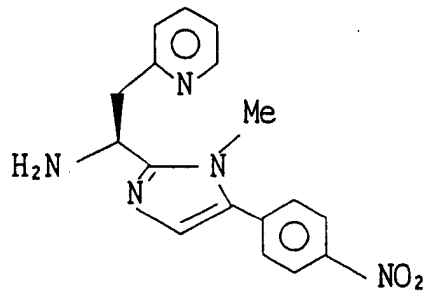
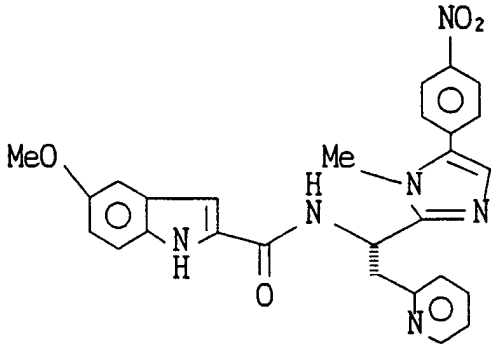
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Example No.	Formula
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83	
	

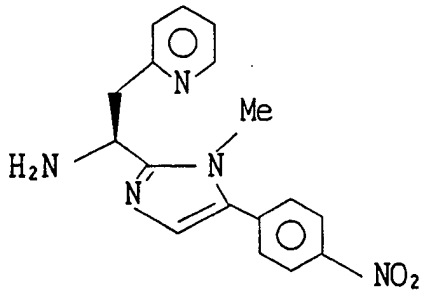
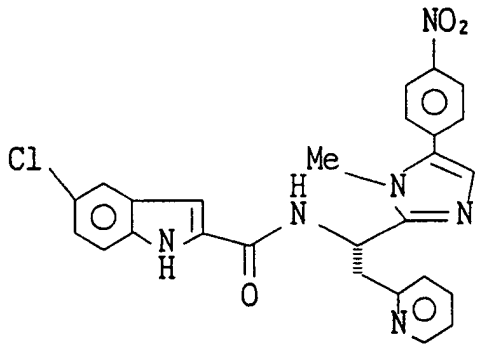
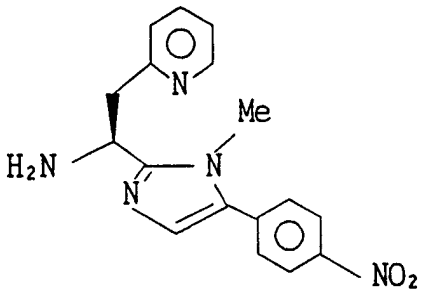
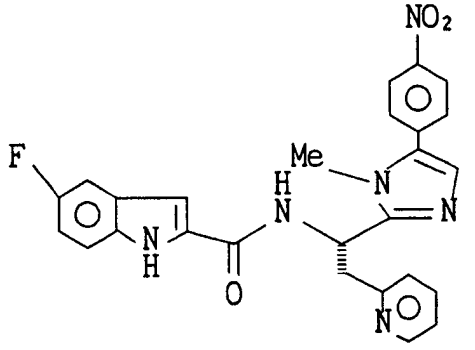
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Example No.	Formula
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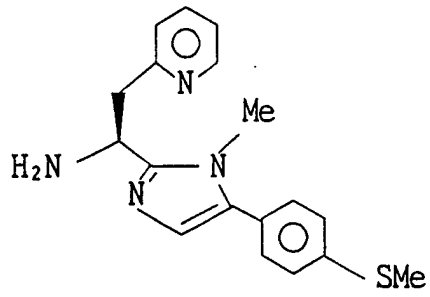
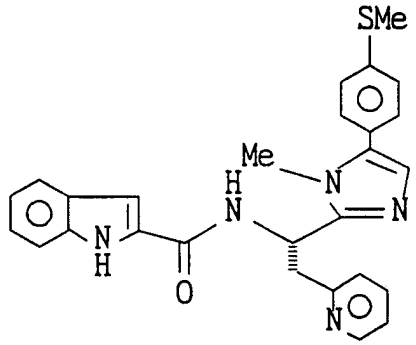
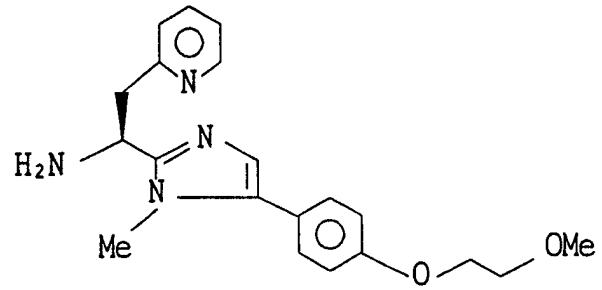
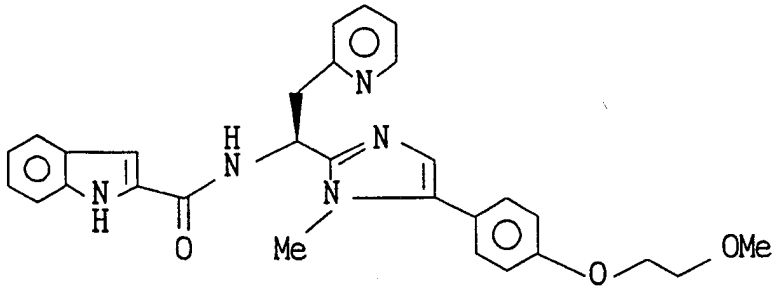
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Example No.	Formula
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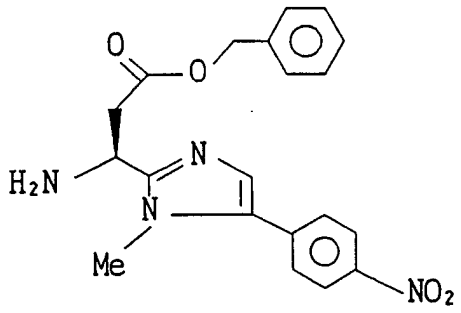
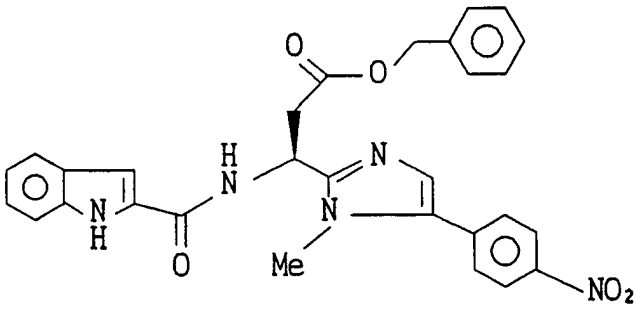
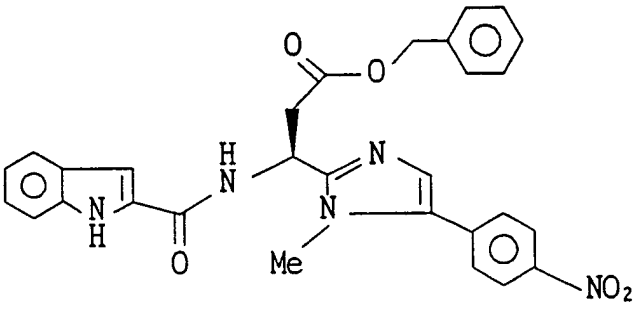
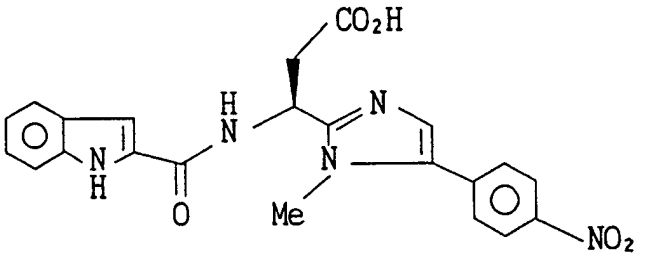
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Example No.	Formula
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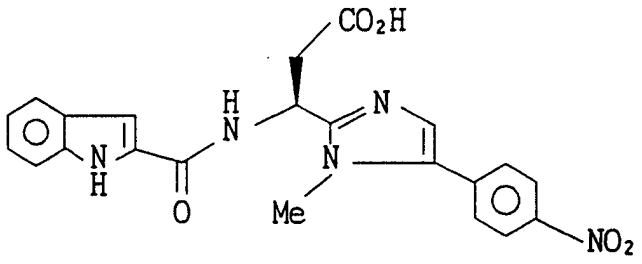
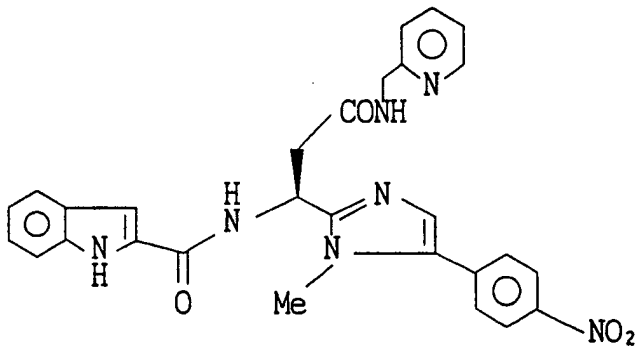
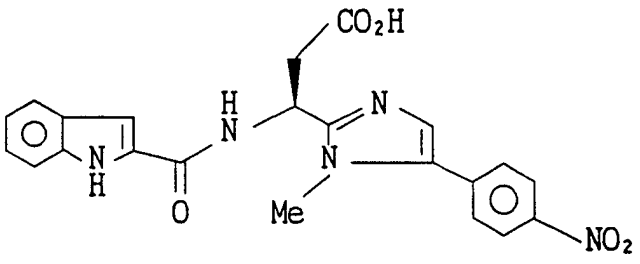
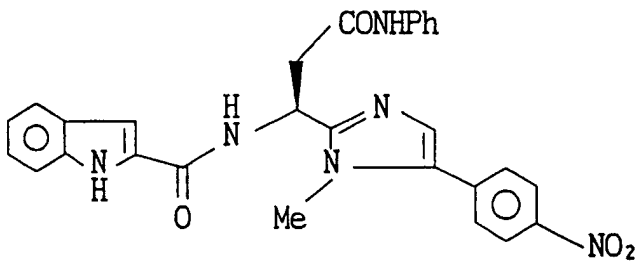
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Example No.	Formula
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91	
	

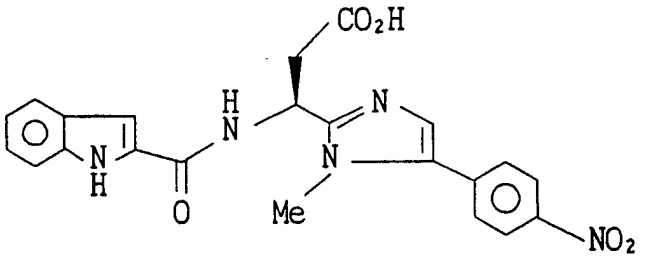
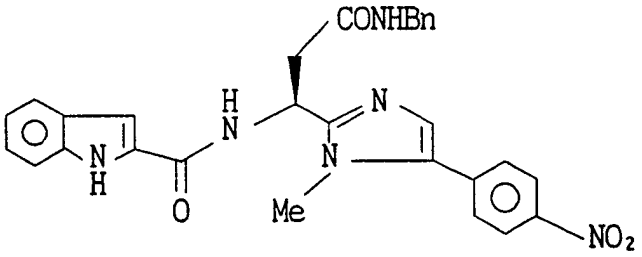
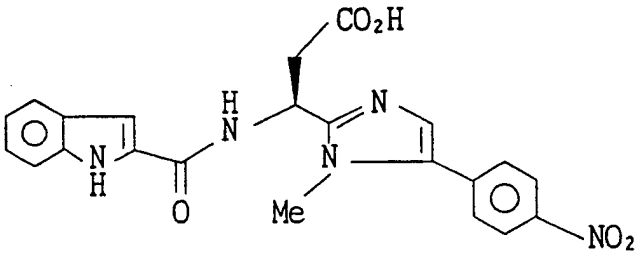
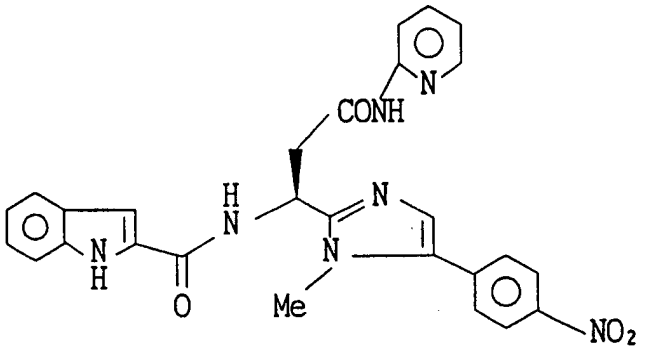
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Example No.	Formula
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93	
	

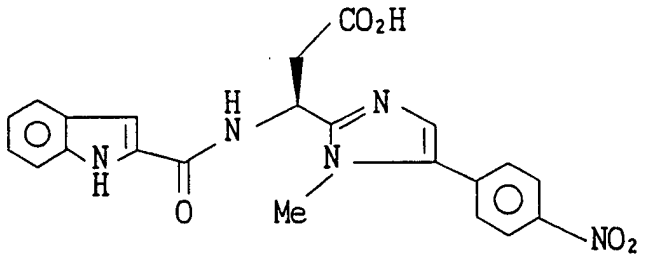
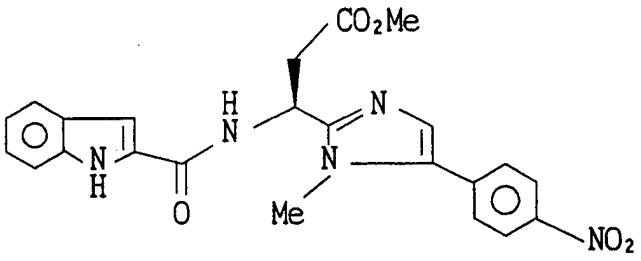
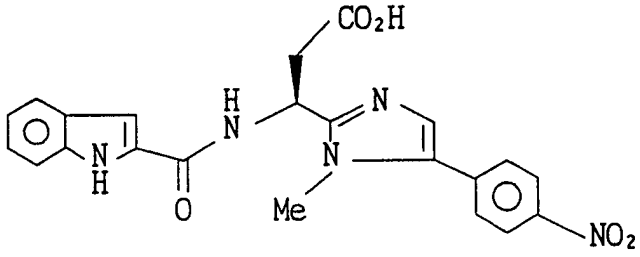
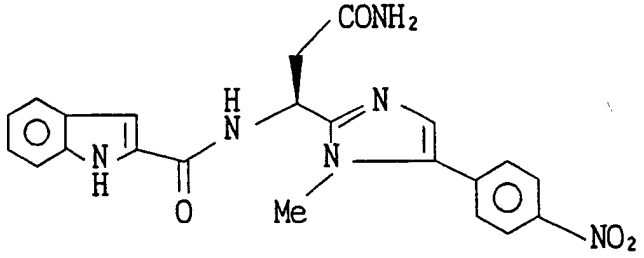
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Example No.	Formula
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95	
	

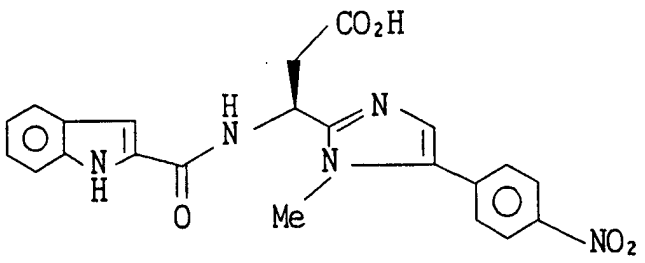
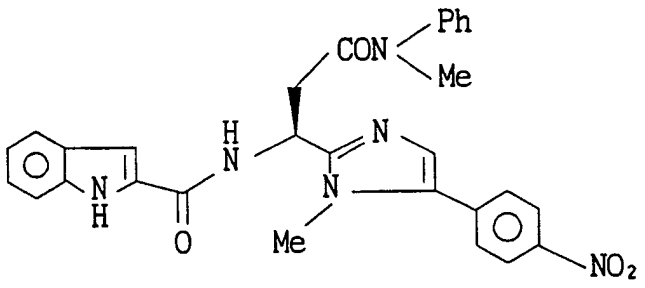
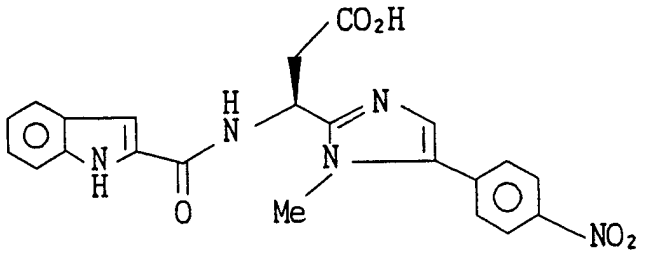
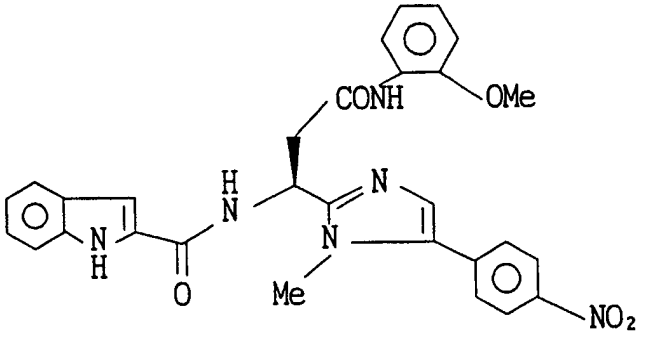
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Example No.	Formula
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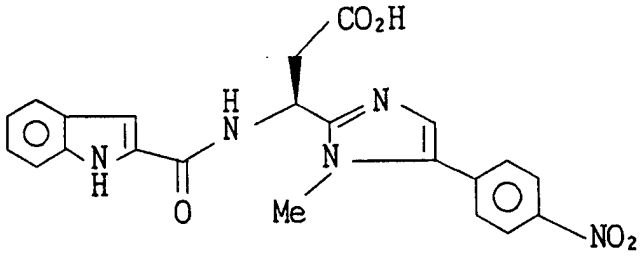
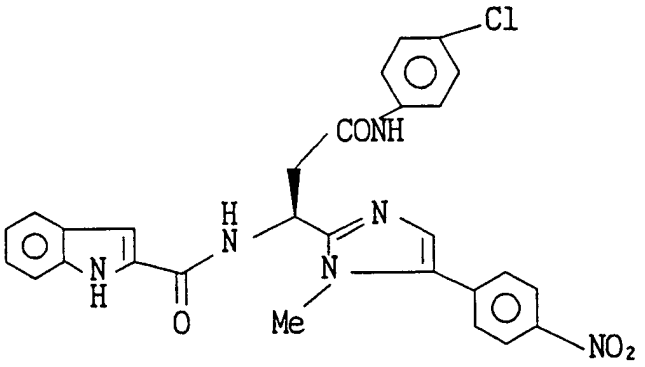
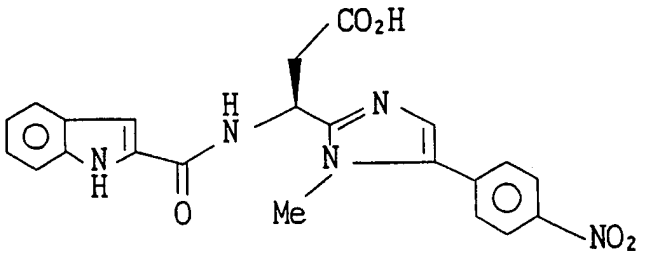
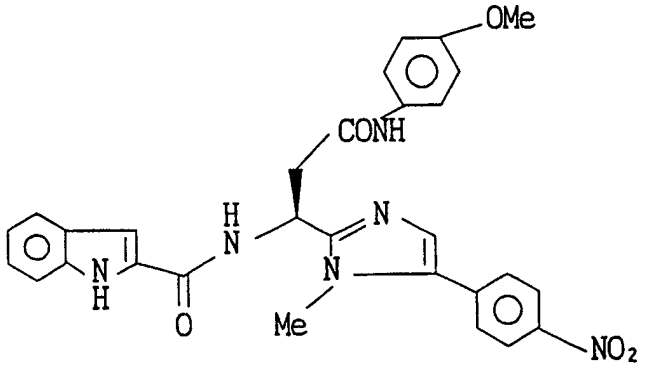
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Example No.	Formula
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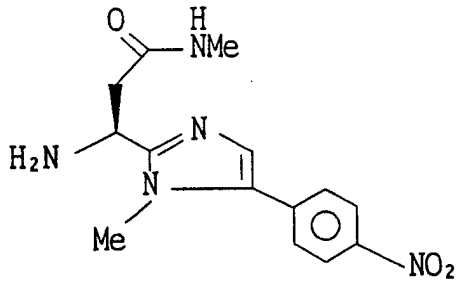
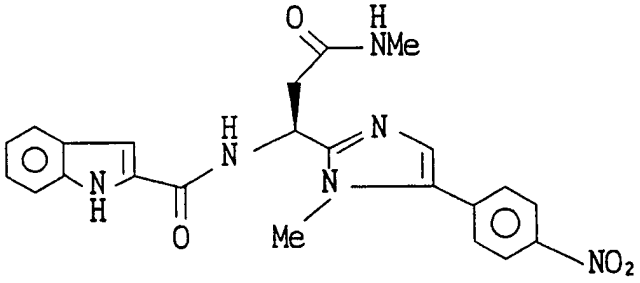
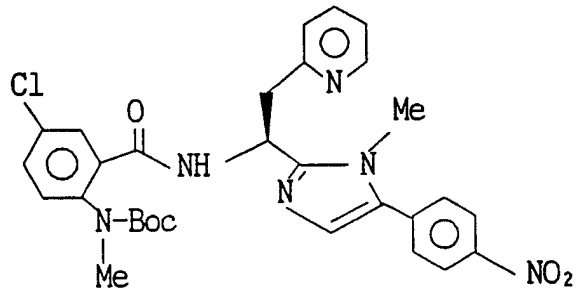
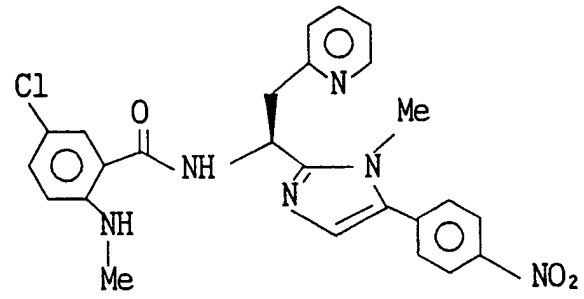
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Example No.	Formula
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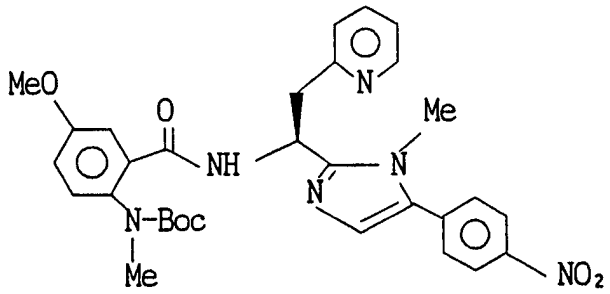
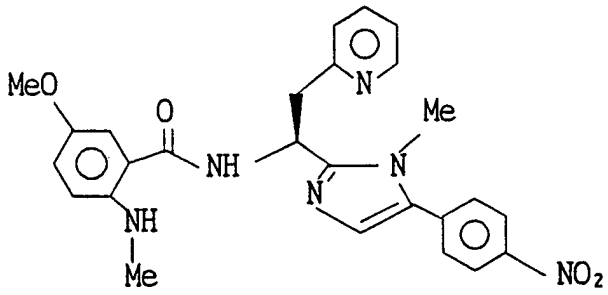
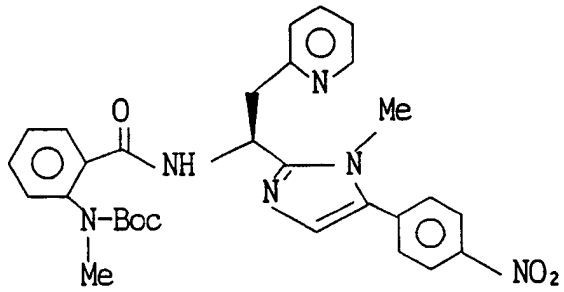
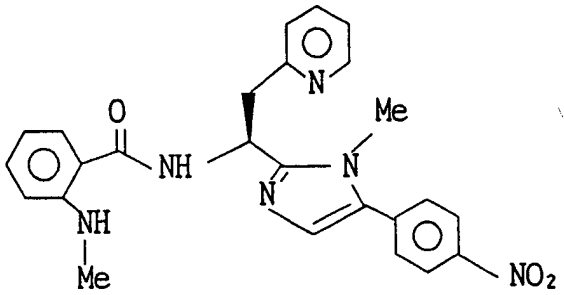
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Example No.	Formula
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103	
	

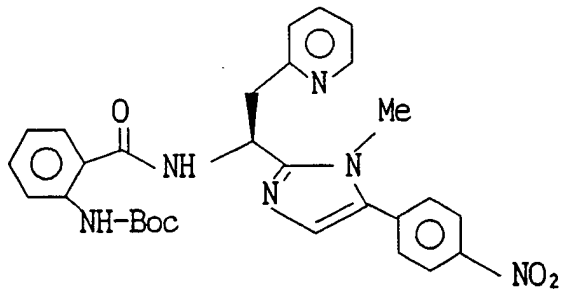
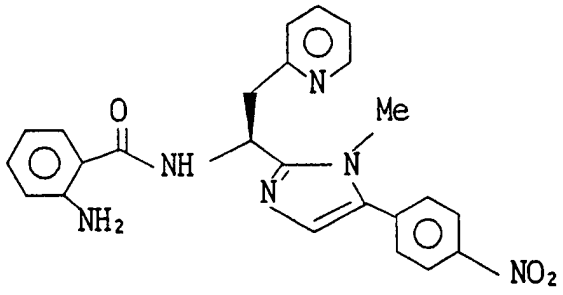
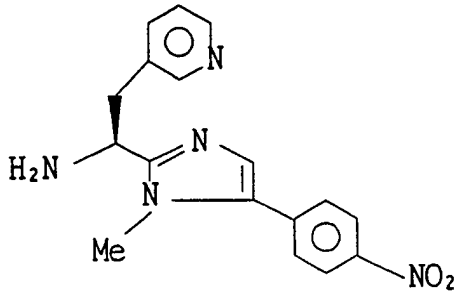
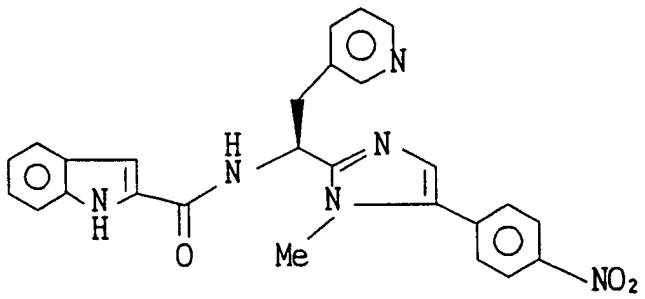
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Example No.	Formula
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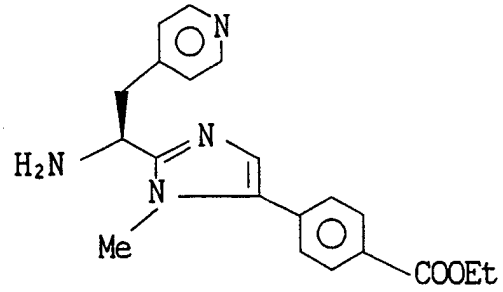
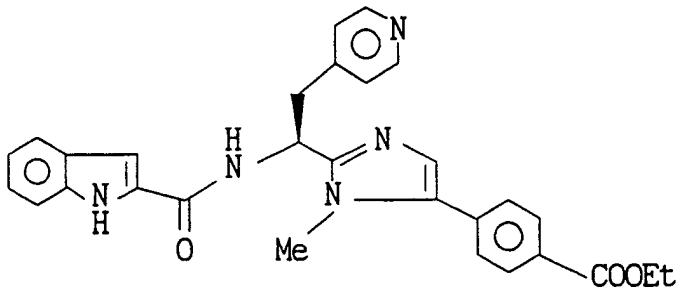
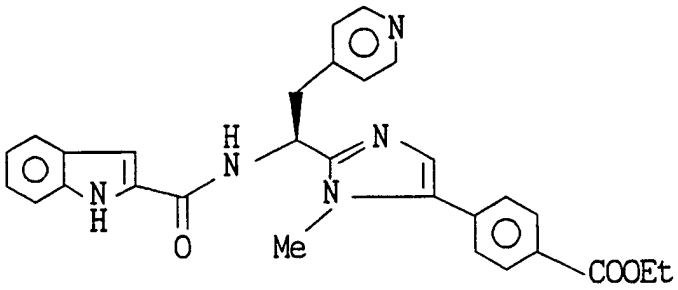
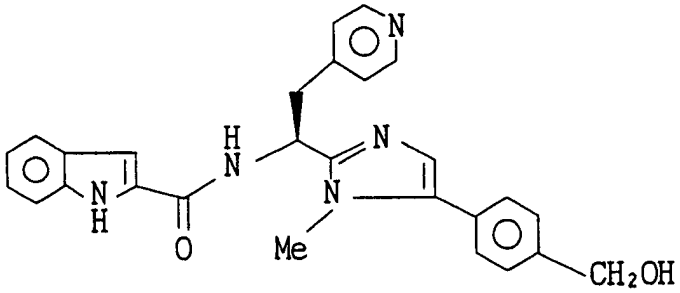
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Example No.	Formula
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107	
	

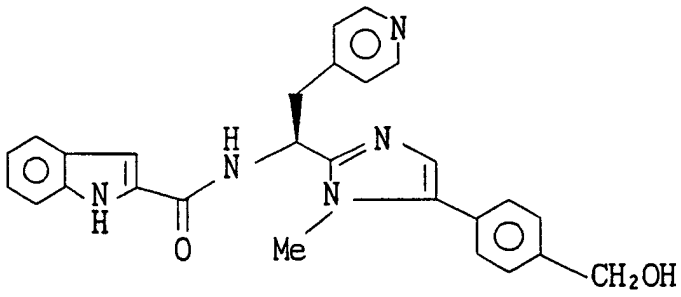
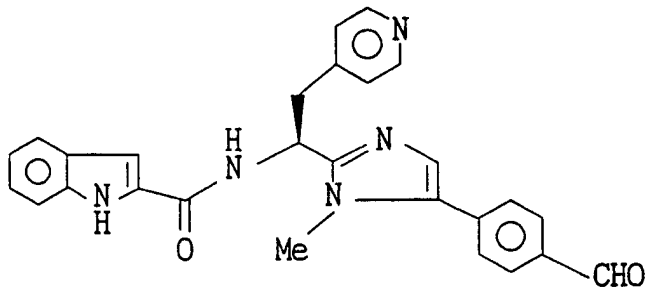
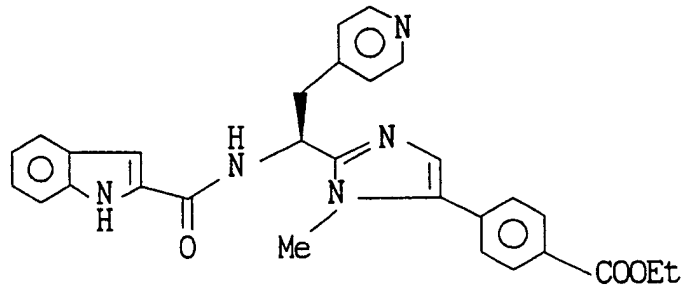
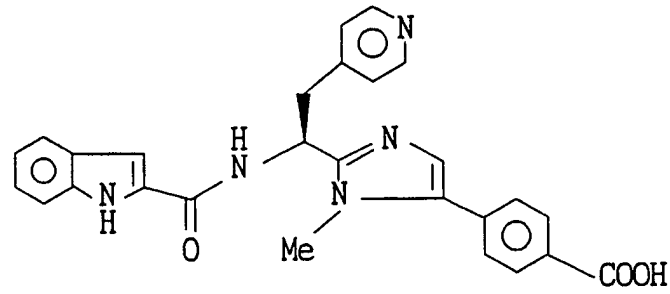
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Example No.	Formula
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109	
	

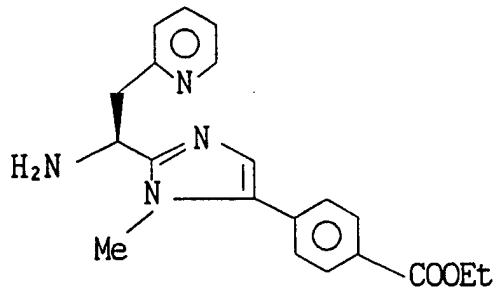
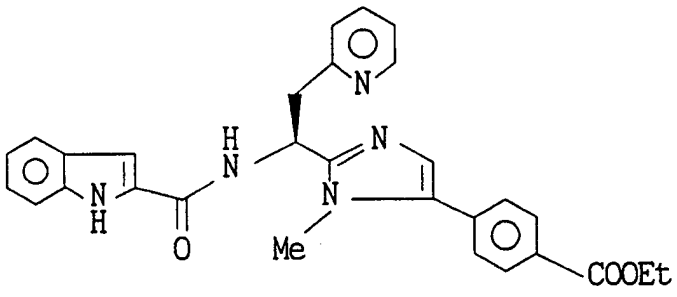
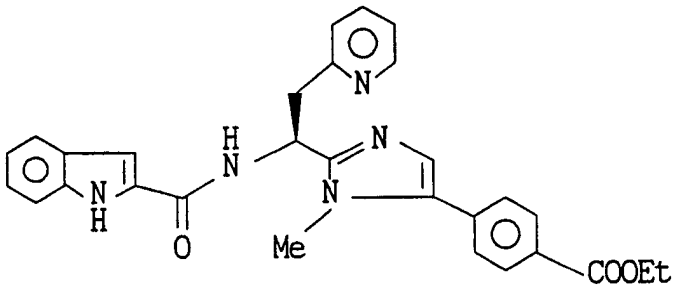
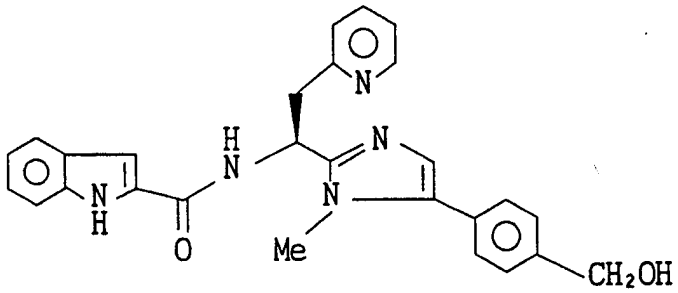
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Example No.	Formula
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111	
	

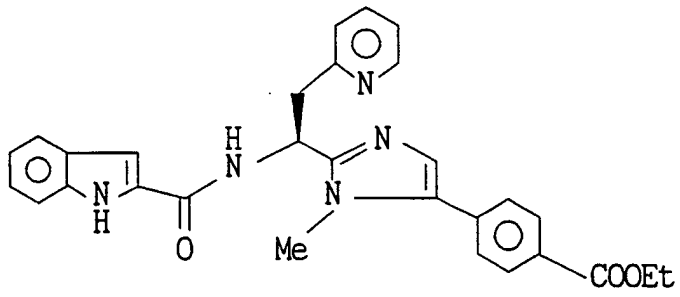
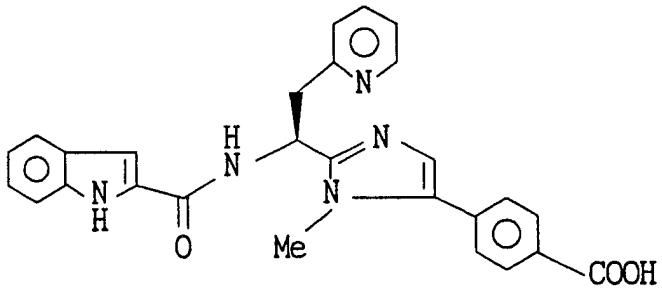
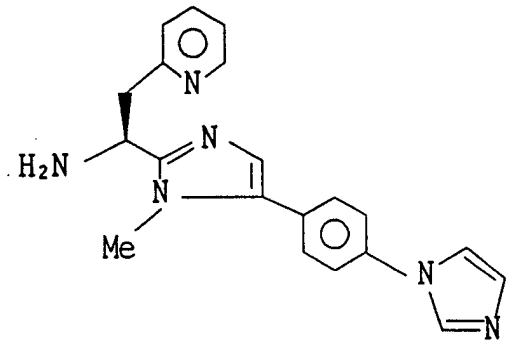
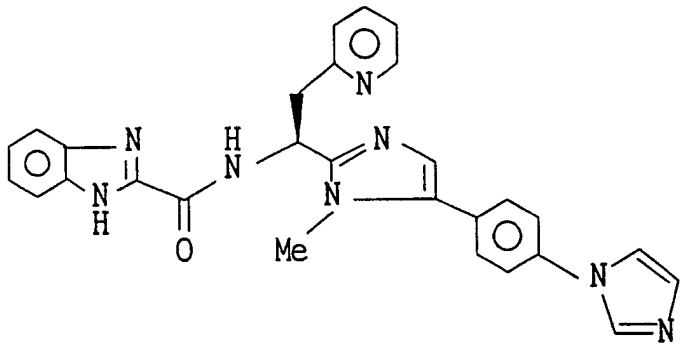
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Example No.	Formula
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113	
	

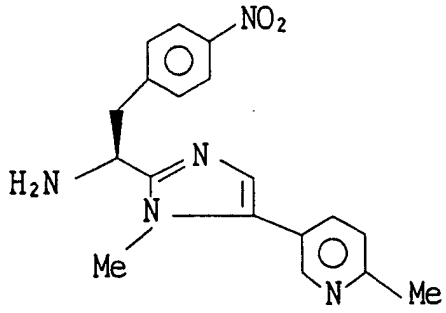
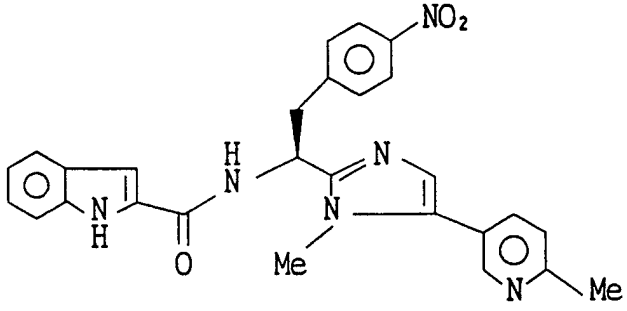
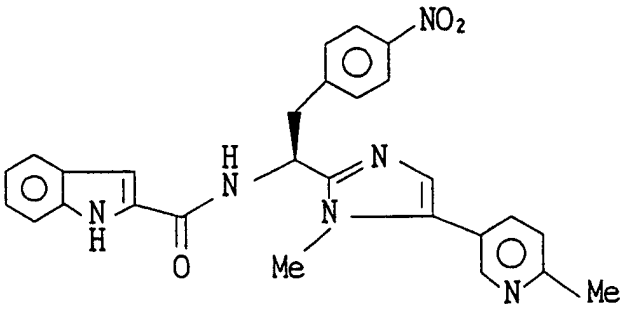
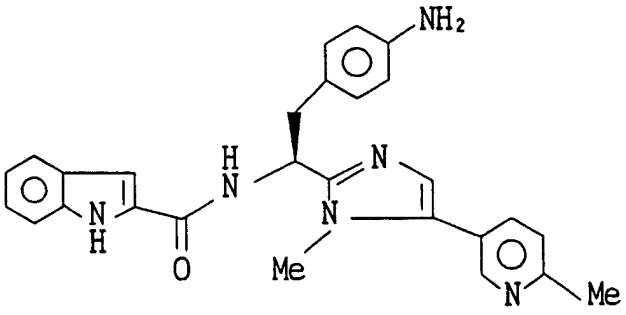
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Example No.	Formula
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115	
	

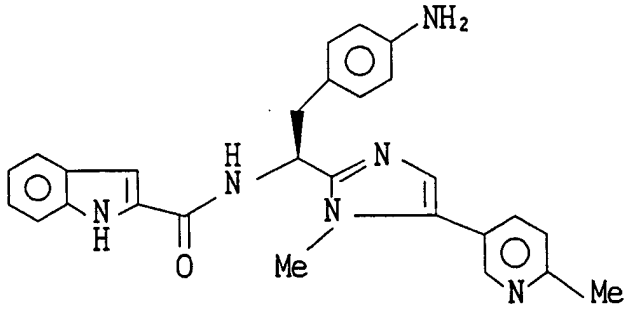
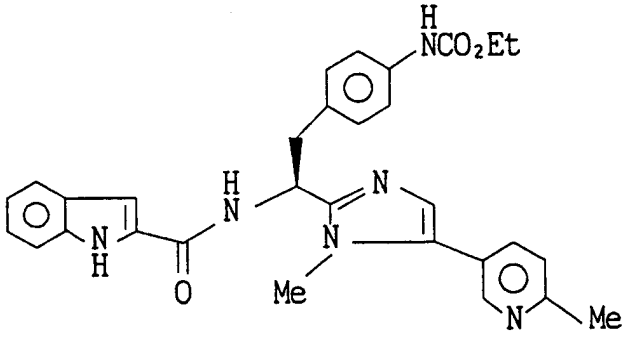
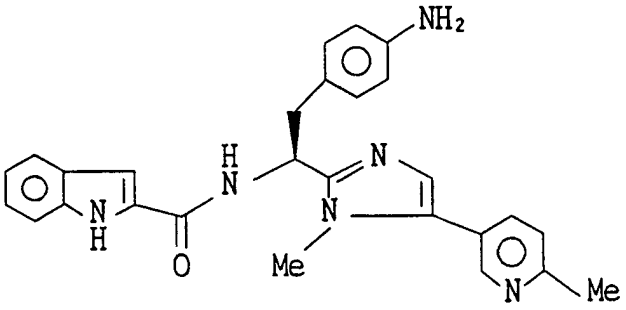
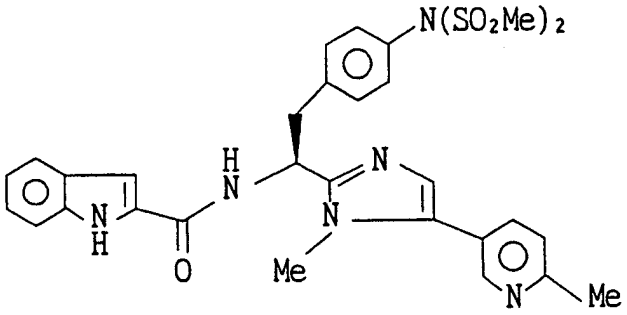
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Example No.	Formula
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117	
	

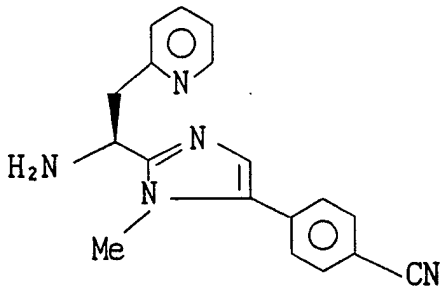
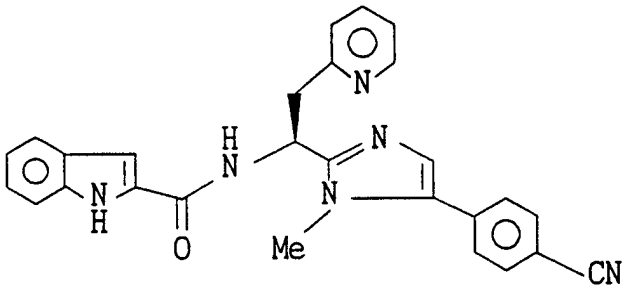
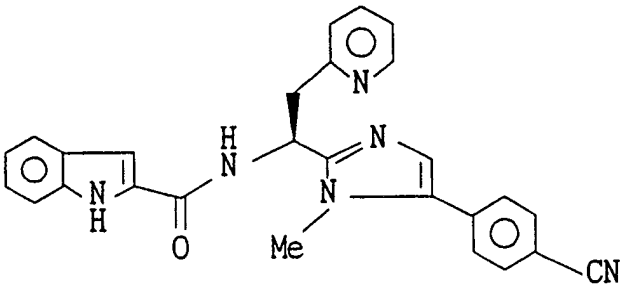
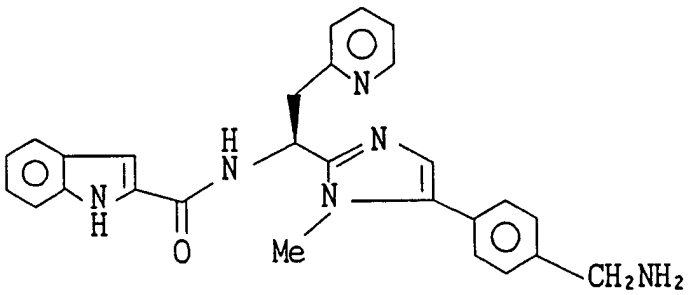
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Example No.	Formula
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119	
	

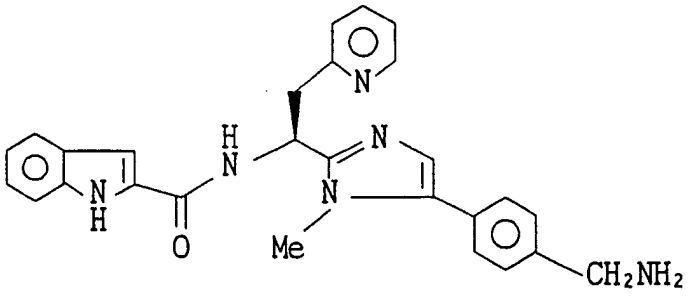
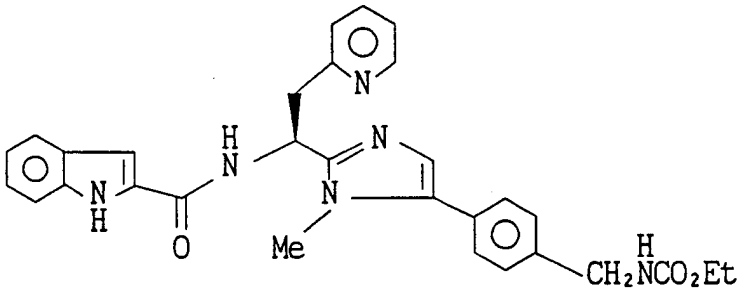
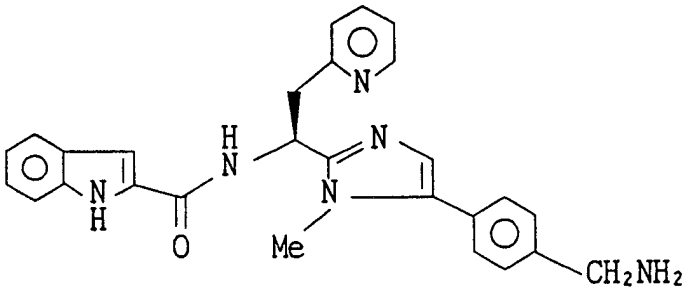
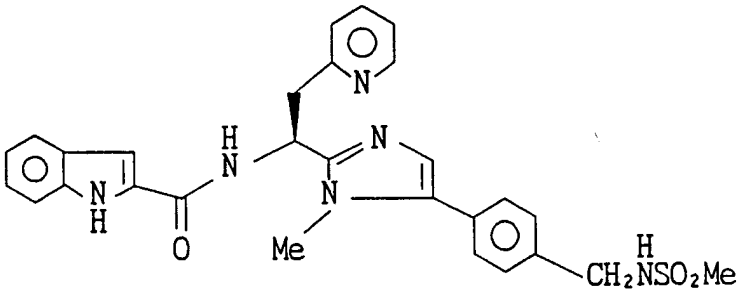
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Example No.	Formula
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121	
	

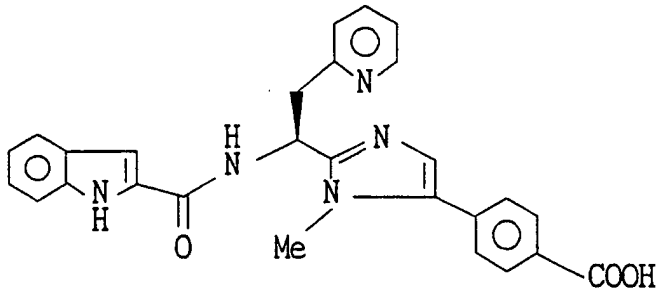
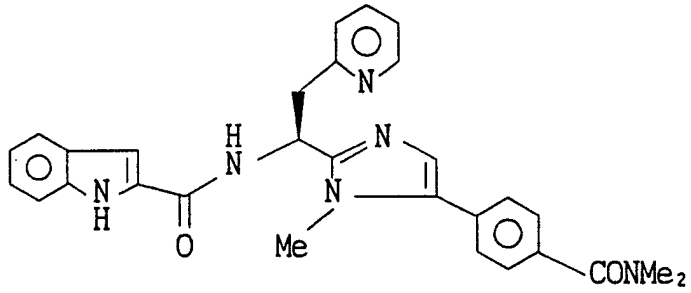
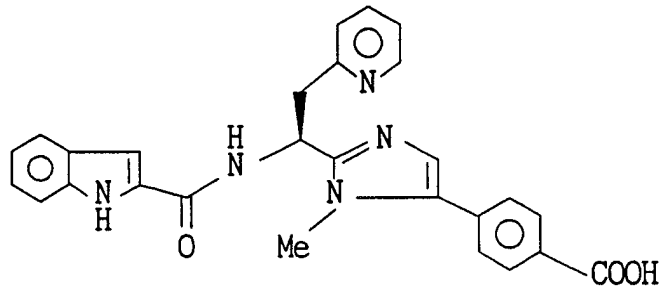
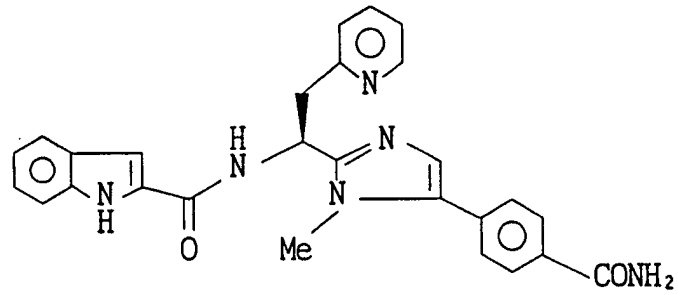
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Example No.	Formula
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123	
	

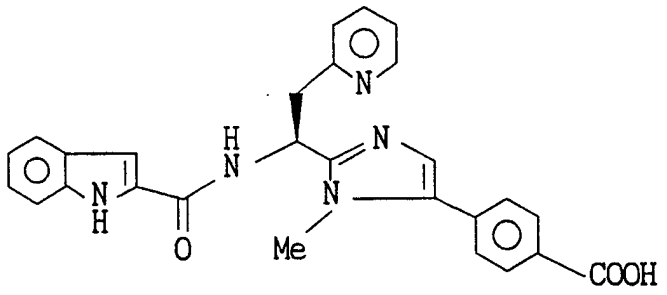
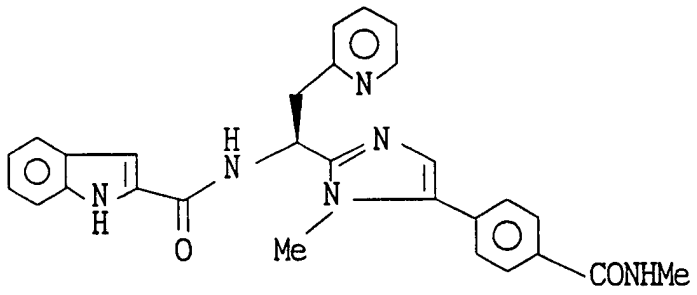
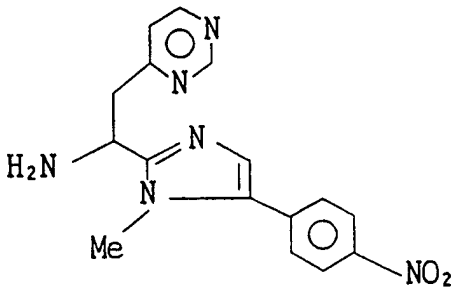
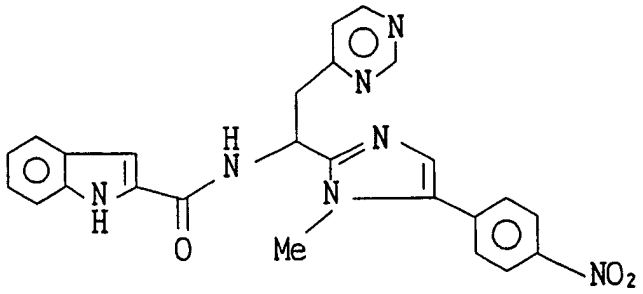
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Example No.	Formula
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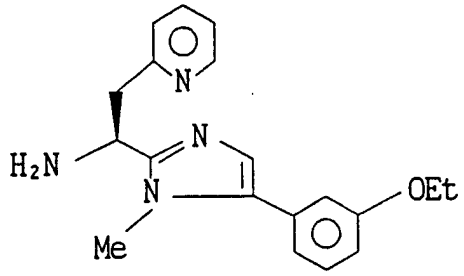
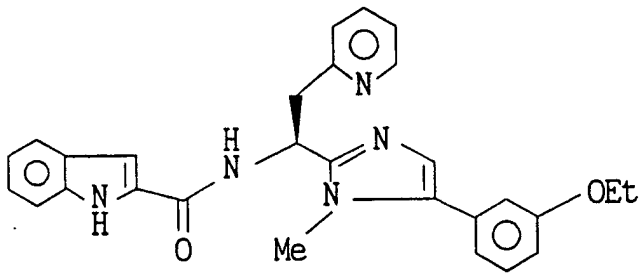
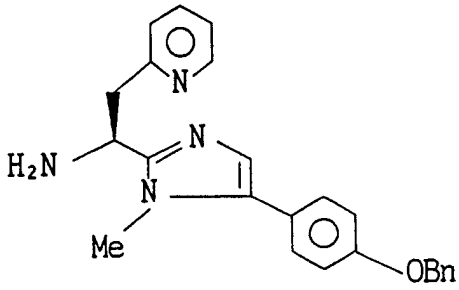
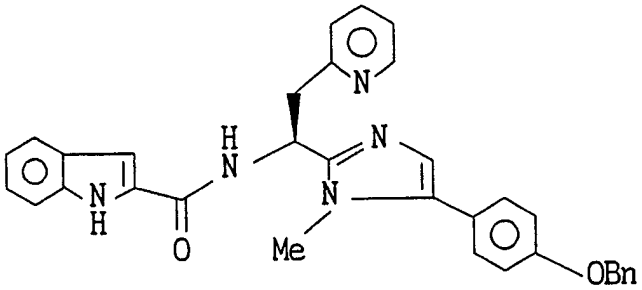
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Example No.	Formula
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127	
	

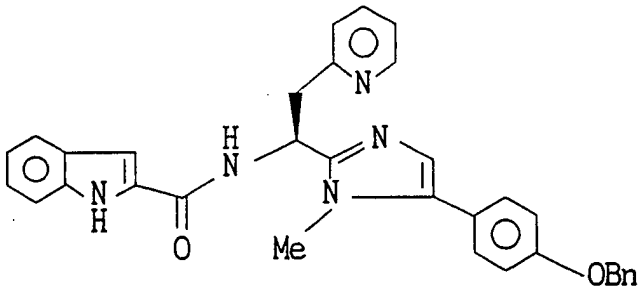
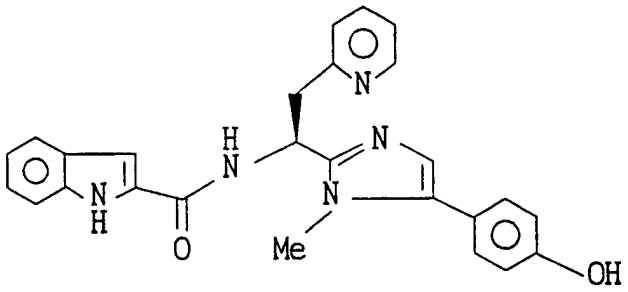
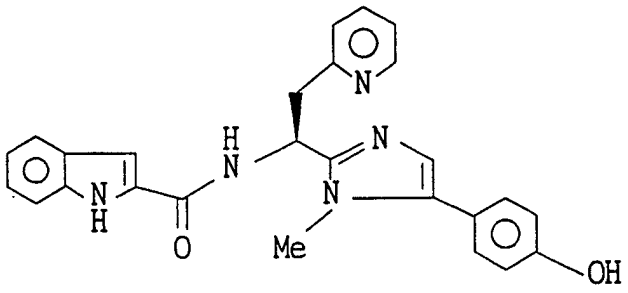
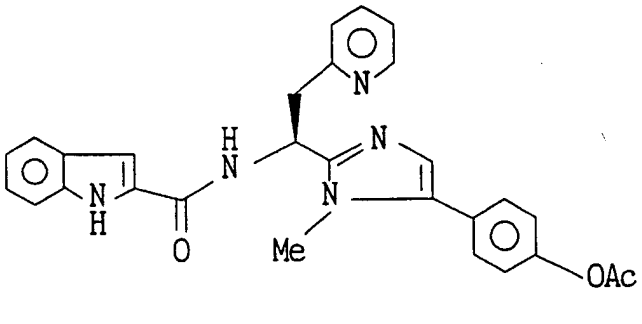
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Example No.	Formula
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129	
	

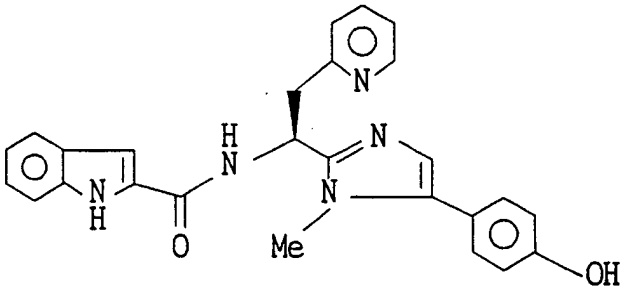
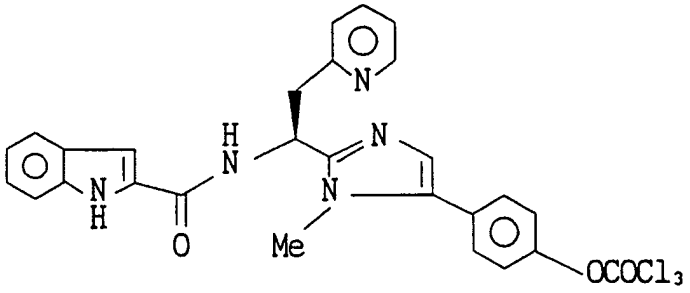
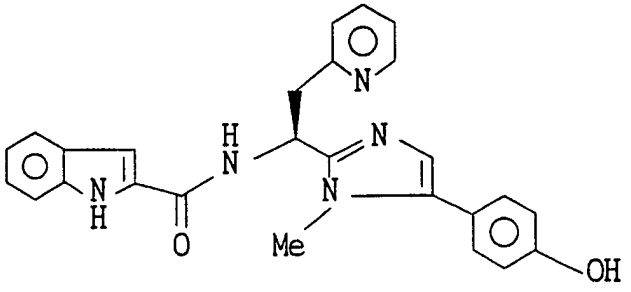
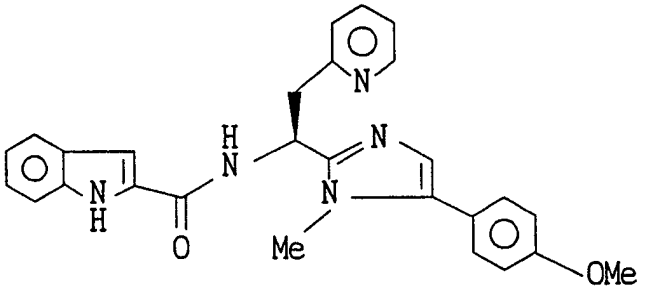
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Example No.	Formula
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131	
	

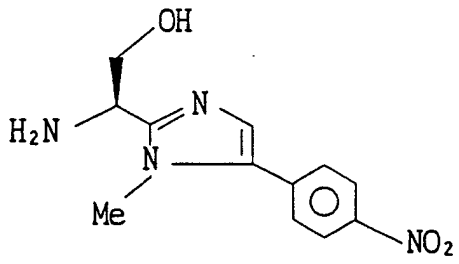
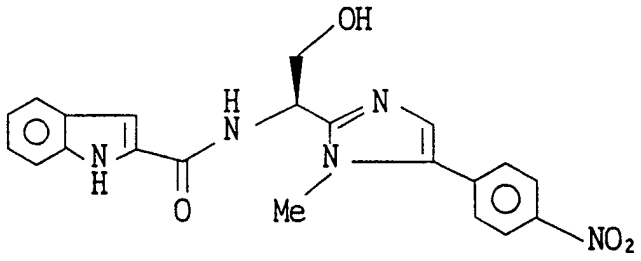
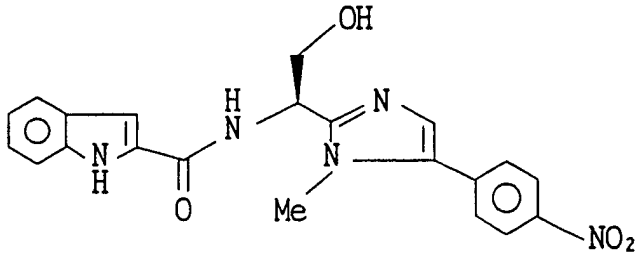
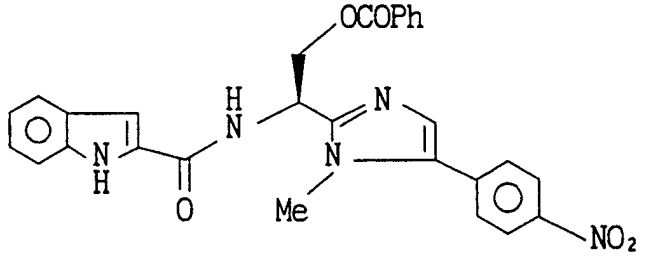
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Example No.	Formula
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133	
	

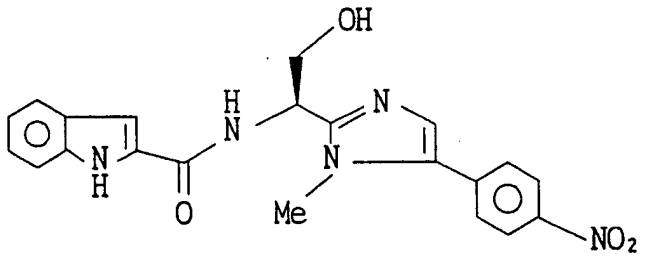
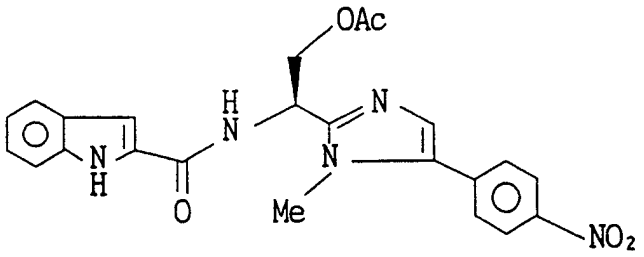
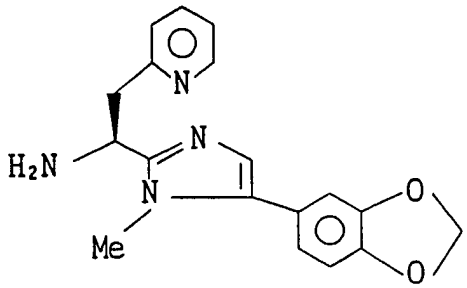
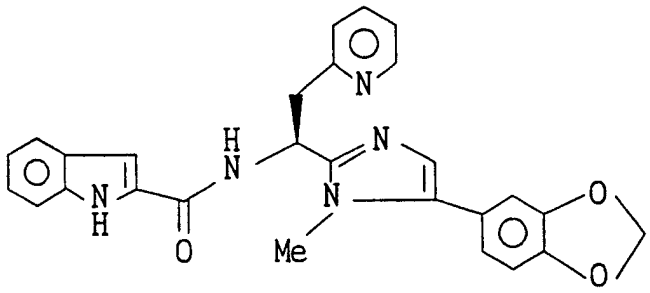
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Example No.	Formula
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135	
	

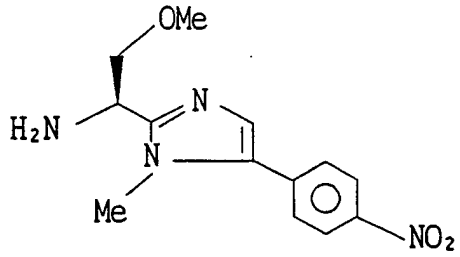
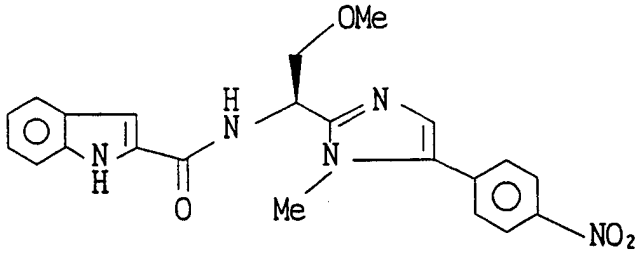
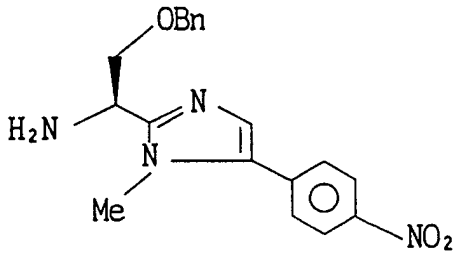
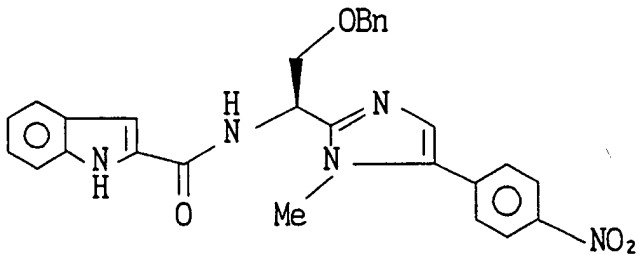
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Example No.	Formula
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137	
	

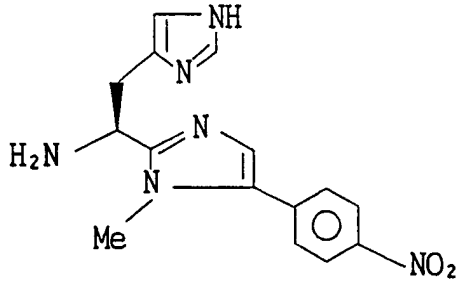
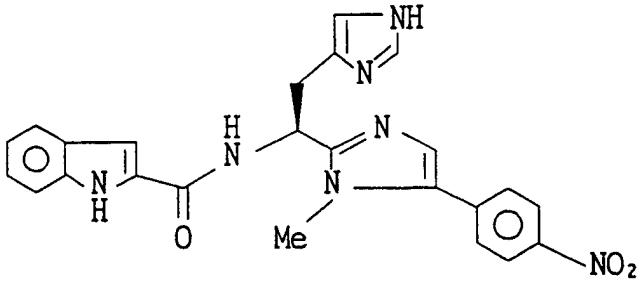
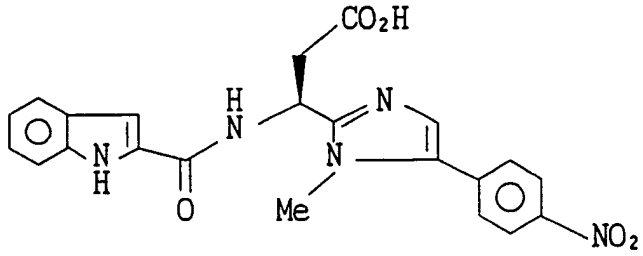
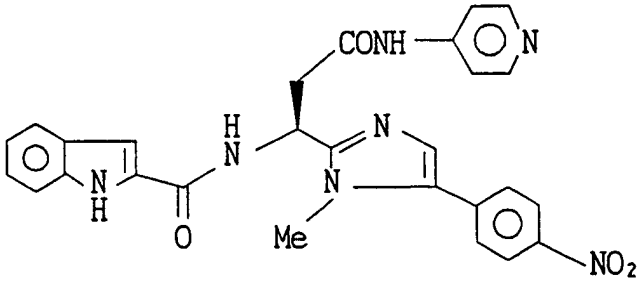
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Example No.	Formula
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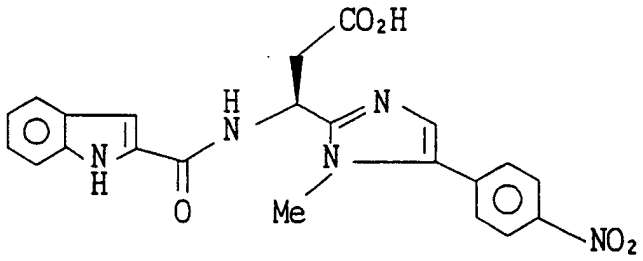
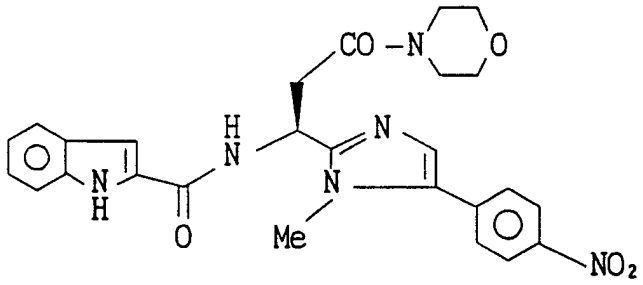
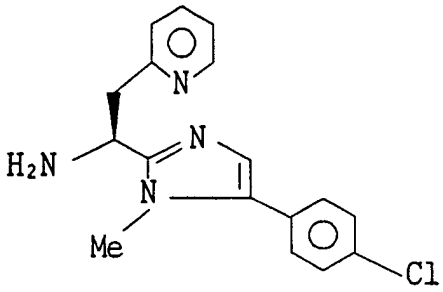
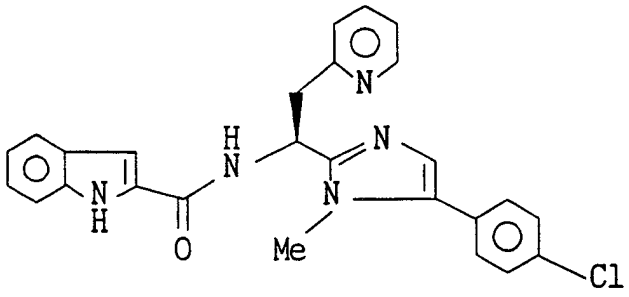
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Example No.	Formula
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141	
	

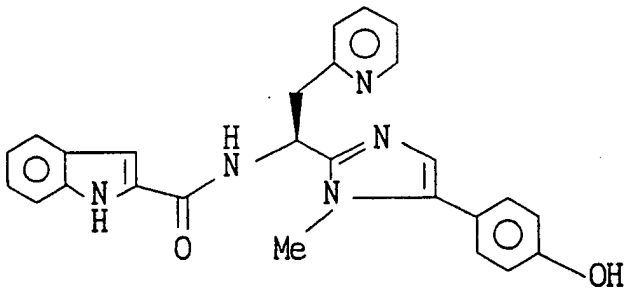
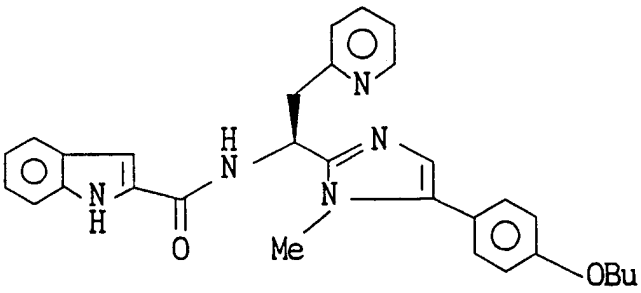
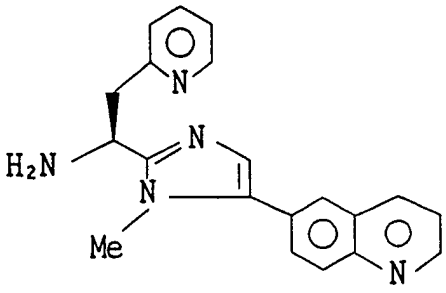
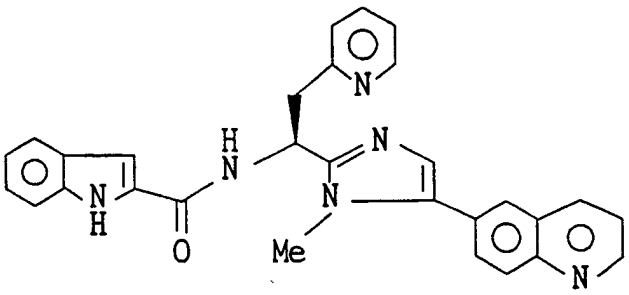
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Example No.	Formula
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143	
	

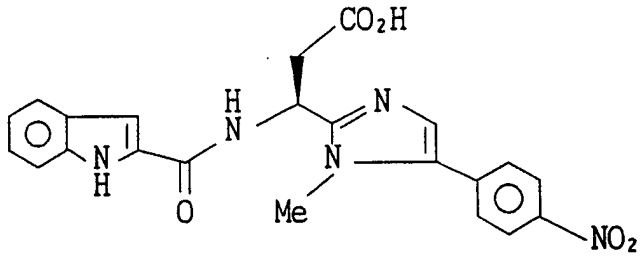
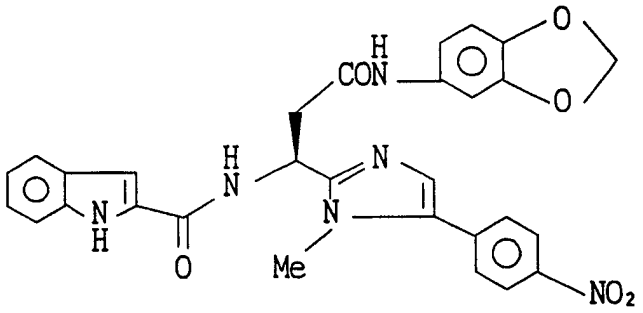
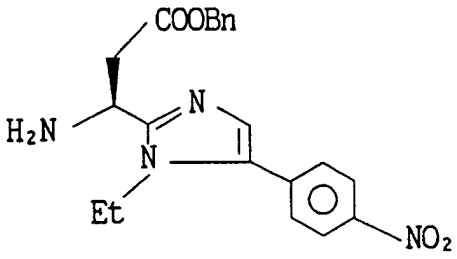
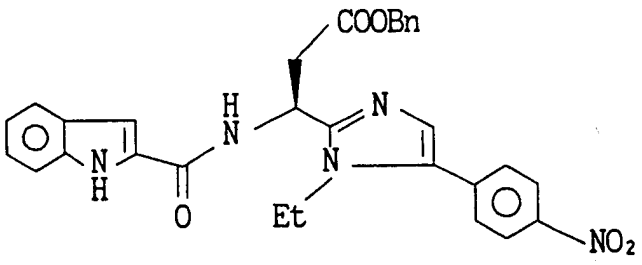
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Example No.	Formula
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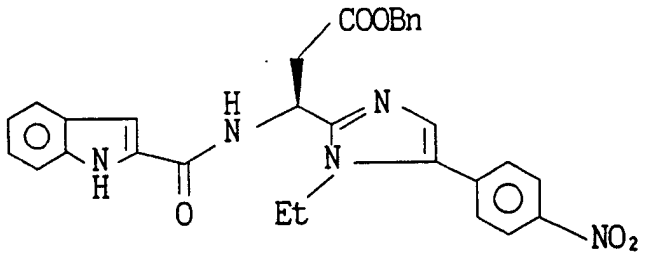
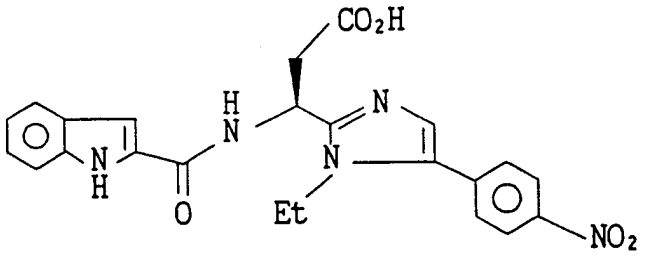
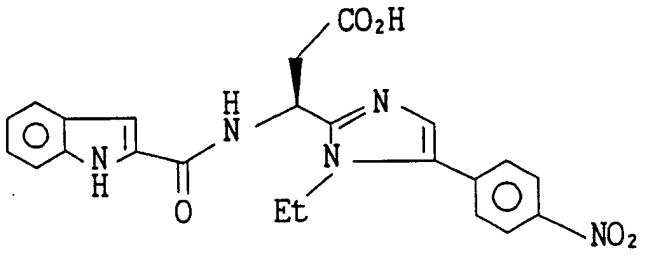
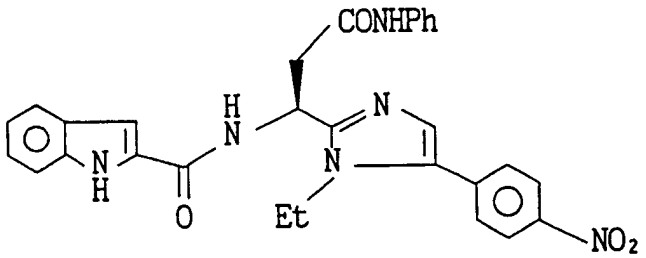
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Example No.	Formula
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147	
	

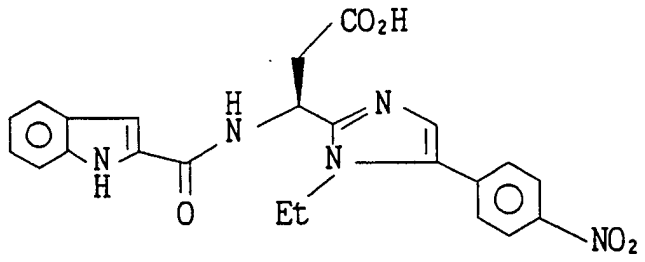
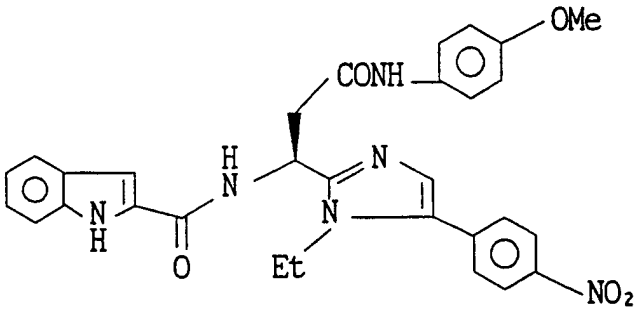
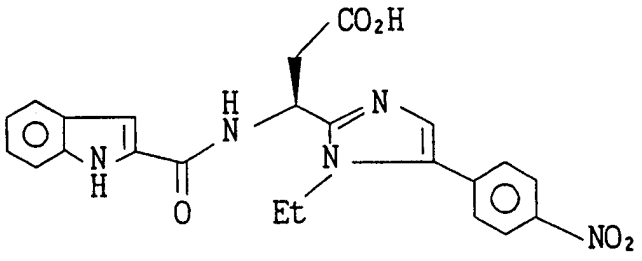
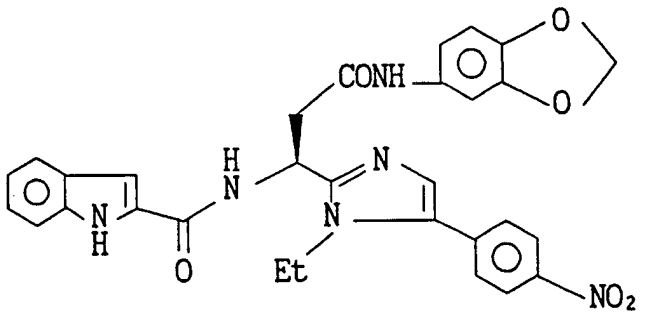
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Example No.	Formula
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149	
	

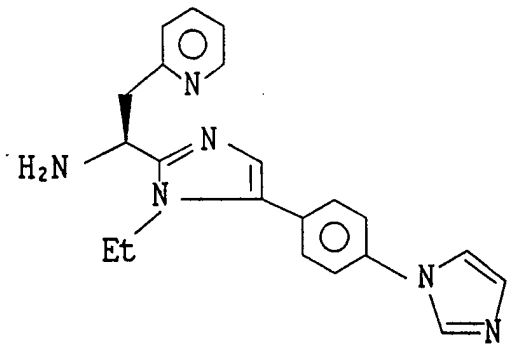
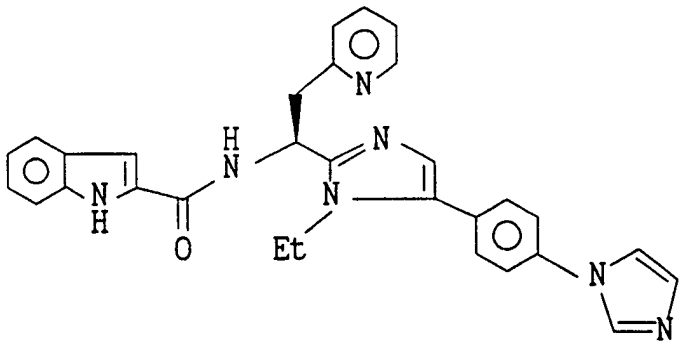
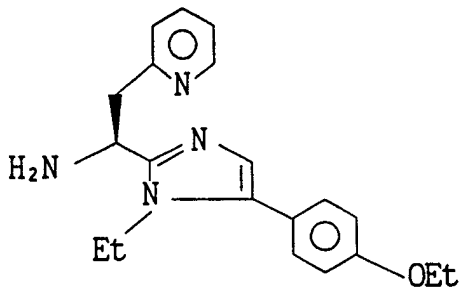
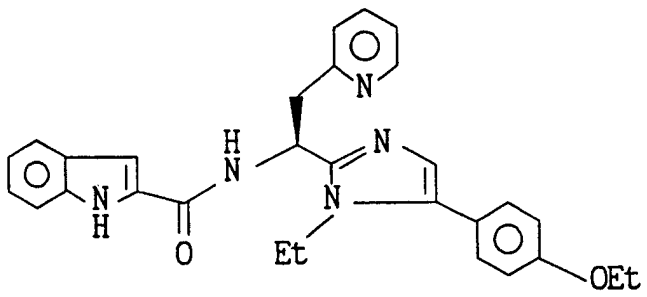
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Example No.	Formula
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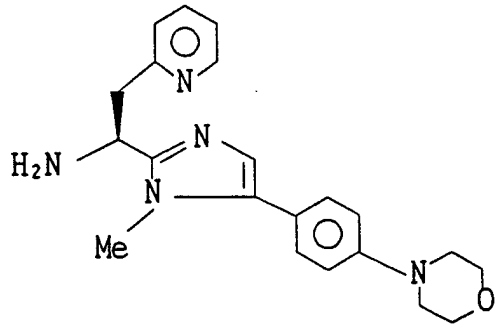
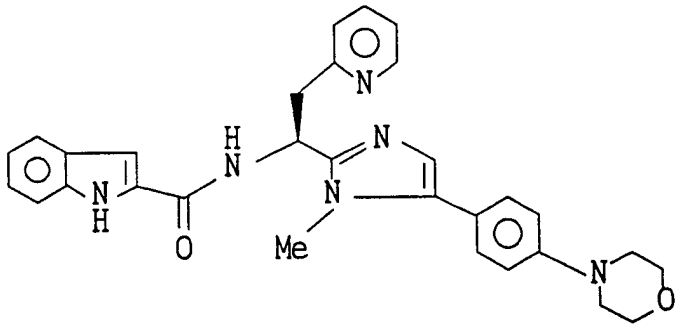
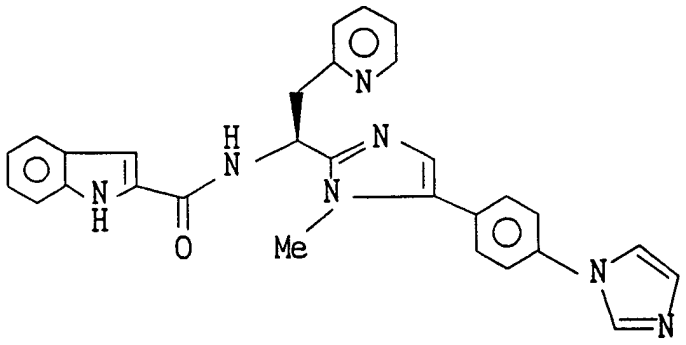
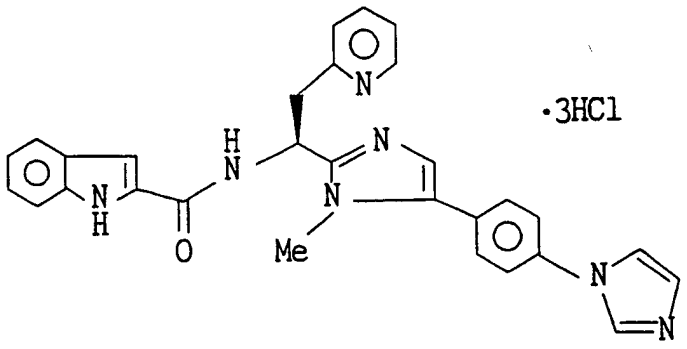
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Example No.	Formula
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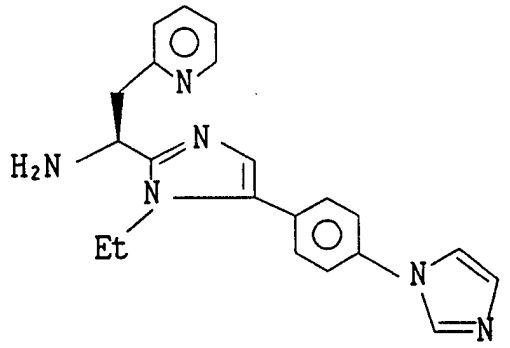
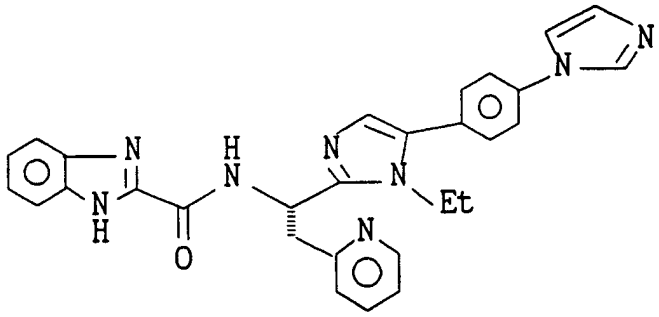
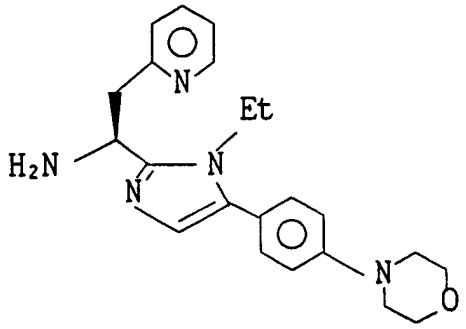
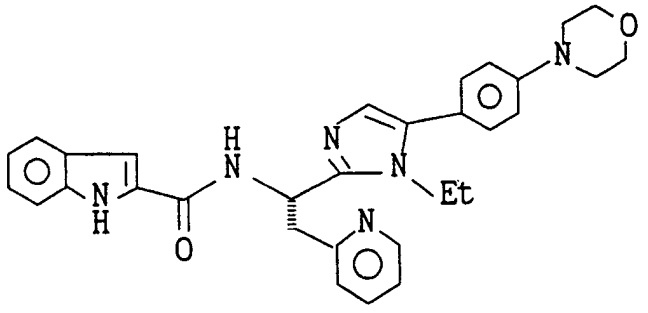
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Example No.	Formula
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155	
	

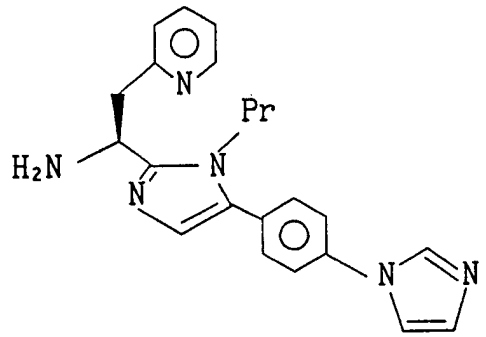
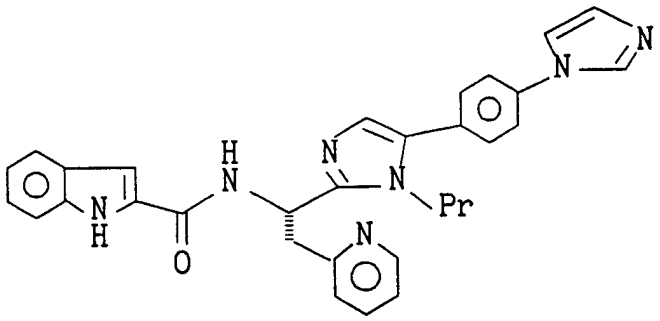
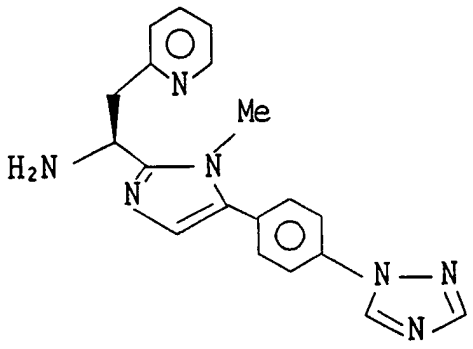
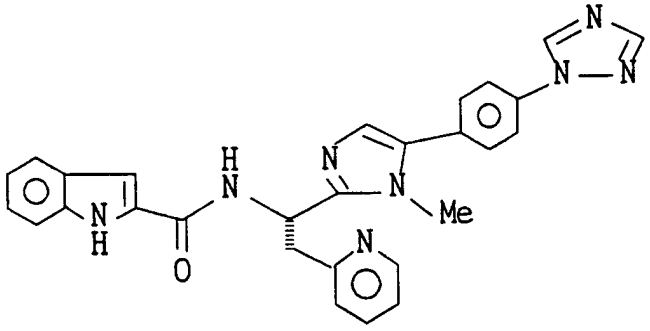
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Example No.	Formula
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157	
	

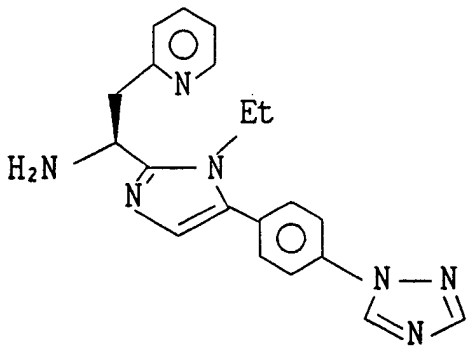
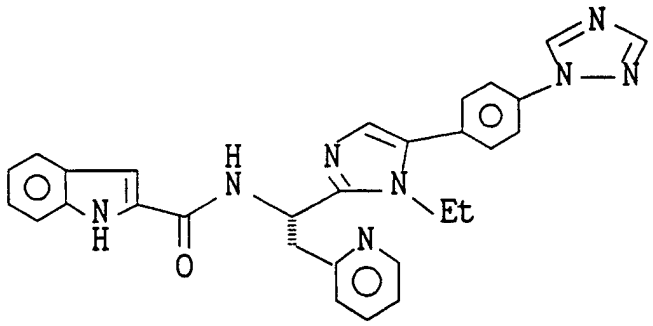
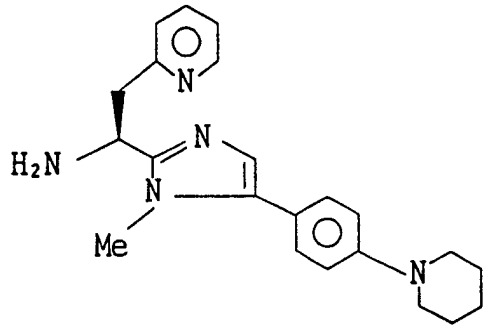
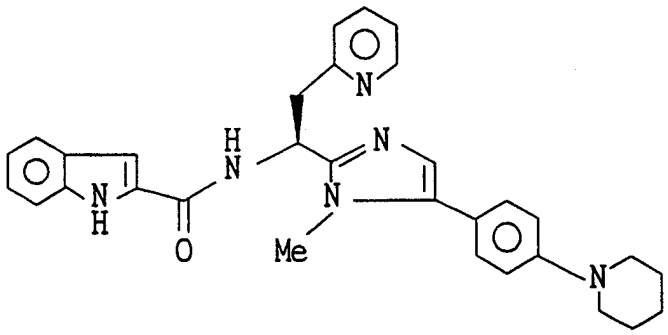
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Example No.	Formula
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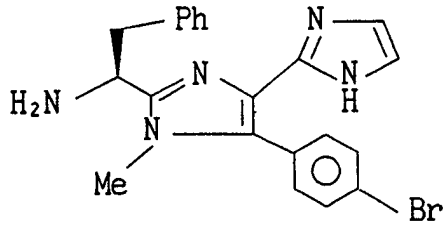
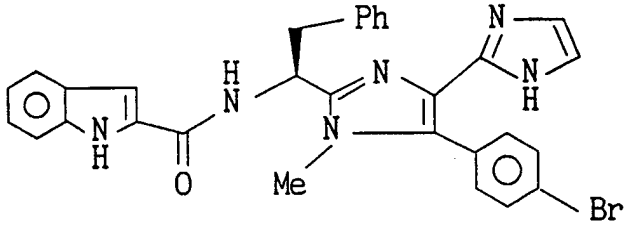
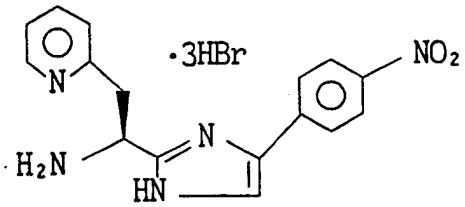
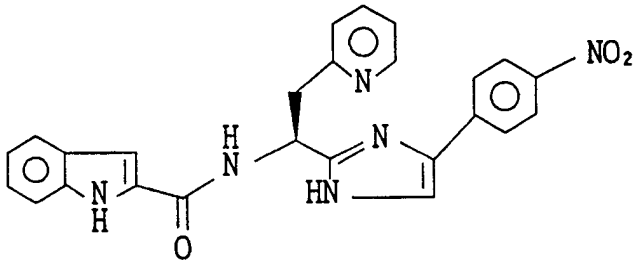
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Example No.	Formula
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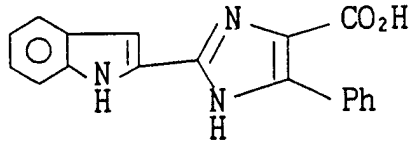
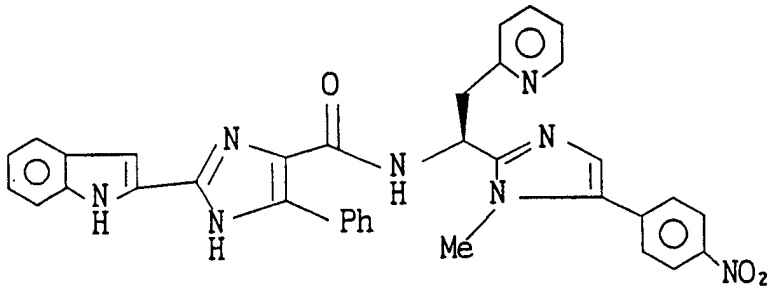
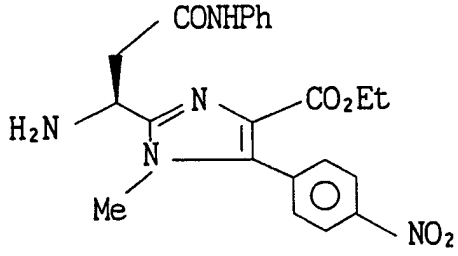
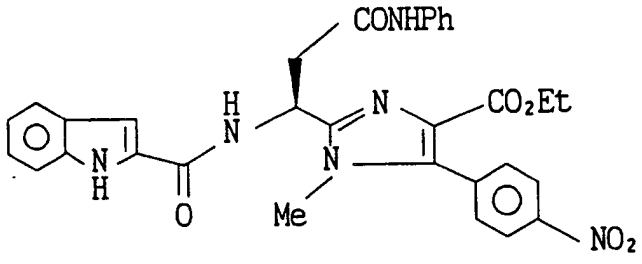
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Example No.	Formula
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163	
	

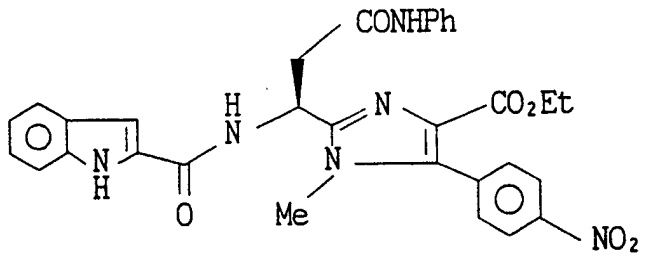
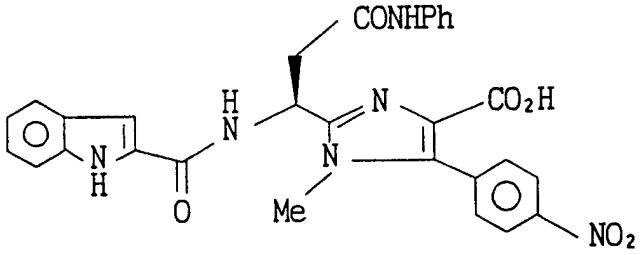
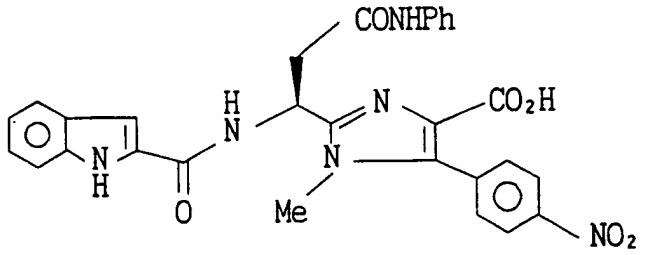
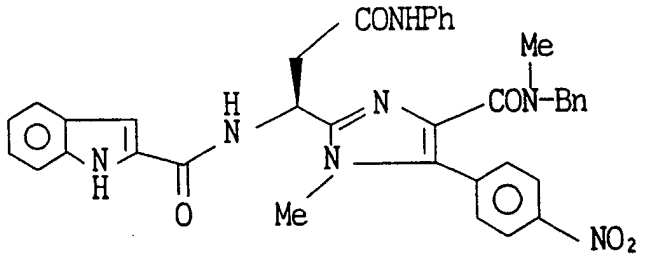
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Example No.	Formula
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165	
	

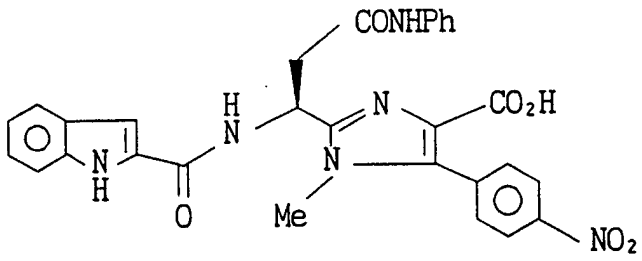
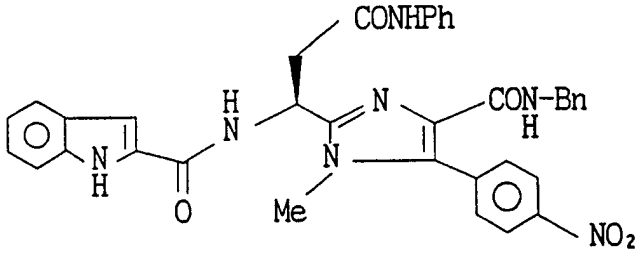
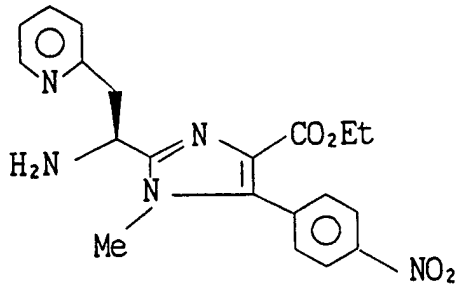
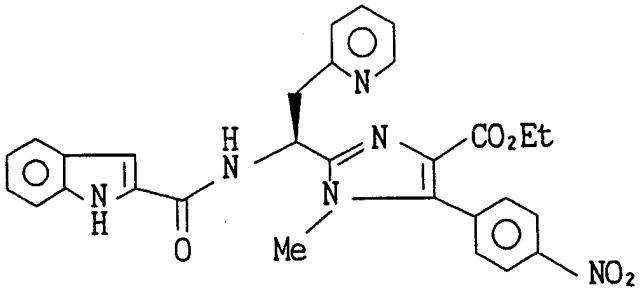
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Example No.	Formula
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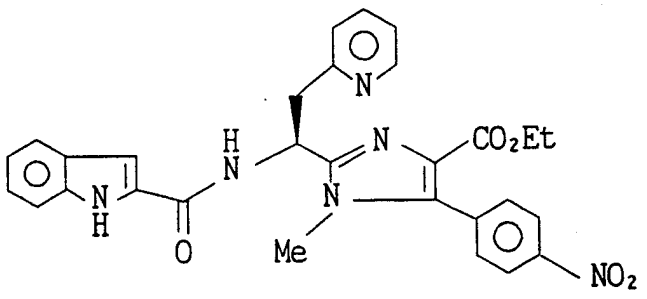
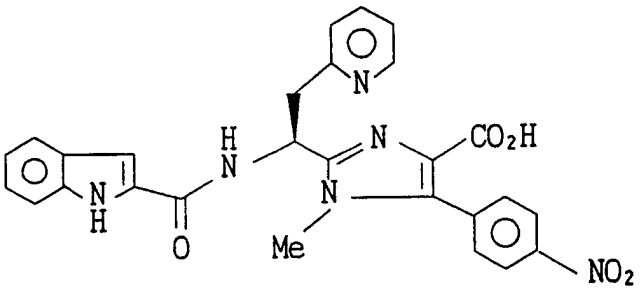
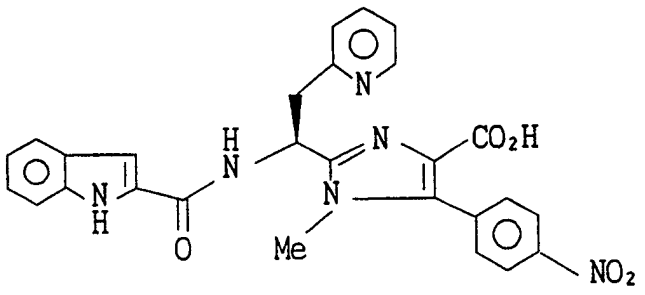
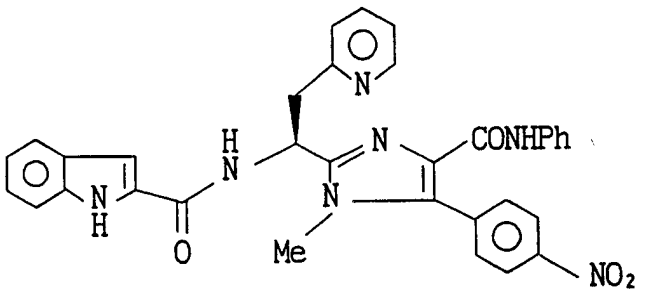
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Example No.	Formula
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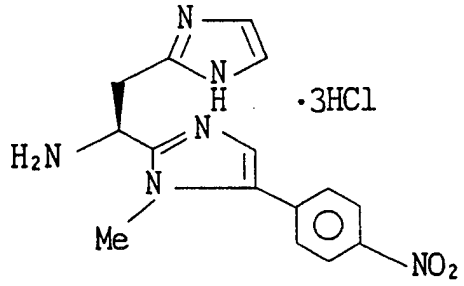
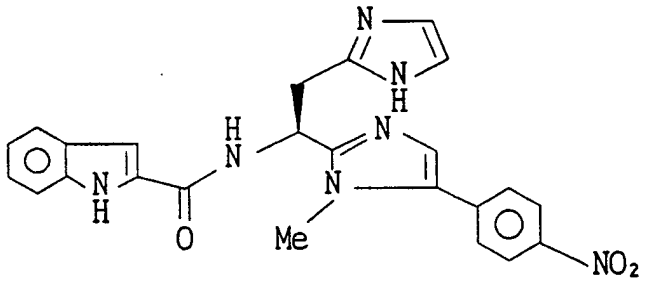
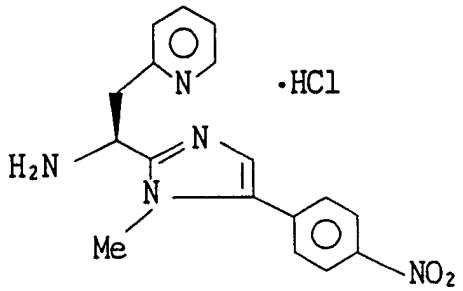
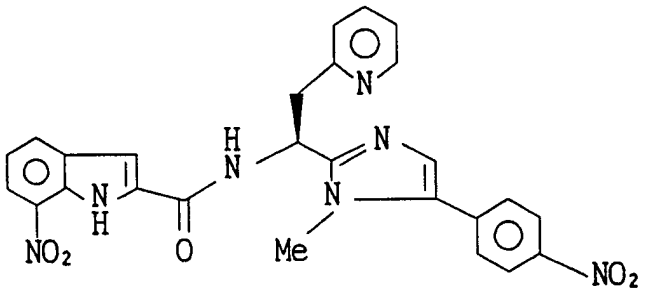
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Example No.	Formula
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171	
	

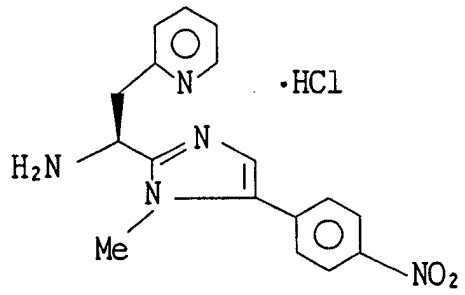
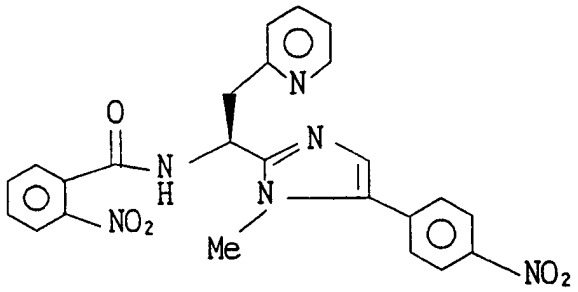
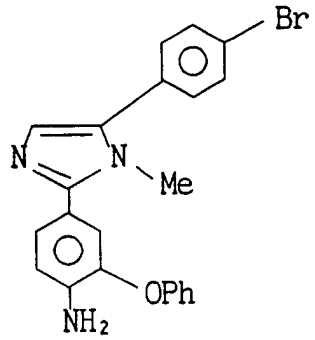
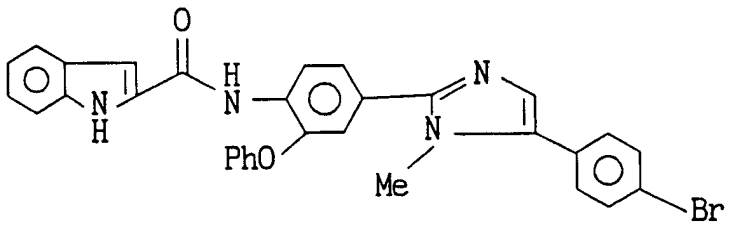
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Example No.	Formula
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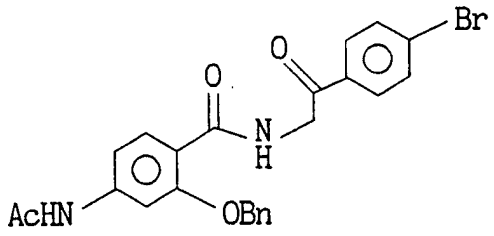
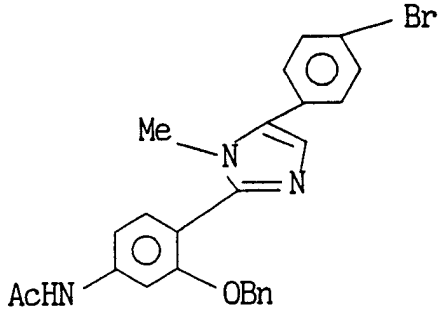
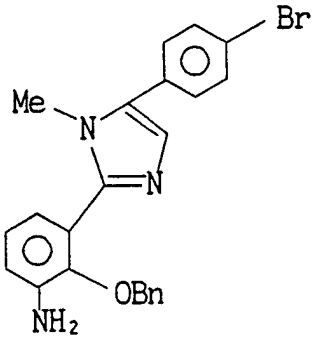
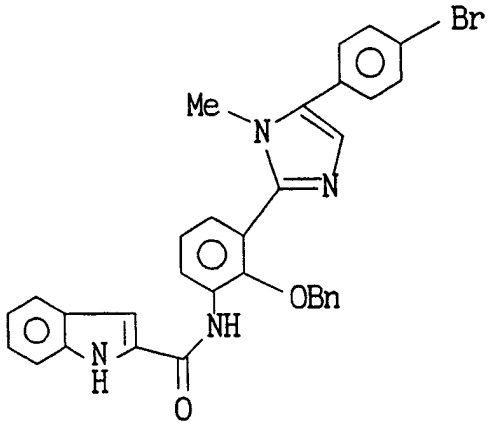
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Example No.	Formula
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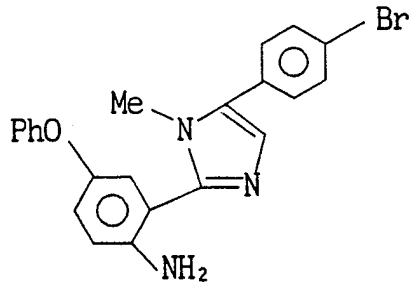
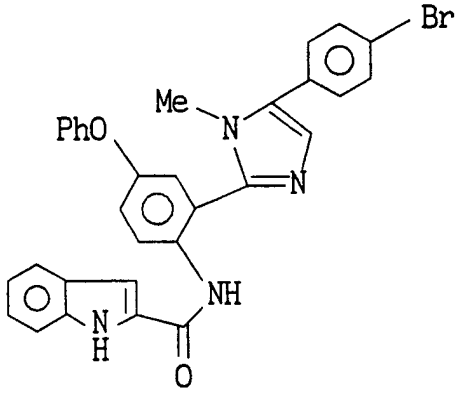
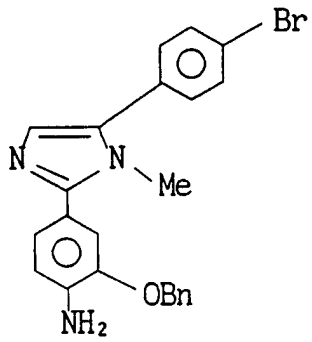
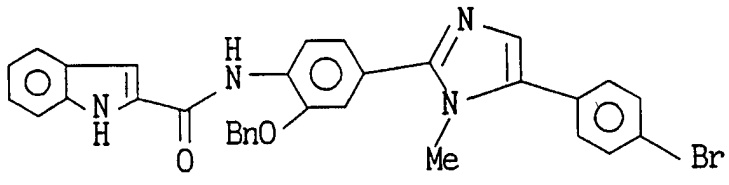
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Example No.	Formula
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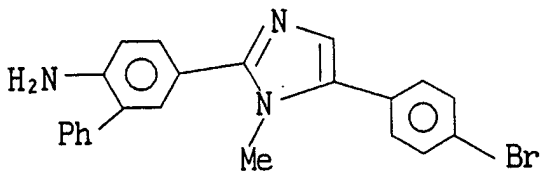
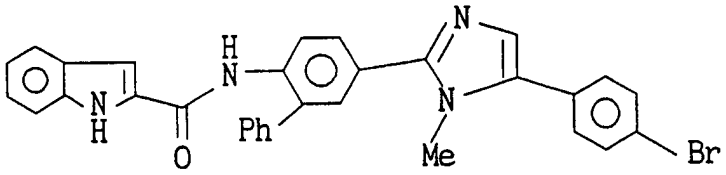
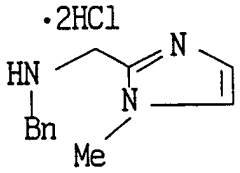
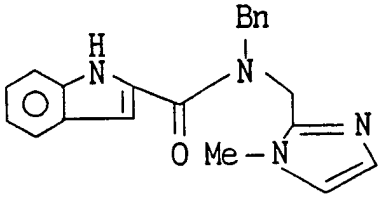
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Example No.	Formula
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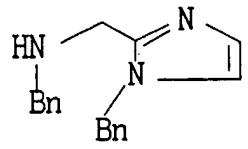
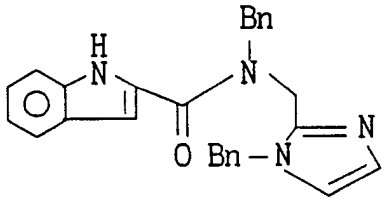
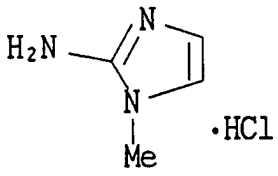
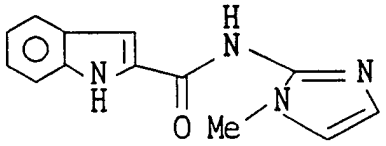
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Example No.	Formula
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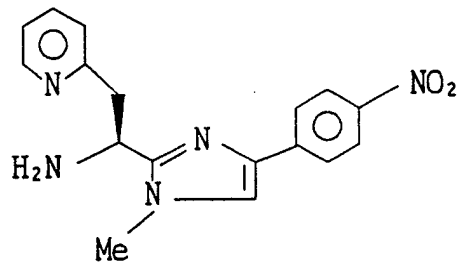
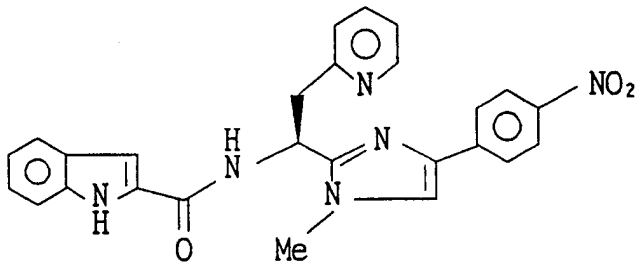
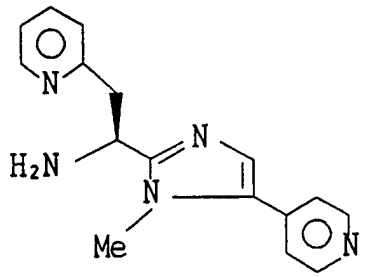
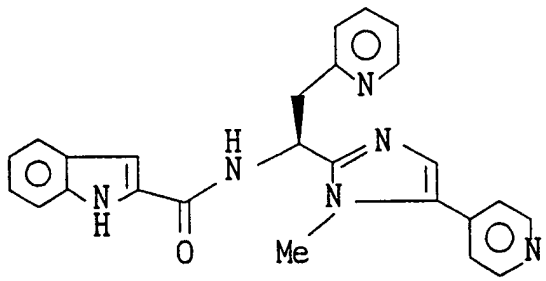
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Example No.	Formula
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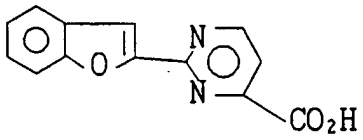
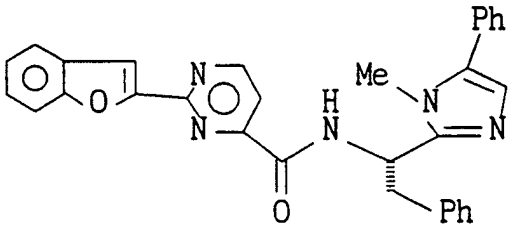
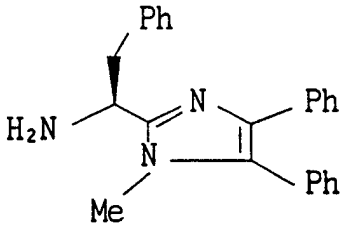
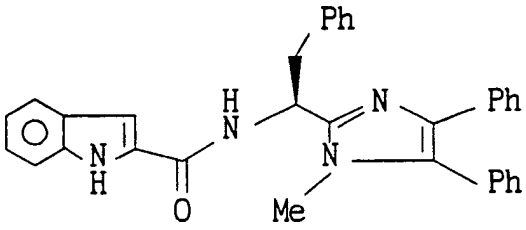
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Example No.	Formula
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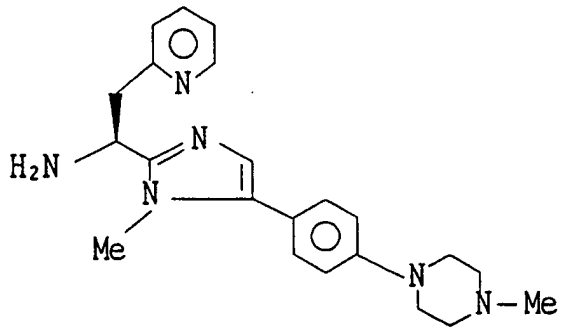
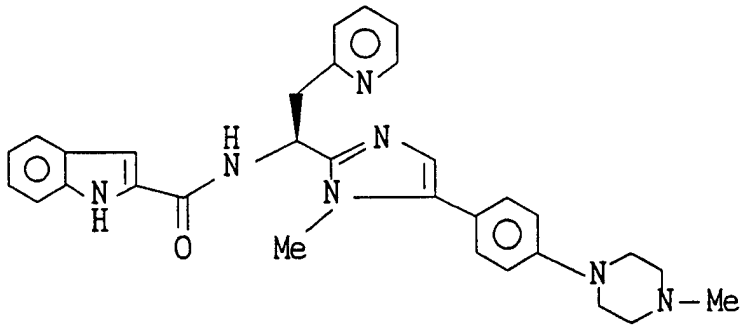
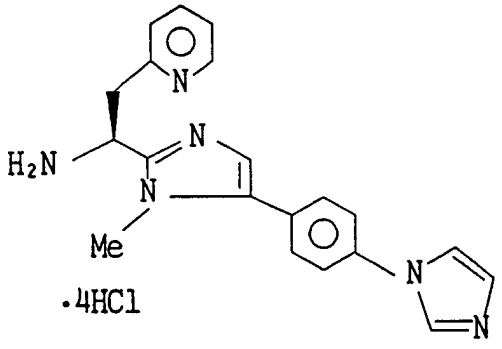
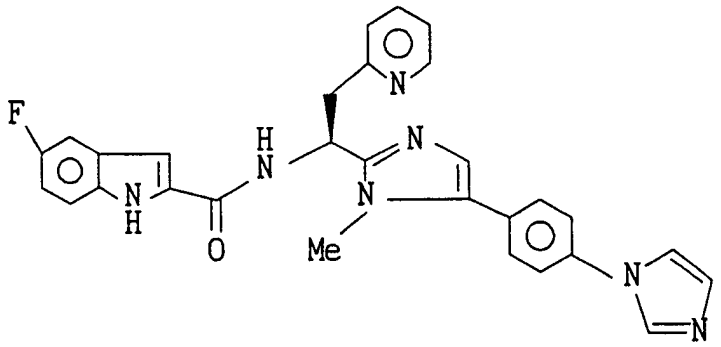
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Example No.	Formula
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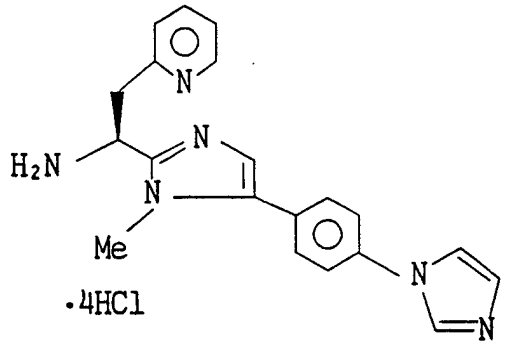
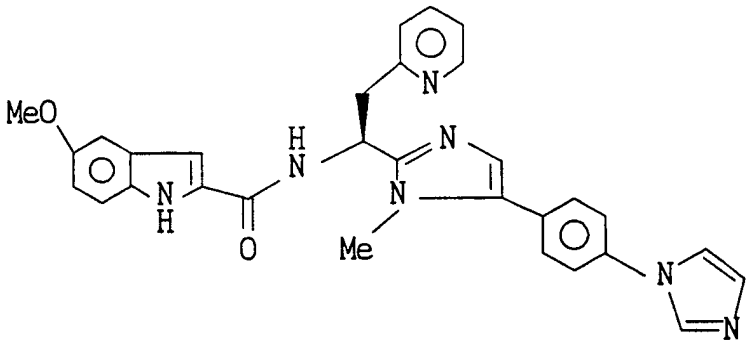
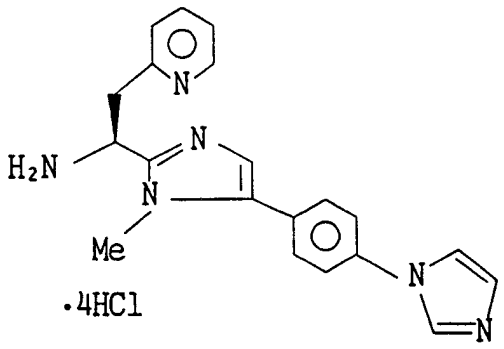
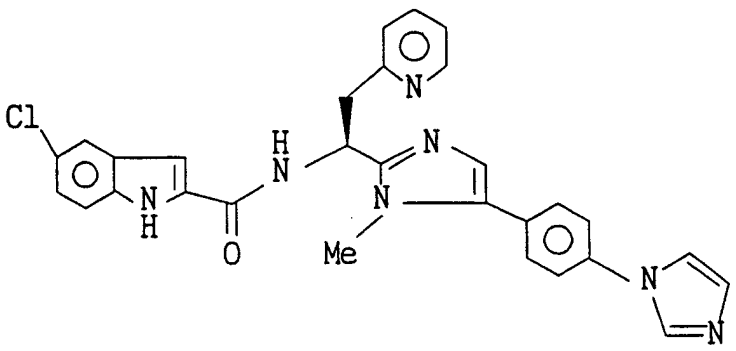
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Example No.	Formula
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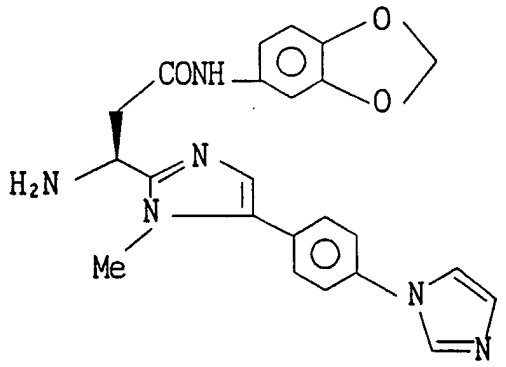
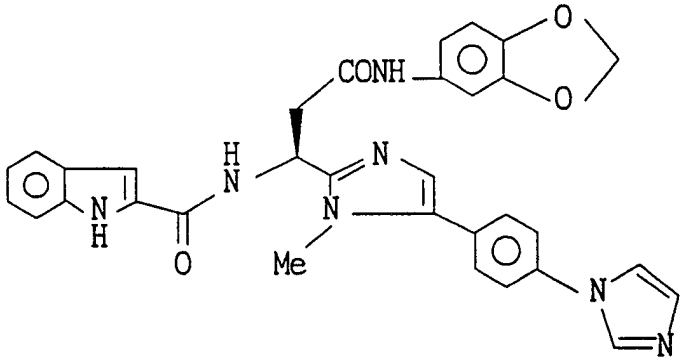
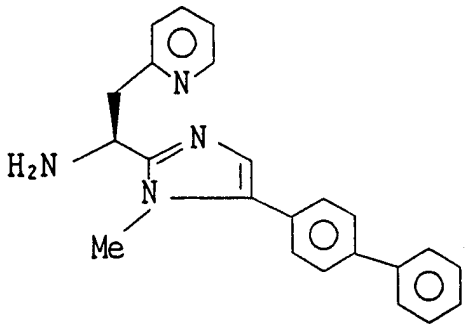
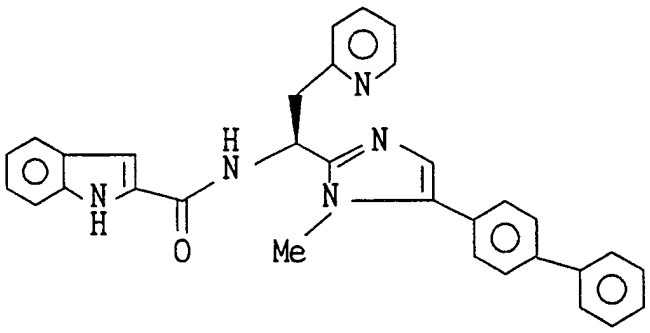
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Example No.	Formula
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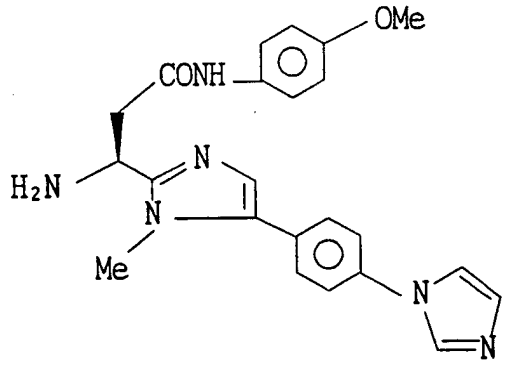
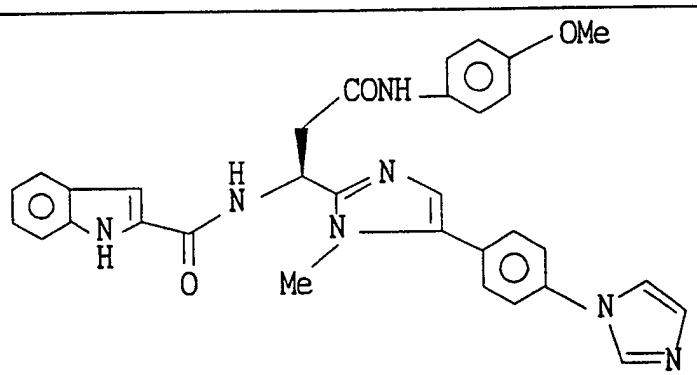
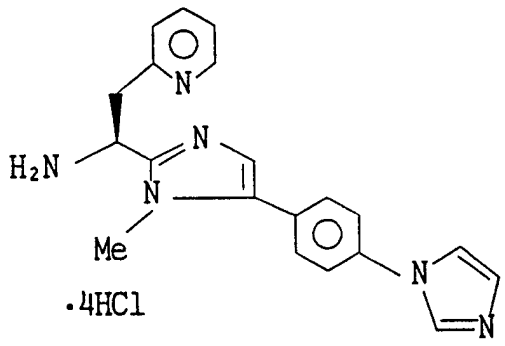
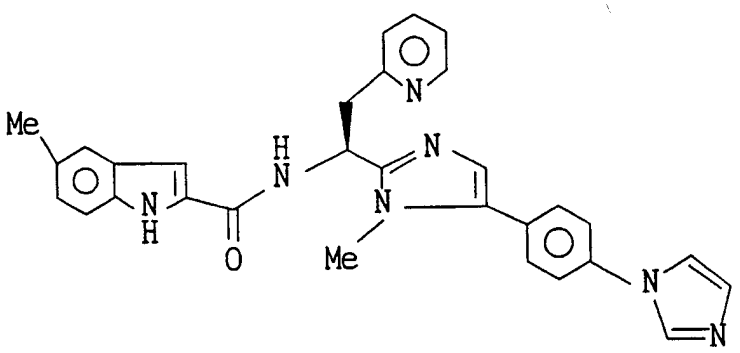
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Example No.	Formula
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193	
	

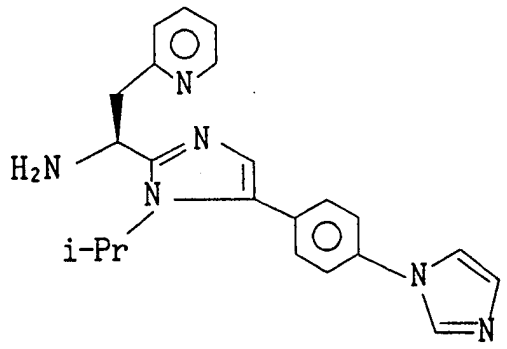
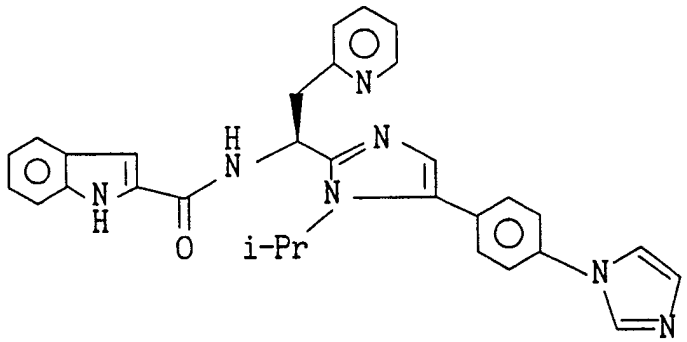
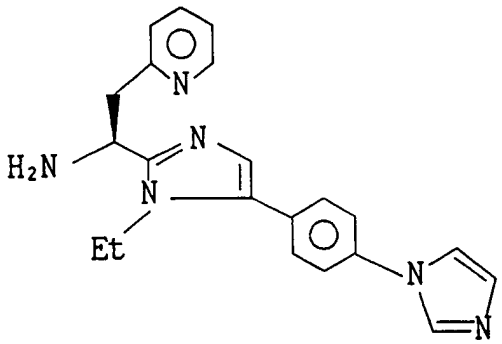
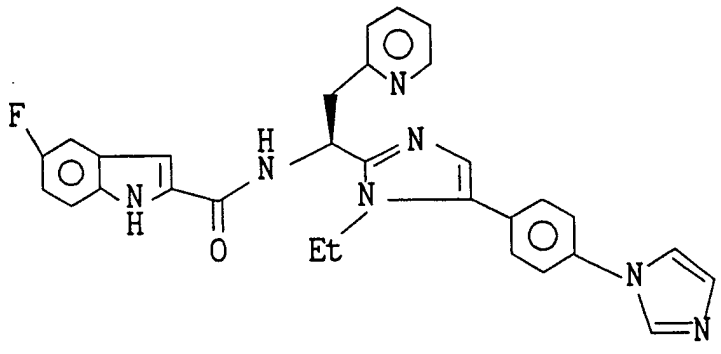
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Example No.	Formula
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195	
	

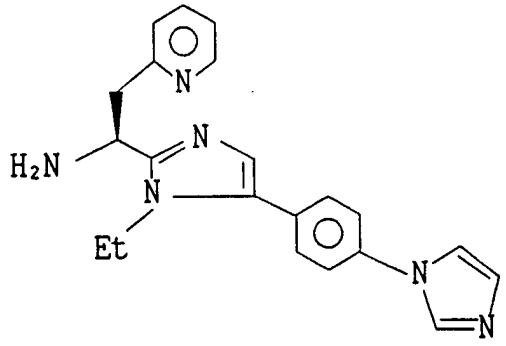
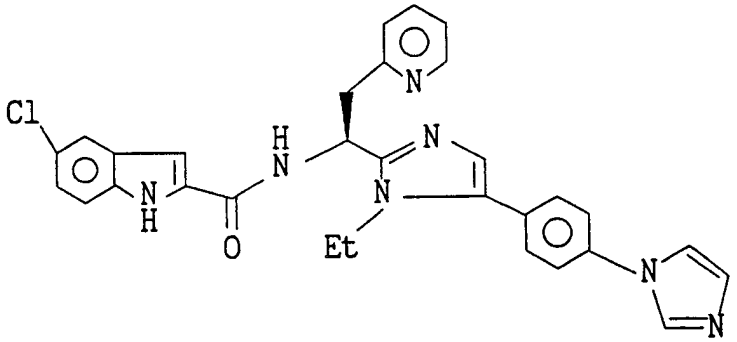
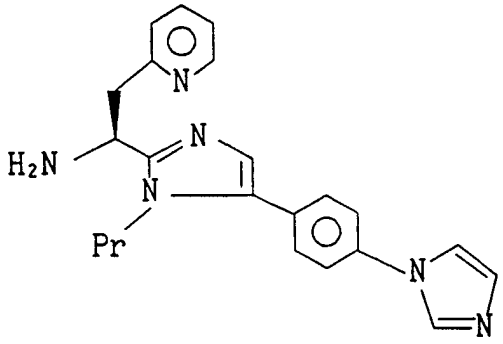
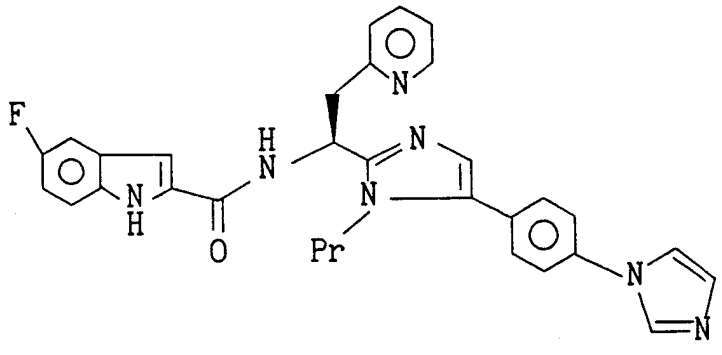
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Example No.	Formula
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197	
	

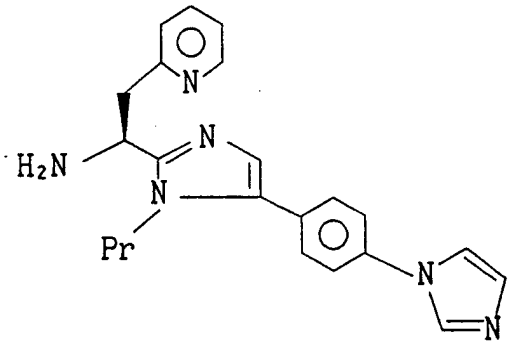
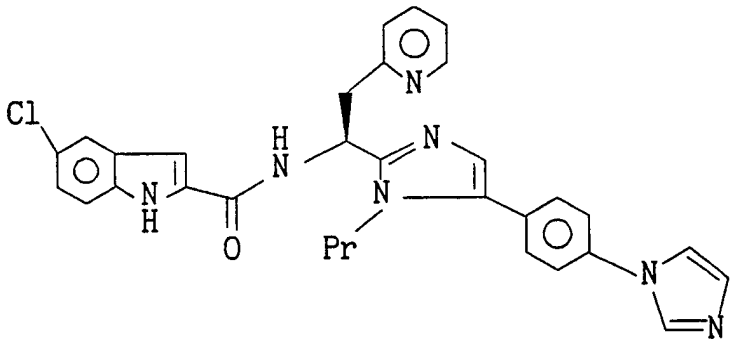
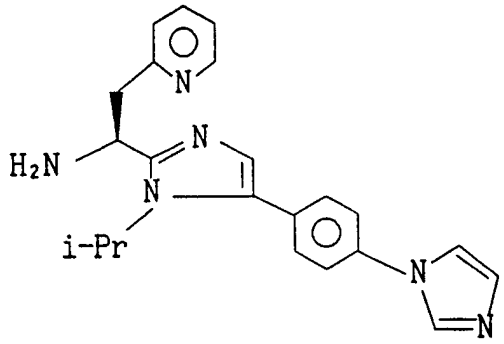
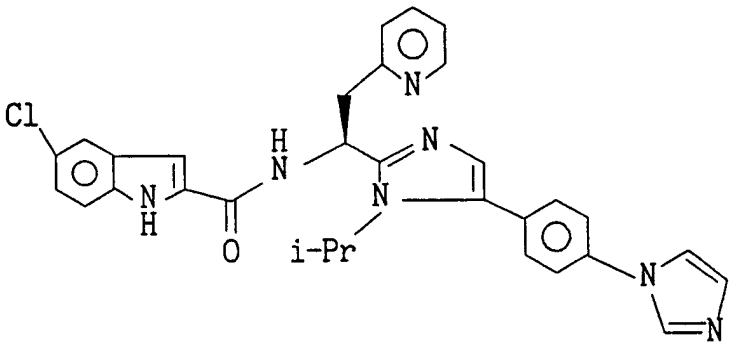
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Example No.	Formula
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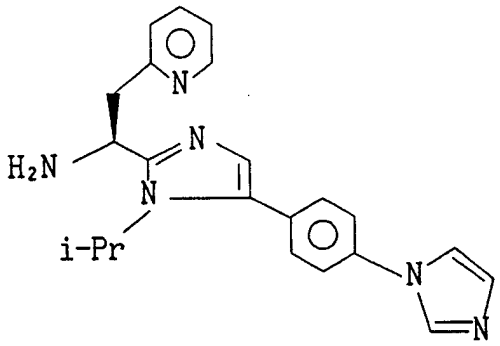
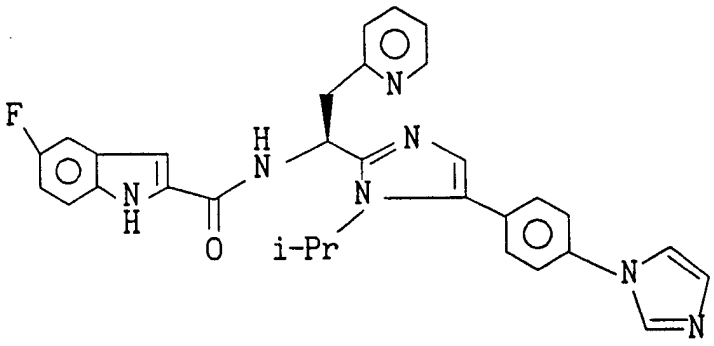
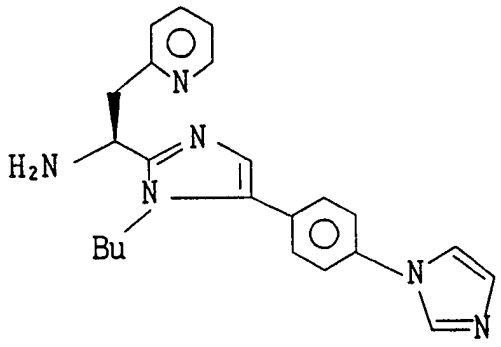
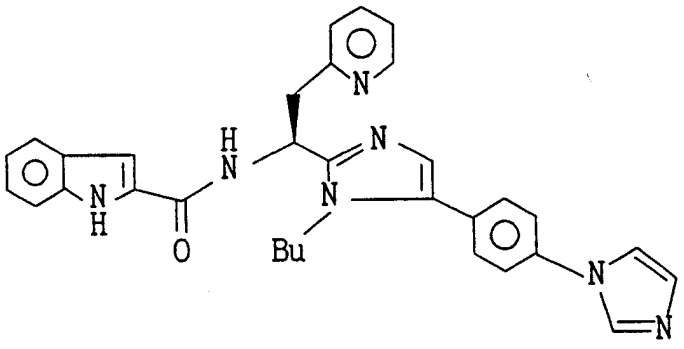
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Example No.	Formula
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201	
	

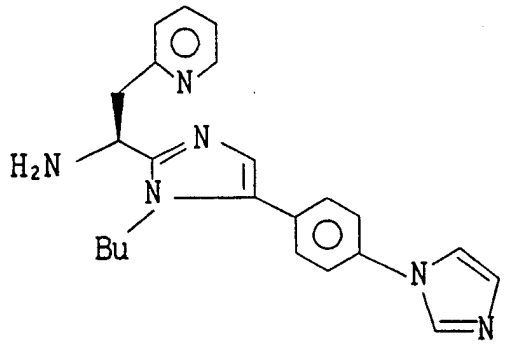
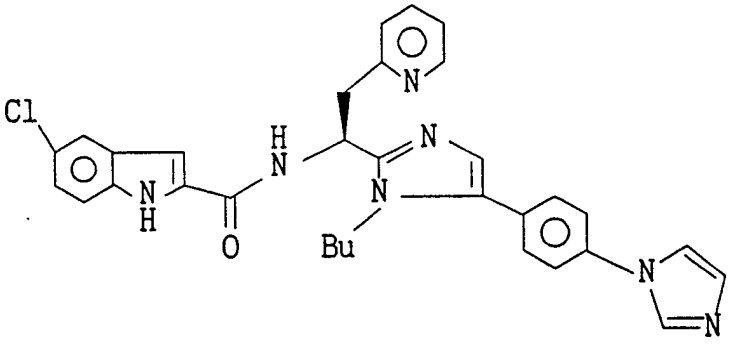
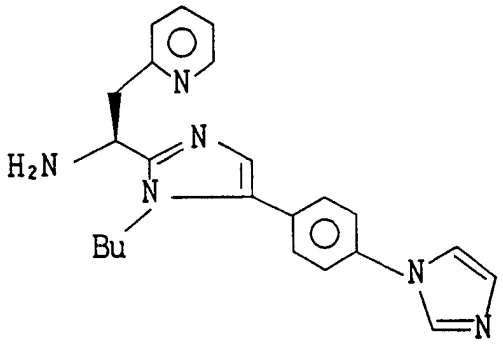
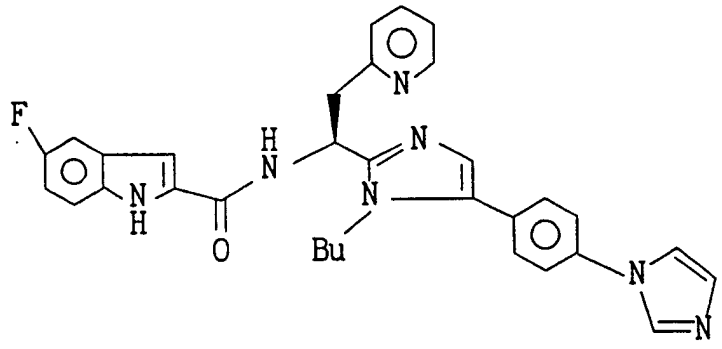
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Example No.	Formula
202	
	
203	
	

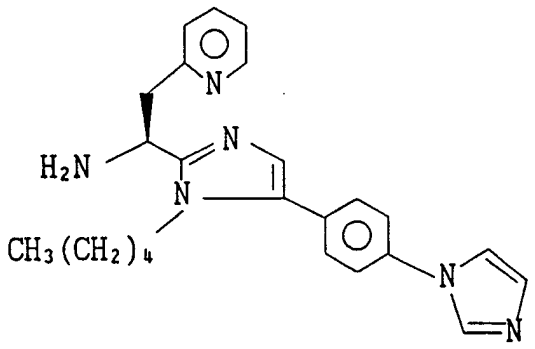
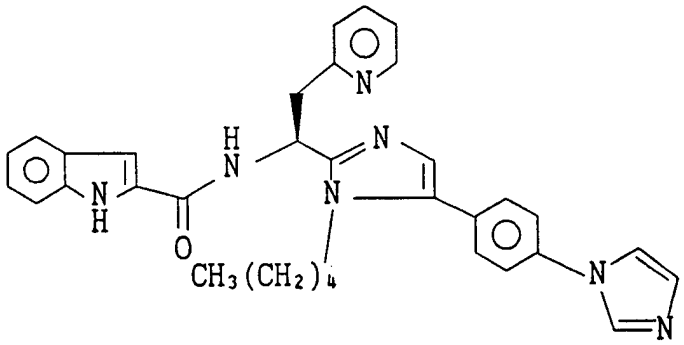
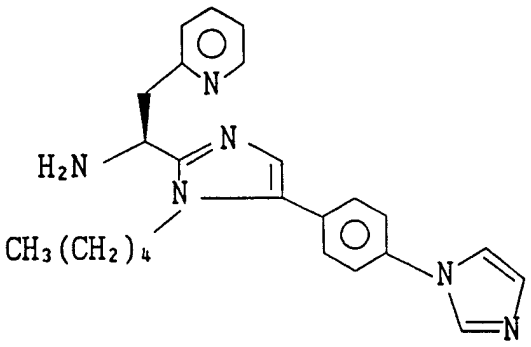
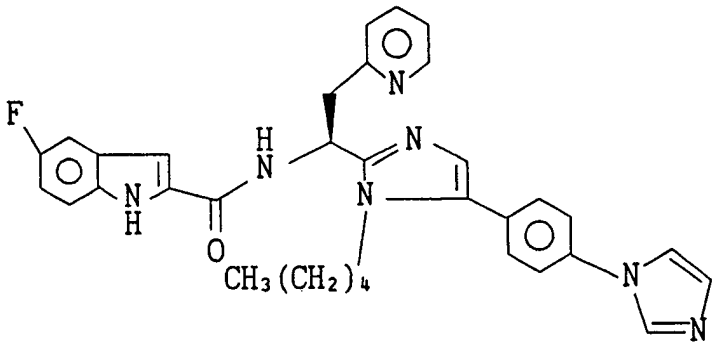
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Example No.	Formula
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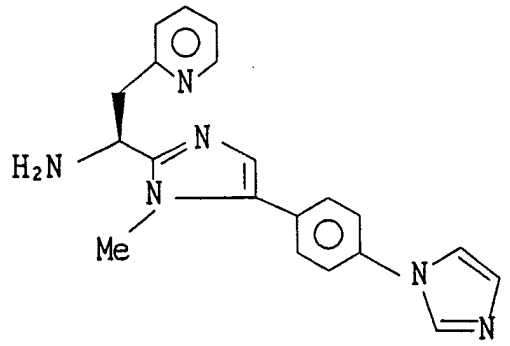
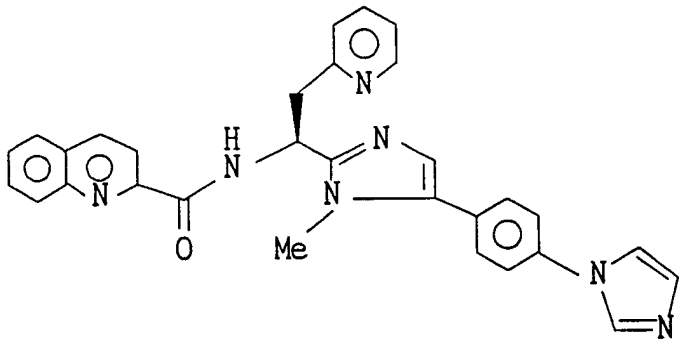
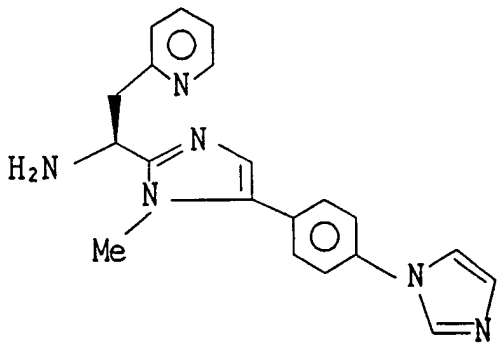
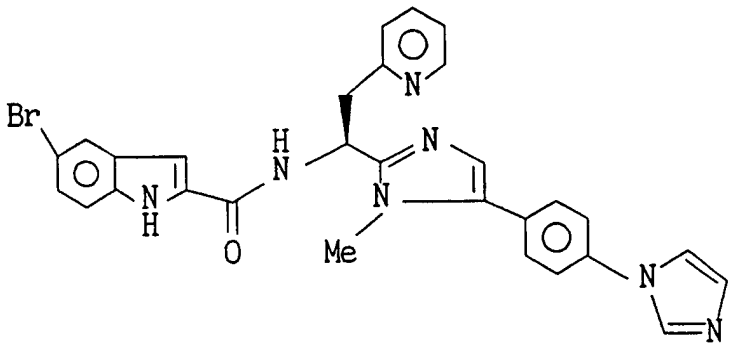
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Example No.	Formula
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207	
	

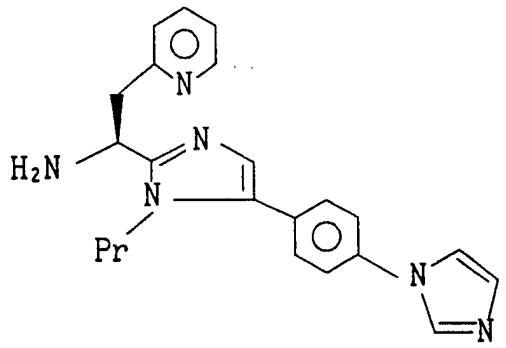
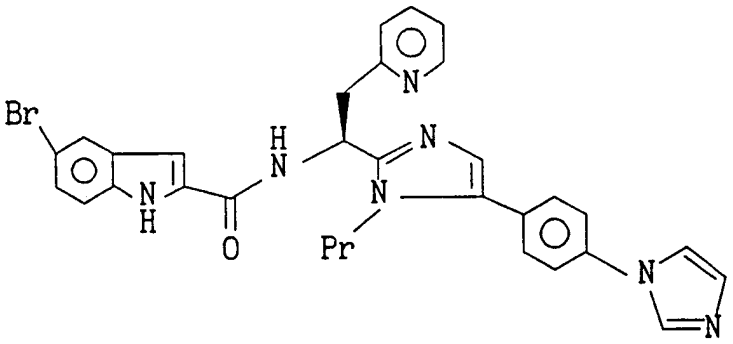
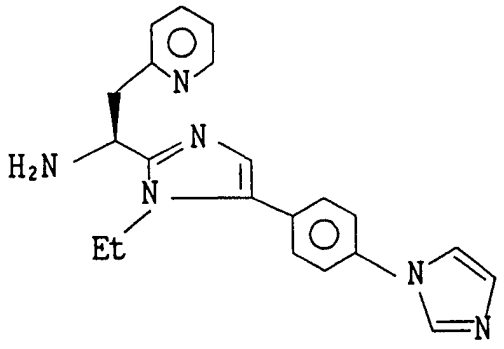
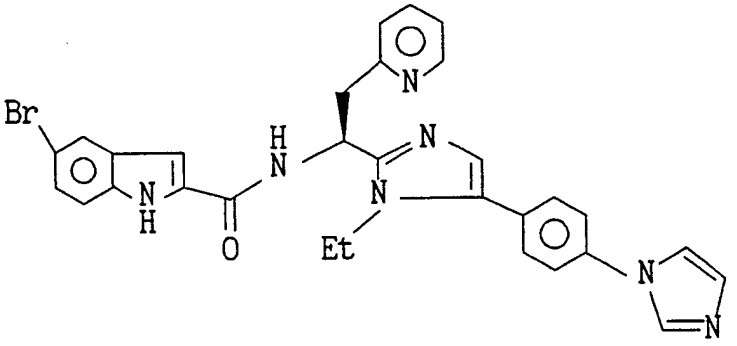
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Example No.	Formula
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209	
	

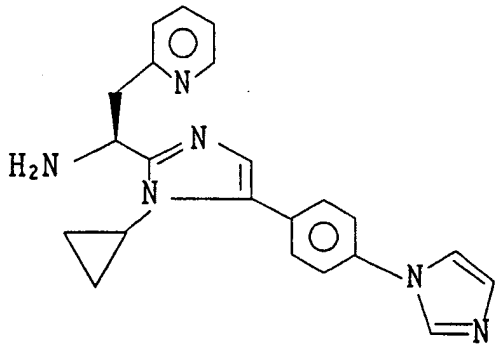
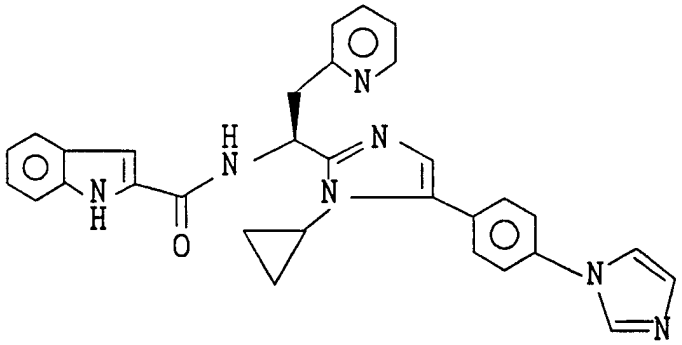
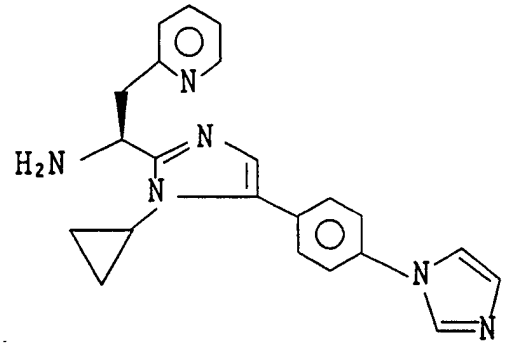
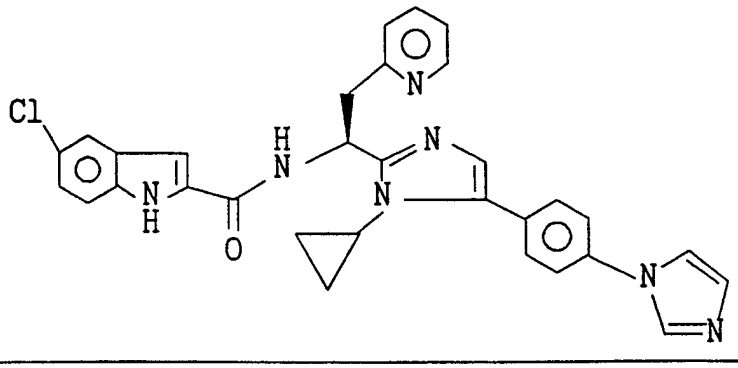
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Example No.	Formula
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211	
	

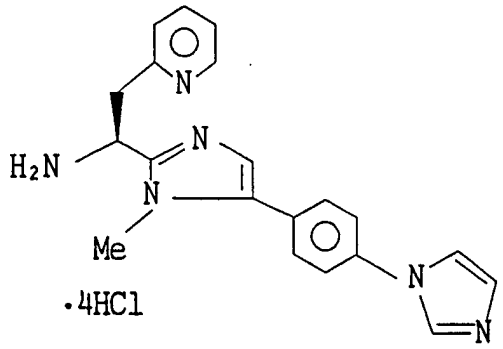
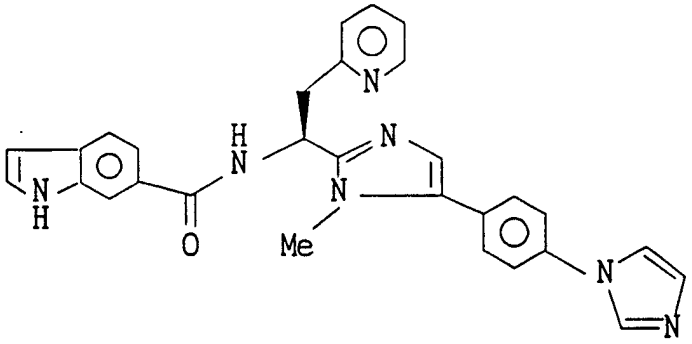
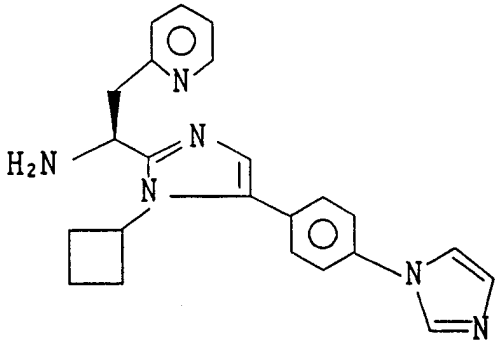
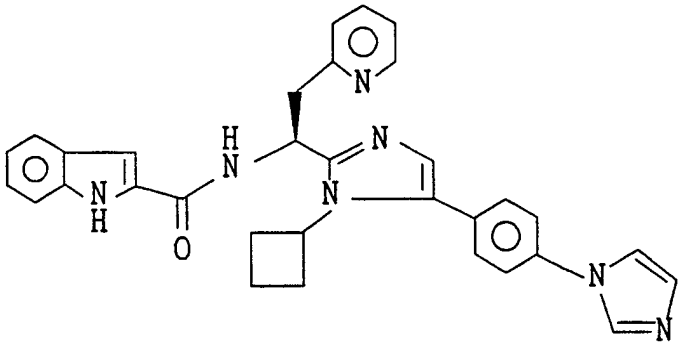
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Example No.	Formula
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213	
	

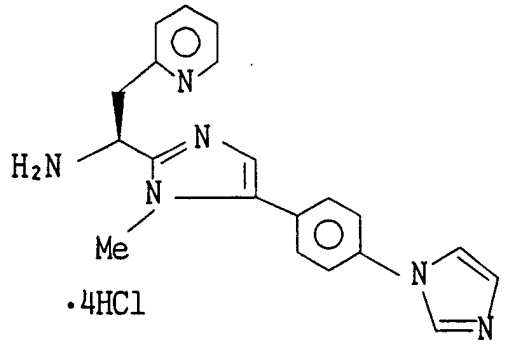
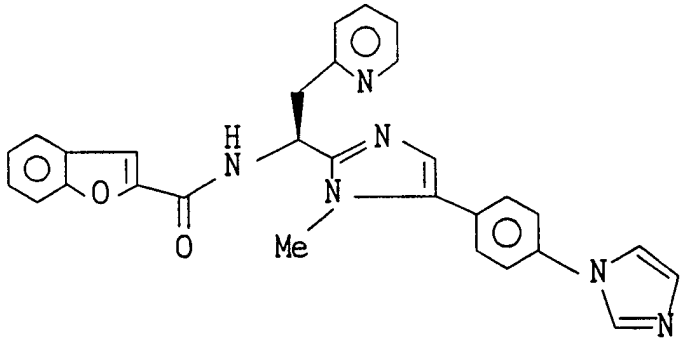
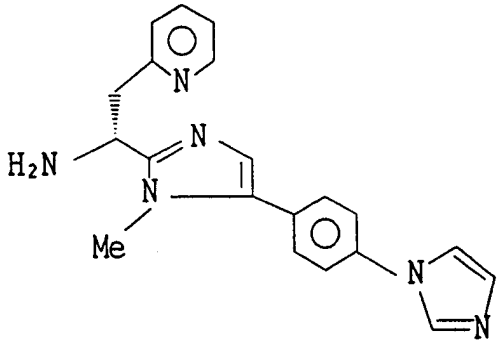
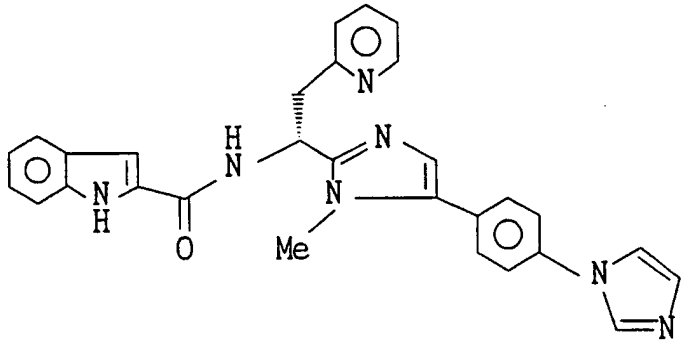
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Example No.	Formula
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215	
	

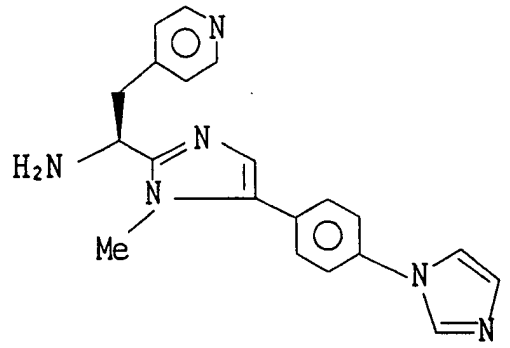
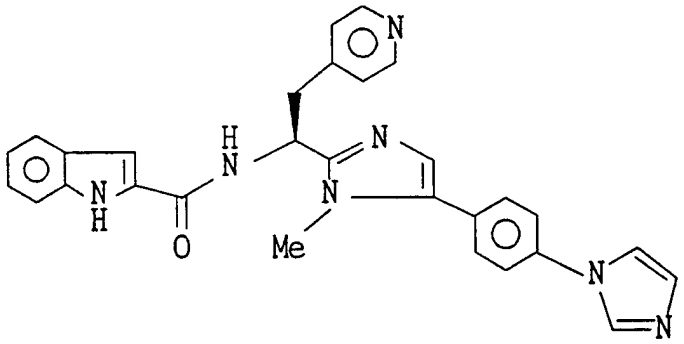
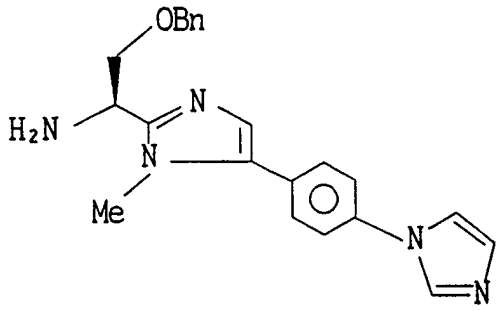
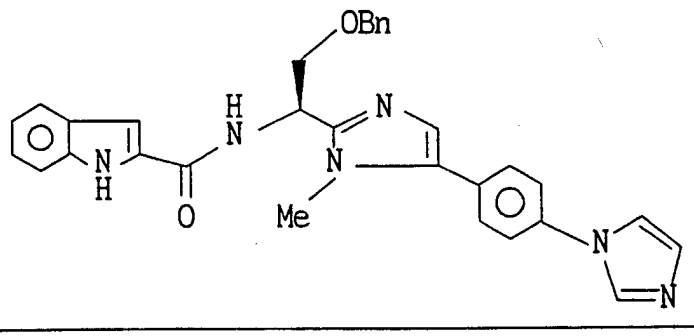
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Example No.	Formula
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217	
	

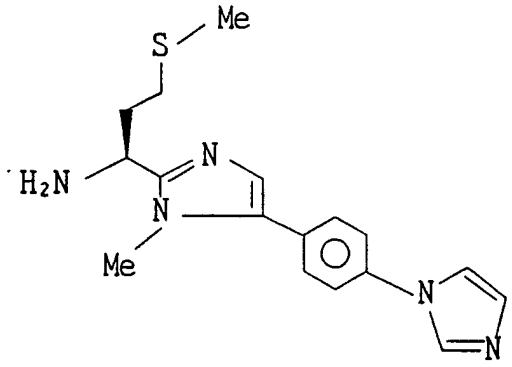
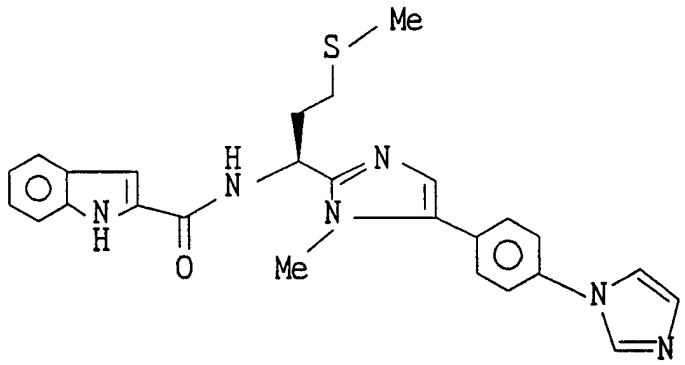
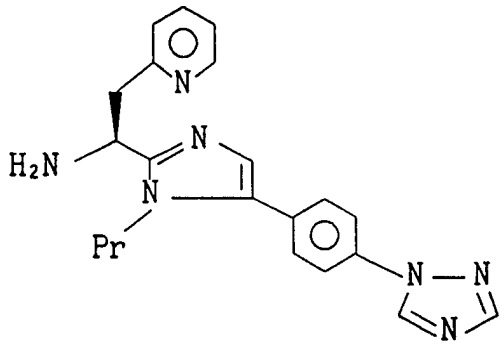
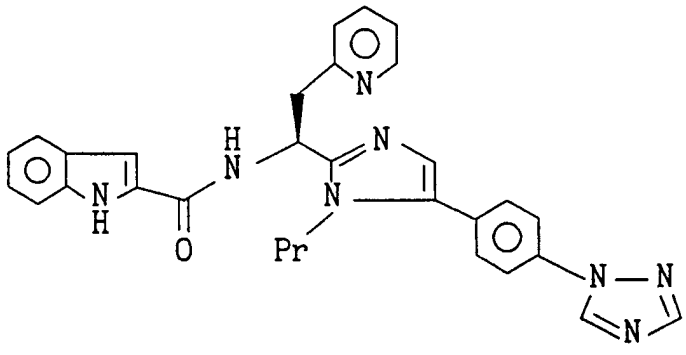
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Example No.	Formula
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219	
	

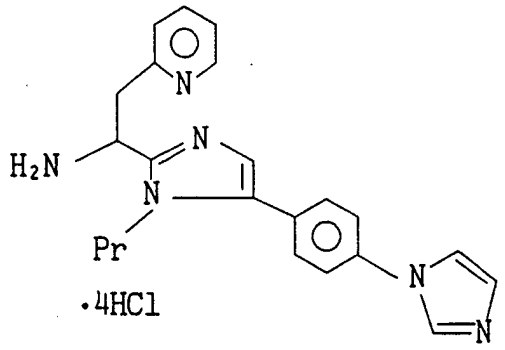
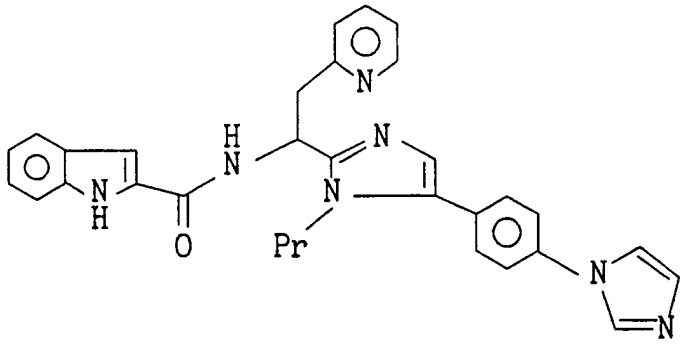
Table

Example No.	Formula
220	
	
221	
	

Table

Example No.	Formula
222	
	
223	
	

Table

Example No.	Formula
224	
	

Preparation 1

To an ice-cooled mixture of N-(tert-butoxycarbonyl)glycine (1.40 g) and 2-aminoacetophenone hydrochloride (1.61 g) in dichloromethane (14 ml) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (1.49 g). The mixture was stirred at room temperature for 12 hours. A saturated aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol= 40/1) to give the object compound as white powder (689 mg).

MASS (ESI) (m/z) : 293 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.47(9H,s), 3.92(2H,d,J=5Hz), 4.78(2H,s), 5.13(1H,br s), 7.05(1H,br s), 7.45-7.70(3H,m), 7.92-8.04(2H,m)

Preparation 2

A solution of the starting compound (669 mg) and 40% methylamine (0.7 ml) in a mixture of acetic acid (0.7 ml) and xylene (7 ml) was refluxed for 4 hours in a flask equipped with a Dean-Stark trap. The mixture was concentrated, neutralized with 1N sodium hydroxide solution, and extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol=50/1) to give the object compound as an oil (445 mg).

MASS (ESI) (m/z) : 288 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.46(9H,s), 3.60(3H,s), 4.48(2H,d,J=5Hz), 5.33(1H,br s), 6.99(1H,s), 7.30-7.52(5H,m)

Preparation 3

The starting compound (430 mg) was dissolved in trifluoroacetic acid (1.5 ml) and the mixture was stirred at room temperature for 1 hour. The mixture was concentrated, made basic with 1N sodium

hydroxide solution and extracted three times with chloroform. The organic layer was dried over magnesium sulfate and filtered. Evaporation of the solvent gave the object compound as an oil (314 mg).

MASS (ESI) (m/z) : 188 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.57(3H,s), 3.98(2H,s), 6.98(1H,s), 7.26-7.50(5H,m)

Preparation 4

To a solution of the starting compound (3.10 g) in methanol (15 ml) was added concentrated hydrochloric acid (3 ml), and the mixture was heated to 50°C for 2 hours. The mixture was concentrated, made basic with a 1N sodium hydroxide solution, and extracted three times with chloroform. The organic layer was dried over magnesium sulfate, and filtered. Evaporation of the solvent gave the object compound(2.35 g).

MASS (ESI) (m/z) : 308 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.02-3.22(2H,m), 3.21(3H,s), 3.78(3H,s), 4.11(1H,t,J=7Hz), 6.81(2H,d,J=8Hz), 6.99(2H,d,J=8Hz), 7.04(1H,s), 7.21-7.48(5H,m)

Preparation 5

To an ice-cooled mixture of the starting compound (599 mg), 2-aminoacetophenone hydrochloride (362 mg) and 1-hydroxybenzotriazole (270 mg) in dichloromethane (6 ml) was added 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide (349 mg). The mixture was stirred at room temperature for 12 hours. A saturated aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol=70/1) to give the object compound (823 mg).

MASS (ESI) (m/z) : 417 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.41(9H,s), 2.96-3.20(2H,m), 4.47(1H,m), 4.70(2H,AB of ABX,J_{AB}=15Hz), 5.01(1H,br s), 6.92(1H,br s), 7.13(2H,d,J=8Hz), 7.24(2H,d,J=8Hz), 7.41-7.68(3H,m), 7.88-8.00(2H,m)

Preparation 6

The starting compound (1.1 g) and glyoxal trimeric dihydrate (930 mg) were stirred in methanol (7 ml) at -10°C. Ammonia was bubbled through the solution for 5 minutes and the mixture was stirred at -10°C for 1 hour. The mixture was allowed to warm to room temperature over 18 hours, then poured into water, and extracted twice with dichloromethane. The combined extracts was dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by flash column chromatography over silica gel with a dichloromethane-methanol gradient (20:1 and 10:1) as eluent to give the object compound as an off-white solid (698.6 mg).

mp : 180.5-184°C

MASS : 288 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 3.29(2H,d,J=7.5Hz), 4.90(1H,q,J=7.5Hz), 5.25(1H,bd,J=7.5Hz), 6.89(1H,bs), 6.99(1H,bs), 7.12(2H,d,J=7.5Hz), 7.18-7.30(3H,m), 9.78(1H,bs)

Preparation 7

The starting compound (600 mg) was heated at 40°C for 2 hours in methyl iodide (10 ml). The reaction mixture was evaporated, and the residue was suspended in an aqueous sodium carbonate solution. The mixture was extracted with chloroform. The organic layer was washed successively with water and a saturated sodium chloride solution, dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was purified by flash column chromatography over silica gel with a chloroform-methanol (20:1) as eluent to give the object compound as a pale yellow oily solid (376.5 mg).

mp : 116-119°C

MASS (ESI) (m/z) : 302 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.40(9H,s), 3.05(3H,s),
3.10(1H,dd,J=14.5, 9.0Hz), 3.29(1H,dd,J=14.5, 4.5Hz),
4.93(1H,m), 5.50(1H,br d,J=7.5Hz), 6.63(1H,s),
6.95-7.02(3H,m), 7.15-7.24(3H,m)

Preparation 8

The object compound was obtained according to a similar manner to that of Preparation 3 except that a mixutre of trifluoroacetic acid and dichloromethane was used instead of trifluoroacetic acid.

MASS : 322 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.43(3H,t,J=8Hz), 3.09-3.27(2H,m), 3.12(3H,s),
4.07(2H,q,J=8Hz), 4.13(1H,t,J=8Hz), 6.91(2H,d,J=8Hz),
7.00(1H,s), 7.10(2H,d,J=7Hz), 7.19(2H,d,J=8Hz),
7.21-7.31(3H,m)

Preparation 9

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS(m/z) : 428 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.43(3H,t,J=7Hz), 1.46(9H,s),
3.25(1H,dd,J=5 and 15Hz), 3.37(1H,m), 4.09(2H,q,J=7Hz),
4.62(2H,d,J=3Hz), 4.67(1H,m), 6.40(1H,m), 6.91(2H,d,J=8Hz),
7.15(1H,dd,J=5 and 7Hz), 7.21(1H,d,J=8Hz),
7.58(1H,dd,J=7 and 8Hz), 7.89(2H,d,J=8Hz), 8.53(1H,d,J=5Hz)

Preparation 10

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS(m/z) : 423 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.43(9H,s), 1.43(3H,t,J=7Hz), 3.38(3H,s),
3.42(2H,d,J=7Hz), 4.04(2H,q,J=7Hz), 5.40(1H,m),
6.91(2H,d,J=8Hz), 6.92(1H,s), 7.11(2H,m), 7.20(2H,d,J=8Hz),
7.54(1H,m), 8.53(1H,d,J=5Hz)

Preparation 11

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS(m/z) : 323 (M+1)

Preparation 12

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS(m/z) : 452 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.48(9H,s), 3.25(1H,dd,J=5 and 15Hz), 3.35(1H,m), 4.69(1H,m), 4.70(2H,d,J=3Hz), 6.44(1H,m), 7.17(1H,dd,J=5 and 7Hz), 7.22(1H,d,J=8Hz), 7.62(1H,dd,J=7 and 8Hz), 7.74(2H,d,J=8Hz), 8.04(2H,d,J=8Hz), 8.55(1H,d,J=5Hz)

Preparation 13

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS(m/z) : 447 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.48(9H,s), 3.46(2H,d,J=7Hz), 3.49(3H,s), 5.44(1H,m), 7.07(1H,s), 7.13(2H,m), 7.42(2H,d,J=8Hz), 7.57(1H,m), 7.68(2H,d,J=8Hz), 8.54(1H,d,J=5Hz)

Preparation 14

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS(m/z) : 347 (M+1)

Preparation 15

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS(m/z) : 428 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 1.43(3H,t,J=7Hz), 3.03(1H,m), 3.22(1H,dd,J=7 and 14Hz), 4.10(2H,q,J=7Hz), 4.57(1H,m), 4.65(2H,m), 5.01(1H,m), 6.94(2H,d,J=8Hz), 7.16(2H,d,J=6Hz), 7.90(2H,d,J=8Hz), 8.51(2H,d,J=6Hz)

Preparation 16

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS(m/z) : 423 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.42(9H,s), 1.44(3H,t,J=7Hz), 3.18(3H,s), 3.29(2H,m), 4.06(2H,q,J=7Hz), 5.41(1H,m), 6.93(2H,d,J=8Hz), 6.97(1H,s), 7.06(2H,d,J=6Hz), 7.17(2H,d,J=8Hz), 8.47(2H,d,J=6Hz)

Preparation 17

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS(m/z) : 323 (M+1)

Preparation 18

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS(m/z) : 415 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.47(9H,s), 4.77(2H,m), 5.42(1H,d,J=5Hz), 6.51(1H,m), 7.25(1H,m), 7.53(1H,d,J=8Hz), 7.73(1H,t,J=8Hz), 8.08(2H,d,J=8Hz), 8.32(2H,d,J=8Hz), 8.57(1H,d,J=5Hz)

Preparation 19

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS(m/z) : 410 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.46(9H,s), 3.78(3H,s), 4.44(1H,d,J=5Hz), 7.17(1H,s), 7.23(1H,m), 7.47(1H,d,J=8Hz), 7.52(2H,d,J=8Hz), 7.70(1H,m), 8.28(2H,d,J=8Hz), 8.55(1H,d,J=5Hz)

Preparation 20

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS(m/z) : 310 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.65(3H,s), 5.48(1H,s), 7.21(1H,s), 7.23(1H,m), 7.40(1H,d,J=8Hz), 7.52(2H,d,J=8Hz), 7.71(1H,t,J=8Hz), 8.28(2H,d,J=8Hz), 8.57(1H,d,J=5Hz)

Preparation 21

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS : 481 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 3.04(2H,d,J=7Hz), 3.78(3H,s), 4.40(1H,br s), 4.52-4.73(2H,m), 5.00(1H,br s), 6.81(2H,d,J=8Hz), 6.82(1H,s), 7.11(2H,d,J=8Hz), 7.59(1H,d,J=8Hz), 7.78(1H,dd,J=8 and 2Hz), 8.02(1H,d,J=2Hz)

Preparation 22

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 476 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.40(9H,s), 3.01(3H,s), 3.02-3.15(1H,m), 3.20-3.31(1H,m), 3.76(3H,s), 4.90-5.00(1H,m), 5.62(1H,d,J=8Hz), 6.77(2H,d,J=8Hz), 6.92(2H,d,J=8Hz), 7.00-7.10(1H,m), 7.03(1H,s), 7.30(1H,d,J=2Hz), 7.48(1H,d,J=8Hz)

Preparation 23

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 376 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.11(2H,d,J=8Hz), 3.20(3H,s), 3.78(3H,s), 4.12(1H,t,J=8Hz), 6.80(2H,d,J=8Hz), 6.99(2H,d,J=8Hz), 7.07(1H,s), 7.10(1H,dd,J=8 and 2Hz), 7.37(1H,s), 7.48(1H,d,J=8Hz)

Preparation 24

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 174-176°C

MASS : 495 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.40(9H,s), 3.09-3.22(2H,m), 4.30-4.58(1H,m), 4.60-4.80(2H,m), 4.92-5.12(1H,m), 6.88(1H,br s), 7.15-7.34(5H,m), 7.80(2H,d,J=8Hz), 8.02(2H,d,J=8Hz)

Preparation 25

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 403 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.46(9H,s), 2.98(3H,s), 3.12(1H,t,J=8Hz), 3.30-3.40(1H,m), 5.01(1H,q,J=8Hz), 5.58(1H,d,J=8Hz), 7.00-7.10(2H,m), 7.19-7.30(4H,m), 7.31(2H,d,J=8Hz), 7.69(2H,d,J=8Hz)

Preparation 26

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 303 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.10-3.28(2H,m), 3.22(3H,s), 4.18(1H,t,J=8Hz), 7.03-7.11(2H,m), 7.16(1H,s), 7.20-7.32(3H,m), 7.39(2H,d,J=8Hz), 7.70(2H,d,J=8Hz)

Preparation 27

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 90-95°C

MASS : 481 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 3.08(2H,d,J=8Hz), 3.78(3H,s), 4.41(1H,br s), 4.61-4.80(2H,m), 5.01(1H,s), 6.81(2H,d,J=8Hz), 6.89(1H,br s), 7.11(2H,d,J=8Hz), 7.76(2H,d,J=8Hz), 8.06(2H,d,J=8Hz)

Preparation 28

The object compound was obtained according to a similar manner to

that of Preparation 2.

mp : 155-159℃

MASS : 476 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.46(9H,s), 3.00-3.18(1H,m), 3.02(3H,s), 3.22-3.32(1H,m), 3.72(3H,s), 4.98(1H,q,J=8Hz), 5.56(1H,d,J=8Hz), 6.78(2H,d,J=8Hz), 6.93(2H,d,J=8Hz), 7.11(1H,s), 7.37(2H,d,J=8Hz), 7.67(2H,d,J=8Hz)

Preparation 29

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 376 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.01-3.20(2H,m), 3.22(3H,s), 3.73(3H,s), 4.11(1H,t,J=8Hz), 6.81(2H,d,J=8Hz), 7.00(2H,d,J=8Hz), 7.10(1H,s), 7.40(2H,d,J=8Hz), 7.68(2H,d,J=8Hz)

Preparation 30

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 153-155℃

MASS : 438 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.42(9H,s), 3.08(2H,d,J=8Hz), 3.78(3H,s), 4.41(1H,br s), 4.60-4.80(2H,m), 4.99(1H,br s), 6.82(2H,d,J=8Hz), 6.83(1H,br s), 7.12(2H,d,J=8Hz), 7.80(2H,d,J=8Hz), 8.05(2H,d,J=8Hz)

Preparation 31

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 433 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 3.01-3.11(1H,m), 3.05(3H,s), 3.20-3.31(1H,m), 3.78(3H,s), 4.90-5.03(1H,m), 5.52(1H,d,J=8Hz), 6.78(2H,d,J=8Hz), 6.92(2H,d,J=8Hz),

7.12(1H,s), 7.33(2H,d,J=8Hz), 7.69(2H,d,J=8Hz)

Preparation 32

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 333 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.05-3.20(2H,m), 3.30(3H,s), 3.80(3H,s), 4.13(1H,t,J=8Hz), 6.81(2H,d,J=8Hz), 7.00(2H,d,J=8Hz), 7.14(1H,s), 7.40(2H,d,J=8Hz), 7.70(2H,d,J=8Hz)

Preparation 33

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 123-125°C

MASS : 511 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 3.20-3.38(2H,m), 4.50-4.78(3H,m), 5.03(1H,br s), 6.90(1H,br s), 7.35(1H,d,J=8Hz), 7.40-7.50(2H,m), 7.59-7.69(3H,m), 7.70-7.81(5H,m)

Preparation 34

The object compound was obtained according to a similar manner to that of Preparation 2.

mp : 204-206°C

MASS : 506 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.40(9H,s), 2.82(3H,s), 3.22-3.38(1H,m), 3.43-3.58(1H,m), 5.01-5.12(1H,m), 5.60(1H,d,J=8Hz), 6.98(2H,d,J=8Hz), 7.05(1H,s), 7.18(1H,d,J=8Hz), 7.40-7.52(5H,m), 7.68-7.72(2H,m), 7.75-7.81(1H,m)

Preparation 35

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 406 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.10(3H,s), 3.22-3.41(2H,m), 4.23(1H,t,J=8Hz),

7.02(1H,s), 7.04-7.11(2H,m), 7.21(1H,d,J=8Hz),
7.40-7.57(5H,m), 7.70-7.88(3H,m)

Preparation 36

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS : 428 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.38(9H,s), 1.42(3H,t,J=8Hz), 2.93-3.11(1H,m),
3.12-3.28(1H,m), 4.10(2H,q,J=8Hz), 4.47-4.58(1H,m),
4.58-4.76(2H,m), 5.11(1H,d,J=8Hz), 6.93(2H,d,J=8Hz),
7.01(1H,s), 7.19-7.30(1H,m), 7.59(1H,d,J=8Hz),
7.90(2H,d,J=8Hz), 8.40-8.59(2H,m)

Preparation 37

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 423 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.39(9H,s), 1.41(3H,t,J=8Hz), 3.18(3H,s),
3.21-3.32(2H,m), 4.08(2H,q,J=8Hz), 5.01(1H,q,J=8Hz),
5.44(1H,d,J=8Hz), 6.91(2H,d,J=8Hz), 6.98(1H,s),
7.19(2H,d,J=8Hz), 7.40(1H,d,J=8Hz), 8.38(1H,s),
8.40-8.50(2H,m)

Preparation 38

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 323 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(3H,t,J=8Hz), 3.10-3.20(1H,m),
3.21-3.30(1H,m), 3.28(3H,s), 4.05(2H,q,J=8Hz),
4.13(1H,t,J=8Hz), 6.91(2H,d,J=8Hz), 6.99(1H,s),
7.19(2H,d,J=8Hz), 7.21(1H,t,J=6Hz), 7.40(1H,d,J=8Hz),
8.41(1H,s), 8.49(1H,d,J=6Hz)

Preparation 39

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS : 429 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.40(9H,s), 2.90-3.12(1H,m), 3.18-3.28(1H,m), 4.59(1H,br s), 4.66-4.88(2H,m), 5.10(1H,d,J=8Hz), 7.10(1H,br s), 7.20(2H,d,J=4Hz), 8.12(2H,d,J=8Hz), 8.37(2H,d,J=8Hz), 8.52(2H,d,J=8Hz)

Preparation 40

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 424 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.39(9H,s), 3.30(2H,d,J=8Hz), 3.31(3H,s), 5.12(1H,q,J=8Hz), 5.38(1H,d,J=8Hz), 7.09(2H,d,J=4Hz), 7.19(1H,s), 7.44(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.49(2H,d,J=4Hz)

Preparation 41

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 324 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.11-3.21(1H,m), 3.28-3.38(1H,m), 3.42(3H,s), 4.21(1H,t,J=8Hz), 7.09(2H,d,J=6Hz), 7.20(1H,s), 7.49(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.52(2H,d,J=7Hz)

Preparation 42

The object compound was obtained according to a similar manner to that of Preparation 1.

MASS (ESI) (m/z) : 491,493 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.41(9H,s), 3.04(2H,d,J=6Hz), 3.75(3H,s), 4.42(1H,br s), 4.54-4.77(2H,m), 5.00(1H,br s),

6.81(2H,d,J=8Hz), 6.85(1H,br s), 7.12(2H,d,J=8Hz),
7.63(2H,d,J=7Hz), 7.80(2H,d,J=7Hz)

Preparation 43

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 486,488 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.41(9H,s), 3.00(3H,s),
3.01-3.32(2H,m), 3.76(3H,s), 4.88-5.02(1H,m),
5.57(1H,d,J=8Hz), 6.76(2H,d,J=8Hz), 6.88-7.18(5H,m),
7.51(2H,d,J=8Hz)

Preparation 44

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 386,388 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.02-3.18(2H,m), 3.20(3H,s),
3.78(3H,s), 4.12(1H,t,J=7Hz), 6.81(2H,d,J=8Hz),
6.98(2H,d,J=8Hz), 7.03(1H,s), 7.15(2H,d,J=8Hz),
7.52(2H,d,J=8Hz)

Preparation 45

The object compound was obtained according to a similar manner to that of Preparation 1.

amorphous solid

MASS : 461 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.39(9H,s), 3.00-3.20(2H,m),
4.40-4.78(3H,m), 5.03(1H,bs), 6.89(1H,bs), 7.19-7.38(5H,m),
7.63(2H,d,J=8Hz), 7.82(2H,d,J=8Hz)

Preparation 46

The object compound was obtained according to a similar manner to that of Preparation 2.

mp : 162-164°C

MASS : 456 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(9H,s), 2.97(3H,s),

3.11(1 x 1/3H,d,J=8Hz), 3.15(1 x 2/3H,d,J=8Hz),
3.31(1 x 2/3H,d,J=8Hz), 3.35(1 x 1/3H,d,J=8Hz),
4.91-5.08(1H,m), 5.59(1H,d,J=8Hz), 6.99-7.07(3H,m),
7.09(2H,d,J=8Hz), 7.18-7.23(3H,m), 7.51(2H,d,J=8Hz)

Preparation 47

The object compound was obtained according to a similar manner to that of Preparation 3.

oil

MASS : 356 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.10-3.25(2H,m), 3.20(3H,s),
4.17(1H,t,J=8Hz), 7.05(1H,s), 7.10(2H,d,J=8Hz),
7.14(2H,d,J=8Hz), 7.20-7.32(3H,m), 7.53(2H,d,J=8Hz)

Preparation 48

A solution of potassium tert-butoxide (4.2 g) in anhydrous tetrahydrofuran (70 ml) was cooled under nitrogen atmosphere to -70°C, and a solution of the starting compound (10 g) in anhydrous tetrahydrofuran (35 ml) was added while maintaining the reaction temperature at -70°C. After 30 minutes, this solution was added dropwise to a solution of 4-bromobenzoyl chloride (8.21 g) in anhydrous tetrahydrofuran (24 ml) with stirring while cooling at -70°C on a cooling bath. The reaction mixture was stirred at -70°C for 1 hour and quenched with 3N-hydrochloric acid (100 ml). The cooling bath was removed and the reaction mixture was concentrated to dryness under reduced pressure. The residue was dissolved in water (15 ml) and extracted with diethyl ether (twice). The aqueous layer was concentrated *in vacuo*, and the residue was dissolved in anhydrous methanol. The precipitated white solid (KCl) was removed by filtration. The filtrate was concentrated *in vacuo* and the residue was crystallized from tetrahydrofuran/diethyl ether to give the object compound as an off-white solid.

mp : 183-188°C

MASS : 286 $(M+H)^+$

^{1}H-NMR (DMSO-d_6, δ) 1.03(3H,t,J=7.0Hz), 4.13(2H,q,J=7.0Hz),
6.24(1H,s), 7.86(2H,d,J=7.5Hz), 8.09(2H,d,J=7.5Hz),
9.10(2H,br s),

Preparation 49

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow amorphous solid

MASS : 531 $(M-H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.14(3H,t,J=7.0Hz), 1.40(9H,s),
2.97-3.18(2H,m), 4.16(2H,q,J=7.0Hz), 4.49(1H,m), 4.96(1H,m),
6.03(1H×3/7,d,J=7.0Hz), 6.06(1H×4/7,d,J=7.0Hz),
7.14-7.31(6H,m), 7.64(2H,d,J=7.5Hz), 7.95(2H×3/7,d,J=7.5Hz),
7.97(2H×4/7,d,J=7.5Hz)

Preparation 50

The object compound was obtained according to a similar manner to that of Preparation 2.

pale yellow amorphous solid

MASS : 528 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.18(3H,t,J=7.0Hz), 1.41(9H,s), 2.69(3H,s),
3.17(1H,dd,J=13.5 and 9.0Hz), 3.37(1H,dd,J=13.5 and 7.0Hz),
4.23(2H,q,J=7.0Hz), 4.98(1H,m), 5.74(1H,d,J=7.5Hz),
6.97-7.08(4H,m), 7.19-7.27(3H,m), 7.55(2H,d,J=7.5Hz)

Preparation 51

To a solution of the starting compound (2.0 g) in ethanol (20 ml) was added 1N-sodium hydroxide solution (4.16 ml) with stirring at room temperature. The reaction mixture was stirred at 60°C for 6.5 hours and concentrated *in vacuo*. Water was added to the residue, and the aqueous solution was washed with ethyl acetate (twice). The aqueous layer was acidified to pH 3 with 1N-hydrochloric acid, and extracted with chloroform (twice). The combined extracts were dried over anhydrous magnesium sulfate and concentrated *in vacuo* to give the object compound (2.13 g) as a pale yellow amorphous solid.

MASS : 498 $(M-H)^+$

^{1}H-NMR ($DMSO-d_6$, δ) 1.27(9H×1/5,s), 1.30(9H×4/5,s),
3.01(3H×1/5,s), 3.07(3H×4/5,s), 3.13-3.21(2H,m),
5.09(1H,m), 6.98-7.31(7H,m), 7.58(2H,d,J=7.5Hz),
8.03(1H,d,J=7.5Hz)

Preparation 52

The object compound was obtained according to a similar manner to that of Preparation 5.

off-white amorphous solid

MASS : 513 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.42(9H×1/5,s), 1.46(9H×4/5,s),
2.70(3H×1/5,s), 2.76(3H×4/5,s), 2.92(3H,d,J=6.0Hz),
3.09(1H,dd,J=13.5 and 9.0Hz), 3.34(1H,dd,J=13.5 and 6.0Hz),
4.97(1H,m), 5.47(1H,d,J=7.5Hz), 6.97-7.06(3H,m),
7.12(2H,d,J=7.5Hz), 7.19-7.25(3H,m), 7.53(2H,d,J=7.5Hz)

Preparation 53

The object compound was obtained according to a similar manner to that of Preparation 3.

pale brown oil

MASS : 413 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 2.91(3H,d,J=4.5Hz), 2.97(3H,s),
3.13(2H,d,J=7.5Hz), 4.17(1H,t,J=7.5Hz), 7.03-7.31(6H,m),
7.19(2H,d,J=7.5Hz), 7.56(2H,d,J=7.5Hz)

Preparation 54

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow amorphous solid

MASS : 543 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.42(9H,s), 2.85(3H,s),
3.15(1H,dd,J=13.5 and 9.0Hz), 3.30(3H,s),
3.34(1H,dd,J=13.5 and 6.0Hz), 3.74(3H,s), 5.00(1H,m),
5.51(1H,d,J=7.5Hz), 6.99-7.06(2H,m), 7.09(2H,d,J=7.5Hz),

7.19-7.27(3H,m), 7.53(2H,d,J=7.5Hz)

Preparation 55

The object compound was obtained according to a similar manner to that of Preparation 3.

pale yellow oil

MASS : 443 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 3.03(3H,s), 3.12-3.25(2H,m), 3.30(3H,s), 3.77(3H,s), 4.17(1H,t,J=7.0Hz), 7.04-7.11(2H,m), 7.16(2H,d,J=7.5Hz), 7.22-7.32(3H,m), 7.54(2H,d,J=7.5Hz)

Preparation 56

The object compound was obtained according to a similar manner to that of Preparation 5.

colorless amorphous solid

MASS : 527 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.42(9H,s), 2.88(3H,s), 2.99(3H,s), 3.03(3H,s), 3.13(1H,dd,J=13.5 and 7.5Hz), 3.33(1H,dd,J=13.5 and 6.0Hz), 5.00(1H,m), 5.52(1H,d,J=7.5Hz), 7.00-7.09(2H,m), 7.11(2H,d,J=7.5Hz), 7.20-7.26(3H,m), 7.52(2H,d,J=7.5Hz)

Preparation 57

The object compound was obtained according to a similar manner to that of Preparation 3.

colorless oil

MASS : 427 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 2.98(3H,s), 3.06(3H,s), 3.07(3H,s), 3.18(2H,d,J=7.5Hz), 4.18(1H,t,J=7.5Hz), 7.04-7.13(2H,m), 7.17(2H,d,J=7.5Hz), 7.22-7.31(3H,m), 7.53(2H,d,J=7.5Hz)

Preparation 58

The object compound was obtained according to a similar manner to that of Preparation 5.

off-white amorphous solid

MASS : 575 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.42(9H×1/5,s), 1.49(9H×4/5,s),
2.70(3H×1/5,s), 2.80(3H×4/5,s),
3.15(1H,dd,J=13.5 and 9.0Hz), 3.39(1H,dd,J=13.5 and 7.0Hz),
5.01(1H,m), 5.51(1H×4/5,d,J=7.5Hz), 5.76(1H×1/5,d,J=7.5Hz),
6.99-7.10(4H,m), 7.17(2H,d,J=7.5Hz), 7.19-7.28(4H,m),
7.31(2H,t,J=7.5Hz), 7.56(2H,d,J=7.5Hz), 9.11(1H,s)

Preparation 59

The object compound was obtained according to a similar manner to that of Preparation 3.

pale yellow oil

MASS : 475 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 3.01(3H,s), 3.16-3.24(2H,m), 4.16-4.26(1H,m),
7.03-7.14(4H,m), 7.22(2H,d,J=7.5Hz), 7.24-7.34(6H,m),
7.58(2H,d,J=7.5Hz), 9.19(1H,s)

Preparation 60

To a solution of the starting compound (2.65 g) and triethylamine (1.5 ml) in tetrahydrofuran (10 ml) was added isobutyl chloroformate (1.3 ml) at -10°C, and the mixture was stirred at -10°C for 10 minutes. To the solution was added dropwise a solution of o-phenylenediamine (1.15 g) in tetrahydrofuran (10 ml) at -5°C. The mixture was allowed to warm to room temperature and stirred for 1 hour. The mixture was concentrated, then the residue was poured into a saturated sodium hydrogencarbonate solution and extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, and filtered. Evaporation of the solvent gave the object compound as an oil (4.11 g).

MASS (ESI) (m/z) : 356 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.40(9H×1/3,s), 1.42(9H×2/3,s),
3.03-3.28(2H,m), 4.38-4.52(1H,m), 5.05-5.26(1H,br s),
6.65-7.42(10H,m)

Preparation 61

A solution of the starting compound (3.55 g) in acetic acid (1

ml) and ethanol (10 ml) was refluxed for 4 hours. The mixture was concentrated, neutralized with 1N sodium hydroxide solution, and extracted three times with chloroform. The organic layer was washed successively with 1N hydrochloric acid, a saturated sodium hydrogencarbonate solution and brine, then dried over magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol=50/1) to give the object compound as a white powder (2.69 g).

MASS (ESI) (m/z) : 338 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.36(9H×1/2,s), 1.39(9H×1/2,s), 2.95-3.46(2H,m), 4.41-4.55(1H×1/2,m), 5.06-5.22(1H×1/2,m), 5.30(1H×1/2,br s), 5.73(1H×1/2,d,J=8Hz), 7.02-7.38(9H,m), 7.68(1H×1/2,br s), 8.46(1H×1/2,br s)

Preparation 62

To a suspension of the starting compound (500 mg) and potassium carbonate (614 mg) in N,N-dimethylformamide (5 ml) was added methyl iodide (0.28 ml) at room temperature under nitrogen atmosphere. The reaction mixture was heated at 30°C for 3 hours. After being cooled to room temperature, the mixture was diluted with chloroform. The organic layer was washed with water and a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography over silica gel with chloroform-methanol (30:1) as eluent to give the object compound (264 mg) as a colorless solid.

mp : 186-189°C

MASS : 352 $(M+H)^+$

^{1}H-NMR (DMSO-d_6, δ) 1.12(9H×1/8,s), 1.28(9H×7/8,s), 3.14-3.30(2H,m), 3.60(3H×1/8,s), 3.62(3H×7/8,s), 5.11(1H,m), 7.11-7.29(7H,m), 7.47(1H,d,J=7.5Hz), 7.54(1H,d,J=7.5Hz), 7.61(1H,d,J=7.5Hz)

Preparation 63

The object compound was obtained according to a similar manner to

that of Preparation 3.

pale yellow oil

MASS : 252 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 3.19(1H,dd,J=13.5 and 7.5Hz), 3.27(1H,dd,J=13.5 and 7.5Hz), 3.46(3H,s), 4.35(1H,t,J=7.5Hz), 7.06-7.12(2H,m), 7.19-7.30(6H,m), 7.77(1H,m)

Preparation 64

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow solid

mp : 153-155°C

MASS : 447 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.41(9H,s), 4.63(1H,dd,J=19.5 and 5.5Hz), 4.77(1H,dd,J=19.5 and 5.5Hz), 5.24(1H,m), 5.71(1H,br d,J=5.5Hz), 6.79(1H,m), 7.29-7.44(5H,m), 7.63(2H,d,J=7.5Hz), 7.80(2H,d,J=7.5Hz)

Preparation 65

The object compound was obtained according to a similar manner to that of Preparation 2.

pale yellow amorphous solid

MASS : 442 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.43(9H,s), 3.40(3H,s), 5.96(1H,d,J=7.5Hz), 6.20(1H,d,J=7.5Hz), 7.06(1H,s), 7.20(2H,d,J=7.5Hz), 7.27-7.37(5H,m), 7.53(2H,d,J=7.5Hz)

Preparation 66

The object compound was obtained according to a similar manner to that of Preparation 3.

brown oil

MASS : 342 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 3.35(3H,s), 5.21(1H,s), 7.08(1H,s), 7.20(2H,d,J=7.5Hz), 7.23-7.40(5H,m), 7.53(2H,d,J=7.5Hz)

Preparation 67

The object compound was obtained according to a similar manner to that of Preparation 1.

amorphous solid

MASS : 417 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 3.11(2H,d,J=8Hz), 4.40-4.60(1H,m), 4.60-4.78(2H,m), 5.00(1H,bs), 6.84(1H,bs), 7.17-7.36(5H,m), 7.49(2H,d,J=8Hz), 7.90(2H,d,J=8Hz)

Preparation 68

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 412 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(9H,s), 2.92(3H,s), 3.00-3.20(1H,m), 3.24-3.40(1H,m), 5.00(1H,q,J=8Hz), 5.59(1H,d,J=8Hz), 7.00-7.10(3H,m), 7.14(2H,d,J=8Hz), 7.18-7.30(3H,m), 7.37(2H,d,J=8Hz)

Preparation 69

The object compound was obtained according to a similar manner to that of Preparation 3.

oil

MASS : 312 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.10-3.28(2H,m), 3.18(3H,s), 4.10-4.24(1H,m), 7.08(2H,d,J=8Hz), 7.11(1H,s), 7.21(2H,d,J=8Hz), 7.22-7.33(3H,m), 7.39(2H,d,J=8Hz)

Preparation 70

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow oil

MASS : 395 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.49(9H,s), 3.03-3.47(2H,m), 4.49-4.77(4H,m), 5.03(1H,m), 6.87(1H,m), 7.03-7.27(4H,m), 7.46(2H,t,J=7.5Hz), 7.60(1H,t,J=7.5Hz), 7.90(2H,d,J=7.5Hz)

Preparation 71

The object compound was obtained according to a similar manner to that of Preparation 2.

pale brown oil

MASS : 390 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.46(9H,s), 3.31(1H,dd,J=16.0 and 7.0Hz), 3.52(1H,dd,J=16.0 and 2.5Hz), 3.60(3H,s), 4.01(1H,d,J=16.0Hz), 4.51-5.93(2H,m), 6.91(1H,s), 7.05(1H,d,J=7.5Hz), 7.11-7.49(8H,m)

Preparation 72

The object compound was obtained according to a similar manner to that of Preparation 3.

pale brown solid

mp : 162-165℃

MASS : 290 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 3.10(1H,dd,J=16.0 and 3.0Hz), 3.55(1H,dd,J=16.0 and 11.5Hz), 3.72(3H,s), 4.05-4.28(3H,m), 7.03(1H,s), 7.08(1H,m), 7.12-7.21(3H,m), 7.32-7.49(5H,m)

Preparation 73

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 436 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 3.12-3.45(2H,m), 3.73(3H,s), 4.44-4.61(1H,m), 4.62(2H,d,J=2Hz), 5.18(1H,br d,J=8Hz), 6.82(1H,br t,J=2Hz), 6.94(1H,s), 7.01-7.30(3H,m), 7.41-7.66(4H,m), 7.90(2H,d,J=8Hz)

Preparation 74

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 431 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 2.87(3H,s), 3.18-3.58(2H,m), 3.70(3H,s), 5.00-5.13(1H,m), 5.70(1H,br d,J=8Hz),

6.80(1H,s), 6.91-7.40(10H,m)

Preparation 75

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 331 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.22-3.43(2H,m), 3.25(3H,s), 3.74(3H,s), 4.25(1H,t,J=7Hz), 6.87(1H,s), 7.00-7.48(10H,m)

Preparation 76

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 506, 508 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.39(9H,s), 3.13(1H,dd,J=13 and 8Hz), 3.29(1H,dd,J=13 and 6Hz), 4.46-4.78(3H,m), 5.10(1H,br d,J=8Hz), 6.98(1H,br s), 7.39(2H,d,J=8Hz), 7.64(2H,d,J=8Hz), 7.80(2H,d,J=8Hz), 8.16(2H,d,J=8Hz)

Preparation 77

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 501, 503 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.39(9H,s), 3.28(3H,s), 3.32-3.50(2H,m), 5.03-5.17(1H,m), 5.33(1H,br d,J=8Hz), 7.02(1H,s), 7.13(2H,d,J=8Hz), 7.32(2H,d,J=8Hz), 7.56(2H,d,J=8Hz), 8.11(2H,d,J=8Hz)

Preparation 78

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 401, 403 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.25(1H,dd,J=13 and 7Hz), 3.36(3H,s), 3.41(1H,dd,J=13 and 7Hz), 4.20(1H,t,J=7Hz), 7.03(1H,s), 7.17(2H,d,J=8Hz), 7.31(2H,d,J=8Hz), 7.55(2H,d,J=8Hz), 8.15(2H,d,J=8Hz)

Preparation 79

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 458 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 2.93-3.15(2H,m), 3.77(3H,s), 4.34-4.51(1H,m), 4.62-4.86(2H,m), 5.00(1H,br d,J=8Hz), 6.82(2H,d,J=8Hz), 6.88(1H,br s), 7.13(2H,d,J=8Hz), 8.11(2H,d,J=8Hz), 8.35(2H,d,J=8Hz)

Preparation 80

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 453 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 3.02-3.33(2H,m), 3.08(3H,s), 3.76(3H,s), 4.90-5.05(1H,m), 5.55(1H,br d,J=8Hz), 6.77(2H,d,J=8Hz), 6.94(2H,d,J=8Hz), 7.19(1H,s), 7.41(2H,d,J=8Hz), 8.26(2H,d,J=8Hz)

Preparation 81

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 353 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.02-3.21(2H,m), 3.29(3H,s), 3.78(3H,s), 4.14(1H,t,J=7Hz), 6.82(2H,d,J=8Hz), 7.00(2H,d,J=8Hz), 7.20(1H,s), 7.46(2H,d,J=8Hz), 8.28(2H,d,J=8Hz)

Preparation 82

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 477, 479 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 3.78(3H,s), 4.56-4.82(2H,m), 5.19(1H,br s), 5.66(1H,br d,J=8Hz), 6.80(1H,br s), 6.89(2H,d,J=8Hz), 7.32(2H,d,J=8Hz), 7.63(2H,d,J=8Hz), 7.89(2H,d,J=8Hz)

Preparation 83

The object compound was obtained according to a similar manner to

that of Preparation 2.

MASS (ESI) (m/z) : 472, 474 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 3.37(3H,s), 3.78(3H,s), 5.91(1H,br d,J=8Hz), 6.18(1H,br d,J=8Hz), 6.86(2H,d,J=8Hz), 7.06(1H,s), 7.19(2H,d,J=8Hz), 7.25(2H,d,J=8Hz), 7.53(2H,d,J=8Hz)

Preparation 84

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 372, 374 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.33(3H,s), 3.78(3H,s), 5.15(1H,s), 6.87(2H,d,J=8Hz), 7.05(1H,s), 7.19(2H,d,J=8Hz), 7.23(2H,d,J=8Hz), 7.52(2H,d,J=8Hz)

Preparation 85

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 479, 481 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 4.55-4.82(2H,m), 5.24(1H,br s), 5.76(1H,br d,J=8Hz), 6.81(1H,br s), 7.28-7.41(4H,m), 7.63(2H,d,J=8Hz), 7.79(2H,d,J=8Hz),

Preparation 86

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 476, 478 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 3.40(3H,s), 5.91(1H,br d,J=8Hz), 6.25(1H,br d,J=8Hz), 7.04(1H,s), 7.18(2H,d,J=8Hz), 7.23-7.36(4H,m), 7.55(2H,d,J=8Hz)

Preparation 87

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 376, 378 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.35(3H,s), 5.20(1H,s), 7.05(1H,s),

7.19(2H,d,J=8Hz), 7.22-7.38(4H,m), 7.54(2H,d,J=8Hz)

Preparation 88

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 471 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 3.09-3.39(2H,m), 4.48-4.62(1H,m), 4.65-4.88(2H,m), 5.04(1H,br d,J=8Hz), 6.97(1H,br s), 7.41(2H,d,J=8Hz), 8.12(2H,d,J=8Hz), 8.17(2H,d,J=8Hz), 8.35(2H,d,J=8Hz)

Preparation 89

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 468 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.39(9H,s), 3.31-3.51(2H,m), 3.39(3H,s), 5.09-5.22(1H,m), 5.33(1H,br d,J=8Hz), 7.18(1H,s), 7.33(2H,d,J=8Hz), 7.45(2H,d,J=8Hz), 8.11(2H,d,J=8Hz), 8.28(2H,d,J=8Hz)

Preparation 90

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 368 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.26(1H,dd,J=13 and 7Hz), 3.45(1H,dd,J=13 and 7Hz), 3.50(3H,s), 4.25(1H,t,J=7Hz), 7.20(1H,s), 7.35(2H,d,J=8Hz), 7.49(2H,d,J=8Hz), 8.15(2H,d,J=8Hz), 8.29(2H,d,J=8Hz)

Preparation 91

To an ice-cooled solution of the starting compound (5.32 g) and N,N-diisopropylethylamine (9.6 ml) in N,N-dimethylformamide (27 ml) was added diphenylphosphoryl azide (6.04 g). After 5 minutes, 2-amino-4'-nitroacetophenone hydrochloride (4.53 g) was added portionwise to the above solution, and the resulting deep-colored mixture was stirred at room temperature for 1 hour. A saturated

aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with ethyl acetate. The organic layer was washed successively with water and brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate=1/1) to give the object compound as a deep-red oil (5.96 g).

MASS (ESI) (m/z) : 429 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.46(9H,s), 3.20-3.43(2H,m), 4.62-4.78(3H,m), 6.43(1H,br d,J=8Hz), 7.12-7.27(2H,m), 7.56-7.67(1H,m), 8.04(1H,br s), 8.10(2H,d,J=8Hz), 8.32(2H,d,J=8Hz), 8.54(1H,d,J=5Hz)

Preparation 92

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 424 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.38(9H,s), 3.38-3.50(2H,m), 3.53(3H,s), 5.37-5.51(1H,m), 5.54(1H,br d,J=8Hz), 7.05-7.20(3H,m), 7.46(2H,d,J=8Hz), 7.55(1H,t,J=8Hz), 8.27(2H,d,J=8Hz), 8.52(1H,d,J=5Hz)

Preparation 93

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 324 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.27-3.50(2H,m), 3.61(3H,s), 4.62(1H,dd,J=8 and 6Hz), 7.11-7.22(3H,m), 7.50(2H,d,J=8Hz), 7.61(1H,t,J=7Hz), 8.29(2H,d,J=8Hz), 8.58(1H,d,J=5Hz)

Preparation 94

The object compound was obtained according to a similar manner to that of Preparation 91.

MASS (ESI) (m/z) : 429 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.45(9H,s), 3.18-3.42(2H,m), 4.61-4.78(3H,m), 6.43(1H,br d,J=8Hz), 7.10-7.29(2H,m),

7.55-7.67(1H,m), 8.05(1H,br s), 8.09(2H,d,J=8Hz),
8.32(2H,d,J=8Hz), 8.54(1H,d,J=5Hz)

Preparation 95

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 424 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.36(9H,s), 3.38-3.50(2H,m), 3.53(3H,s),
5.36-5.54(2H,m), 7.06-7.18(3H,m), 7.46(2H,d,J=8Hz),
7.56(1H,t,J=8Hz), 8.27(2H,d,J=8Hz), 8.52(1H,d,J=5Hz)

Preparation 96

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 324 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.28-3.51(2H,m), 3.62(3H,s),
4.62(1H,dd,J=8 and 6Hz), 7.11-7.22(3H,m), 7.50(2H,d,J=8Hz),
7.60(1H,t,J=7Hz), 8.29(2H,d,J=8Hz), 8.58(1H,d,J=5Hz)

Preparation 97

The object compound was obtained according to a similar manner to that of Preparation 91.

oil

MASS : 399 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.45(9H,s), 2.62(3H,s), 3.20-3.30(1H,m),
3.31-3.42(1H,m), 4.68(2H,d,J=4Hz), 4.62-4.73(1H,m),
6.43(1H,br s), 7.11-7.30(3H,m), 7.60(1H,t,J=8Hz),
7.99(1H,br s), 8.09(1H,d,J=8Hz), 8.57(1H,d,J=4Hz), 9.02(1H,s)

Preparation 98

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS : 394 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.33(9H,s), 2.60(3H,s), 3.40(3H,s),
3.42(2H,d,J=8Hz), 5.40(1H,q,J=8Hz), 5.49(1H,d,J=8Hz),

7.01(1H,s), 7.07-7.19(2H,m), 7.20(1H,d,J=8Hz),
7.49-7.59(2H,m), 8.42(1H,d,J=2Hz), 8.52(1H,d,J=2Hz)

Preparation 99

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 294 (M+1)

^{1}H-NMR ($CDCl_3$) δ 2.59(3H,s), 3.29-3.50(2H,m), 3.51(3H,s),
4.60(1H,t,J=8Hz), 7.02(1H,s), 7.10-7.22(3H,m),
7.50-7.63(2H,m), 8.48(1H,s), 8.58(1H,d,J=4Hz)

Preparation 100

The object compound was obtained according to a similar manner to that of Preparation 91.

oil

MASS : 385 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 3.21-3.41(2H,m), 4.68(1H,br s),
4.70(2H,d,J=6Hz), 6.42(1H,br s), 7.11-7.23(2H,m),
7.42(1H,dd,J=8 and 6Hz), 7.61(1H,t,J=8Hz), 8.02(1H,br s),
8.20(1H,dd,J=8 and 2Hz), 8.54(1H,d,J=2Hz), 8.81(1H,d,J=2Hz),
9.16(1H,d,J=2Hz)

Preparation 101

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 380 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.38(9H,s), 3.40-3.50(2H,m), 3.43(3H,s),
5.41(1H,q,J=8Hz), 5.50(1H,d,J=8Hz), 7.07(1H,s),
7.11(2H,t,J=8Hz), 7.35(1H,dd,J=8 and 6Hz), 7.55(1H,t,J=8Hz),
7.61(1H,d,J=8Hz), 8.49-8.62(3H,m)

Preparation 102

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 280 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.30-3.39(1H,m), 3.40-3.49(1H,m), 3.52(3H,s), 4.60(1H,dd,J=8 and 6Hz), 7.09(1H,s), 7.10-7.19(2H,m), 7.37(1H,dd,J=8 and 6Hz), 7.59(1H,d,J=8Hz), 7.63(1H,dd,J=8 and 2Hz), 8.53-8.62(3H,m)

Preparation 103

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 469 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 1.45(3H,t,J=7Hz), 3.01(2H,d,J=7Hz), 4.11(2H,q,J=7Hz), 4.29-4.52(1H,m), 4.53-4.74(2H,m), 4.94-5.12(1H,m), 5.90(2H,s), 6.59-6.78(3H,m), 6.93(1H,br s), 6.94(2H,d,J=8Hz), 7.92(2H,d,J=8Hz)

Preparation 104

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 466 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 1.42(3H,t,J=7Hz), 3.01-3.28(2H,m), 3.08(3H,s), 4.05(2H,q,J=7Hz), 4.87-5.01(1H,m), 5.56(1H,br d,J=8Hz), 5.90(2H,s), 6.51(1H,d,J=8Hz), 6.52(1H,s), 6.68(1H,d,J=8Hz), 6.91(2H,d,J=8Hz), 6.96(1H,s), 7.17(2H,d,J=8Hz)

Preparation 105

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 366 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.44(3H,t,J=7Hz), 2.98-3.20(2H,m), 3.25(3H,s), 4.07(2H,q,J=7Hz), 4.09(1H,t,J=7Hz), 5.91(2H,s), 6.55(1H,d,J=8Hz), 6.58(1H,s), 6.72(1H,d,J=8Hz), 6.92(2H,d,J=8Hz), 6.97(1H,s), 7.19(2H,d,J=8Hz)

Preparation 106

The object compound was obtained according to a similar manner to that of Preparation 2 except that ethylamine was used instead of methylamine.

MASS (ESI) (m/z) : 438 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.14(3H,t,J=7Hz), 1.36(9H,s), 3.35-3.57(2H,m), 3.92-4.18(2H,m), 5.32-5.52(2H,m), 7.05-7.18(3H,m), 7.49(2H,d,J=8Hz), 7.50-7.60(1H,m), 8.28(2H,d,J=8Hz), 8.53(1H,d,J=5Hz)

Preparation 107

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 338 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.20(3H,t,J=7Hz), 3.29-3.52(2H,m), 3.94-4.20(2H,m), 4.62(1H,t,J=7Hz), 7.09-7.20(3H,m), 7.51(2H,d,J=8Hz), 7.53-7.63(1H,m), 8.28(2H,d,J=8Hz), 8.58(1H,d,J=5Hz)

Preparation 108

To a solution of the starting compound (50.25 g) in acetic acid (400 ml) was added 30% hydrogen bromide/acetic acid (d 1.35, 80 ml). Bromine (40.9 g) was added dropwise to the mixture for 20 minutes while the temperature of the reaction mixture was maintained between 20-25°C. After the addition was complete, the mixture was heated at 50°C for 1 hour and allowed to cool to room temperature. The mixture was diluted with diisopropyl ether (400 ml) and the product was filtered and washed with diisopropyl ether. Recrystallization from methanol (750 ml) gave the object compounhd as a white powder (68.83 g).

MASS (ESI)(m/z) : 265, 267 (free, $M+H)^+$

^{1}H-NMR (DMSO-d_6, 300MHz) δ : 5.01(2H,s), 7.94(1H,s), 8.02(2H,d,J=8Hz), 8.24(2H,d,J=8Hz), 8.41(1H,s), 9.89(1H,s)

Preparation 109

To a suspension of the starting compound (48.7 g) in N,N-dimethylformamide (500 ml) was added sodium azide (9.15 g) at 5 ℃. The mixture was stirred at the same temperature for 30 minutes, then at room temperature for 1 hour. The mixture was poured into diluted sodium hydrogencarbonate solution (1.6 L) and extracted three times with ethyl acetate. The extract was washed twice with brine and dried over magnesium sulfate. Evaporation of the solvent gave the object compound as a white solid (18.9g).

MASS (ESI)(m/z) : 228 $(M+H)^+$

^{1}H-NMR (DMSO-d_6, 300MHz) δ : 4.92(2H,s), 7.16(1H,s), 7.88(2H,d,J=8Hz), 7.92(1H,s), 8.07(2H,d,J=8Hz), 8.46(1H,s)

Preparation 110

A solution of the starting compound (18.9 g) in a mixture of 2N hydrochloric acid (90 ml) and methanol (90 ml) was hydrogenated (3 atm) over 10% palladium on carbon (1.9 g) at room temperature for 3 hours. After the catalyst was filtered off, the filtrate was concentrated to give a white powder. The white powder was collected by filtration, washed with methanol and dried *in vacuo* to give the object compound (16.0 g).

MASS (ESI)(m/z) : 202 (free, $M+H)^+$

^{1}H-NMR (DMSO-d_6, 300MHz) δ : 4.67(2H,q,J=5Hz), 7.89(1H,s), 8.08(2H,d,J=8Hz), 8.27(2H,d,J=8Hz), 8.41(1H,s), 8.52(3H,br s), 9.78(1H,s)

Preparation 111

The object compound was obtained according to a similar manner to that of Preparation 5.

oil

MASS : 450 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.42(9H,s), 3.20-3.30(1H,m), 3.31-3.42(1H,m), 4.62-4.73(1H,m), 4.70(2H,d,J=6Hz), 6.42(1H,br s), 7.15(1H,t,J=6Hz), 7.21(1H,d,J=6Hz), 7.23(1H,s), 7.33(1H,s),

7.50(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.97(1H,s), 8.00(1H,br s),
8.08(2H,d,J=8Hz), 8.57(1H,d,J=8Hz)

Preparation 112

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 445 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.38(9H,s), 3.39-3.52(2H,m), 3.49(3H,s),
5.38-5.52(1H,m), 5.49(1H,br s), 7.01(1H,s), 7.12(2H,d,J=8Hz),
7.22(2H,d,J=8Hz), 7.30(1H,s), 7.38-7.50(3H,m),
7.57(1H,t,J=8Hz), 7.90(1H,s), 8.53(1H,d,J=2Hz)

Preparation 113

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 345 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.29-3.39(1H,m), 3.40-3.50(1H,m), 3.55(3H,s),
4.58-4.65(1H,m), 7.09(1H,s), 7.15(2H,d,J=8Hz),
7.23(2H,d,J=8Hz), 7.31(1H,s), 7.41-7.48(3H,m),
7.61(1H,t,J=8Hz), 7.90(1H,s), 8.59(1H,d,J=2Hz)

Preparation 114

The object compound was obtained according to a similar manner to that of Preparation 5 except that a mixture of dichloromethane and dimethylformamide was used instead of dichloromethane.

MASS (ESI) (m/z) : 430 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.40(9H,s), 2.52(3H,s),
2.98-3.28(2H,m), 4.48-4.79(3H,m), 5.06(1H,br d,J=8Hz),
7.04(1H,br s), 7.16(2H,d,J=5Hz), 7.28(2H,d,J=8Hz)
7.85 (2H,d,J=8Hz), 8.51 (2H,d,J=5Hz)

Preparation 115

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 425 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.39 (9H,s), 2.50(3H, s), 3.21(3H, s)
3.23-3.34(2H,m), 5.01-5.15(1H,m), 5.40(1H,br d,J=8Hz)
7.00(1H,s), 7.06(2H,d,J=6Hz), 7.17(2H,d,J=8Hz)
7.28(2H,d,J=8Hz), 8.47(2H,d,J=6Hz)

Preparation 116

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 325 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 2.50(3H,s), 3.09-3.35(2H,m), 3.31(3H,s)
4.19(1H,d,J=7Hz), 7.02(1H,s), 7.06(2H,d,J=6Hz),
7.13-7.33(4H,m), 8.50(2H,d,J=6Hz)

Preparation 117

To an ice-cooled solution of the starting compound (172 mg) in acetic acid (0.8 ml)- water (0.8 ml) was added potassium permanganate (69 mg), and the mixture was stirred under ice-cooling for 30 minutes. 2-Propanol was added to the mixture and the mixture was stirred for 5 minutes. The mixture was diluted with ethyl acetate and neutralized with 1N sodium hydroxide solution. After the precipitate formed was filtered off, the filtrate was extracted three times with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. Evaporation of the solvent gave the object compound as a white powder (214 mg).

MASS (ESI) (m/z) : 457 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.39(9H,s), 3.08(3H,s),
3.22-3.38(2H,m), 3.37(3H,s), 5.09-5.25(1H,m)
6.35(1H, br d,J=8Hz), 7.03-7.22(3H, broad), 7.46(2H,d,J=8Hz),
8.00(2H,d,J=8Hz) 8.38-8.61(2H, broad)

Preparation 118

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 357 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.09(3H,s), 3.12-3.38(2H,m)
3.40(3H,s), 4.28(1H,t,J=7Hz), 7.08(2H,d,J=6Hz), 7.15(1H,s)
7.50(2H,d,J=8Hz), 7.99(2H,d,J=8Hz), 8.50(2H,d,J=6Hz)

Preparation 119

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 427 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 3.04(6H,s),
3.18-3.43(2H,m), 4.56(2H,d,J=5Hz), 4.61-4.74(1H,m),
6.36(1H,br d,J=8Hz), 6.62 (2H,d,J=8Hz),
7.11(1H,dd,J=8 and 5Hz), 7.20(1H,d,J=8Hz)
7.58(1H,t,J=8Hz), 7.80(1H,br d,J=8Hz), 7.81(2H,d,J=8Hz),
8.54(1H,d,J=5Hz)

Preparation 120

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 422 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.35(9H,s), 2.98(6H,s), 3.37(3H,s),
3.38-3.48(2H,m), 5.28-5.42(1H,m), 5.46(1H,br d,J=8Hz),
6.72(2H,d,J=8Hz), 6.89(1H,s), 7.03-7.11(2H,m),
7.13(2H,d,J=8Hz), 7.52(1H,t,J=8Hz), 8.52(1H,d,J=5Hz)

Preparation 121

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 322 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 2.98(6H,s), 3.23-3.43(2H,m),
3.44(3H,s), 4.55(1H,dd,J=8 and 5Hz), 6.74(2H,d,J=8Hz),
6.91(1H,s), 7.07-7.16(2H,m), 7.18(2H,d,J=8Hz),
7.58(1H,t,J=8Hz), 8.57(1H,d,J=5Hz)

Preparation 122

The object compound was obtained according to a similar manner to that of Preparation 91.

MASS (ESI) (m/z) : 429 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.45(9H,s), 3.18-3.42(2H,m), 4.60-4.77(1H,m), 4.72(2H,d,J=5Hz), 6.42(1H,br d,J=8Hz), 7.16(1H,dd,J=8 and 5Hz), 7.21(1H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.70(1H,t,J=8Hz), 8.04(1H,br s), 8.24(1H,dd,J=8 and 2Hz), 8.45(1H,dd,J=8 and 2Hz), 8.54(1H,d,J=5Hz), 8.76(1H,t,J=2Hz)

Preparation 123

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 424 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.38(9H,s), 3.38-3.51(2H,m), 3.50(3H,s), 5.36-5.50(1H,m), 5.52(1H,br d,J=8Hz), 7.09(1H,s), 7.10-7.19(2H,m), 7.50-7.68(3H,m), 8.11-8.23(2H,m), 8.53(1H,d,J=5Hz)

Preparation 124

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 324 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.30-3.51(2H,m), 3.58(3H,s), 4.68(1H,dd,J=8 and 5Hz), 7.04-7.21(2H,m), 7.12(1H,s), 7.52-7.72(3H,m), 8.11-8.25(2H,m), 8.57(1H,d,J=5Hz)

Preparation 125

To a solution of the starting compound (1.92 g) in carbon tetrachloride (19 ml) were added N-bromosuccinimide (3.34 g) and 2,2'-azobis(2,4-dimethyl-4-methoxyvaleronitrile) (Wako V-70, 153 mg), and the mixture was heated at 50°C for 15 minutes. After the precipitate formed was filtered off, the residue was purified by column chromatography (silica gel, hexane/ethyl acetate = 1/1) to give the object compound as a red oil (806 mg).

MASS (ESI) (m/z) : 202,204 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.89(3H,s), 4.61(2H,s),

7.28(1H,dd,J=8 and 2Hz), 7.43(1H,d,J=8Hz), 8.26(1H,d,J=2Hz)

Preparation 126

In a nitrogen atmosphere, an ice-cooled solution of diethyl acetamidomalonate (758 mg) in N,N-dimethylformamide (3.5 ml) was added potassium tert-butoxide (437 mg), and the mixture was stirred under ice-cooling for 1.5 hours. To the mixture was added the starting compound (726 mg), and the mixture was heated at 60 °C for 1 hour. A saturated sodium hydrogencarbonate solution was added to the mixture, and the mixture was extracted three times with ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate = 1/2) to give the object compound as white crystals (362 mg).

MASS (ESI) (m/z) : 339 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.28(6H,t,J=7Hz), 1.95(3H,s), 3.75(2H,s), 3.81(3H,s), 4.28(4H,q,J=7Hz), 6.78(1H,br s), 6.99(1H,d,J=8Hz), 7.08(1H,dd,J=8 and 2Hz), 8.13(1H,d,J=2Hz)

Preparation 127

A mixture of the starting compound (345 mg) and 6N hydrochloric acid (1.7 ml) was heated under reflux for 2 hours. The solvent was evaporated to give the object compound as a pale yellow powder (285 mg).

MASS (ESI) (m/z) : 197 (free, $M+H)^+$

^{1}H-NMR (D_2O,300MHz) δ 3.63(2H,d,J=7Hz), 4.01(3H,s), 4.46(1H,t,J=7Hz), 7.96(1H,d,J=8Hz), 8.15(1H,dd,J=8 and 2Hz), 8.45(1H,d,J=2Hz)

Preparation 128

To an ice-cooled solution of the starting compound (238 mg) in 1N sodium hydroxide solution (3.0 ml) - 1,4-dioxane (0.6 ml) was added di-tert-butyl dicarbonate (263 mg), and the mixture was stirred at room temperature for 12 hours. After the mixture was concentrated, citric acid monohydrate (93 mg) was slowly added to the mixture. The mixture

was extracted three times with chloroform. The organic layer was dried over magnesium sulfate. Evaporation of the solvent gave the object compound as a white powder (194 mg).

MASS (ESI) (m/z) : 297 $(M+H)^+$

^{1}H-NMR ($CHCl_3$,300MHz) δ 1.44(9H,s), 3.19-3.41(2H,m), 3.87(3H,s), 4.34-4.48(1H,m), 5.86(1H,br d, J=8Hz), 7.32(2H,s), 8.17(1H,s)

Preparation 129

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 459 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.49(9H,s), 3.12-3.37(2H,m), 3.82(3H,s), 4.56-4.69(1H,m), 4.72(2H,d,J=5Hz), 6.38(1H,br d,J=8Hz), 7.40-7.52(2H,m), 7.88(1H,br s), 8.09(2H,d,J=8Hz), 8.22(1H,d,J=2Hz), 8.31(2H,d,J=8Hz)

Preparation 130

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 454 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.38(9H,s), 3.29-3.46(2H,m), 3.53(3H,s), 3.82(3H,s), 5.31-5.45(1H,m), 5.52(1H,br d,J=8Hz), 6.98-7.12(2H,m), 7.13(1H,s), 7.47(2H,d,J=8Hz), 8.12(1H,d,J=2Hz), 8.28(2H,d,J=8Hz)

Preparation 131

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 354 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.21-3.43(2H,m), 3.62(3H,s), 3.84(3H,s), 4.53-4.63(1H,m), 7.03-7.16(2H,m), 7.18(1H,s), 7.51(2H,d,J=8Hz), 8.26(1H,d,J=2Hz), 8.28(2H,d,J=8Hz)

Preparation 132

A mixture of the starting compound (5.92 g), dichlorobis(triphenylphosphine)palladium(II) (843 mg), triethylamine (20 ml), and

methanol (20 ml) was heated at 110°C under a carbon monoxide (10 atm) atmosphere for 11 hours. After being allowed to cool to room temperature, the mixture was dissolved in chloroform and evaporated. Water was added to the residue and the mixture was extracted three times with ether. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate = 4/1) to give the object compound as a white powder (5.48 g).

MASS (ESI) (m/z) : 172 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 4.00(3H,s), 7.82(1H,dd,J=8 and 2Hz), 8.10(1H,d,J=8Hz), 8.69(1H,d,J=2Hz)

Preparation 133

In a nitrogen atmosphere, to a suspention of lithium aluminum hydride (873 mg) in tetrahydrofuran (52 ml) was added the starting compound (5.24 g) in tetrahydrofuran (26 ml) dropwise at a temperature below -30°C for 10 minutes. The mixture was stirred at -30°C for 30 minutes. After the mixture was diluted with ether (60 ml), water (0.9 ml), 15% sodium hydroxide solution (0.9 ml), and water (2.7 ml) were successively added dropwise to the mixture with vigorous stirring. After the precipitate was filtered off, the residue was purified by column chromatography (silica gel, hexane/ethyl acetate = 1/1) to give the object compound as an oil (801 mg).

MASS (ESI) (m/z) : 144 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.35(1H,br t,J=5Hz), 4.74(2H,d,J=5Hz), 7.23(1H,d,J=8Hz), 7.67(1H,dd,J=8 and 2Hz), 8.52(1H,d,J=2Hz)

Preparation 134

To an ice-cooled solution of the starting compound (742 mg) in dichloromethane (2.5 ml) was added thionyl chloride (681 mg) in dichloromethane (1 ml) dropwise for 5 minutes, and the mixture was stirred under ice-cooling for 30 minutes. After the solvent was evaporated, the residue was dissolved in 1N sodium hydroxide solution with ice-cooling, and the product was extracted three times with

chloroform. The organic layer was dried over magnesium sulfate. Evaporation of the solvent gave the object compound as an oil (927 mg).

MASS (ESI) (m/z) : 162 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 4.76(2H,s), 7.58(1H,d,J=8Hz), 7.85(1H,dd,J=8 and 2Hz), 8.57(1H,d,J=2Hz)

Preparation 135

The object compound was obtained according to a similar manner to that of Preparation 126.

MASS (ESI) (m/z) : 343 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.28(6H,t,J=7Hz), 1.94(3H,s), 3.83(2H,s), 4.28(4H,q,J=7Hz), 6.71(1H,br s), 7.03(1H,d,J=8Hz), 7.54(1H,dd,J=8 and 2Hz), 8.39(1H,d,J=2Hz)

Preparation 136

The object compound was obtained according to a similar manner to that of Preparation 127.

MASS (ESI) (m/z) : 201 (free, $M+H)^+$

^{1}H-NMR (D_2O,300MHz) δ 3.59(2H,d,J=7Hz), 4.50(1H,t,J=7Hz), 7.75(1H,d,J=8Hz), 8.28(1H,dd,J=8 and 2Hz), 8.72(1H,d,J=2Hz)

Preparation 137

The object compound was obtained according to a similar manner to that of Preparation 128

MASS (ESI) (m/z) : 301 $(M+H)^+$

^{1}H-NMR ($CHCl_3$,300MHz) δ 1.42(9H,s), 3.35(2H,br s), 4.50(1H,br s), 5.74(1H,br s), 7.27(1H,br s), 7.69(1H,br s), 8.48(1H,br s)

Preparation 138

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 463 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.48(9H,s), 3.16-3.43(2H,m), 4.61-4.82(3H,m), 6.26(1H,br d,J=8Hz), 7.19(1H,d,J=8Hz),

7.59(1H,dd,J=8 and 2 Hz), 7.74(1H,br s), 8.10(2H,d,J=8Hz)
8.33(2H,d,J=8Hz), 8.50(1H,d,J=2Hz)

Preparation 139

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 458 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.39(9H,s), 3.33-3.57(2H,m), 3.61(3H,s),
5.33-5.52(2H,m), 7.11(1H,d,J=8Hz), 7.12(1H,s),
7.49(2H,d,J=8Hz), 7.53(1H,dd,J=8 and 2Hz), 8.29(2H,d,J=8Hz),
8.48(1H,d,J=2Hz)

Preparation 140

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 358 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.23-3.52(2H,m), 3.67(3H,s),
4.59(1H,t,J=7Hz), 7.13(1H,d,J=8Hz), 7.15(1H,s),
7.51(2H,d,J=8Hz), 7.58(1H,dd,J=8 and 2Hz), 8.29(2H,d,J=8Hz),
8.51(1H,d,J=2Hz)

Preparation 141

The object compound was obtained according to a similar manner to that of Preparation 126.

MASS (ESI) (m/z) : 310 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.28(6H,t,J=7Hz), 1.95(3H,s), 3.90(2H,s),
4.29(4H,q,J=7Hz), 6.65(1H,br s), 8.36(1H,s), 8.41(2H,s)

Preparation 142

The object compound was obtained according to a similar manner to that of Preparation 127.

MASS (ESI) (m/z) : 168 (free, $M+H)^+$

^{1}H-NMR (D_2O,300MHz) δ 3.49-3.69(2H,m), 4.59(1H,t,J=7Hz),
8.57(1H,d,J=2Hz), 8.62(1H,s), 8.67(1H,d,J=2Hz)

Preparation 143

The object compound was obtained according to a similar manner to

that of Preparation 128.

MASS (ESI) (m/z) : 266 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 3.32-3.51(2H,m), 4.56-4.70(1H,m), 5.73(1H,br d, J=8Hz), 8.50(1H,s), 8.58(1H,s), 8.62(1H,s)

Preparation 144

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 428 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.45(9H,s), 3.21-3.48(2H,m), 4.62-4.83(3H,m), 6.10(1H,br d,J=8Hz), 7.59(1H,br s), 8.10(2H,d,J=8Hz), 8.32(2H,d,J=8Hz), 8.42-8.55(3H,m)

Preparation 145

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 425 $(M+H)^+$

^{1}H-NMR($CDCl_3$,300MHz) δ 1.38(9H,s), 3.38-3.62(2H,m), 3.63(3H,s), 5.41-5.60(2H,m) 7.12(1H,s), 7.50(2H,d,J=8Hz), 8.28(2H,d,J=8Hz), 8.38-8.53(3H,m)

Preparation 146

The object compound was obtained according to a similar manner tothat of Preparation 4.

MASS (ESI) (m/z) : 325 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.29-3.60(2H,m), 3.66(3H,s), 4.61(1H,t,J=7Hz), 7.16(1H,s), 7.51(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.39-8.55(3H,m)

Preparation 147

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 500 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.44(9H,s), 1.91-2.31(2H,m), 2.42-2.68(2H,m), 4.22-4.40(1H,m), 4.68-4.86(2H,m),

5.13(2H,s), 5.30(1H,br d,J=8Hz), 7.14(1H,br s)
7.27-7.41(5H,m), 8.12(2H,d,J=8Hz), 8.34(2H,d,J=8Hz)

Preparation 148

The object compound was obtained according to a similar manner tothat of Preparation 2.

MASS (ESI) (m/z) : 495 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 2.08-2.39(2H,m),
2.40-2.65(2H,m), 3.16(3H,s), 4.98-5.11(1H,m),
5.11(2H,s), 5.39(1H,br d,J=8Hz), 7.12(1H,s),
7.28-7.41(5H,m), 7.52(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 149

The object compound was obtained according to a similar manner tothat of Preparation 3.

MASS (ESI) (m/z) : 395 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 2.38-2.82(4H,m), 3.71(3H,s),
5.07(2H,ABq,Δ=0.08, J=13Hz), 5.17(1H,t,J=7Hz),
7.23-7.38(6H,m), 7.55(2H,d,J=8Hz), 8.39(2H,d,J=8Hz)

Preparation 150

To an ice-cooled solution of the starting compound (1.17 g) in 1N soduim hydroxide solution (17.5 ml) - 1,4-dioxane (3.5 ml) was added acetic anhydride (0.75 ml). The mixture was stirred under ice-cooling for 1 hour, then at room temperature for 3 hours. The mixture was concentrated, made acidic (pH=3) with 6N hydrochloric acid, extracted three times with chloroform, and dried over magnesium sulfate. Evaporation of the solvent gave the object compound as a colorless oil (1.03 g).

MASS (ESI) (m/z) : 273 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 1.51-1.97(4H,m),
2.00(3H,s), 3.17-3.42(2H,m), 4.25-4.42(1H,m),
5.29(1H,br d,J=8Hz), 6.19(1H,br t,J=8Hz)

Preparation 151

The object compound was obtained according to a similar manner to

that of Preparation 5.

MASS (ESI) (m/z) : 437 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 1.52-2.00(4H,m), 2.00(3H,s), 3.11-3.28(1H,m), 3.42-3.60(1H,m), 4.31-4.49(1H,m), 4.60-4.97(2H,m), 5.35(1H,br d,J=8Hz), 5.99(1H,br t,J=8Hz), 7.46(1H,br t,J=8Hz), 8.12(2H,d,J=8Hz), 8.33(2H,d,J=8Hz)

Preparation 152

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 432 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 1.48-2.16(4H,m), 1.98(3H,s), 3.18-3.40(2H,m), 3.68(3H,s), 4.88-5.02(1H,m), 5.19(1H,br d,J=9Hz), 6.05(1H,br t,J=8Hz), 7.12(1H,s), 7.54(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 153

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 332 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.49-2.15(4H,m), 1.98(3H,s), 3.28(2H,q,J=7Hz), 3.72(3H,s), 4.04(1H,t,J=7Hz), 6.20(1H,br s), 7.15(1H,s), 7.56(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 154

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 399 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 2.85-3.15(2H,m), 4.55-4.68(1H,m), 5.19(2H,ABq, Δ=0.05,J=13Hz), 5.79(1H,br d,J=8Hz), 7.04-7.53(11H,m)

Preparation 155

To a solution of the starting compound (1.04 g) in a mixture of methanol (21 ml) and 1,4-dioxane (21 ml) was added palladium-carbon

(10%, 104 mg). The resultig mixture was stirred under hydrogen at 25°C for 8 hours. The catalyst was filtered off and the filtrate was concentrated to give an oil. The oil was purified by column chromatography (silica gel, chloroform/methanol=10/1) to give the object compound as an amorphous solid (915 mg).

MASS (ESI) (m/z) : 307 $(M-H)^-$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.45(9H,s), 2.84-3.20(2H,m), 4.45-4.59(1H,m), 5.95(1H,br d.J=8Hz), 7.10-7.53(5H,m), 8.05(1H,br s)

Preparation 156

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 470 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(3H,t,J=7Hz), 1.48(9H,s), 2.72-3.22(2H,m), 4.09(2H,q,J=7Hz), 4.54-4.74(3H,m), 6.22(1H,br d,J=8Hz), 6.89(2H,d,J=8Hz), 6.98-7.52(5H,m), 7.72(1H,br s), 7.88(2H,d,J=8Hz), 8.27(1H,br s)

Preparation 157

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 465 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 1.47(3H,t,J=7Hz), 3.05-3.26(2H,m), 3.59(3H,s), 4.07(2H,q,J=7Hz), 5.32-5.49(1H,m), 5.53(1H,br d,J=8Hz), 6.91(1H,s), 6.94(2H,d,J=8Hz), 6.98-7.55(7H,m), 9.62(1H,br s)

Preparation 158

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 365 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(3H,t,J=7Hz), 3.68-4.22(2H,m), 3.88(3H,s), 3.99(2H,q,J=7Hz), 5.33-5.53(1H,m), 6.67-7.58(11H,m)

Preparation 159

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 418 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.45(9H,s), 3.06-3.27(2H,m), 4.43-4.62(1H,m), 4.65-4.87(2H,m), 5.18(1H,br d,J=8Hz), 6.13(1H,t,J=2Hz), 6.29(1H,d,J=2Hz), 7.05(1H,br s), 7.34(1H,d,J=2Hz), 8.12(2H,d,J=8Hz), 8.35(2H,d,J=8Hz)

Preparation 160

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 413 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 3.16-3.41(2H,m), 3.43(3H,s), 5.13-5.28(1H,m), 5.47(1H,br d,J=8Hz), 6.01(1H,d,J=2Hz), 6.27(1H,t,J=2Hz), 7.17(1H,s), 7.32(1H,d,J=2Hz), 7.49(2H,d,J=8Hz), 8.29(2H,d,J=8Hz)

Preparation 161

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 313 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.13-3.33(2H,m), 3.56(3H,s), 4.32(1H,t,J=7Hz), 6.07(1H,d,J=2Hz), 6.31(1H,t,J=2Hz), 7.18(1H,s), 7.35(1H,d,J=2Hz), 7.51(2H,d,J=8Hz), 8.29(2H,d,J=8Hz)

Preparation 162

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 500 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 3.29-3.56(2H,m), 4.20(2H,s), 4.97-5.11(1H,m), 6.16(1H,br d,J=8Hz), 7.00-7.91(11H,J=4Hz), 8.22(2H,d,J=8Hz), 8.28(1H,d,J=2Hz)

Preparation 163

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 400 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.16-3.48(2H,m), 4.21(2H,s), 4.52(1H,J=7Hz), 7.10-7.68(9H,m), 7.79(2H,d,J=8Hz), 8.22(2H,d,J=8Hz), 8.29(1H,d,J=2Hz)

Preparation 164

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (ESI) (m/z) : 472 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 2.91-3.10(2H,m), 4.32-4.51(1H,m), 4.67-4.80(2H,m), 5.05(1H,br d,J=8Hz), 5.90(2H,d,J=1Hz), 6.59-6.76(3H,m), 6.95(1H,br s), 8.11(2H,d,J=8Hz), 8.33(2H,d,J=8Hz)

Preparation 165

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 467 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.41(9H,s), 3.01-3.29(2H,m), 3.20(3H,s), 4.89-5.06(1H,m), 5.49(1H,br d,J=8Hz), 5.90(2H,s), 6.46-6.73(3H,m), 7.18(1H,s), 7.43(2H,d,J=8Hz), 8.27(1H,d,J=8Hz)

Preparation 166

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 367 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 2.98-3.22(2H,m), 3.39(3H,s), 4.13(1H,t,J=7Hz), 5.92(2H,s), 6.51-6.78(3H,m), 7.19(1H,s), 7.48(2H,d,J=8Hz), 8.28(2H,d,J=8Hz)

Preparation 167

The object compound was obtained according to a similar manner to that of Preparation 91.

MASS (ESI) (m/z) : 462, 464 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.44(9H,s), 3.18-3.43(2H,m), 4.58-4.75(1H,m), 4.64(2H,d,J=5Hz), 6.42(1H,br d,J=8Hz), 7.10-7.23(2H,m), 7.53-7.65(1H,m), 7.61(2H,d,J=8Hz), 7.79(2H,d,J=8Hz), 7.92(1H,br s), 8.53(1H,d,J=5Hz)

Preparation 168

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 457, 459 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.37(9H,s), 3.33-3.52(2H,m), 3.42(3H,s), 5.31-5.52(2H,m), 6.99(1H,s), 7.05-7.15(2H,m), 7.18(2H,d,J=8Hz), 7.48-7.61(1H,m), 7.53(2H,d,J=8Hz), 8.53(1H,d,J=5Hz)

Preparation 169

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 357, 359 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 3.23-3.47(2H,m), 3.49(3H,s), 4.59(1H,t,J=7Hz), 7.01(1H,s), 7.05-7.22(4H,m), 7.54(2H,d,J=8Hz), 7.55-7.64(1H,m), 8.57(1H,d,J=5Hz)

Preparation 170

A mixture of acetic anhydride (3.7 ml) and formic acid (1.8 ml) was heated at 50°C for 1.5 hours. After the mixture was allowed to cool to room temperature, sodium formate (896 mg) was suspended in the mixture and stirred for 10 minutes. The starting compound (2.15 g) was added and stirring at room temperature was continued for 3 hours. The reaction mixture was poured into water (30 ml) and the product was extracted three times with chloroform. The organic layer was dried over potassium carbonate. Evaporation of the solvent gave the object compound as a white powder (1.59 g).

MASS (ESI) (m/z) : 208 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.45(3H,t,J=7Hz), 4.12(2H,q,J=7Hz),

4.74(2H,d,J=2Hz), 6.78(1H,br s), 6.96(2H,d,J=8Hz)
7.96(2H,d,J=8Hz), 8.34(1H,s)

Preparation 171

In a nitrogen atmosphere, the starting compound (1.56 g) in N,N-dimethylformamide (12.5 ml) was added to a stirred and ice-cooled suspension of sodium hydride (70%, 285 mg) in N,N-dimethylformamide (25 ml). After 30 minutes, benzyl bromide (1.65 g) was added dropwise at 0°C and the mixture was stirred at the same temperature for 2 hours. The reaction mixture was poured into water and the product was extracted three times with ethyl acetate. The organic layer was washed three times with water, once with brine, and dried over magnesium sulfate. Evaporation of the solvent gave the object compound as an oil (2.53 g).

MASS (ESI) (m/z) : 298 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.44(3H,t,J=7Hz), 3.01-3.38(2H,m),
4.11(2H,q,J=7Hz), 5.81-5.92(1H,m), 6.51(1H,br d,J=8Hz)
6.93(2H,d,J=8Hz), 6.95-7.25(5H,m), 7.92(2H,d,J=8Hz),
8.22(1H,s)

Preparation 172

A solution of the starting compound (2.15 g) in concentrated hydrochloric acid (2 ml)-ethanol (10 ml) was heated at 50°C for 1.5 hours. The object compound began to precipitate. After cooling, the mixture was diluted with diisopropyl ether (3 ml) and filtration gave the object compound as a white powder (1.20 g).

MASS (ESI) (m/z) : 270 (free, $M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ 1.35(3H,t,J=7Hz), 3.03-3.23(2H,m),
4.13(2H,q,J=7Hz), 5.33(1H,t,J=6Hz), 7.02(2H,d,J=8Hz)
7.08-7.31(5H,m), 7.95(2H,d,J=8Hz), 8.41(3H,br s)

Preparation 173

The object compound was obtained according to a similar manner to that of Preparation 91.

MASS (ESI) (m/z) : 518 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(9H,s), 1.44(3H,t,J=7Hz),
2.85-3.40(4H,m), 4.01-4.18(2H,m), 4.49-4.72(1H,m),
4.61-4.75(1H,m), 6.29(1H,br s), 6.98-7.23(9H,m),
7.42-7.62(1H,m), 7.71-7.93(3H,m), 8.39-8.51(1H,m)

Preparation 174

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 513 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.37(9H,s), 1.42(3H,t,J=7Hz),
3.24(3H,s), 3.32-3.48(2H,m), 3.81(2H,s), 4.04(2H,q,J=7Hz),
5.25-5.42(1H,m), 5.50(1H,br d,J=8Hz), 6.82-7.55(12H,m),
8.52(1H,d,J=5Hz)

Preparation 175

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 413 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.42(3H,t,J=7Hz), 3.33(3H,s),
3.35-3.50(2H,m), 3.84(2H,s), 4.05(2H,q,J=7Hz),
4.68(1H,t,J=7Hz), 6.81-7.25(11H,m), 7.46-7.59(1H,m),
8.51(1H,d,J=5Hz)

Preparation 176

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 452 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 0.93(3H,t,J=7Hz), 1.36(9H,s),
1.43-1.61(2H,m), 3.35-3.58(2H,m), 3.82-4.06(2H,m),
5.34(1H,br d,J=8Hz), 5.36-5.53(1H,m), 7.06-7.18(3H,m),
7.48(2H,d,J=8Hz), 7.50-7.63(1H,m), 8.28(2H,d,J=8Hz),
8.54(1H,d,J=5Hz)

Preparation 177

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 352 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 0.92(3H,t,J=7Hz), 1.41-1.60(2H,m), 3.28-3.52(2H,m), 3.82-4.08(2H,m), 4.60(1H,t,J=7Hz), 7.07-7.20(3H,m), 7.48(2H,d,J=8Hz), 7.51-7.65(1H,m), 8.28(2H,d,J=8Hz), 8.58(1H,d,J=5Hz)

Preparation 178

A mixture of the starting compound (6.88 g), pyrazole (10.20 g), and powdered potassium carbonate (6.91 g) in N,N-dimethylformamide (35 ml) was heated at 140°C for 8 hours. After cooling, the mixture was poured into water and the product was extracted three times with ethyl acetate. The organic layer was washed three times with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate=2/1) to give the object compound as a pale yellow powder (4.71 g).

MASS (ESI) (m/z) : 187 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 2.61(3H,s), 6.51(1H,d,J=2Hz), 7.78(1H,d,J=2Hz), 7.82(2H,d,J=8Hz), 8.01(1H,t,J=2Hz), 8.06(2H,d,J=8Hz)

Preparation 179

To a solution of the starting compound (4.66 g) in 5% hydrogen bromide/acetic acid (54 ml) was added bromine (4.34 g) dropwise at room temperature for 10 minutes. A white precipitate was formed. The mixture was heated at 50°C for 20 minutes. After cooling, the precipitate was collected by filtration and purified by recrystallization from methanol-diisopropyl ether to give the object compound (2.61 g).

^{1}H-NMR (DMSO-d_6,300MHz) δ 4.95(2H,s), 6.62(1H,t,J=2Hz), 7.83(1H,d,J=2Hz), 8.03(2H,d,J=8Hz), 8.13(2H,d,J=8Hz), 8.68(1H,d,J=2Hz)

Preparation 180

2-Bromo-4'-(pyrazol-1-yl)acetophenone hydrobromide (3.04 g) was

dissolved in 1N sodium hydroxide solution. The free acetophenone compound was extracted three times with chloroform, dried over magnesium sulfate. After the solvent was evaporated, the residue was redissolved in chloroform (20 ml) and added all at once to a suspension of hexamethylenetetramine (1.35 g) in chloroform (4.4 ml) at room temperature. The mixture was heated at 50°C for 2 hours. After cooling, the mixture was diluted with chloroform (20 ml) and the white precipitate was collected by filtration. The precipitate was washed twice with ethanol and dried *in vacuo* to give the object compound (3.75 g).

Preparation 181

To a suspension of the starting compound (3.50 g) in ethanol (17.6 ml) was added concentrated hydrochloric acid (4.4 ml) at room temperature and the mixture was stirred at room temperature for 4 hours. The mixture was cooled with ice, and the precipitate was collected by filtration and washed with cold ethanol. The crude product was suspended in water (4.4 ml) and stirred at room temperature for 10 minutes. The suspension was cooled in an ice bath and ethanol (2.2 ml) was added thereto. The precipitate was collected by filtration, washed with cold ethanol, and dried *in vacuo* to give the object compound (2.00 g).

MASS (ESI) (m/z) : 202 (free, $M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ 4.62(2H,q,J=2Hz),
6.64(1H,t,J=2Hz), 7.87(1H,d,J=2Hz), 8.09(2H,d,J=8Hz),
8.17(2H,d,J=8Hz), 8.44(3H,br s), 8.73(1H,d,J=2Hz)

Preparation 182

The object compound was obtained according to a similar manner to that of Preparation 91.

MASS (ESI) (m/z) : 450 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.43(9H,s), 3.27-3.49(2H,m),
4.60-4.81(3H,m), 6.37(1H,br d,J=8Hz), 6.52(1H,t,J=2Hz),
7.18-7.33(2H,m), 7.62-7.73(1H,m), 7.78(1H,d,J=2Hz),

7.83(2H,d,J=8Hz), 8.01(1H,d,J=2Hz), 8.05(2H,d,J=8Hz),
8.05(1H,br d,J=8Hz), 8.58(1H,d,J=5Hz)

Preparation 183

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 445 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.37(9H,s), 3.36-3.60(2H,m),
3.48(3H,s), 5.35-5.51(1H,m), 5.58(1H,br d,J=8Hz),
6.49(1H,t,J=2Hz), 7.03(1H,s), 7.06-7.18(2H,m),
7.38(2H,d,J=8Hz), 7.48-7.62(1H,m), 7.74(1H,d,J=2Hz),
7.76(2H,d,J=8Hz), 7.95(1H,d,J=2Hz), 8.53(1H,d,J=5Hz)

Preparation 184

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 345 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 2.25(2H,br s), 3.28-3.51(2H,m),
3.55(3H,s), 4.64(1H,t,J=7Hz), 6.49(1H,t,J=2Hz),
7.06(1H,s), 7.10-7.21(2H,m), 7.41(2H,d,J=8Hz),
7.52-7.67(1H,m), 7.73(1H,d,J=2Hz), 7.75(2H,d,J=8Hz),
7.95(1H,d,J=2Hz), 8.58(1H,d,J=5Hz)

Preparation 185

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 459 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.10(3H,t,J=7Hz), 1.36(9H,s),
3.37-3.62(2H,m), 3.85-4.10(2H,m), 5.29-5.60(2H,m),
6.49(1H,t,J=2Hz), 7.01(1H,s), 7.05-7.21(2H,m),
7.39(2H,d,J=8Hz), 7.48-7.61(1H,m), 7.73(1H,d,J=2Hz),
7.76(2H,d,J=8Hz), 7.96(1H,d,J=2Hz), 8.53(1H,d,J=5Hz)

Preparation 186

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 359 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ 1.14(3H,t,J=7Hz), 2.26(2H,br s,NH_2),
3.31-3.52(2H,m), 3.87-4.13(2H,m), 4.62(1H,t,J=7Hz),
6.49(1H,t,J=2Hz), 7.03(1H,s), 7.07-7.21(2H,m),
7.40(2H,d,J=8Hz), 7.52-7.65(1H,m), 7.73(1H,d,J=2Hz),
7.75(2H,d,J=8Hz), 7.95(1H,d,J=2Hz), 8.57(1H,d,J=5Hz)

Preparation 187

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (m/z) : 430 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.46(9H,s), 2.52(3H,s),
3.25(1H,d,J=4,15Hz), 3.37(1H,m), 4.63(2H,d,J=4Hz),
4.68(1H,m), 6.40(1H,m), 7.13-7.27(4H,m), 7.59(1H,m),
7.83(2H,d,J=8Hz), 7.87(1H,m), 8.54(1H,d,J=5Hz)

Preparation 188

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (m/z) : 425 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.36(9H,s), 2.51(3H,s), 3.42(3H,s),
3.43(2H,d,J=7Hz), 5.42(1H,m), 6.96(1H,s), 7.07-7.30(6H,m),
7.53(1H,m), 8.53(1H,d,J=5Hz)

Preparation 189

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 325 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.51(3H,s), 3.32(1H,dd,J=7 and 14Hz),
3.43(1H,dd,J=5 and 14Hz), 3.50(3H,s), 4.59(1H,dd,J=5 and 7Hz),
6.96(1H,s), 7.02(1H,s), 7.13-7.32(6H,m), 7.59(1H,m),
8.56(1H,d,J=5Hz)

Preparation 190

The object compound was obtained according to a similar manner to that of Example 146 from the starting compound and 2-bromoethyl methyl

ether.

MASS (m/z) : 195 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.55(3H,s), 3.46(3H,s), 3.76(2H,m), 4.19(2H,m), 6.96(2H,d,J=8Hz), 7.92(2H,d,J=8Hz)

Preparation 191

The object compound was obtained according to a similar manner to that of Preparation 179.

^{1}H-NMR ($CDCl_3$) δ : 3.47(3H,s), 3.78(2H,m), 4.20(2H,m), 4.40(2H,s), 6.99(2H,d,J=8Hz), 7.97(2H,d,J=8Hz)

Preparation 192

The object compound was obtained according to a similar manner to that of Preparation 180.

Preparation 193

The object compound was obtained according to a similar manner to that of Preparation 181.

MASS (m/z) : 210 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.37(3H,s), 3.68(2H,t,J=5Hz), 4.23(2H,t,J=5Hz), 4.51(2H,s), 7.12(2H,d,J=8Hz), 7.99(2H,d,J=8Hz), 8.40(2H,s)

Preparation 194

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (m/z) : 458 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.44(9H,s), 3.24(1H,dd,J=7 and 15Hz), 3.37(1H,m), 3.45(3H,s), 3.76(2H,t,J=5Hz), 4.18(2H,t,J=5Hz), 4.62(2H,d,J=4Hz), 4.68(1H,m), 6.41(1H,m), 6.96(2H,d,J=8Hz), 7.13(1H,m), 7.20(1H,d,J=8Hz), 7.58(1H,m), 7.86(1H,m) 7.90(2H,d,J=8Hz), 8.54(1H,d,J=5Hz)

Preparation 195

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (m/z) : 453 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.35(9H,s), 3.39(3H,s), 3.43(2H,m), 3.46(3H,s), 3.78(2H,t,J=5Hz), 4.15(2H,m), 6.93(1H,s), 6.97(2H,d,J=8Hz), 7.12(2H,m), 7.21(2H,d,J=8Hz), 7.54(1H,m), 8.53(1H,d,J=5Hz)

Preparation 196

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 353 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.32(1H,dd,J=7 and 15Hz), 3.42(1H,dd,J=5 and 15Hz), 3.46(6H,s), 3.77(2H,t,J=5Hz), 4.15(2H,t,J=5Hz), 4.57(1H,dd,J=5 and 7Hz), 6.95(1H,s), 6.98(2H,d,J=8Hz), 7.12-7.17(2H,m), 7.22(2H,d,J=8Hz), 7.58(1H,m), 8.57(1H,d,J=5Hz)

Preparation 197

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (m/z) : 486 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.48(9H,s), 2.78(1H,dd,J=7 and 15Hz), 3.14(1H,dd,J=5 and 15Hz), 4.65(1H,m), 4.75(2H,t,J=4Hz), 5.13(1H,d,J=13Hz), 5.19(1H,d,J=13Hz), 5.71(1H,m), 7.28-7.40(5H,m), 8.13(2H,d,J=8Hz), 8.35(2H,d,J=8Hz)

Preparation 198

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (m/z) : 481 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.43(9H,s), 3.07(1H,dd,J=5 and 15Hz), 3.23(1H,dd,J=7 and 15Hz), 3.67(3H,s), 5.05(1H,d,J=13Hz), 5.15(1H,d,J=13Hz), 5.33(2H,m), 7.11(1H,s), 7.29-7.37(5H,m), 7.52(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 199

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 381 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.02(1H,dd,J=7 and 15Hz),
3.20(1H,dd,J=5 and 15Hz), 3.73(3H,s), 4.50(1H,dd,J=5 and 7Hz),
5.15(1H,d,J=13Hz), 5.20(1H,d,J=13Hz), 7.15(1H,s),
7.32-7.38(5H,m), 7.53(2H,d,J=8Hz), 8.31(2H,d,J=8Hz)

Preparation 200

A mixture of the starting compound (4.6 g) and 40% methylamine solution (5 ml) in acetic acid (4.6 ml) and xylene (46 ml) was refluxed in a flask equipped with a Dean-Stark trap for 2 hours. The mixture was concentrated, neutralized with 1N sodium hydroxide solution, and extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol) to give the object compound (1.55 g).

MASS (m/z) : 404 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.44(9H,s), 2.75(3H,d,J=6Hz),
2.93(1H,dd,J=5 and 15Hz), 3.02(1H,dd,J=7 and 15Hz),
3.75(3H,s), 5.39(1H,m), 5.76(1H,m), 6.43(1H,m),
7.12(1H,s), 7.53(2H,d,J=8Hz), 8.29(2H,d,J=8Hz)

Preparation 201

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 304 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.77(1H,dd,J=5 and 15Hz), 2.81(3H,d,J=6Hz),
2.90(1H,dd,J=7 and 15Hz), 3.73(3H,s), 4.48(1H,dd,J=5 and 7Hz),
7.13(1H,s), 7.54(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 202

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (m/z) : 591 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.34(9H,s), 3.12(3H,s), 3.55-3.64(2H,m),

3.61(3H,s), 5.93(1H,m), 7.11-7.17(4H,m),
7.40(1H,dd,J=2 and 8Hz), 7.47-7.52(3H,m), 7.59(1H,t,J=8Hz),
8.30(2H,d,J=8Hz), 8.56(1H,d,J=4Hz)

Preparation 203

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (m/z) : 587 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.37(9H,s), 3.09(3H,s), 3.57(2H,m),
3.62(3H,s), 5.97(1H,m), 6.95-7.17(5H,m), 7.47(2H,d,J=8Hz),
7.57(2H,t,J=8Hz), 8.27(2H,d,J=8Hz), 8.53(1H,d,J=5Hz)

Preparation 204

The object compound was obtained according to a similar manner to that of Preparation 5.

MASS (m/z) : 557 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.34(9H,s), 3.13(3H,s), 3.57(2H,d,J=7Hz),
3.61(3H,s), 5.96(1H,d,J=7Hz), 7.13-7.17(4H,m),
7.31(1H,d,J=8Hz), 7.40-7.59(5H,m), 8.27(2H,d,J=8Hz),
8.53(1H,d,J=5Hz)

Preparation 205

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 90-94°C

MASS (m/z) : 429 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.42(9H,s), 3.00-3.12(1H,m),
3.17-3.25(1H,m), 4.51(1H,q,J=8Hz), 4.66-4.89(2H,m),
5.09(1H,d,J=8Hz), 7.01(1H,br s), 7.20-7.29(1H,m),
7.60(1H,d,J=8Hz), 8.12(2H,d,J=8Hz), 8.35(2H,d,J=8Hz),
8.48(1H,s), 8.49-8.58(1H,m)

Preparation 206

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 424 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 3.25-3.35(2H,m), 3.30(3H,s)
5.09(1H,q,J=8Hz), 5.41(1H,d,J=8Hz), 7.19(1H,s),
7.20(1H,t,J=8Hz), 7.45(2H,d,J=8Hz), 7.46(1H,d,J=8Hz),
8.29(2H,d,J=8Hz), 8.32(1H,s), 8.49(1H,d,J=2Hz)

Preparation 207

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 324 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.11-3.21(1H,m), 3.22-3.33(1H,m),
3.39(3H,s), 4.20(1H,t,J=8Hz), 7.16-7.23(1H,m),
7.20(1H,s), 7.43(1H,t,J=8Hz), 7.48(2H,d,J=8Hz),
8.29(2H,d,J=8Hz), 8.42(1H,s), 8.50(1H,d,J=6Hz)

Preparation 208

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 138-141℃

MASS (m/z) : 455 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 1.41(3H,t,J=8Hz),
2.98-3.10(1H,m), 3.18-3.28(1H,m), 4.41(2H,q,J=8Hz),
4.59(1H,br s), 4.63-4.83(2H,m), 5.22(1H,d,J=8Hz),
7.09(1H,br s), 7.19(2H,d,J=7Hz), 8.00(2H,d,J=8Hz),
8.17(2H,d,J=8Hz), 8.52(2H,d,J=7Hz)

Preparation 209

The object compound was obtained according to a similar manner to that of Preparation 2.

mp : 165-167℃

MASS (m/z) : 451 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.39(3H,t,J=8Hz), 1.40(9H,s)
3.30(3H,s), 3.31(2H,d,J=8Hz), 4.40(2H,q,J=8Hz),
5.11(1H,q,J=8Hz), 5.41(1H,d,J=8Hz), 7.09(2H,d,6Hz),

7.10(1H,s), 7.34(2H,d,J=8Hz), 8.09(2H,d,J=8Hz),
8.49(2H,d,J=6Hz)

Preparation 210

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 351 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.42(3H,t,J=8Hz), 3.11-3.22(1H,m),
3.23-3.38(1H,m), 3.40(3H,s), 4.22(1H,t,J=8Hz),
4.40(2H,q,J=8Hz), 7.09(2H,d,J=6Hz), 7.11(1H,s),
7.39(2H,d,J=8Hz), 8.10(2H,d,J=8Hz), 8.51(2H,d,J=6Hz)

Preparation 211

The object compound was obtained according to a similar manner to that of Preparation 91.

oil

MASS (m/z) : 456 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(3H,t,J=8Hz), 1.42(9H,s),
3.20-3.30(1H,m), 3.30-3.40(1H,m), 4.40(2H,q,J=8Hz),
4.68(1H,br s), 4.70(2H,d,J=4Hz), 6.41(1H,d,J=6Hz),
7.12-7.22(2H,m), 7.60(1H,t,J=8Hz), 7.95(1H,br s)
7.99(2H,d,J=8Hz), 8.12(2H,d,J=8Hz), 8.55(1H,d,J=4Hz)

Preparation 212

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 451 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.38(9H,s), 1.40(3H,t,J=8Hz),
3.43(2H,t,J=7Hz), 3.49(3H,s), 4.40(2H,q,J=8Hz),
5.33-5.50(2H,m), 7.08(1H,s), 7.09-7.20(2H,m),
7.38(2H,d,J=8Hz), 7.57(1H,t,J=8Hz), 8.09(2H,d,J=8Hz),
8.52(1H,d,J=6Hz)

Preparation 213

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 351 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(3H,t,J=8Hz), 3.27-3.39(1H,m), 3.39-3.49(1H,m), 3.51(3H,s), 4.40(2H,q,J=8Hz), 4.57-4.67(1H,m), 7.10(1H,s), 7.10-7.20(2H,m), 7.40(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 8.09(2H,d,J=8Hz), 8.59(1H,d,J=4Hz)

Preparation 214

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 157-160°C

MASS (m/z) : 443 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.43(9H,s), 2.62(3H,s), 3.10-3.21(1H,m), 3.25-3.35(1H,m), 4.56(1H,br s), 4.61-4.80(2H,m), 5.07(1H,br s), 6.93(1H,t,J=8Hz), 7.30(1H,d,J=8Hz), 7.40(2H,d,J=8Hz), 8.11(1H,dd,J=8 and 2Hz), 8.18(2H,d,J=8Hz), 9.03(1H,d,J=2Hz)

Preparation 215

The object compound was obtained according to a similar manner to that of Preparation 2.

mp : 194-196°C

MASS (m/z) : 438 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 2.59(3H,s), 3.29(3H,s), 3.32-3.52(2H,m), 5.11(1H,q,J=8Hz), 5.38(1H,d,J=8Hz), 7.06(1H,s), 7.21(1H,d,J=8Hz), 7.31(2H,d,J=8Hz), 7.49(1H,dd,J=8 and 2Hz), 8.11(2H,d,J=8Hz), 8.42(1H,d,J=2Hz)

Preparation 216

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 338 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.61(3H,s), 3.20-3.31(1H,m), 3.40(3H,s), 3.41-3.50(1H,m), 4.21(1H,t,J=8Hz), 7.09(1H,s) 7.23(1H,d,J=8Hz), 7.34(2H,d,J=8Hz), 7.51(1H,d,J=8Hz), 8.18(2H,d,J=8Hz), 8.49(1H,d,J=2Hz)

Preparation 217

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 409 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(9H,s), 3.20-3.42(2H,m), 4.60-4.72(1H,m), 4.70(2H,d,J=4Hz), 6.41(1H,br s), 7.11-7.26(2H,m), 7.60(1H,t,J=8Hz), 7.78(2H,d,J=8Hz), 8.00(1H,s), 8.01(2H,d,J=8Hz), 8.53(1H,d,J=2Hz)

Preparation 218

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 404 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 3.43(2H,d,J=2Hz), 3.50(3H,s), 5.46(2H,br s), 7.10(1H,s), 7.12(2H,d,J=8Hz), 7.41(2H,d,J=8Hz), 7.57(1H,t,J=8Hz), 7.70(2H,d,J=8Hz), 8.53(1H,d,J=2Hz)

Preparation 219

The object compound was obtained according to a similar manner to that of Preparation 8.

amorphous solid

MASS (m/z) : 304 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.46(2H,d,J=8Hz), 3.60(3H,s), 4.80(1H,t,J=8Hz), 7.11(1H,s), 7.12-7.22(2H,m), 7.43(2H,d,J=8Hz), 7.61(1H,t,J=8Hz), 7.70(2H,d,J=8Hz), 8.58(1H,d,J=2Hz)

Preparation 220

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 430 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.50(9H,s), 3.18-3.28(1H,m),
3.32-3.47(1H,m), 4.70-4.78(2H,m), 4.80(1H,br s),
6.29(1H,br s), 7.27(1H,d,J=6Hz), 7.71(1H,br s),
8.10(2H,d,J=8Hz), 8.32(2H,d,J=8Hz), 8.62(1H,d,J=6Hz),
9.14(1H,s)

Preparation 221

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 425 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 3.38-3.48(1H,m),
3.50-3.60(1H,m), 3.69(3H,s), 5.43(1H,d,J=8Hz),
5.58(1H,q,J=8Hz), 7.10(1H,s), 7.21(1H,d,J=4Hz),
7.50(2H,d,J=8Hz), 8.30(2H,d,J=8Hz), 8.59(1H,d,J=4Hz),
9.11(1H,s)

Preparation 222

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 325 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.29-3.39(1H,m), 3.48-3.58(1H,m),
3.73(3H,s), 4.70(1H,t J=8Hz), 7.17(1H,s),
7.29(1H,d,J=6Hz), 7.52(2H,d,J=8Hz), 8.30(2H,d,J=8Hz),
8.62(1H,d,J=6Hz), 9.19(1H,s)

Preparation 223

The object compound was obtained according to a similar manner to that of Preparation 5.

oil

MASS (m/z) : 428 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(3H,t,J=8Hz), 1.43(9H,s), 3.10-3.30(1H,m), 3.31-3.42(1H,m), 4.08(2H,q,J=8Hz), 4.68(2H,d,J=4Hz), 4.70(1H,br s), 6.40(1H,br s), 7.09-7.19(2H,m), 7.21(1H,d,J=8Hz), 7.38(1H,t,J=8Hz), 7.41(1H,s), 7.50(1H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.90(1H,br s), 8.57(1H,d,J=2Hz)

Preparation 224

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 423 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.39(9H,s), 1.44(3H,t,J=8Hz), 3.33-3.50(2H,m), 3.43(3H,s), 4.03(2H,q,J=8Hz), 5.30-5.51(2H,m), 6.80-6.91(3H,m), 7.00(1H,s), 7.03-7.18(2H,m), 7.30(1H,t,J=8Hz), 7.53(1H,t,J=6Hz), 8.52(1H,d,J=2Hz),

Preparation 225

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 323 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.43(3H,t,J=8Hz), 3.24-3.38(1H,m), 3.39-3.50(1H,m), 3.50(3H,s), 4.07(2H,q,J=8Hz), 4.52-4.61(1H,m), 6.80-6.92(3H,m), 7.00(1H,s), 7.10-7.20(2H,m), 7.31(1H,t,J=8Hz), 7.60(1H,t,J=8Hz), 8.59(1H,d,J=2Hz)

Preparation 226

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 490 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.42(9H,s), 3.19-3.30(1H,m), 3.30-3.41(1H,m), 4.61(2H,d,J=4Hz), 4.62-4.73(1H,m), 5.11(2H,s), 6.41(1H,br s),

7.00(2H,d,J=8Hz), 7.12(1H,t,J=8Hz), 7.20(1H,d,J=8Hz),
7.30-7.48(5H,m), 7.59(1H,t,J=8Hz), 7.84(1H,br s),
7.91(2H,d,J=8Hz), 8.52(1H,d,J=4Hz)

Preparation 227

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 485 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.38(9H,s), 3.38(3H,s), 3.41(2H,d,J=8Hz),
5.10(2H,s), 5.30-5.42(1H,m), 5.42-5.50(1H,m), 6.91(1H,s),
7.00(2H,d,J=8Hz), 7.10(2H,t,J=8Hz), 7.20(2H,d,J=8Hz),
7.30-7.48(5H,m), 7.53(1H,t,J=8Hz), 8.52(1H,d,J=2Hz)

Preparation 228

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 385 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.20-3.48(2H,m), 3.48(3H,s), 4.58(1H,t,J=8Hz),
5.10(2H,s), 6.97(1H,s), 7.00(2H,d,J=8Hz), 7.13(2H,d,J=8Hz),
7.21(2H,d,J=8Hz), 7.30-7.50(5H,m), 7.59(1H,t,J=8Hz),
8.58(1H,d,J=2Hz)

Preparation 229

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 368 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.50(9H,s), 3.18(1H,br s), 3.70-3.80(1H,m),
4.12(1H,d,J=10Hz), 4.28-4.38(1H,m), 4.71-4.91(2H,m),
5.62(1H,d,J=8Hz), 7.53(1H,br s), 8.13(2H,d,J=8Hz),
8.33(2H,d,J=8Hz)

Preparation 230

The object compound was obtained according to a similar manner to

that of Preparation 2.

oil

MASS (m/z) : 363 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.47(9H,s), 3.70(3H,s),
3.91(1H,dd,J=15 and 2Hz), 4.22(1H,dd,J=15 and 2Hz),
4.92-5.01(1H,m), 5.58(1H,d,J=8Hz), 7.10(1H,s),
7.58(2H,d,J=8Hz), 8.31(2H,d,J=8Hz)

Preparation 231

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 263 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.71(3H,s), 3.81-3.91(1H,m), 4.00-4.12(2H,m),
7.10(1H,s), 7.54(2H,d,J=8Hz), 8.30(2H,d,J=8Hz),

Preparation 232

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 428 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.48(9H,s), 3.20-3.30(1H,m), 3.31-3.42(1H,m),
4.61(2H,d,J=4Hz), 4.63-4.72(1H,m), 6.09(2H,s), 6.41(1H,br s),
6.88(1H,d,J=8Hz), 7.11-7.23(2H,m), 7.41(1H,s),
7.50-7.67(2H,m), 7.89(1H,br s), 8.58(1H,d,J=2Hz)

Preparation 233

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 423 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.38(9H,s), 3.40(3H,s), 3.42(2H,d,J=8Hz),
5.30-5.50(2H,m), 5.99(2H,s), 6.70-6.77(2H,m),
6.82(1H,d,J=8Hz), 6.90(1H,s), 7.10(2H,t,J=8Hz),
7.52(1H,t,J=8Hz), 8.52(1H,d,J=8Hz)

Preparation 234

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 323 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.27-3.37(1H,m), 3.38-3.47(1H,m), 3.50(3H,s), 4.52-4.60(1H,m), 6.00(2H,s), 6.72-6.80(2H,m), 6.85(1H,d,J=8Hz), 6.93(1H,s), 7.10-7.20(2H,m), 7.60(1H,t,J=8Hz), 8.59(1H,d,J=2Hz)

Preparation 235

The object compound was obtained according to a similar manner to that of Preparation 5.

oil

MASS (m/z) : 380 (M-1)

^{1}H-NMR ($CDCl_3$) δ 1.49(9H,s), 3.40(3H,s), 3.51(1H,dd,J=10 and 7Hz), 3.90(1H,dd,J=8 and 2Hz), 4.30-4.40(1H,m), 4.70-4.90(2H,m), 5.42(1H,br s), 7.43(1H,br s), 8.13(2H,d,J=8Hz), 8.35(2H,d,J=8Hz),

Preparation 236

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 377 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.46(9H,s), 3.33(3H,s), 3.62-3.72(1H,m), 3.70(3H,s), 3.79-3.88(1H,m), 5.11(1H,q,J=8Hz), 5.41(1H,d,J=8Hz), 7.19(1H,s), 7.53(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 237

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 277 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.40(3H,s), 3.71(3H,s), 3.77-3.88(2H,m), 4.22(2H,br s), 4.37-4.50(1H,m), 7.19(1H,s), 7.51(2H,d,J=8Hz), 8.30(2H,d,J=8Hz),

Preparation 238

The object compound was obtained according to a similar manner to that of Preparation 5.

oil

MASS (m/z) : 458 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.49(9H,s), 3.59-3.68(1H,m), 3.90-4.02(1H,m), 4.30-4.42(1H,m), 4.50-4.62(2H,m), 4.78-7.84(2H,m), 5.43(1H,br s), 7.28-7.39(5H,m), 7.42(1H,br s), 8.13(2H,d,J=8Hz), 8.37(2H,d,J=8Hz)

Preparation 239

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 453 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.41(9H,s), 3.68(3H,s), 3.78(1H,t,J=8Hz), 3.97(1H,t,J=8Hz), 4.52(2H,s), 5.15(1H,q,J=8Hz), 5.45(1H,d,J=8Hz), 7.19(1H,s), 7.20-7.38(5H,m), 7.51(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 240

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 353 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.70(3H,s), 3.83(2H,d,J=8Hz), 4.30(1H,t,J=8Hz), 4.59(2H,s), 7.18(1H,s), 7.20-7.38(5H,m), 7.51(2H,d,J=8Hz), 8.30(2H,d,J=8Hz)

Preparation 241

The object compound was obtained according to a similar manner to that of Preparation 5 except that a mixture of dichloromethane and

dimethylformamide was used instead of dichloromethane.

amorphous solid

MASS (m/z) : 416 (M-1)

^{1}H-NMR (DMSO-d_6) δ 1.31(9H,s), 2.70-2.98(2H,m), 4.19-4.30(1H,m), 4.57-4.75(2H,m), 6.79(1H,s), 6.99(1H,d,J=8Hz), 7.53(1H,s), 8.11-8.30(4H,m), 8.33(2H,d,J=8Hz)

Preparation 242

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 413 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.48(9H,s), 3.33(2H,d,J=7Hz), 3.62(3H,s), 5.09-5.19(1H,m), 5.19-5.30(1H,m), 6.90(1H,s), 7.19(1H,s), 7.28(1H,s), 7.51(1H,s), 7.58(2H,d,J=8Hz), 8.31(2H,d,J=8Hz)

Preparation 243

The object compound was obtained according to a similar manner to that of Preparation 8.

amorphous solid

MASS (m/z) : 313 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.22(2H,d,J=7Hz), 3.69(3H,s), 4.33(1H,t,J=8Hz), 6.89(1H,s), 7.19(1H,s), 7.28(1H,s), 7.52(2H,d,J=8Hz), 7.59(1H,s), 8.30(2H,d,J=8Hz)

Preparation 244

The object compound was obtained according to a similar manner to that of Preparation 5.

oil

MASS (m/z) : 418 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.48(9H,s), 3.20-3.30(1H,m), 3.32-3.43(1H,m), 4.62-4.72(1H,m), 4.67(2H,d,J=2Hz), 6.42(1H,br s), 7.12-7.23(2H,m), 7.47(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.89(2H,d,J=8Hz), 7.93(1H,br s), 8.53(1H,d,J=2Hz)

Preparation 245

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 413 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.37(9H,s), 3.38-3.48(2H,m), 3.44(3H,s), 5.33-5.52(2H,m), 6.90(1H,s), 7.10(2H,t,J=8Hz), 7.21(2H,d,J=8Hz), 7.40(2H,d,J=8Hz), 7.57(1H,t,J=8Hz) 8.52(1H,d,J=2Hz)

Preparation 246

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 313 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.27-3.38(1H,m), 3.39-3.50(1H,m), 3.50(3H,s), 4.53-4.62(1H,m), 7.01(1H,s), 7.13(1H,d,J=8Hz), 7.18(1H,t,J=8Hz), 7.25(2H,d,J=8Hz), 7.40(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 8.59(1H,d,J=2Hz)

Preparation 247

A mixture of 6-acetylquinoline (2.0 g), hydroxylamine hydrochloride (1.0 g) and sodium carbonate (1.7 g) in ethanol (20 ml) was refluxed for 1 hour. After cooling to room temperature, water was added to the mixture. The precipitate was collected and washed with diethyl ether to give the object compound as a pale yellow solid (1.7 g).

mp : 170-173°C

MASS (ESI) (m/z) : 187 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 2.43(3H,s), 7.44(1H,dd,J=7.5, 4.5Hz), 8.00(1H,s), 8.16-8.23(3H,m), 8.94(1H,d,J=4.5Hz), 9.46(1H,s)

Preparation 248

To a solution of the starting compound (1.50 g) in pyridine (15 ml) cooled to 0°C was added p-toluenesulfonyl chloride (1.84 g) with

stirring under an atmosphere of nitrogen, and the mixture was stirred at 0°C for 9 hours. After the reaction mixture was poured into ice-water, the precipitate was collected and washed successively with water and 2-propanol to give the object compound as a pale brown solid (1.62 g).

mp : 119.5-121°C

MASS (ESI) (m/z) : 341 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 2.43(3H,s), 2.48(3H,s),
7.36(2H,d,J=7.5Hz), 7.44(1H,dd,J=7.5, 4.5Hz), 7.92-8.03(4H,m),
8.07(1H,d,J=7.5Hz), 8.18(1H,d,J=7.5Hz), 8.95(1H,d,J=4.5Hz)

Preparation 249

Potassium (258.4 mg) was added to a suspension of the starting compound (1.5 g) in ethanol (40 ml), and the mixture was stirred at room temperature for 72 hours. The precipitate of potassium p-toluenesulfonate was removed by filtration, and the filtrate was diluted with diethyl ether (400 ml). A further precipitate of the potassium salt was filtered off, and the ethereal solution was extracted twice with 1.5N hydrochloric acid (50 ml). The combined extracts were evaporated in vacuo, and the residue was recrystallized from 2-propanol to give the object compound as an off-white solid (1.31 g).

mp : 293.5-296°C

MASS (ESI) (m/z) : 187 $(M+H)^+$

^{1}H-NMR (DMSO-d_6, δ) 4.72(1H,d,J=5.5Hz),
4.77(1H,d,J=5.5Hz), 7.83(1H,dd,J=7.5, 5.5Hz),
8.30(1H,d,J=7.5Hz), 8.37(1H,d,J=7.5Hz), 8.55(2H,br s),
8.81(1H,d,J=7.5Hz), 8.97(1H,s), 9.20(1H,d,J=5.5Hz)

Preparation 250

The object compound was obtained according to a similar manner to that of Preparation 5.

oil

MASS (m/z) : 435 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.50(9H,s), 3.20-3.31(1H,m), 3.31-3.48(1H,m), 4.68-4.80(1H,m), 4.87(2H,d,J=4Hz), 6.49(1H,br s), 7.18(1H,t,J=6Hz), 7.22(1H,d,J=8Hz), 7.51(1H,dd,J=8 and 2Hz), 7.61(1H,t,J=8Hz), 8.02(1H,br s), 8.13-8.31(3H,m), 8.49(1H,s), 8.58(1H,d,J=2Hz), 9.08(1H,d,J=2Hz)

Preparation 251

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 430 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.40(9H,s), 3.49(2H,d,J=6Hz), 3.51(3H,s), 5.38-5.60(2H,m), 7.10(1H,s), 7.11-7.20(2H,m), 7.43(1H,dd,J=8 and 2Hz), 7.59(1H,t,J=8Hz), 7.63(1H,d,J=8Hz), 7.77(1H,s), 8.17(2H,t,J=8Hz), 8.56(1H,d,J=2Hz), 8.92(1H,d,J=2Hz),

Preparation 252

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 330 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.40-3.60(2H,m), 3.65(3H,s), 4.88(1H,t,J=8Hz), 7.10-7.21(3H,m), 7.46(1H,dd,J=8 and 2Hz), 7.58-7.70(2H,m), 7.79(1H,s), 8.10-8.20(2H,m), 8.59(1H,d,J=2Hz), 8.99(1H,d,J=2Hz)

Preparation 253

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 495 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.20(3H,t,J=8Hz), 1.40(9H,s), 3.00-3.10(1H,m), 3.20-3.33(1H,m), 4.12(2H,q,J=8Hz), 5.13(1H,d,J=10Hz), 5.18(1H,d,J=10Hz), 5.28(1H,d,J=8Hz),

5.32-5.45(1H,m), 7.09(1H,s), 7.28-7.40(5H,m),
7.51(2H,d,J=8Hz), 8.30(2H,d,J=8Hz),

Preparation 254

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 395 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.25(3H,t,J=8Hz), 3.00-3.10(1H,m),
3.18-3.30(1H,m), 4.02-4.30(2H,m), 4.55(1H,t,J=8Hz),
5.11(1H,d,J=8Hz), 5.18(1H,d,J=8Hz), 7.10(1H,s),
7.28-7.40(5H,m), 7.51(2H,d,J=8Hz), 8.29(2H,d,J=8Hz)

Preparation 255

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 459 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.18(3H,t,J=8Hz), 1.40(9H,s),
3.42-3.52(1H,m), 3.53-3.70(1H,m), 3.95-4.12(2H,m),
5.50(1H,q,J=8Hz), 5.70(1H,br s), 7.08(1H,s), 7.10-7.20(2H,m),
7.21-7.30(2H,m), 7.31(1H,s), 7.40-7.51(3H,m),
7.58(1H,t,J=8Hz), 7.90(1H,s), 8.52(1H,d,J=2Hz)

Preparation 256

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 359 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.20(3H,t,J=8Hz), 3.35-3.60(2H,m),
3.90-4.17(2H,m), 4.62-4.72(1H,m), 7.03(1H,s),
7.18(2H,d,J=8Hz), 7.23(2H,d,J=8Hz), 7.31(1H,s),
7.40-7.50(2H,m), 7.61(1H,t,J=8Hz), 7.89-7.92(2H,m),
8.59(1H,d,J=2Hz)

Preparation 257

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS (m/z) : 437 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.07(3H,t,J=8Hz), 1.32(9H,s),
1.42(3H,t,J=8Hz), 3.12-3.33(1H,m), 3.40-3.60(1H,m),
3.80-4.00(1H,m), 4.05(2H,q,J=8Hz), 5.41(1H,q,J=8Hz),
5.59(1H,d,J=8Hz), 6.90(1H,s), 6.92(2H,d,J=8Hz),
7.08-7.19(2H,m), 7.21(2H,d,J=8Hz), 7.53(1H,t,J=8Hz),
8.52(1H,d,J=2Hz),

Preparation 258

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 337 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.12(3H,t,J=8Hz), 1.48(3H,t,J=8Hz),
3.20-3.31(1H,m), 3.33-3.50(1H,m), 3.80-4.00(2H,m),
4.03(2H,q,J=8Hz), 4.56-4.70(1H,m), 6.90(1H,s),
6.92(2H,d,J=8Hz), 7.13(2H,d,J=8Hz), 7.19-7.30(2H,m),
7.60(1H,t,J=8Hz), 8.60(1H,d,J=8Hz),

Preparation 259

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 469 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.44(9H,s), 3.23-3.42(6H,m), 3.80-3.90(4H,m),
4.60(2H,d,J=2Hz), 4.63-4.78(1H,m), 6.39(1H,br s),
6.87(2H,d,J=8Hz), 7.12-7.30(2H,m), 7.62(1H,t,J=8Hz),
7.88(3H,d,J=8Hz), 8.58(1H,d,J=2Hz)

Preparation 260

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 464 (M+1)

^{1}H-NMR ($CDCl_3$) δ 1.39(9H,s), 3.10-3.22(4H,m), 3.28-3.60(2H,m), 3.42(3H,s), 3.80-3.92(4H,m), 5.40(1H,q,J=8Hz), 5.60(1H,d,J=6Hz), 6.91(2H,d,J=8Hz), 6.92(1H,s), 7.11(2H,d,J=8Hz), 7.20(2H,d,J=8Hz), 7.52(1H,t,J=8Hz), 8.52(1H,d,J=2Hz)

Preparation 261

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 364 (M+1)

^{1}H-NMR ($CDCl_3$) δ 3.10-3.28(4H,m), 3.28-3.50(2H,m), 3.46(3H,s), 3.78-3.91(4H,m), 4.60(1H,t,J=8Hz), 6.92(2H,d,J=8Hz), 6.93(1H,s), 7.12(2H,t,J=8Hz), 7.20(2H,d,J=8Hz), 7.59(1H,t,J=8Hz), 8.59(1H,d,J=8Hz),

Preparation 262

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 478 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.10(3H,t,J=7Hz), 1.34(9H,s), 3.10-3.25(4H,m), 3.38-3.65(2H,m), 3.76-4.04(6H,m), 5.38-5.52(1H,m), 5.65(1H,br d,J=8Hz), 6.91(2H,d,J=8Hz), 6.93(1H,s), 7.02-7.30(4H,m), 7.45-7.60(1H,m), 8.51(1H,d,J=5Hz)

Preparation 263

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 378 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.15(3H,t,J=7Hz), 3.11-3.31(4H,m), 3.36-3.57(2H,m), 3.75-4.10(6H,m), 4.68(1H,t,J=7Hz), 6.93(2H,d,J=8Hz), 6.97(1H,s), 7.08-7.29(4H,m), 7.53-7.66(1H,m), 8.54(1H,d,J=5Hz)

Preparation 264

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 473 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 0.76(3H,t,J=7Hz), 1.38(9H,s), 1.40-1.60(2H,m), 3.48-3.80(2H,m), 3.88-4.08(2H,m), 5.40-5.60(2H,m), 7.02-7.65(10H,m), 7.92(1H,s), 8.52(1H,d,J=5Hz)

Preparation 265

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 373 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 0.78(3H,t,J=7Hz), 1.36-1.72(2H,m), 3.42-3.74(2H,m), 3.85-4.24(2H,m), 4.81-5.02(1H,m), 7.08(1H,s), 7.15-7.72(9H,m), 7.93(1H,s), 8.55(1H,d,J=5Hz)

Preparation 266

To an ice-cooled suspension of sodium hydride (60%, 2.21 g) in N,N-dimethylformamide (35 ml) was added 1,2,4-triazole (3.80 g) portionwisely. After the evolution of hydrogen was ceased, the mixture was heated at 40°C for 20 minutes and allowed to cool to room temperature. To this mixture was added the starting compound (6.91 g) and the mixture was heated at 80°C for 4 hours. The mixture was poured into water and extracted three times with ethyl acetate. The extract was washed three times with brine, dried over magnesium sulfate, filtered, and concentrated. The crude product was purified by recrystallization from ethyl acetate-diisopropyl ether to give the object compound (3.36 g).

MASS (ESI) (m/z) : 188 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.65(3H,s), 7.83(2H,d,J=8Hz), 8.12(2H,d,J=8Hz), 8.15(1H,s), 8.67(1H,s)

Preparation 267

The object compound was obtained according to a similar manner to

that of Preparation 108.

MASS (ESI) (m/z) : 266, 268 (free, M+H)$^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 4.98(2H,s), 8.08(2H,d,J=8Hz), 8.20(2H,d,J=8Hz), 8.33(1H,s), 9.51(1H,s)

Preparation 268

The object compound was obtained according to a similar manner to that of Preparation 109.

MASS (ESI) (m/z) : 229 (M+H)$^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 4.68(2H,s), 7.86(2H,d,J=8Hz), 8.08(2H,d,J=8Hz), 8.16(1H,s), 8.68(1H,s)

Preparation 269

The object compound was obtained according to a similar manner to that of Preparation 110 except that a mixture of methanol and tetrahydrofuran was used instead of methanol.

MASS (ESI) (m/z) : 203 (free, M+H)$^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 4.65(2H,q,J=5Hz), 8.00-8.27(4H,m), 8.34(1H,s), 8.46(3H,br s), 9.54(1H,s)

Preparation 270

The object compound was obtained according to a similar manner to that of Preparation 91.

MASS (ESI) (m/z) : 451 (M+H)$^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.46(9H,s), 3.20-3.44(2H,m), 4.61-4.78(3H,m), 6.44(1H,br d,J=8Hz), 7.10-7.25(2H,m), 7.54-7.65(1H,m), 7.84(2H,d,J=8Hz), 8.00(1H,br s), 8.09(2H,d,J=8Hz), 8.14(1H,s), 8.55(1H,d,J=5Hz), 8.68(1H,s)

Preparation 271

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 446 (M+H)$^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.36(9H,s), 3.36-3.50(2H,m), 3.49(3H,s), 5.35-5.49(1H,m), 5.53(1H,br d,J=8Hz), 7.05(1H,s), 7.07-7.18(2H,m), 7.44(2H,d,J=8Hz), 7.50-7.62(1H,m),

7.74(2H,d,J=8Hz), 8.12(1H,s), 8.54(1H,d,J=5Hz), 8.59(1H,s)

Preparation 272

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 346 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.26-3.51(2H,m), 3.56(3H,s), 4.61(1H,t,J=7Hz), 7.09(1H,s), 7.15(2H,d,J=8Hz), 7.48(2H,d,J=8Hz), 7.55-7.65(1H,m), 7.74(2H,d,J=8Hz), 8.12(1H,s), 8.57(1H,d,J=5Hz), 8.59(1H,s)

Preparation 273

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS (ESI) (m/z) : 460 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.13(3H,t,J=7Hz), 1.34(9H,s), 3.34-3.60(2H,m), 3.84-4.13(2H,m), 5.33(1H,br d,J=8Hz), 5.35-5.51(1H,m), 7.03(1H,s), 7.06-7.18(2H,m), 7.47(2H,d,J=8Hz), 7.50-7.60(1H,m), 7.74(2H,d,J=8Hz), 8.12(1H,s), 8.53(1H,d,J=5Hz), 8.59(1H,s)

Preparation 274

The object compound was obtained according to a similar manner to that of Preparation 4.

MASS (ESI) (m/z) : 360$(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.16(3H,t,J=7Hz), 3.29-3.52(2H,m), 3.89-4.14(2H,m), 4.60(1H,t,J=7Hz), 7.07(1H,s), 7.10-7.20(2H,m), 7.48(2H,d,J=8Hz), 7.54-7.64(1H,m), 7.75(2H,d,J=8Hz), 8.13(1H,s), 8.58(1H,d,J=5Hz), 8.60(1H,s)

Preparation 275

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 467 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.48(9H,s), 1.68(6H,s), 3.20-3.42(2H,m),

3.39(4H,s), 4.57(2H,d,J=2Hz), 4.61-4.72(1H,m),
6.38(1H,d,J=2Hz), 6.81(2H,d,J=8Hz), 7.12(1H,t,J=6Hz),
7.20(1H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.80(2H,d,J=8Hz),
7.81(1H,s), 8.54(1H,d,J=2Hz)

Preparation 276

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS (m/z) : 462 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.39(9H,s), 1.67-1.78(6H,m), 3.17-3.23(4H,m),
3.38(3H,s), 3.47(2H,t,J=8Hz), 5.40(1H,q,J=8Hz),
5.58(1H,d,J=8Hz), 6.91(1H,s), 6.93(2H,d,J=8Hz),
7.06-7.20(2H,m), 7.17(2H,d,J=8Hz), 7.53(1H,t,J=8Hz),
8.51(1H,d,J=2Hz)

Preparation 277

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS (m/z) : 362 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.53-1.68(2H,m), 1.68-1.80(4H,m),
3.17-3.28(4H,m), 3.28-3.41(2H,m), 3.48(3H,s),
4.60(1H,t,J=8Hz), 6.90-7.00(3H,m), 7.10-7.22(4H,m),
7.59(1H,t,J=8Hz), 8.59(1H,d,J=2Hz)

Preparation 278

The starting compound (3.6 g) was dissolved in tetrahydrofuran (36 ml) under a nitrogen atmosphere and cooled to -30°C. 1M Lithium aluminum hydride solution in tetrahydrofuran (11.7 ml) was added dropwise to the solution at -30°C, and the reaction mixture was stirred at -30°C for 1 hour. Water was added carefully, and the mixture was stirred at room temperature for 30 minutes. Ethyl acetate and 1N-hydrochloric acid were added to the suspension and extracted. The organic layer was washed with water, a saturated

sodium hydrogencarbonate solution and a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* to give the object compound (501.3 mg) as a pale yellow amorphous solid.

MASS (m/z) : 484 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.41(9H,s), 2.80(3H,s),
3.17(1H,dd,J=12.0 and 9.0Hz), 3.37(1H,dd,J=12.0 and 7.0Hz),
5.01(1H,m), 5.69(1H,d,J=7.5Hz), 6.99-7.06(2H,m),
7.09(2H,d,J=7.5Hz), 7.19-7.26(3H,m), 7.61(2H,d,J=7.5Hz),
9.68(1H,s)

Preparation 279

The object compound was obtained according to a similar manner to that of Preparation 6.

MASS (m/z) : 522 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.47(9H,s), 2.77(3H,s), 3.14(1H,m),
3.38(1H,dd,J=13.5 and 5.5Hz), 4.99(1H,m), 5.80(1H,m),
6.97-7.12(5H,m), 7.19-7.29(5H,m), 7.56(2H,d,J=7.5Hz)

Preparation 280

The object compound was obtained according to a similar manner to that of Preparation 3.

yellow amorphous solid

MASS (m/z) : 422 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.93(3H,s), 3.19(2H,d,J=7.5Hz),
4.21(1H,t,J=7.5Hz), 6.98(1H,s), 7.02-7.09(2H,m),
7.12(1H,d,J=7.5Hz), 7.20-7.31(5H,m), 7.56(2H,d,J=7.5Hz)

Preparation 281

The object compound was obtained according to a similar manner to that of Preparation 91.

brown oil

MASS (m/z) : 463 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.28(1H,dd,J=15.0 and 7.0Hz), 3.40(1H,m),
4.72(2H,br s), 4.76(1H,m), 5.15(2H,s), 6.83(1H,m),

7.13-7.42(7H,m), 7.61(1H,t,J=7.5Hz), 8.10(2H,d,J=7.5Hz), 8.15(1H,m), 8.32(2H,d,J=7.5Hz), 8.53(1H,d,J=5.5Hz)

Preparation 282

The starting compound (420 mg), xylene (6 ml) and acetic acid (1 ml) were mixed, and ammonium acetate (462 mg) was added to the solution at room temperature. The reaction mixture was refluxed for 2.5 hours with azeotropic removal of water and allowed to cool. The mixture was concentrated *in vacuo*, and the residue was dissolved in ethyl acetate. The organic solution was washed with a saturated sodium hydrogen carbonate solution and saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography over silica gel with a chloroform-methanol (20:1) as eluent to give the object compound as a brown amorphous solid.

MASS (m/z) : 444 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.45(1H,dd,J=15.0 and 7.0Hz), 3.60(1H,m), 5.13(2H,s), 5.19(1H,m), 6.68(1H,m), 7.18-7.41(9H,m), 7.67(1H,t,J=7.5Hz), 7.89(2H,d,J=7.5Hz), 8.21(2H,d,J=7.5Hz), 8.54(1H,d,J=5.5Hz)

Preparation 283

The starting compound (340 mg) and 30%-hydrogen bromide solution in acetic acid (3 ml) were mixed at 0°C. The reaction mixture was stirred at room temperature for 1.5 hours and diethyl ether was added to the mixture at 0°C. The precipitate was collected to give the object compound (376.4 mg) as a pale brown solid.

mp : 178-181°C

MASS (m/z) : 310 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.61(1H,dd,J=15.0 and 7.0Hz), 3.68(1H,dd,J=15.0 and 7.0Hz), 5.01(1H,m), 7.57(1H,d,J=7.5Hz), 7.61(1H,t,J=7.5Hz), 7.99(1H,s), 8.03(2H,d,J=7.5Hz), 8.11(1H,t,J=7.5Hz), 8.27(2H,d,J=7.5Hz), 8.72(1H,d,J=5.5Hz)

Preparation 284

The object compound was obtained according to a similar manner to that of Preparation 5.

off-white solid

mp : 190-191.5°C

MASS (m/z) : 349 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 1.18(3H,t,J=7.5Hz), 4.21(2H,q,J=7.5Hz), 6.37(1H,d,J=7.5Hz), 7.03(1H,t,J=7.5Hz), 7.20(1H,t,J=7.5Hz), 7.28(1H,d,J=1.0Hz), 7.41(1H,d,J=7.5Hz), 7.52-7.63(3H,m), 7.69(1H,t,J=7.5Hz), 8.02(2H,d,J=7.5Hz), 9.40(1H,d,J=7.5Hz)

Preparation 285

The object compound was obtained according to a similar manner to that of Preparation 282.

yellow amorphous solid

MASS (m/z) : 332 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 1.29(3H,t,J=7.5Hz), 4.21(2H,q,J=7.5Hz), 6.92-7.74(7H,m), 7.31(1H,s), 7.93(2H,d,J=7.5Hz)

Preparation 286

The object compound was obtained according to a similar manner to that of Example 73.

off-white solid

mp : 228-230°C

MASS (m/z) : 302 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 7.02(1H,t,J=7.5Hz), 7.10-7.61(6H,m), 7.59(1H,d,J=7.5Hz), 7.67-7.79(1H,m), 7.89-8.04(1H,m)

Preparation 287

The object compound was obtained according to a similar manner to that of Preparation 5.

orange solid

mp : 114-117°C

MASS (m/z) : 541 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.12(3H,t,J=7.0Hz), 1.48(9H,s), 2.76(1H,dd,J=14.5 and 7.0Hz), 3.04(1H,m), 4.19(2H,q,J=7.0Hz),

4.67(1H,m), 6.05(1H,dd,J=8.5 and 7.0Hz), 6.17(1H,m),
7.10(1H,t,J=7.5Hz), 7.21-7.49(4H,m), 7.68-7.79(1H,m),
8.03-8.32(5H,m)

Preparation 288

The object compound was obtained according to a similar manner to that of Preparation 2.

yellow amorphous solid

MASS (m/z) : 538 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.12(3H,t,J=7.0Hz), 1.43(9H,s), 3.19(1H,m),
3.32(1H,m), 3.59(3H,s), 4.20(2H,q,J=7.0Hz), 5.49(1H,m),
5.71(1H,m), 7.08(1H,t,J=7.5Hz), 7.23-7.37(2H,m),
7.47-7.57(2H,m), 7.53(2H,d,J=7.5Hz), 8.33(2H,d,J=7.5Hz),
8.96(1H,br s)

Preparation 289

The object compound was obtained according to a similar manner to that of Preparation 3.

yellow amorphous solid

MASS (m/z) : 438 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.19(3H,t,J=7.0Hz),
3.07(1H,dd,J=14.5 and 7.5Hz), 3.17(1H,dd,J=14.5 and 7.5Hz),
3.56(3H,s), 4.22(2H,q,J=7.0Hz), 4.52(1H,t,J=7.5Hz),
7.08(1H,t,J=7.5Hz), 7.30(2H,t,J=7.5Hz), 7.52(2H,d,J=7.5Hz),
7.58(2H,d,J=7.5Hz),8.32(2H,d,J=7.5Hz), 9.45(1H,br s)

Preparation 290

The object compound was obtained according to a similar manner to that of Preparation 91.

brown oil

MASS (m/z) : 501 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.17(3H,t,J=7.0Hz), 1.47(9H,s),
3.10-3.33(2H,m), 4.17(2H,q,J=7.0Hz), 4.67(1H,m), 6.07(1H,m),
7.09-7.27(3H,m), 7.51-7.66(2H,m), 8.16-8.57(3H,m)

Preparation 291

The object compound was obtained according to a similar manner to that of Preparation 2.

dark brown amorphous solid

MASS (m/z) : 496 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.19(3H,t,J=7.0Hz), 1.39(9H,s), 3.32(3H,s), 3.49(2H,m), 4.20(2H,q,J=7.0Hz), 4.39(1H,m), 6.03(1H,m), 7.04-7.18(2H,m), 7.45(2H,d,J=7.5Hz), 7.55(1H,m), 8.30(2H,d,J=7.5Hz), 8.52(1H,m)

Preparation 292

The object compound was obtained according to a similar manner to that of Preparation 3.

yellow oil

MASS (m/z) : 396 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.20(3H,t,J=7.5Hz), 3.35-3.52(2H,m), 3.43(3H,s), 4.23(2H,q,J=7.5Hz), 4.66(1H,t,J=7.5Hz), 7.19(2H,d,J=7.5Hz), 7.52(2H,d,J=7.5Hz), 7.63(1H,t,J=7.5Hz), 8.35(2H,d,J=7.5Hz), 8.59(1H,d,J=7.5Hz)

Preparation 293

The object compound was obtained according to a similar manner to that of Example 73.

MASS (m/z) : 389 (M-1)

^{1}H-NMR ($CDCl_3$) δ : 1.45(9H,s), 3.07(1H,dd,J=5 and 15Hz), 3.18(1H,dd,J=7 and 15Hz), 3.73(3H,s), 5.36(1H,m), 5.73(1H,d,J=7Hz), 7.14(1H,s), 7.55(2H,d,J=8Hz), 8.33(2H,d,J=8Hz)

Preparation 294

The object compound was obtained according to a similar manner to that of Preparation 5.

yellow amorphous solid

MASS (m/z) : 434 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.43(9H,s), 3.13(1H,m), 3.15(3H,s), 3.35(1H,m), 3.73(3H,s), 3.79(3H,s), 5.41(2H,m), 7.11(1H,s),

7.53(2H,d,J=8.5Hz), 8.30(2H,d,J=8.5Hz)

Preparation 295

The object compound was obtained according to a similar manner to that of Preparation 278.

yellow amorphous solid

MASS (m/z) : 375 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.45(9H,s), 3.17(1H,m), 3.40(1H,m), 3.77(3H,s), 5.27(1H,m), 5.41(1H,m), 7.10(1H,s), 7.53(2H,d,J=8.5Hz), 8.30(2H,d,J=8.5Hz), 9.85(1H,s)

Preparation 296

The object compound was obtained according to a similar manner to that of Preparation 6.

yellow solid

mp : 217-218.5°C

MASS (m/z) : 413 $(M+H)^+$

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 1.40(9H,s), 3.29(2H,d,J=7.5Hz), 3.61(3H,s), 5.22(1H,t,J=7.5Hz), 6.92(2H,s), 7.10(1H,s), 7.53(2H,d,J=8.5Hz), 8.31(2H,d,J=8.5Hz)

Preparation 297

The starting compound (85 mg) and 4N hydrogen chloride solution in ethyl acetate (2 ml) were mixed at 0 °C. The reaction mixture was stirred at room temperature for 2 hours and concentrated *in vacuo*. The residue was washed with diethyl ether to give the object compound (89.4 mg) as a pale yellow solid.

mp : 88-91°C

MASS (m/z) : 313 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.79(1H,dd,J=15.0 and 7.5Hz), 3.85(3H,s), 3.89(1H,dd,J=15.0 and 7.5Hz), 5.66(1H,t,J=7.5Hz), 7.42(1H,s), 7.59(2H,s), 7.75(2H,d,J=7.5Hz), 8.33(2H,d,J=7.5Hz)

Preparation 298

A mixture of the starting compound (5 g) and phenol (3.03 g) in N,N-dimethylacetamide (50 ml) was stirred until the solids were

dissolved. Then potassium carbonate (4.9 g) was added and the solution was refluxed for 1.5 hours. The cooled reaction mixture was treated with water (100 ml) and $CHCl_3$ (60 ml). The organic phase was separated, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography over silica gel with a n-hexane/ethyl acetate (6:1) as eluent to give the object compound (4.85 g) as an orange solid.

mp : 64-66°C

MASS (m/z) : 228 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.33(3H,s), 6.79(1H,s), 6.93-7.07(3H,m), 7.17(1H,t,J=7.5Hz), 7.33-7.42(2H,m), 7.89(1H,d,J=7.5Hz)

Preparation 299

Potassium permanganate (4.14 g) was added portionwise, with stirring, over 1 hour to a mixture of the starting compound (2.0 g) and anhydrous magnesium sulfate (2.1 g) in 2-methyl-2-propanol (30 ml) and water (30 ml) at 90 °C. The reaction mixture was stirred at 90°C for 3 hours, and cooled to room temperature. 2-Propanol was added to the reaction mixture, and the mixture was stirred at room temperature for 1 hour. Water (60 ml) was added, and the suspension was filtered through a celite pad. The filtrate was acidified with 1N hydrochloric acid, and the precipitate was collected by filtration to give the object compound (845.5 mg) as a pale yellow solid.

mp : 181-186°C

MASS (m/z) : 258 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 7.19(2H,d,J=7.5Hz), 7.29(1H,t,J=7.5Hz), 7.43-7.53(3H,m), 7.83(1H,d,J=7.5Hz), 8.17(1H,d,J=7.5Hz)

Preparation 300

The object compound was obtained according to a similar manner to that of Preparation 5.

orange amorphous solid

MASS (m/z) : 455 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 4.85(2H,d,J=2.5Hz), 7.09(2H,d,J=7.5Hz),

7.16(1H,br t,J=2.5Hz), 7.23(1H,m), 7.37-7.48(2H,m),
7.51(1H,s), 7.61(1H,d,J=7.5Hz), 7.69(2H,d,J=7.5Hz),
7.87(2H,d,J=7.5Hz), 8.03(1H,d,J=7.5Hz)

Preparation 301

The object compound was obtained according to a similar manner to that of Preparation 2.

pale brown solid

mp : 134-136°C

MASS (m/z) : 450 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.59(3H,s), 7.12(2H,d,J=7.5Hz), 7.19(1H,s),
7.21-7.28(1H,m), 7.28(2H,d,J=7.5Hz), 7.33(1H,d,J=1.0Hz),
7.41(2H,d,J=7.5Hz), 7.53(1H,d,J=7.5Hz), 7.60(2H,d,J=7.5Hz),
8.09(1H,d,J=7.5Hz)

Preparation 302

The object compound was obtained according to a similar manner to that of Example 60.

off-white amorphous solid

MASS (m/z) : 420 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.57(3H,s), 4.03(2H,br s),
6.90(1H,d,J=7.5Hz), 7.02(2H,d,J=7.5Hz), 7.08(1H,t,J=7.5Hz),
7.11(1H,s), 7.18(1H,s), 7.23-7.36(5H,m), 7.57(2H,d,J=7.5Hz)

Preparation 303

The object compound was obtained according to a similar manner to that of Example 146 from the starting compound and benzyl bromide.

colorless oil

^{1}H-NMR ($CDCl_3$) δ : 2.18(3H,s), 3.89(3H,s), 5.19(2H,s),
6.82(1H,dd,J=8.5 and 1.5Hz), 7.27-7.43(4H,m),
7.51(2H,d,J=8.5Hz), 7.70(1H,br s), 7.83(1H,d,J=8.5Hz)

Preparation 304

The object compound was obtained according to a similar manner to that of Example 73.

colorless solid

mp : 108-111°C

MASS (m/z) : 284 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 2.07(3H,s), 5.13(2H,s), 7.19(1H,d,J=7.5Hz), 7.29-7.45(3H,m), 7.52(2H,d,J=7.5Hz), 7.55(1H,s), 7.69(1H,d,J=7.5Hz)

Preparation 305

The object compound was obtained according to a similar manner to that of Preparation 5.

off-white solid

mp : 194-197°C

MASS (m/z) : 481 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 2.06(3H,s), 4.83(2H,d,J=6.0Hz), 5.31(2H,s), 7.20(1H,d,J=8.5Hz), 7.25-7.43(4H,m), 7.53(2H,d,J=8.5Hz), 7.66(1H,s), 7.77(2H,d,J=8.5Hz), 7.84(1H,d,J=8.5Hz), 7.97(2H,d,J=8.5Hz), 8.67(1H,br t,J=6.0Hz)

Preparation 306

The object compound was obtained according to a similar manner to that of Preparation 303.

colorless oil

MASS (m/z) : 288 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.90(3H,s), 5.18(2H,s), 7.31(1H,t,J=8.5Hz), 7.34-7.43(3H,m), 7.47-7.51(2H,m), 7.93(1H,d,J=8.5Hz), 8.07(1H,d,J=8.5Hz)

Preparation 307

The object compound was obtained according to a similar manner to that of Example 73.

colorless solid

mp : 125-128°C

MASS (m/z) : 272 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 5.10(2H,s), 7.32-7.47(5H,m), 7.45(1H,t,J=8.5Hz), 8.05(1H,d,J=8.5Hz), 8.09(1H,d,J=8.5Hz)

Preparation 308

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow solid

mp : 141.5-143°C

MASS (m/z) : 467 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 4.82(2H,d,J=6.0Hz), 5.18(2H,s), 7.33-7.42(5H,m), 7.44(1H,t,J=8.5Hz), 7.78(2H,d,J=8.5Hz), 7.83(1H,d,J=8.5Hz), 7.99(2H,d,J=8.5Hz), 8.02(1H,d,J=8.5Hz), 9.01(1H,br t,J=6.0Hz)

Preparation 309

The object compound was obtained according to a similar manner to that of Preparation 2.

brown amorphous solid

MASS (m/z) : 464 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.30(3H,s), 4.78(2H,s), 7.09-7.69(9H,m), 7.82(1H,d,J=8.5Hz), 7.98(2H,d,J=8.5Hz), 8.27(1H,d,J=8.5Hz)

Preparation 310

The object compound was obtained according to a similar manner to that of Example 60.

brown oil

MASS (m/z) : 434 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.41(3H,s), 4.63(2H,s), 6.90-7.66(10H,m), 7.99(1H,d,J=8.5Hz), 8.34(2H,d,J=8.5Hz)

Preparation 311

The object compound was obtained according to a similar manner to that of Preparation 298.

pale brown oil

^{1}H-NMR ($CDCl_3$) δ : 2.60(3H,s), 6.83(1H,d,J=7.5Hz), 6.85(1H,s), 7.08(2H,d,J=7.5Hz), 7.23(1H,t,J=7.5Hz), 7.42(2H,t,J=7.5Hz), 8.06(1H,d,J=7.5Hz)

Preparation 312

The object compound was obtained according to a similar manner to

that of Preparation 299.

pale yellow solid

mp : 142-144°C

MASS (m/z) : 258 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 7.16-7.25(4H,m), 7.32(1H,t,J=7.5Hz), 7.50(2H,t,J=7.5Hz), 8.08(1H,d,J=7.5Hz)

Preparation 313

The object compound was obtained according to a similar manner to that of Preparation 5.

off-white solid

mp : 160-163.5°C

MASS (m/z) : 453 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 4.76(2H,d,J=6.0Hz), 7.09(1H,d,J=1.5Hz), 4.17(1H,dd,J=8.5 and 1.5Hz), 7.22(2H,d,J=8.5Hz), 7.33(1H,t,J=8.5Hz), 7.53(2H,t,J=8.5Hz), 7.78(2H,d,J=8.5Hz), 7.94(2H,d,J=8.5Hz), 8.13(1H,d,J=8.5Hz), 9.07(1H,t,J=6.0Hz)

Preparation 314

The object compound was obtained according to a similar manner to that of Preparation 2.

yellow amorphous solid

MASS (m/z) : 450 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.41(3H,s), 7.10-7.19(4H,m), 7.21(1H,s), 7.24-7.33(1H,m), 7.30(2H,d,J=8.5Hz), 7.45(2H,t,J=8.5Hz), 7.60(2H,d,J=8.5Hz), 8.22(1H,d,J=8.5Hz)

Preparation 315

The object compound was obtained according to a similar manner to that of Example 60.

off-white amorphous solid

MASS (m/z) : 420 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.55(3H,s), 6.80(1H,d,J=8.5Hz), 6.91-6.98(4H,m), 7.02(1H,t,J=8.5Hz),7.21(1H,s), 7.23-7.32(4H,m), 7.59(2H,d,J=8.5Hz)

Preparation 316

The object compound was obtained according to a similar manner to that of Preparation 303.

pale orange solid

mp : 90.5-91.5°C

^{1}H-NMR ($CDCl_3$) δ : 3.96(3H,s), 5.28(2H,s), 7.30-7.49(5H,m), 7.70(1H,d,J=7.5Hz), 7.83(1H,d,J=2.5Hz), 7.85(1H,d,J=7.5Hz)

Preparation 317

The object compound was obtained according to a similar manner to that of Example 73.

off-white solid

mp : 207-210°C

MASS (m/z) : 272 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 5.40(2H,s), 7.31-7.49(5H,m), 7.65(1H,d,J=8.5Hz), 7.87(1H,s), 7.99(1H,d,J=8.5Hz)

Preparation 318

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow solid

mp : 171-174°C

MASS (m/z) : 467 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 4.90(2H,d,J=2.5Hz), 5.32(2H,s), 7.31-7.51(6H,m), 7.70(2H,d,J=8.5Hz), 7.72(1H,d,J=1.5Hz), 7.90(2H,d,J=8.5Hz), 7.91(1H,d,J=8.5Hz)

Preparation 319

The object compound was obtained according to a similar manner to that of Preparation 2.

pale yellow solid

mp : 142-144°C

MASS (m/z) : 464 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.59(3H,s), 5.32(2H,s), 7.23-7.52(9H,m), 7.56(1H,s), 7.61(2H,d,J=8.5Hz), 7.99(1H,d,J=8.5Hz)

Preparation 320

The object compound was obtained according to a similar manner to that of Example 60.

pale orange amorphous solid

MASS (m/z) : 434 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.56(3H,s), 4.03(2H,br s), 5.17(2H,s), 6.80(1H,d,J=8.5Hz), 7.08(1H,d,J=8.5Hz), 7.17(1H,s), 7.24-7.48(6H,m), 7.30(2H,d,J=8.5Hz), 7.57(2H,d,J=8.5Hz)

Preparation 321

Trifluoromethanesulfonic anhydride (3.15 g) in dichloromethane (10 ml) was added dropwise, with stirring, over 10 minutes to the starting compound (2.0 g) and 4-dimethylaminopyridine (1.49 g) in dichloromethane (40 ml) at 0°C under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 2.5 hours, then washed with 1N hydrochloric acid, water, and a saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was washed with diethyl ether to give the object compound (3.11 g) as an off-white solid.

mp : 90-93.5°C

MASS (m/z) : 328 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 4.01(3H,s), 8.09(1H,s), 8.22(2H,s)

Preparation 322

A mixture of the starting compound (1.5 g), phenylboric acid (1.11 g), tetrakis(triphenylphosphine)palladium(0) (158 mg), potassium carbonate (945 mg), and toluene (30 ml) was heated at 80°C for 1 hour under a nitrogen atmosphere. After the mixture was allowed to cool to room temperature, ethyl acetate and water were added to the mixture. The suspension was filtered through a celite pad. The aqueous layer was separated, and the organic layer was washed with a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column

chromatography over silica gel with a n-hexane/ethyl acetate (10:1) as eluent to give the object compound (1.15 g) as a pale yellow wax.

mp : 51-53°C

^{1}H-NMR ($CDCl_3$) δ : 3.97(3H,s), 7.31-7.37(2H,m), 7.43-7.49(3H,m), 7.86(1H,d,J=8.5Hz), 8.13(1H,d,J=8.5Hz), 8.14(1H,s)

Preparation 323

The object compound was obtained according to a similar manner to that of Example 73.

pale yellow solid

mp : 224-227°C

MASS (m/z) : 242 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 7.37-7.43(2H,m), 7.46-7.53(3H,m), 8.00(1H,s), 8.07-8.17(2H,m)

Preparation 324

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow amorphous solid

MASS (m/z) : 437 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 4.94(2H,d,J=3.0Hz), 7.31(1H,br t,J=3.0Hz), 7.32-7.39(2H,m), 7.42-7.50(3H,m), 7.70(2H,d,J=8.5Hz), 7.89(2H,d,J=8.5Hz), 7.42-7.50(3H,m)

Preparation 325

The object compound was obtained according to a similar manner to that of Preparation 2.

off-white solid

mp : 156-159°C

MASS (m/z) : 434 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.73(3H,s), 7.24(1H,s), 7.28-7.47(5H,m), 7.32(2H,d,J=8.5Hz), 7.61(2H,d,J=8.5Hz), 7.81(1H,d,J=8.5Hz), 7.82(1H,s), 8.00(1H,d,J=8.5Hz)

Preparation 326

The object compound was obtained according to a similar manner to

that of Example 60.

pale yellow solid

mp : 176-178.5°C

MASS (m/z) : 404 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.67(3H,s), 3.97(2H,br s),
6.84(1H,d,J=8.5Hz), 7.17(1H,s),7.31(2H,d,J=8.5Hz),
7.31-7.40(1H,m), 7.42-7.52(6H,m), 7.59(2H,d,J=8.5Hz)

Preparation 327

Sodium hydride (60%, 1.92 g) was added portionwise to a solution of the starting compound (4.0 g) in anhydrous N,N-dimethylformamide (40 ml) at 0°C under a nitrogen atmosphere. The mixture was stirred at 0°C for 30 minutes. Then benzyl bromide (5.7 ml) was added dropwise at 0°C, and the mixture was stirred at room temperature for 3 hours. The reaction mixture was poured into ice-water, and the product was extracted with ethyl acetate. The organic layer was washed with a saturated sodium hydrogencarbonate solution, water and a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* . The residue (6.39 g), 1N sodium hydroxide solution (22.8 ml) and ethyl alcohol (50 ml) were combined. The reaction mixture was stirred at room temperature for 3 hours, and concentrated *in vacuo*. Water was added to the residue, and the aqueous solution was washed with diethyl ether. The aqueous layer was acidified to pH3.5 with 1N hydrochloric acid, and extracted with ethyl acetate. The combined extracts were dried over anhydrous magnesium sulfate and concentrated *in vacuo* to give the object compound (3.6 g) as a colorless oil.

MASS (m/z) : 264 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.47(9H,s),3.81(1H,s),3.96(1H,s),
4.52(2H,d,J=10.0Hz),7.19-7.41(5H,m)

Preparation 328

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow oil

MASS (m/z) : 309 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.46(9H,s), 3.17(3H,s), 3.59(3H x 2/5,s), 3.63(3H x 3/5,s), 3.94(2H x 2/5,s), 4.10(2H x 3/5,s), 4.53(2H x 3/5,s), 4.58(2H x 2/5,s), 7.19-7.39(5H,m)

Preparation 329

The object compound was obtained according to a similar manner to that of Preparation 278.

colorless oil

MASS (m/z) : 248 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.45(9H x 1/2,s), 1.49(9H x 1/2,s), 3.79(1H,s), 3.93(1H,s), 4.50(1H,s), 4.55(1H,s), 7.15-7.40(5H,m), 9.41(1H x 1/2,s), 9.50(1H x 1/2,s)

Preparation 330

The object compound was obtained according to a similar manner to that of Preparation 6.

brown oil

MASS (m/z) : 288 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 1.35(9H,s), 4.22-4.47(4H,m), 6.83(1H,s), 7.03(1H,s), 7.17-7.38(5H,s)

Preparation 331

The object compound was obtained according to a similar manner to that of Preparation 7.

MASS (m/z) : 302 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.48(9H,s), 3.59(3H,s), 4.38(1H,d,J=12.5Hz), 4.42(1H,d,J=12.5Hz), 4.56(2H,s), 6.79(1H,s), 6.94(1H,s), 7.15-7.37(5H,m)

Preparation 332

The object compound was obtained according to a similar manner to that of Preparation 297.

off-white solid

mp : 230-233°C

MASS (m/z) : 202 $(M+H)^+$

^{1}H-NMR ($DMSO-d_6$) δ : 3.94(3H,s), 4.33(2H,s), 4.55(2H,s), 7.38-7.49(4H,m), 7.57-7.65(2H,m), 7.70-7.75(2H,m)

Preparation 333

To a precooled solution of the starting compound (400 mg) in N,N-dimethylformamide (4 ml) was added 85% potassium hydroxide powder (91.9 mg). After the mixture was stirred for 1 hour on an ice bath, benzyl bromide (0.174 ml) was added dropwise to the reaction mixture. The reaction mixture was stirred for 7 hours at room temperature, then poured into water, and extracted with chloroform. The organic layer was washed with water (twice) and a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography over silica gel with a chloroform-methanol (60:1) as eluent to give the object compound (556.6mg) as a yellow oil.

MASS (m/z) : 378 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.38(9H,s), 4.38(2H,s), 4.57(2H,s), 5.22(2H,s), 6.83(1H,s), 6.98-7.06(3H,m), 7.21-7.40(8H,m)

Preparation 334

The object compound was obtained according to a similar manner to that of Preparation 297.

yellow oil

MASS (m/z) : 278 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.78(2H,s), 3.80(2H,s), 5.18(2H,s), 6.85(1H,s), 6.98(1H,s), 7.01-7.07(2H,m), 7.20-7.38(9H,m)

Preparation 335

The object compound was obtained according to a similar manner to that of Preparation 91.

dark brown oil

MASS (m/z) : 352 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.37(9H,s), 3.02(1H,dd,J=13.5 and 6.0Hz), 3.15(3H,s), 3.23(1H,dd,J=13.5 and 6.0Hz), 3.71(3H,s),

3.93(1H,d,J=17.5Hz), 4.28(1H,d,J=17.5Hz), 5.11(1H,m), 5.46(1H,m), 7.12(1H,m), 7.18(1H,d,J=7.5Hz), 7.59(1H,m), 8.54(1H,d,J=4.0Hz)

Preparation 336

The object compound was obtained according to a similar manner to that of Example 73.

brown amorphous solid

MASS (m/z) : 338 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.19(9H,s), 2.80(1H,dd,J=13.5 and 10.5Hz), 3.08(3H,s), 3.35(1H,dd,J=13.5 and 10.5Hz), 4.01(1H,d,J=17.5Hz), 5.06(1H,m), 5.13(1H,d,J=17.5Hz), 5.67(1H,d,J=9.0Hz), 7.21-7.38(2H,m), 7.75(1H,m), 8.66(1H,d,J=5.5Hz)

Preparation 337

The starting compound (1.3 g), N-(4-nitrophenylmethylene)benzenesulfonamide (1.68 g) and toluene (6 ml) were mixed, and then N,N-dicyclohexylcarbodiimide (954 mg) in toluene (4 ml) was added to the mixture. The reaction mixture was stirred at 60°C for 15 hours under a nitrogen atmosphere. The suspension was filtered and the solvent was evaporated *in vacuo*. The residue was taken up in chloroform, washed with a saturated sodium hydrogencarbonate solution (twice) and a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography over silica gel with a chloroform-methanol gradient (30:1 and 20:1) as eluent to give the object compound (919.6 mg) as a brown amorphous solid.

MASS (m/z) : 424 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.37(9H,s), 3.41-3.52(2H,m), 4.06(3H,s), 4.93(1H,m), 7.09-8.33(5H,m), 7.53(2H,d,J=7.5Hz), 7.93(2H,d,J=7.5Hz), 8.52(1H,m)

Preparation 338

The object compound was obtained according to a similar manner to

that of Preparation 3.

brown amorphous solid

MASS (m/z) : 324 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.12(1H,m), 3.42(1H,m), 3.63(3H,s), 5.12(1H,m), 7.11-8.23(8H,m), 8.46-8.59(1H,m)

Preparation 339

The object compound was obtained according to a similar manner to that of Preparation 247.

colorless solid

mp : 160.5-161°C

MASS (m/z) : 137 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.28(3H,s), 7.57(2H,d,J=5.5Hz), 8.65(2H,d,J=5.5Hz), 9.85(1H,s)

Preparation 340

The object compound was obtained according to a similar manner to that of Preparation 248.

off-white solid

mp : 74-76°C

MASS (m/z) : 291 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.34(3H,s), 2.46(3H,s), 7.37(2H,d,J=8.5Hz), 7.46(2H,d,J=6.0Hz), 7.93(2H,d,J=8.5Hz), 8.64(2H,d,J=6.0Hz)

Preparation 341

The object compound was obtained according to a similar manner to that of Preparation 249.

pale brown solid

mp : 192-194°C

^{1}H-NMR (DMSO-d_6) δ : 4.64(2H,q,J=5.5Hz), 7.96(2H,d,J=7.0Hz), 8.50(2H,m), 8.91(2H,d,J=7.0Hz)

Preparation 342

The object compound was obtained according to a similar manner to that of Preparation 91.

brown oil

MASS (m/z) : 385 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.43(9H,s), 3.36(2H,d,J=5.5Hz),
4.70(2H,d,J=5.5Hz), 4.73(1H,m), 6.40(1H,m), 7.19-7.29(1H,m),
7.56(1H,d,J=7.0Hz), 7.68(1H,t,J=7.0Hz), 7.71(2H,d,J=5.5Hz),
8.55(1H,t,J=7.0Hz), 8.61(1H,d,J=7.0Hz), 8.81(2H,d,J=5.5Hz)

Preparation 343

The object compound was obtained according to a similar manner to that of Preparation 2.

brown oil

MASS (m/z) : 380 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.37(9H,s), 3.45(1H,dd,J=13.5 and 7.5Hz),
3.55(1H,dd,J=13.5 and 7.5Hz), 3.59(3H,s), 5.49(1H,m),
5.69(1H,m), 7.09-7.17(2H,m), 7.17(1H,s), 7.22(2H,d,J=5.5Hz),
7.56(1H,t,J=7.5Hz), 8.51(1H,m), 8.63(2H,d,J=5.5Hz)

Preparation 344

The object compound was obtained according to a similar manner to that of Preparation 3.

brown oil

MASS (m/z) : 280 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.43(2H,t,J=7.0Hz), 3.66(3H,s),
4.72(1H,t,J=7.0Hz), 7.12-7.19(2H,m), 7.19(1H,s),
7.25(2H,d,J=5.5Hz), 7.61(1H,t,J=7.0Hz), 8.58(1H,d,J=7.0Hz),
8.63(2H,d,J=5.5Hz)

Preparation 345

The starting compound (230 mg) was dissolved in absolute ethanol (11.5 ml) under an atmosphere of nitrogen. Sodium ethoxide (1M solution) in ethanol (1.17 ml) was added to the solution at room temperature. To the mixture was added a solution of ethyl 4-(dimethylamino)-2-oxo-3-butenoate (240.4 mg) in absolute ethanol (1.5 ml). The reaction mixture was then stirred at 50°C for 2 hours. The reaction mixture was refluxed for 30 minutes. After cooling the solution, sodium chloride was filtered off. The filtrate was

concentrated *in vacuo*, and the residue was purified by flash column chromatography over silica gel with a chloroform-methanol (40:1) as eluent to give the object compound (170.7 mg) as a dark blue solid.

mp : 95-98°C

MASS (m/z) : 269 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.51(3H,t,J=7.0Hz), 4.53(2H,q,J=7.0Hz), 7.30(1H,t,J=7.5Hz), 7.41(1H,t,J=7.5Hz), 7.67(1H,d,J=7.5Hz), 7.71(1H,d,J=7.5Hz), 7.85(1H,s), 7.88(1H,d,J=5.5Hz), 9.06(1H,d,J=5.5Hz)

Preparation 346

The object compound was obtained according to a similar manner to that of Preparation 51.

off-white solid

mp : 211-218°C

MASS (m/z) : 239 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 7.36(1H,t,J=7.5Hz), 7.48(1H,t,J=7.5Hz), 7.78(1H,d,J=7.5Hz), 7.81(1H,d,J=7.5Hz), 7.87(1H,s), 7.90(1H,d,J=5.5Hz), 9.13(1H,d,J=5.5Hz)

Preparation 347

The object compound was obtained according to a similar manner to that of Preparation 5.

pale yellow oil

MASS (m/z) : 425 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 2.31(3H,s), 2.97-3.19(2H,m), 3.63-3.75(1H,m), 3.70(3H,s), 4.37(1H,m), 7.00-7.42(11H,m)

Preparation 348

The object compound was obtained according to a similar manner to that of Example 73 except that a mixture of methanol and 1,4-dioxane was used instead of 1,4-dioxane.

colorless solid

mp : 74-78°C

MASS (m/z) : 411 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 1.30(9H,s), 2.67-3.03(5H,m),
4.13-4.35(1H,m), 5.33-5.37(1H,m), 7.06-7.49(10H,m)

Preparation 349

The object compound was obtained according to a similar manner to that of Preparation 337.

pale yellow oil

MASS (m/z) : 454 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.43(9H,s), 2.74(3H,s),
3.20(1H,dd,J=13.5 and 6.0Hz), 3.40(1H,dd,J=13.5 and 6.0Hz),
5.13(1H,m), 5.77(1H,d,J=7.5Hz), 7.03-8.03(15H,m)

Preparation 350

The object compound was obtained according to a similar manner to that of Preparation 3.

off-white amorphous solid

MASS (m/z) : 354 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.99(3H,s), 3.24(1H,dd,J=13.5 and 7.5Hz),
3.46(1H,dd,J=13.5 and 7.5Hz), 5.02(1H,m), 7.05-7.69(15H,m)

Preparation 351

The object compound was obtained according to a similar manner to that of Preparation 91.

amorphous solid

MASS : 482 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.42(9H,s), 2.34(3H,s), 2.53(4H,t,J=4Hz),
3.19-3.30(1H,m), 3.30-3.42(1H,m), 3.39(4H,t,J=4Hz),
4.59(2H,d,J=2Hz), 4.62-4.73(1H,m), 6.39(1H,br s),
6.84(2H,d,J=8Hz), 7.11(1H,t,J=4Hz), 7.19(1H,d,J=7Hz),
7.59(1H,d,J=8Hz), 7.81(3H,d,J=8Hz), 8.52(1H,d,J=2Hz)

Preparation 352

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS : 477 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.38(9H,s), 2.38(3H,s), 2.50-2.61(4H,m),
3.27(3H,t,J=4Hz), 3.32-3.48(2H,m), 3.39(3H,s),
5.32-5.41(1H,m), 5.42-5.50(1H,m), 6.39(1H,br s),
6.88(1H,d,J=8Hz), 6.91(1H,s), 6.93(1H,d,J=8Hz),
7.08-7.20(3H,m), 7.50-7.62(1H,m), 7.83(1H,d,J=8Hz),
8.52(1H,t,J=4Hz)

Preparation 353

The object compound was obtained according to a similar manner to that of Preparation 3.

oil

MASS : 377 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.38(3H,s), 2.59-2.68(4H,m),
3.20-3.30(4H,m), 3.31-3.52(2H,m), 3.48(3H,s),
4.60(1H,dd,J=12Hz and 7Hz), 6.88(1H,t,J=8Hz),
6.97(2H,d,J=8Hz), 6.98(1H,s), 7.10-7.20(1H,m),
7.21(2H,d,J=8Hz), 7.59(1H,t,J=8Hz), 8.59(1H,d,J=4Hz)

Preparation 354

The object compound was obtained according to a similar manner to that of Preparation 297.

mp : 253-256°C

^{1}H-NMR (DMSO-d_6) δ : 3.80-4.03(2H,m), 3.88(3H,s),
5.54(1H,t,J=6Hz), 7.65(1H,t,J=5Hz), 7.69-7.85(4H,m),
7.98-8.08(3H,m), 8.16(1H,t,J=8Hz), 8.40(1H,s),
8.69(1H,d,J=5Hz)

Preparation 355

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 182-185°C

MASS : 536 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.40(9H,s), 2.51-2.68(1H,m),
2.70-2.81(1H,m), 4.41-4.52(1H,m), 4.54-4.77(2H,m), 5.97(2H,s),
6.81(1H,d,J=8Hz), 6.92(1H,dd,J=8Hz and 2Hz), 7.11(1H,d,J=8Hz),

7.17(1H,s), 7.30(1H,s), 7.84(2H,d,J=8Hz), 7.90(1H,s),
8.11(2H,d,J=8Hz), 8.12(1H,s), 8.48(1H,s), 9.82(1H,s)

Preparation 356

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS : 529 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 1.40(9H,s), 2.70-2.83(1H,m),
3.12-3.25(1H,m), 3.61(3H,s), 5.19(1H,q,J=8Hz), 5.92(2H,s),
6.81(1H,d,J=8Hz), 6.92(1H,d,J=8Hz), 7.00(1H,s), 7.11(1H,s),
7.29(1H,s), 7.48(1H,d,J=8Hz), 7.59(2H,d,J=8Hz),
7.73(2H,d,J=8Hz), 7.80(1H,s), 8.31(1H,s), 9.93(1H,s)

Preparation 357

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 431 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.91-3.10(2H,m), 3.67(3H,s),
4.51(1H,t,J=8Hz), 5.90(2H,s), 6.70(1H,d,J=8Hz),
6.83(1H,d,J=8Hz), 7.06(1H,s), 7.26(1H,s), 7.20-7.29(2H,m),
7.40-7.58(4H,m), 7.90(1H,s), 9.72(1H,s)

Preparation 358

The object compound was obtained according to a similar manner to that of Preparation 91.

mp : 129-132°C

MASS : 460 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.29(9H,s), 2.90-3.11(1H,m),
3.17-3.23(1H,m), 4.47-4.55(1H,m), 4.56-4.78(2H,m),
7.09(1H,d,J=8Hz), 7.20(1H,t,J=8Hz), 7.30(1H,d,J=8Hz),
7.40-7.58(3H,m), 7.70(1H,t,J=8Hz), 7.78(2H,d,J=8Hz),
7.85(2H,d,J=8Hz), 8.09(2H,d,J=8Hz), 8.21(1H,t,J=6Hz),
8.50(1H,d,J=4Hz)

Preparation 359

The object compound was obtained according to a similar manner to that of Preparation 2.

solid

MASS : 455 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.30(9H,s), 3.20-3.30(1H,m), 3.33-3.47(1H,m), 3.59(3H,s), 5.30(1H,q,J=8Hz), 7.00(1H,s), 7.15-7.30(3H,m), 7.33-7.58(4H,m), 7.61-7.80(4H,m), 7.82(1H,d,J=8Hz), 8.09(1H,d,J=8Hz), 8.50(1H,d,J=4Hz)

Preparation 360

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 355 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.10-3.20(1H,m), 3.28-3.38(1H,m), 3.60(3H,s), 4.48(1H,t,J=8Hz), 6.99(1H,s), 7.18-7.30(2H,m), 7.36-7.59(4H,m), 7.60-7.80(6H,m), 8.51(1H,d,J=2Hz)

Preparation 361

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 180-185°C

MASS : 522 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.40(9H,s), 2.52-2.68(1H,m), 2.70-2.81(1H,m), 3.70(3H,s), 4.49(1H,q,J=8Hz), 4.55-4.78(2H,m), 6.86(2H,d,J=8Hz), 7.11(1H,d,J=8Hz), 7.18(1H,s), 7.50(2H,d,J=8Hz), 7.87(2H,d,J=8Hz), 7.91(1H,s), 8.11(2H,d,J=8Hz), 8.11(1H,s), 8.45(1H,s), 9.75(1H,s)

Preparation 362

The object compound was obtained according to a similar manner to that of Preparation 2.

mp : 187-193°C

MASS : 517 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.41(9H,s), 2.70-2.81(1H,m),
3.15-3.28(1H,m), 3.61(3H,s), 3.69(3H,s), 5.30(1H,q,J=8Hz),
6.83(2H,d,J=8Hz), 7.00(1H,s), 7.11(1H,s), 7.48(1H,s),
7.50(2H,d,J=8Hz), 7.58(2H,d,J=8Hz), 7.73(2H,d,J=8Hz),
7.81(1H,s), 8.31(1H,s), 9.90(1H,s)

Preparation 363

The object compound was obtained according to a similar manner to that of Preparation 8.

solid

MASS : 415 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 2.73-2.85(1H,m), 2.90-3.00(1H,m),
3.71(3H,s), 3.72(3H,s), 4.41(1H,t,J=8Hz), 6.87(2H,d,J=8Hz),
6.99(1H,s), 7.11(1H,s), 7.50(2H,d,J=8Hz), 7.58(2H,d,J=8Hz),
7.76(2H,d,J=8Hz), 7.81(1H,s), 8.31(1H,s)

Preparation 364

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS : 473 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.21(3H,d,J=8Hz), 1.28(3H,d,J=8Hz),
1.37(9H,s), 3.72(2H,q,J=8Hz), 4.70(1H,d,J=2Hz),
4.11(1H,q,J=8Hz), 5.78(1H,br s), 7.09(1H,s), 7.11-7.70(8H,m),
7.93(1H,d,J=8Hz), 8.09(1H,d,J=8Hz), 8.52(1H,dd,J=8Hz and 2Hz)

Preparation 365

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 373 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.37(3H,d,J=8Hz), 1.43(3H,d,J=8Hz),
3.32-3.42(1H,m), 3.43-3.53(1H,m), 4.59-4.60(1H,m),
4.72-4.81(1H,m), 6.99(1H,s), 7.11-7.72(7H,m), 7.83(1H,s),
7.89(1H,s), 7.90(1H,s), 8.58(1H,d,J=2Hz)

Preparation 366

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

MASS : 487 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.79(3H,t,J=7Hz), 1.08-1.20(2H,m), 1.30-1.40(2H,m), 1.40(9H,s), 3.40-3.60(2H,m), 3.80-4.01(2H,m), 5.35-5.50(1H,m), 5.41(1H,br s), 7.00(1H,s), 7.11(1H,d,J=7Hz), 7.13(1H,d,J=7Hz), 7.23(1H,s), 7.32(1H,s), 7.41(2H,d,J=8Hz), 7.48(2H,d,J=8Hz), 7.59(1H,t,J=8Hz), 7.90(1H,s), 8.53(1H,d,J=4Hz)

Preparation 367

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 387 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.79(3H,t,J=8Hz), 1.09-1.21(2H,m), 1.31-1.55(2H,m), 3.28-3.40(1H,m), 3.41-3.51(1H,m), 3.80-4.01(2H,m), 4.58(1H,t,J=8Hz), 7.03(1H,s), 7.12(2H,d,J=8Hz), 7.22(2H,d,J=8Hz), 7.31(1H,s), 7.38-7.50(3H,m), 7.59(1H,t,J=8Hz), 7.90(1H,s), 8.59(1H,d,J=4Hz)

Preparation 368

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

MASS : 501 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.79(3H,t,J=8Hz), 1.00-1.20(4H,m), 1.37(9H,s), 1.43-1.52(2H,m), 3.39-3.58(2H,m), 3.80-4.00(2H,m), 5.30-5.50(2H,m), 7.00(1H,s), 7.11(2H,d,J=8Hz), 7.22(1H,s), 7.31(1H,s), 7.38-7.50(4H,m), 7.50-7.60(1H,m), 7.91(1H,s), 8.52(1H,d,J=2Hz)

Preparation 369

The object compound was obtained according to a similar manner to that of Preparation 8.

oil

MASS : 401 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.77(3H,t,J=8Hz), 1.01-1.20(4H,m), 1.38-1.57(2H,m), 3.33-3.53(2H,m), 3.80-4.09(2H,m), 4.62(1H,t,J=8Hz), 7.02(1H,s), 7.10-7.20(2H,m), 7.22(1H,s), 7.31(1H,s), 7.41(2H,d,J=6Hz), 7.49(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.91(1H,s), 8.59(1H,d,J=8Hz)

Preparation 370

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS : 471 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(9H,s), 1.43-1.52(4H,m), 3.22-3.30(1H,m), 3.40-3.49(1H,m), 3.43-3.49(1H,m), 5.55(1H,d,J=8Hz), 5.72(1H,d,J=8Hz), 7.00(1H,s), 7.07-7.70(8H,m), 7.98(1H,s), 8.09(1H,d,J=8Hz), 8.59(1H,s)

Preparation 371

The object compound was obtained according to a similar manner to that of Preparation 8.

MASS : 371 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.90-1.10(4H,m), 3.30-3.45(2H,m), 3.60(1H,q,J=8Hz), 4.91(1H,t,J=8Hz), 7.03(1H,s), 7.09-7.60(9H,m), 7.90(1H,s), 8.60(1H,d,J=2Hz)

Preparation 372

To a solution of methyl indole-6-carboxylate (300 mg) in methanol (20 ml) was added 1N aqueous sodium hydroxide solution (6 ml) at 0°C. The solution was stirred at room temperature for 2 hours. After evaporation of solvent, the residue was dissolved in water and acidified with 1N hydrochloric acid. The precipitate was dried to give indole-6-carboxylic acid as colorless crystals (204 mg).

mp : 250-255°C

MASS : 162 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 6.50-6.53(1H,m), 7.55-7.59(1H,m), 7.60(2H,s), 8.08(1H,s)

Preparation 373

The object compound was obtained according to a similar manner to that of Preparation 2.

MASS : 485 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(9H,s), 1.65-1.89(2H,m), 2.10-2.30(2H,m), 2.30-2.50(2H,m), 3.22-3.32(1H,m), 3.40-3.43(1H,m), 4.48-4.62(1H,m), 5.43-5.50(2H,m), 6.93(1H,s), 7.07-7.70(8H,m), 7.91(1H,s), 8.09(1H,d,J=8Hz), 8.59(1H,s)

Preparation 374

The object compound was obtained according to a similar manner to that of Preparation 8.

MASS : 385 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.61-1.80(2H,m), 2.20-2.42(4H,m), 3.28-3.38(1H,m), 3.41-3.50(1H,m), 4.60-4.73(2H,m), 6.98(1H,s), 7.10-7.20(2H,m), 7.22(1H,s), 7.31(1H,s), 7.39(2H,d,J=8Hz), 7.41(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.90(1H,s), 8.60(1H,d,J=2Hz)

Preparation 375

The object compound was obtained according to a similar manner to that of Preparation 91.

amorphous solid

ESI-MS : 450 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.45(9H,s), 3.21-3.44(2H,m), 4.61-4.79(3H,m), 6.42(1H,d,J=8Hz), 7.11-7.30(3H,m), 7.34(1H,s), 7.51(2H,d,J=8Hz), 7.55-7.68(1H,m), 7.96(1H,s), 8.01(1H,s), 8.07(2H,d,J=8Hz), 8.55(1H,d,J=5Hz),

Preparation 376

The object compound was obtained according to a similar manner to

that of Preparation 2.

oil

ESI-MS : 445 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.37(9H,s), 3.40-3.52(2H,m), 3.51(3H,m), 5.35-5.55(3H,m), 7.05(1H,s), 7.08-7.18(2H,m), 7.22(1H,s), 7.31(1H,s), 7.33-7.63(5H,m), 7.89(1H,s), 8.53(1H,d,J=5Hz)

Preparation 377

The object compound was obtained according to a similar manner to that of Preparation 4.

oil

ESI-MS : 345 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.75-2.10(2H,br s), 3.28-3.51(2H,m), 3.58(3H,s), 4.64(1H,t,J=6Hz), 7.08(1H,s), 7.10-7.21(2H,m), 7.23(1H,s), 7.31(1H,s), 7.38-7.51(4H,m), 7.54-7.65(1H,m), 7.89(1H,s), 8.58(1H,d,J=5Hz)

Preparation 378

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

ESI-MS : 450 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.42(9H,s), 3.00-3.37(2H,m), 4.58(1H,br s), 4.65-4.85(2H,m), 5.08(1H,d,J=6Hz), 7.07(1H,br s), 7.18(2H,d,J=8Hz), 7.38(1H,s), 7.55(2H,d,J=8Hz), 7.98(1H,s), 8.10(2H,d,J=8Hz), 8.55(2H,d,J=8Hz)

Preparation 379

The object compound was obtained according to a similar manner to that of Preparation 2.

oil

ESI-MS : 445 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(9H,s), 3.29(3H,s), 3.38(2H,d,J=8Hz), 5.15(1H,q,J=8Hz), 5.62(1H,d,J=8Hz), 7.10(2H,d,J=8Hz), 7.12(1H,s), 7.25(1H,s), 7.32(1H,s), 7.39(2H,d,J=8Hz),

7.48(2H,d,J=8Hz), 7.91(1H,s), 8.50(2H,d,J=8Hz)

Preparation 380

The object compound was obtained according to a similar manner to that of Preparation 4.

oil

ESI-MS : 345 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.15-3.40(5H,m), 4.28(1H,t,J=6Hz), 7.05-7.13(3H,m), 7.25(1H,s), 7.32(1H,s), 7.38-7.52(4H,m), 7.90(1H,s), 8.51(2H,d,J=4Hz)

Preparation 381

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

ESI-MS : 479 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.48(9H,s), 3.65(2H,dd,J=6Hz and 10Hz), 4.59(2H,d,J=6Hz), 4.79(2H,d,J=6Hz), 5.45(1H,br s), 7.18-7.40(6H,m), 7.48(1H,br s), 7.55(2H,d,J=8Hz), 8.00(1H,s), 8.12(2H,d,J=8Hz)

Preparation 382

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

ESI-MS : 474 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.45(9H,s), 3.64(3H,s), 3.35-4.03(2H,m), 4.54(2H,s), 5.22(1H,br s), 7.12(1H,s), 7.20-7.38(8H,m), 7.48(2H,d,J=4Hz), 7.91(1H,s)

Preparation 383

The object compound was obtained according to a similar manner to that of Preparation 4.

amorphous solid

ESI-MS : 382 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.66(3H,s), 3.88(2H,d,J=6Hz), 4.60(2H,s),

7.08(1H,s), 7.18-7.40(8H,m), 7.46(2H,s), 7.90(1H,s)

Preparation 384

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

ESI-MS : 433 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.48(9H,s), 1.90-2.24(2H,m), 2.14(3H,s), 2.63(2H,t,J=6Hz), 4.42(1H,br s), 4.80(2H,t,J=4Hz), 5.28(1H,br s), 7.20(1H,s), 7.38(1H,s), 7.55(2H,d,J=8Hz), 7.99(1H,s), 8.12(2H,d,J=8Hz)

Preparation 385

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

ESI-MS : 429 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.47(9H,s), 2.02-2.40(2H,m), 2.13(3H,s), 2.55-2.80(2H,m), 3.69(3H,s), 4.23(1H,t,J=6Hz), 7.07(1H,s), 7.25(1H,s), 7.34(1H,s), 7.49(4H,s), 7.91(1H,s)

Preparation 386

The object compound was obtained according to a similar manner to that of Preparation 4.

ESI-MS : 328 (M+1)

Preparation 387

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

ESI-MS : 474 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.75(3H,t,J=6Hz), 1.38(9H,s), 1.40-1.65(2H,m), 3.53-3.83(2H,m), 3.93-4.07(2H,m), 4.72(1H,d,J=6Hz), 5.60(1H,q,J=6Hz), 7.13(1H,s), 7.24(2H,d,J=8Hz), 7.46(2H,d,J=8Hz), 7.60(1H,t,J=8Hz), 7.80(2H,d,J=8Hz), 8.15(1H,s), 8.50-8.54(1H,m), 8.63(1H,s)

Preparation 388

The object compound was obtained according to a similar manner to that of Preparation 4.

amorphous solid

ESI-MS : 374 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.75(3H,t,J=6Hz), 1.37-1.65(2H,m), 3.48(2H,d,J=6Hz), 3.80-4.10(2H,m), 4.71(1H,t,J=6Hz), 7.08(1H,s), 7.13-7.23(2H,m), 7.48(2H,d,J=8Hz), 7.62(1H,t,J=8Hz), 7.75(2H,d,J=8Hz), 8.14(1H,s), 8.04-8.60(1H,m), 8.61(1H,s)

Preparation 389

The object compound was obtained according to a similar manner to that of Preparation 91.

amorphous solid

ESI-MS : 450 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.45(9H,s), 3.21-3.44(2H,m), 4.61-4.79(3H,m), 6.42(1H,d,J=8Hz), 7.11-7.30(3H,m), 7.34(1H,s), 7.51(2H,d,J=8Hz), 7.55-7.68(1H,m), 7.96(1H,s), 8.01(1H,s), 8.07(2H,d,J=8Hz), 8.55(1H,d,J=5Hz)

Preparation 390

The object compound was obtained according to a similar manner to that of Preparation 2.

amorphous solid

ESI-MS : 473 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.70(3H,t,J=6Hz), 1.36(9H,s), 1.35-1.55(2H,m), 3.37-3.55(2H,m), 3.77-4.00(2H,m), 5.44(1H,s), 7.02(1H,s), 7.07-7.20(2H,m), 7.25(1H,s), 7.34(1H,s), 7.38-7.50(4H,m), 7.58(1H,t,J=8Hz), 7.91(1H,s), 8.55(1H,d,J=4Hz)

Preparation 391

The object compound was obtained according to a similar manner to that of Preparation 297.

ESI-MS : 373 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.65(3H,t,J=6Hz), 1.30-1.53(2H,m), 3.70-3.98(2H,m), 4.08-4.35(2H,m), 5.48(1H,t,J=6Hz), 7.55-7.63(2H,m), 7.69(1H,d,J=8Hz), 7.75(2H,d,J=8Hz), 7.99(1H,s), 8.01(2H,d,J=8Hz), 8.12(1H,t,J=8Hz), 8.40(1H,s), 8.63(1H,d,J=4Hz), 9.97(1H,s)

Example 1

To an ice-cooled solution of the starting compound (100 mg), indole-2-carboxylic acid (50 mg) and 1-hydroxybenzotriazole (41.9 mg) in dichloromethane (10 ml) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (71.4 mg). The mixture was stirred at room temperature for 12 hours. A saturated aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol=70/1) to give the object compound as white powder (50 mg).

MASS(m/z) : 466 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.43(3H,t,J=7Hz), 3.48(3H,s), 3.60(2H,m), 4.03(2H,q,J=7Hz), 5.97(1H,m), 6.91(2H,d,J=8Hz), 6.94(1H,s), 6.99(1H,s), 7.10-7.12(3H,m), 7.17(2H,d,J=8Hz), 7.37(1H,d,J=8Hz), 7.50(1H,t,J=8Hz), 7.63(1H,d,J=8Hz), 9.41(1H,s)

Example 2

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 490 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.59(3H,s), 3.63(2H,m), 6.02(1H,m), 7.00(1H,s), 7.08(1H,s), 7.11-7.16(3H,m), 7.38-7.43(3H,m), 7.52(1H,t,J=8Hz), 7.64-7.68(3H,m), 7.86(1H,m), 8.54(1H,d,J=5Hz), 9.48(1H,m)

Example 3

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 466 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.43(3H,t,J=7Hz), 3.19(3H,s), 3.43(2H,m), 4.04(2H,q,J=7Hz), 5.64(1H,m), 6.91(2H,d,J=8Hz), 7.01(2H,s), 7.05(2H,d,J=6Hz), 7.12-7.16(3H,m), 7.31(1H,d,J=8Hz), 7.41(1H,d,J=8Hz), 7.64(1H,d,J=8Hz), 8.45(2H,d,J=6Hz)

Example 4

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 453 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.84(3H,s), 6.65(1H,d,J=7Hz), 7.17(2H,m), 7.20(1H,s), 7.22(1H,m), 7.31(1H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.51(1H,d,J=8Hz), 7.53(2H,d,J=8Hz), 7.71(2H,m), 8.29(2H,d,J=8Hz), 8.41(1H,d,J=8Hz), 8.61(1H,d,J=5Hz), 9.26(1H,s)

Example 5

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 543 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.50(9H,s), 3.55(2H,m), 3.60(3H,s), 5.93(1H,q,J=7Hz), 6.97(1H,t,J=8Hz), 7.10-7.17(3H,m), 7.40-7.67(6H,m), 8.27(2H,d,J=8Hz), 8.34(1H,d,J=8Hz), 8.54(1H,d,J=4Hz)

Example 6

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 483 (M-1)

^{1}H-NMR ($CDCl_3$) δ : 2.62(3H,s), 3.45(3H,s), 3.60(2H,m), 4.28(1H,m), 7.04-7.17(2H,m), 7.40-7.59(5H,m), 7.48(2H,d,J=8Hz), 7.72(1H,m), 8.17(1H,d,J=8Hz),

8.27(2H,d,J=8Hz), 8.45(1H,d,J=5Hz)

Example 7

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 543 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.30(2H,m), 3.62(3H,s), 5.89(1H,q,J=7Hz), 6.77(1H,d,J=8Hz), 6.90(1H,d,J=8Hz), 7.07(1H,s), 7.11(2H,m), 7.29(1H,m), 7.42-7.52(10H,m), 8.24(2H,d,J=8Hz), 8.48(1H,d,J=4Hz), 9.47(1H,s)

Example 8

The object compound was obtained according to a similar manner to that of Example 1.

MASS(m/z) : 467 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.60(2H,m), 3.63(3H,s), 6.01(1H,q,J=7Hz), 6.54(1H,s), 7.08-7.17(4H,m), 7.30(1H,m), 7.48(3H,m), 7.57(1H,t,J=8Hz), 7.73(1H,m), 7.79(1H,d,J=8Hz), 8.26(2H,d,J=8Hz), 8.54(1H,d,4Hz)

Example 9

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 519 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.09(3H,s), 3.30-3.50(2H,m), 3.72(3H,s), 5.61(1H,q,J=8Hz), 6.71(2H,d,J=8Hz), 6.98(2H,d,J=8Hz), 6.99-7.13(4H,m), 7.17-7.30(2H,m), 7.38(1H,d,J=8Hz), 7.41(1H,d,J=8Hz), 7.59(1H,d,J=8Hz), 8.49(1H,d,J=8Hz)

Example 10

The object compound was obtained according to a similar manner to that of Example 1.

mp : 193-195°C

MASS : 446 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.37-3.48(2H,m), 3.60(3H,s),

5.55(1H,q,J=8Hz), 7.00(1H,t,J=8Hz), 7.10-7.30(6H,m),
7.31-7.40(3H,m), 7.60(1H,d,J=8Hz), 7.65(2H,d,J=8Hz),
7.90(2H,d,J=8Hz), 9.03(1H,d,J=8Hz)

Example 11

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 519 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.13(3H,s), 3.33-3.52(2H,m), 3.71(3H,s),
5.70(1H,q,J=8Hz), 5.72(2H,d,J=8Hz), 7.00(2H,d,J=8Hz),
7.09(1H,t,J=8Hz), 7.14(1H,s), 7.19-7.29(2H,m),
7.30-7.41(3H,m), 7.58-7.70(3H,m), 8.61(1H,d,J=8Hz)

Example 12

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 476 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.11(3H,s), 3.27-3.50(2H,m), 3.73(3H,s),
5.61(1H,q,J=8Hz), 6.71(2H,d,J=8Hz), 6.97(2H,d,J=8Hz),
7.07(1H,s), 7.10(1H,d,J=8Hz), 7.18-7.28(2H,m),
7.29-7.40(3H,m), 7.59(1H,d,J=8Hz), 7.67(2H,d,J=8Hz),
8.30(1H,d,J=8Hz)

Example 13

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 549 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.89(3H,s), 3.31-3.59(2H,m), 5.53-5.67(1H,m),
6.88(2H,d,J=8Hz), 7.00(1H,s), 7.07(1H,t,J=8Hz),
7.10-7.30(2H,m), 7.20(1H,s), 7.30-7.50(6H,m), 7.59-7.80(5H,m)

Example 14

The object compound was obtained according to a similar manner to

that of Example 1.

mp : 143-147°C

MASS : 466 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.43(3H,t,J=8Hz), 3.20(3H,s),
3.32-3.52(2H,m), 4.07(2H,q,J=8Hz), 5.61(1H,q,J=8Hz),
5.91(2H,d,J=8Hz), 7.00(2H,s), 7.10-7.20(3H,m),
7.30(1H,t,J=8Hz), 7.41(2H,d,J=8Hz), 7.63(2H,t,J=8Hz),
8.39(1H,s), 8.48(1H,d,J=4Hz), 9.40(1H,s)

Example 15

The object compound was obtained according to a similar manner to that of Example 1.

mp : 130-135°C

MASS : 467 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.29(3H,s), 3.48(2H,d,J=8Hz),
5.70(1H,q,J=8Hz), 7.00(1H,s), 7.08(2H,d,J=6Hz),
7.15(1H,t,J=8Hz), 7.24(1H,s), 7.30(1H,t,J=8Hz),
7.39-7.49(1H,m), 7.45(2H,d,J=8Hz)

Example 16

The object compound was obtained according to a similar manner to that of Example 1.

mp : 191-192°C

MASS : 543 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.06(3H,s), 3.13-3.23(1H,m), 3.37-3.48(1H,m),
3.78(3H,s), 4.01(3H,s), 5.43-5.52(1H,m), 6.80(2H,d,J=8Hz),
6.98(1H,s), 7.00(2H,d,J=8Hz), 7.05-7.20(4H,m),
7.28-7.40(3H,m), 7.52(2H,d,J=8Hz), 7.63(1H,d,J=8Hz)

Example 17

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 542 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.11(3H,s), 3.29-3.40(1H,m), 3.41-3.50(1H,m),

3.69(3H,s), 5.50-5.61(1H,m), 6.79(2H,d,J=8Hz),
7.02(2H,d,J=8Hz), 7.08-7.20(3H,m), 7.52(2H,d,J=8Hz),
7.80-7.92(2H,m), 8.12-8.22(2H,m), 8.89(1H,d,J=8Hz), 9.62(1H,s)

Example 18

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 541 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.17(3H,s), 3.30-3.51(2H,m), 3.71(3H,s),
5.49-5.62(1H,m), 6.73(2H,d,J=8Hz), 7.04(2H,d,J=8Hz),
7.09-7.20(3H,m), 7.50(2H,d,J=8Hz), 7.60(1H,t,J=8Hz),
7.78(1H,t,J=8Hz), 7.83(1H,d,J=8Hz), 8.18(1H,d,J=8Hz),
8.20-8.33(2H,m), 9.08(1H,d,J=8Hz)

Example 19

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 479 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.11(3H,s), 3.21-3.40(2H,m), 3.72(3H,s),
5.52-5.63(1H,m), 6.13-6.21(1H,m), 6.72(2H,d,J=8Hz),
6.89(1H,s), 6.90(1H,s), 6.99(2H,d,J=8Hz), 7.03(1H,s),
7.08(2H,d,J=8Hz), 7.50(2H,d,J=8Hz), 8.11(1H,d,J=8Hz)

Example 20

The object compound was obtained according to a similar manner to that of Example 1.

mp : 249-251°C

MASS : 530 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.21-3.40(2H,m), 3.49(3H,s), 3.70(3H,s),
5.48(1H,q,J=8Hz), 6.79(2H,d,J=8Hz), 7.08(1H,s),
7.13(2H,d,J=8Hz), 7.23-7.32(2H,m), 7.38(2H,d,J=8Hz),
7.59(1H,br s), 7.63(3H,d,J=8Hz), 9.04(1H,d,J=8Hz)

Example 21

The object compound was obtained according to a similar manner to that of Example 1.

mp : 125-128°C

MASS : 546 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.01(3H,s), 3.17-3.29(1H,m), 3.40-3.50(1H,m), 3.78(3H,s), 5.41-5.53(1H,m), 6.89(2H,d,J=8Hz), 6.99(2H,d,J=8Hz), 7.03-7.17(3H,m), 7.34-7.48(2H,m), 7.49-7.60(3H,m), 7.79-7.90(3H,m)

Example 22

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 547 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.09(3H,s), 3.27-3.39(1H,m), 3.40-3.50(1H,m), 3.72(3H,s), 5.40-5.51(1H,m), 6.78(2H,d,J=8Hz), 7.01(2H,d,J=8Hz), 7.08-7.17(3H,m), 7.42-7.60(4H,m), 7.93(1H,d,J=8Hz), 8.10(1H,d,J=8Hz), 8.40(1H,d,J=8Hz)

Example 23

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 531 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.10(3H,s), 3.21-3.38(1H,m), 3.39-3.49(1H,m), 3.72(3H,s), 5.42-5.56(1H,m), 6.80(2H,d,J=8Hz), 7.02(2H,d,J=8Hz), 7.10(1H,s), 7.11(2H,d,J=8Hz), 7.39-7.51(2H,m), 7.52(2H,d,J=8Hz), 7.62(1H,d,J=8Hz), 7.80(1H,d,J=8Hz), 8.31(1H,d,J=8Hz)

Example 24

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS : 531 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.91-2.96(1×1/2H,m), 3.00(3×1/2H,s), 3.01-3.28(1H,m), 3.17(3×1/2H,s), 3.30-3.40(1×1/2H,m), 3.43-3.60(1H,m), 3.73(3×1/2H,s), 3.78(3×1/2H,s), 4.27-4.50(2H,m), 5.20-5.40(1H,m), 6.62-6.82(4H,m), 6.89(1H,d,J=8Hz), 6.95(1H,d,J=8Hz), 7.00-7.17(5H,m), 7.52(2H,t,J=8Hz), 7.98(1H,d,J=8Hz)

Example 25

The object compound was obtained according to a similar manner to that of Example 1.

colorless solid

mp : 231-234.5°C

MASS : 501 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.27-3.41(2H,m), 3.44(3H,s), 5.32(1H,m), 7.07(1H,s), 7.12(1H,t,J=7.5Hz), 7.16-7.27(6H,m), 7.31(1H,d,J=7.5Hz), 7.35(1H,t,J=7.5Hz), 7.36(2H,d,J=7.5Hz), 7.64(2H,d,J=7.5Hz), 7.78(2H,d,J=7.5Hz), 9.27(1H,d,J=7.5Hz)

Example 26

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS : 526 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.08(3H,s), 3.38-3.51(2H,m), 5.51(1H,m), 7.06-7.16(5H,m), 7.20-7.25(4H,m), 7.29(1H,t,J=7.5Hz), 7.36-7.43(3H,m), 7.52(2H,d,J=7.5Hz), 7.55(1H,t,J=7.5Hz), 7.80(1H,d,J=7.5Hz), 8.18(1H,d,J=7.5Hz)

Example 27

To a solution of the starting compound (88.2 mg) in dichloromethane (1 ml) was added phenyl isocyanate (32.4 mg) under nitrogen atmosphere at 0°C. The reaction mixture was stirred at room temperature for 5 hours and concentrated *in vacuo*. The residue was purified by flash column chromatography over silica gel with chloroform-methanol (10:1) as eluent to give the object compound (80.0

mg) as an off-white solid.

mp : 172-175°C

MASS : 475 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.03(3H,s), 3.21(1H,dd,J=13.5 and 9.0Hz), 3.42(1H,dd,J=13.5 and 6.0Hz), 5.31(1H,m), 6.91(1H,m), 6.99-7.40(11H,m), 7.06(2H,d,J=7.5Hz), 7.52(2H,d,J=7.5Hz), 7.49-7.58(1H,m)

Example 28

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS : 556 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.85(3H,s), 2.98(3H,d,J=4.5Hz), 3.24(1H,dd,J=13.5 and 9.0Hz), 3.48(1H,dd,J=13.5 and 4.5Hz), 5.52(1H,m), 7.01(1H,d,J=1.0Hz), 7.03-7.33(8H,m), 7.10(2H,d,J=7.5Hz), 7.42(2H,d,J=7.5Hz), 7.49(2H,d,J=7.5Hz), 7.45-7.59(1H,m), 7.69(1H,d,J=7.5Hz), 9.23(1H,br s)

Example 29

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS : 586 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.92(3H,s), 3.24-3.35(1H,m), 3.28(3H,s), 3.49(1H,dd,J=13.5 and 4.5Hz), 3.70(3H,s), 5.57(1H,m), 6.98(1H,d,J=1.0Hz), 7.04-7.11(1H,m), 7.09(2H,d,J=7.5Hz), 7.15(1H,t,J=7.5Hz), 7.20-7.33(5H,m), 7.40-7.55(2H,m), 7.52(2H,d,J=7.5Hz), 7.67(1H,d,J=7.5Hz), 9.23(1H,br s)

Example 30

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS : 570 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.96(3H,s), 2.99(6H,s),
3.30(1H,dd,J=13.5 and 8.5Hz), 3.49(1H,dd,J=13.5 and 6.0Hz),
5.57(1H,m), 6.97(1H,s), 7.07-7.18(5H,m), 7.20-7.28(3H,m),
7.29(1H,t,J=7.5Hz), 7.40-7.48(2H,m), 7.53(2H,d,J=7.5Hz),
7.67(1H,d,J=7.5Hz), 9.31(1H,br s)

Example 31

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS : 618 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.91(3H,s), 3.30(1H,dd,J=13.5 and 8.5Hz),
3.49(1H,dd,J=13.5 and 6.0Hz), 5.58(1H,m), 7.03-7.43(13H,m),
7.12(2H,d,J=7.5Hz), 7.50(2H,d,J=7.5Hz), 7.70(2H,t,J=7.5Hz),
9.12(1H,s), 9.27(1H,s)

Example 32

The object compound was obtained according to a similar manner to that of Example 1.

colorless solid

mp : 287-291℃

MASS : 395 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.48(2H,d,J=7.5Hz), 3.77(3H,s),
5.71(1H,q,J=7.5Hz), 7.01(1H,t,J=7.5Hz), 7.10-7.30(7H,m),
7.33-7.40(3H,m), 7.51(1H,d,J=7.5Hz), 7.60(1H,d,J=7.5Hz),
7.66(1H,d,J=7.5Hz), 9.14(1H,d,J=7.5Hz)

Example 33

The object compound was obtained according to a similar manner to that of Example 1.

pale brown amorphous solid

MASS : 485 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.44(3H,s), 6.48(1H,d,J=7.5Hz), 7.06(2H,s),
7.11(1H,t,J=7.5Hz), 7.20(2H,d,J=7.5Hz), 7.20-7.45(7H,m),
7.56(2H,d,J=7.5Hz), 7.62(1H,d,J=7.5Hz), 8.30(1H,d,J=7.5Hz),

9.26(1H,s)

Example 34

The object compound was obtained according to a similar manner to that of Exmaple 1.

yellow amorphous solid

MASS : 531 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.53(9H,s), 2.98(3H,s),
3.21(1H,dd,J=13.0 and 8.5Hz), 3.46(1H,dd,J=13.0 and 5.5Hz),
5.51(1H,m), 7.00(1H,t,J=7.5Hz), 7.03-7.09(2H,m), 7.05(1H,s),
7.15(2H,d,J=7.5Hz), 7.21-7.27(3H,m), 7.39(2H,d,J=7.5Hz),
7.40-7.53(3H,m), 7.57(1H,d,J=7.5Hz), 8.38(1H,d,J=7.5Hz)

Example 35

The object compound was obtained according to a similar manner to that of Preparation 3.

yellow amorphous solid

MASS : 431 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 2.97(3H,s), 3.21(1H,dd,J=13.0 and 8.5Hz),
3.46(1H,dd,J=13.0 and 7.0Hz), 5.44-5.57(3H,m),
6.66(1H,t,J=7.5Hz), 6.68(1H,d,J=7.5Hz), 7.05(1H,s),
7.05-7.10(2H,m), 7.16(2H,d,J=7.5Hz), 7.17-7.27(5H,m),
7.38(2H,d,J=7.5Hz),
7.43(1H,d,J=7.5Hz)

Example 36

The object compound was obtained according to a similar manner to that of Example 1.

off-white amorphous solid

MASS : 574 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.08(3H,s), 3.27(1H,dd,J=13.5 and 8.5Hz),
3.50(1H,dd,J=13.5 and 6.0Hz), 5.60(1H,m), 7.07(1H,s),
7.11(2H,d,J=7.5Hz), 7.12-7.35(10H,m), 7.37(2H,d,J=7.5Hz),
7.48(1H,d,J=7.5Hz), 7.52(1H,t,J=7.5Hz), 7.66(2H,d,J=7.5Hz),
7.75(1H,d,J=7.5Hz), 8.74(1H,d,J=7.5Hz), 9.42(1H,br s)

Example 37

The object compound was obtained according to a similar manner to that of Example 1.

off-white amorphous solid

MASS : 575 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.07(3H,s), 3.25(1H,dd,J=13.5 and 8.5Hz), 3.50(1H,dd,J=13.5 and 5.5Hz), 5.59(1H,m), 7.06(1H,s), 7.07-7.28(9H,m), 7.32(1H,t,J=7.5Hz), 7.37(2H,d,J=7.5Hz), 7.45(1H,d,J=7.5Hz), 7.47-7.52(1H,m), 7.53(1H,d,J=7.5Hz), 7.58(1H,s), 7.64(2H,t,J=7.5Hz), 7.71(1H,d,J=7.5Hz), 8.78(1H,d,J=7.5Hz)

Example 38

The object compound was obtained according to a similar manner to that of Example 1.

yellow amorphous solid

MASS : 531 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 1.53(9H,s), 3.07(3H,s), 3.37(1H,dd,J=13.5 and 8.5Hz), 3.50(1H,dd,J=13.5 and 7.0Hz), 5.60(1H,m), 7.05(1H,s) 7.07-7.16(2H,m), 7.13(2H,d,J=7.5Hz), 7.21-7.85(8H,m), 7.37(2H,d,J=7.5Hz), 7.50(1H,d,J=7.5Hz)

Example 39

The object compound was obtained according to a similar manner to that of Preparation 3.

off-white solid

mp : 198-201°C

MASS : 431 $(M+H)^+$

^{1}H-NMR ($CDCl_3$, δ) 2.97(3H,s), 3.20(1H,dd,J=12.0 and 8.5Hz), 3.47(1H,dd,J=12.0 and 7.0Hz), 3.78(2H,s), 5.50(1H,m), 6.79(1H,dd,J=7.5 and 1.0Hz), 7.03(1H,s), 7.03-7.09(2H,m), 7.12-7.26(8H,m), 7.29(1H,d,J=7.5Hz), 7.37(2H,d,J=7.5Hz)

Example 40

The object compound was obtained according to a similar manner to

that of Example 1.

MASS : 574 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.91(3H,s), 3.58-3.75(2H,m), 5.60(1H,m), 6.78(2H,d,J=7.5Hz), 7.00(1H,s), 7.06-7.19(3H,m), 7.16(2H,d,J=7.5Hz), 7.20-7.26(4H,m), 7.31(2H,t,J=7.5Hz), 7.43(1H,d,J=7.5Hz), 7.53-7.60(2H,m), 7.67(1H,d,J=7.5Hz), 7.84(1H,d,J=7.5Hz), 8.14(1H,m), 9.61(1H,s), 9.84(1H,br s)

Example 41

The object compound was obtained according to a similar manner to that of Example 1.

off-white amorphous solid

MASS : 575 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.98(3H,s), 3.27(1H,dd,J=13.0 and 8.5Hz), 3.50(1H,dd,J=13.0 and 5.5Hz), 5.53(1H,m), 7.03-7.10(2H,m), 7.06(1H,s), 7.13(2H,d,J=7.5Hz), 7.20-7.28(3H,m), 7.30-7.40(3H,m), 7.42-7.51(2H,m), 7.55-7.69(4H,m), 7.71(1H,d,J=7.5Hz), 7.99(1H,s), 8.07(1H,d,J=7.5Hz), 8.46(1H,s)

Example 42

The object compound was obtained according to a similar manner to that of Example 1.

yellow amorphous solid

MASS : 433 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.49(1H,dd,J=16.0 and 7.0Hz), 3.61(3H,s), 3.67(1H,dd,J=16.0 and 2.5Hz), 4.60(1H,m), 5.52(1H,d,J=16.0Hz), 6.29(1H,m), 6.96(2H,s), 7.05(1H,d,J=7.5Hz), 7.15(1H,d,J=7.5Hz), 7.19(1H,d,J=7.5Hz), 7.21-7.47(9H,m), 7.70(1H,d,J=7.5Hz), 9.20(1H,br s)

Example 43

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 474 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.91(3H,s), 3.45(1H,dd,J=13 and 9Hz),

3.66(1H,dd,J=13 and 5Hz), 3.68(3H,s), 5.58-5.70(1H,m), 6.81(1H,s), 6.95-7.45(14H,m), 7.64(1H,d,J=8Hz), 7.84(1H,br s), 9.51(1H,br s)

Example 44

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 475 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.91(3H,s), 3.43(1H,dd,J=13 and 9Hz), 3.66(1H,dd,J=13 and 5Hz), 3.72(3H,s), 5.54-5.67(1H,m), 6.85(1H,s), 6.96-7.72(15H,m), 7.83(1H,d,J=8Hz)

Example 45

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 544, 546 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.30(3H,s), 3.44-3.65(2H,m), 5.61-5.78(1H,m), 6.95-7.70(13H,m), 8.06(2H,d,J=8Hz), 9.49(1H,br s)

Example 46

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 545, 547 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.31(3H,s), 3.47-3.67(2H,m), 5.60-5.72(1H,m), 7.07-7.71(13H,m), 8.11(2H,d,J=8Hz)

Example 47

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 496 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.12(3H,s), 3.19-3.49(2H,m), 3.75(3H,s), 5.48-5.62(1H,m), 6.75(2H,d,J=8Hz), 6.97(2H,d,J=8Hz), 7.00(1H,s), 7.07-7.82(8H,m), 8.25(2H,d,J=8Hz), 9.55(1H,br s)

Example 48

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 497 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.16(3H,s), 3.20-3.49(2H,m), 3.77(3H,s), 5.45-5.59(1H,m), 6.78(2H,d,J=8Hz), 7.00(2H,d,J=8Hz), 7.21-7.75(9H,m), 8.26(2H,d,J=8Hz)

Example 49

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 515, 517 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.41(3H,s), 3.75(3H,s), 6.43(1H,d,J=8Hz), 6.84(2H,d,J=8Hz), 6.99-7.38(9H,m), 7.49-7.67(3H,m), 8.39(1H,d,J=8Hz), 9.41(1H,br s)

Example 50

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 519, 521 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.42(3H,s), 6.42(1H,d,J=8Hz), 7.02-7.41(11H,m), 7.50-7.68(3H,m), 8.31(1H,d,J=8Hz), 9.22(1H,br s)

Example 51

The object compound was obtained according to a similar manner to that of Example 1.

mp : 157-159°C

MASS (ESI) (m/z) : 511 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.44(3H,s), 3.60-3.68(2H,m), 5.76(1H,q,J=8Hz), 7.07-7.70(10H,m), 7.98(1H,br d,J=8Hz), 8.11(2H,d,J=8Hz), 8.31(2H,d,J=8Hz), 9.41(1H,br s)

Example 52

The object compound was obtained according to a similar manner to that of Example 1.

mp : 187-188°C

MASS (ESI) (m/z) : 467 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.43-3.68(2H,m), 3.73(3H,s), 5.86-5.99(1H,m), 6.96-7.68(9H,m), 7.73(2H,d,J=8Hz), 8.26(2H,d,J=8Hz), 8.49(1H,d,J=5Hz), 9.08(1H,br d,J=8Hz), 10.50(1H,br s)

Example 53

The object compound was obtained according to a similar manner to that of Example 1.

mp : 259-260°C

MASS (ESI) (m/z) : 468 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.50-3.64(2H,m), 3.70(3H,s), 5.81-5.95(1H,m), 7.12-7.38(5H,m), 7.44-7.68(2H,m), 7.72(1H,br d,J=8Hz), 7.73(2H,d,J=8Hz), 8.27(2H,d,J=8Hz), 8.50(1H,d,J=5Hz), 9.24(1H,br d,J=8Hz), 10.50(1H,br s)

Example 54

The object compound was obtained according to a similar manner to that of Example 1.

mp : 174-175°C

MASS (ESI) (m/z) : 467 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.42-3.68(2H,m), 3.72(3H,s), 5.84-6.00(1H,m), 6.97-7.70(9H,m), 7.73(2H,d,J=8Hz), 8.27(2H,d,J=8Hz), 8.49(1H,d,J=5Hz), 9.09(1H,br d,J=8Hz), 10.50(1H,br s)

Example 55

The object compound was obtained according to a similar manner to that of Example 1.

mp : 180-184°C

MASS : 437 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.59(3H,s), 3.49(3H,s), 3.50-3.70(2H,m), 6.01(1H,q,J=8Hz), 7.01(1H,s), 7.02(1H,s), 7.08-7.16(3H,m), 7.16-7.29(2H,m), 7.39(1H,d,J=8Hz), 7.48(1H,d,J=8Hz), 7.50(1H,t,J=8Hz), 7.62(1H,d,J=8Hz), 7.99(1H,d,J=8Hz),

8.41(1H,s), 8.52(1H,d,J=2Hz), 9.69(1H,s)

Example 56

The object compound was obtained according to a similar manner to that of Example 1.

mp : 197-199°C

MASS : 423 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.53(3H,s), 3.57-3.70(2H,m), 6.00(1H,q,J=8Hz), 7.00(1H,s), 7.09(1H,s), 7.10-7.18(3H,m), 7.27(1H,t,J=8Hz), 7.31-7.41(2H,m), 7.50-7.70(3H,m), 7.82(1H,d,J=8Hz), 8.50-8.62(3H,m), 9.49(1H,s)

Example 57

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 509 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.42(3H,t,J=7Hz), 3.13(3H,s), 3.19-3.43(2H,m), 4.04(2H,q,J=7Hz), 5.46-5.62(1H,m), 5.88(2H,s), 6.54(1H,d,J=8Hz), 6.56(1H,s), 6.64(1H,d,J=8Hz), 6.89(2H,d,J=8Hz), 7.00(1H,s), 7.02-7.68(7H,m), 7.95(1H,br d,J=8Hz), 9.74(1H,br s)

Example 58

The object compound was obtained according to a similar manner to that of Example 1.

mp : 214-215°C

MASS (ESI) (m/z) : 481 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 1.11(3H,t,J=7Hz), 3.41-3.68(2H,m), 4.02-4.42(2H,m), 5.85-6.00(1H,m), 6.95-7.68(9H,m), 7.72(2H,d,J=8Hz), 8.28(2H,d,J=8Hz), 8.49(1H,d,J=2Hz), 9.12(1H,br d,J=8Hz), 10.50(1H,br s)

Example 59

The object compound was obtained according to a similar manner to that of Example 1.

mp : 145-150°C

MASS : 488 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.41-3.53(1H,m), 3.54-3.63(1H,m), 3.69(3H,s), 5.91(1H,q,J=8Hz), 7.02(1H,t,J=8Hz), 7.08(1H,s), 7.10-7.20(3H,m), 7.28(1H,s), 7.32-7.41(2H,m), 7.52-7.68(4H,m), 7.72(2H,d,J=8Hz), 7.80(1H,d,J=2Hz), 8.31(1H,s), 8.50(1H,d,J=2Hz), 9.07(1H,d,J=8Hz)

Example 60

A solution of the starting compound (360 mg) and ammonium chloride (5 mg) in ethanol (14.5 ml) - water (1.5 ml) was heated to 70°C. Powdered iron (440 mg) and one drop of concentrated hydrochloric acid were added. The mixture was stirred at 70°C for 15 minutes then allowed to cool to room temperature. The mixture was filtered, concentrated, made basic with 1N sodium hydroxide solution and extracted three times with chloroform. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol=20/1) to give the object compound as a pale yellow powder (291 mg).

mp : 145-150°C

MASS (ESI) (m/z) : 437 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.44(3H,s), 3.55-3.71(2H,m), 3.78(2H,br s), 5.98-6.12(1H,m), 6.67(2H,d,J=8Hz), 6.89(1H,s), 6.96-7.66(10H,m), 8.25(1H,br d,J=8Hz), 8.51(1H,d,J=5Hz), 10.00(1H,br s)

Example 61

To a solution of the starting compound (82 mg) in dichloromethane (4 ml) were added triethylamine (0.5 ml) and methanesulfonyl chloride (0.1 ml) at room temperature and the mixture was stirred for 1.5 hours. A saturated aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was

purified by column chromatography (silica gel, chloroform/methanol= 20/1) to give the object compound as pale yellow crystals (84 mg).

mp : 160-165°C

MASS (ESI) (m/z) : 593 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.45-3.68(2H,m), 3.55(6H,s), 3.71(3H,s), 5.86-5.99(1H,m), 6.98-7.73(13H,m), 8.51(1H,d,J=2Hz), 9.13(1H,br d,J=8Hz), 10.50(1H,br s)

Example 62

To a solution of the starting compound (86 mg) in dichloromethane (1 ml) was added acetic anhydride (30 mg) at room temperature and the mixture was stirred for 1 hour. The mixture was diluted with chloroform (2 ml), and then diisopropyl ether was added. The pale yellow precipitate was collected by filtration, washed with diisopropyl ether, and dried *in vacuo* to give the object compound (84.5 mg).

mp : 226-227°C

MASS (ESI) (m/z) : 479 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 2.04(3H,s), 3.40-3.66(2H,m), 3.60(3H,s), 5.81-5.94(1H,m), 6.93(1H,s), 6.96-7.70(12H,m), 8.48(1H,d,J=5Hz), 9.02(1H,br d,J=8Hz), 10.05(1H,br s), 11.52(1H,br s)

Example 63

To an ice-cooled solution of the starting compound (196 mg) in dichloromethane (4 ml) were added pyridine (0.12 ml) and ethyl chloroformate (0.07 ml). The mixture was stirred under ice-cooling for 1 hour. A saturated aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol=20/1) to give the object compound as a pale yellow powder (216 mg).

MASS (ESI) (m/z) : 509 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 1.26(3H,t,J=7Hz), 3.41-3.65(2H,m), 3.60(3H,s), 4.14(2H,q,J=7Hz), 5.81-5.95(1H,m), 6.91(1H,s), 6.95-7.67(12H,m), 8.48(1H,d,J=5Hz), 9.01(1H,br d,J=8Hz), 9.71(1H,br s), 11.48(1H,br s)

Example 64

To an ice-cooled solution of the starting compound (84 mg) in dichloromethane (1.7 ml) were added pyridine (0.05 ml) and methanesulfonyl chloride (0.02 ml). The mixture was stirred under ice-cooling for 3 hours. A saturated aqueous sodium hydrogencarbonate solution was added to the mixture, and then the mixture was extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated.

The residue was purified by column chromatography (silica gel, chloroform/methanol=20/1) to give the object compound as a white powder (69 mg).

MASS (ESI) (m/z) : 513 $(M-H)^-$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.01(3H,s), 3.31-3.62(2H,m), 3.60(3H,s), 5.81-5.95(1H,m), 6.94(1H,s),6.97-7.68(12H,m), 8.48(1H,d,J=5Hz), 9.02(1H,br d,J=8Hz), 9.88(1H,br s), 11.50(1H,br s)

Example 65

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 468 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.50(3H,s), 3.22(3H,s), 3.38-3.50(2H,m), 5.59-5.72(1H,m), 6.97-7.78(13H,m), 8.44(2H,d,J=6Hz), 9.50(1H,br s)

Example 66

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 500 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.09(3H,s), 3.32(3H,s),

3.38-3.50(2H,m), 5.62-5.77(1H,m), 6.96-7.69(11H,m),
7.99(2H,d,J=8Hz), 8.45(2H,d,J=6Hz), 9.55(1H,br s)

Example 67

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 465 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.97(6H,s), 3.49(3H,s),
3.52-3.65(2H,m), 5.91-6.04(1H,m), 6.71(2H,d,J=8Hz),
6.91(1H,s), 6.96-7.68(10H,m), 7.97(1H,br d,J=8Hz),
8.52(1H,d,J=5Hz), 9.51(1H,br s)

Example 68

The object compound was obtained according to a similar manner to that of Example 1.

mp : 200-201°C

MASS (ESI) (m/z) : 467 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.41-3.66(2H,m), 3.69(3H,s),
5.82-5.98(1H,m), 6.95-7.96(11H,m), 8.13-8.23(2H,m),
8.48(1H,d,J=5Hz), 9.05(1H,br d,J=8Hz), 10.50(1H,br s)

Example 69

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 497 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.47-3.61(2H,m), 3.67(3H,s),
3.78(3H,s), 5.92-6.07(1H,m), 6.92-8.15(11H,m),
8.21(1H,d,J=2Hz), 8.25(2H,d,J=8Hz), 9.62(1H,br s)

Example 70

The object compound was obtained according to a similar manner to that of Example 1.

mp : 154-155°C

MASS (ESI) (m/z) : 501 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.43-3.68(2H,m), 3.72(3H,s),
5.83-5.97(1H,m), 6.97-7.63(7H,m), 7.75(2H,d,J=8Hz),

7.78(1H,dd,J=8 and 2Hz), 8.27(2H,d,J=8Hz),
8.52(1H,d,J=2Hz), 9.07(1H,br d,J=8Hz), 10.50(1H,br s)

Example 71

The object compound was obtained according to a similar manner to that of Example 1.

mp : 208-209°C

MASS (ESI) (m/z) : 466 $(M-H)^-$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.49-3.72(2H,m), 3.71(3H,s),
5.86-6.01(1H,m), 6.97-7.64(6H,m), 7.75(2H,d,J=8Hz),
8.27(2H,d,J=8Hz), 8.42(1H,d,J=2Hz), 8.55(1H,d,J=2Hz),
8.66(1H,s), 9.11(1H,br d,J=8Hz), 10.50(1H,br s)

Example 72

The object compound was obtained according to a similar manner to that of Example 1.

mp : 190-192°C

MASS (ESI) (m/z) : 538 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.29-2.72(4H,m), 3.69(3H,s),
5.07(2H,s), 5.53-5.67(1H,m), 6.93-7.68(14H,m),
8.29(2H,d,J=8Hz), 9.31(1H,br s)

Example 73

A solution of the starting compound (186 mg) in 1N sodium hydroxide solution (2.7 ml) - 1,4-dioxane (5.4 ml) was stirred at room temperature for 1 hour. After the mixture was concentrated, 1N hydrochloric acid was added to the residue. The yellow precipitate formed was collected by filtration and dried *in vacuo* to give the object compound (157 mg).

mp : 170-175°C

MASS (ESI) (m/z) : 448 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.22-2.56(4H,m), 3.79(3H,s),
5.41-5.55(1H,m), 6.98-7.68(6H,m), 7.84(2H,d,J=8Hz),
8.33(2H,d,J=8Hz), 9.14(1H,br d,J=8Hz), 10.50(1H,br s)

Example 74

To a solution of the starting compound (41 mg) in chloroform (0.4 ml) - methanol (0.4 ml) was added trimethylsilyldiazomethane/hexane (2.0 M) at room temperature, and the mixture was stirred for 2 hours. After adding acetic acid (0.1 ml), the mixture was neutralized with a saturated sodium hydrogencarbonate solution and extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica gel, chloroform/methanol= 20/1) to give the object compound as a pale yellow powder (22 mg).

mp : 177-179°C

MASS (ESI) (m/z) : 462 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 2.28-2.68(4H,m), 3.62(3H,s), 3.74(3H,s), 5.52-5.65(1H,m), 7.04-7.68(8H,m), 7.88(1H,br d,J=8Hz), 8.28(2H,d,J=8Hz), 10.50(1H,br s)

Example 75

The object compound was obtained according to a similar manner to that of Example 1 except that a mixture of dichloromethane and dimethylformamide was used instead of dichloromethane.

mp : 230-231°C

MASS (ESI) (m/z) : 523 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 2.22-2.60(4H,m), 3.75(3H,s), 5.38-5.52(1H,m), 6.94-7.64(11H,m), 7.77(2H,d,J=8Hz), 8.28(2H,d,J=8Hz), 8.94(1H,br d,J=8Hz), 10.50(2H,br s)

Example 76

The object compound was obtained according to a similar manner to that of Example 1.

mp : 150-155°C

MASS (ESI) (m/z) : 475 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 1.41-1.62(2H,m), 1.78(3H,s), 1.98-2.16(2H,m), 3.01-3.20(2H,m), 3.72(3H,s), 5.31-5.46(1H,m), 6.96-7.64(6H,m), 7.76(2H,d,J=8Hz), 7.86(1H,br t,J=5Hz), 8.28(2H,d,J=8Hz), 8.88(1H,br d,J=8Hz), 10.50(1H,br s)

Example 77

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 508 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.41(3H,t,J=7Hz), 3.24-3.42(2H,m), 3.61(3H,s), 4.02(2H,q,J=7Hz), 5.96-6.11(1H,m), 6.81-7.58(15H,m), 8.03(1H,br d,J=8Hz), 9.01(1H,br s), 9.76(1H,br s)

Example 78

The object compound was obtained according to a similar manner to that of Example 1.

mp : 196-197°C

MASS (ESI) (m/z) : 456 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.38-3.55(2H,m), 3.70(3H,s), 5.61-5.77(1H,m), 6.16(1H,d,J=4Hz), 6.29(1H,d,J=4Hz), 6.98-7.64(7H,m), 7.77(2H,d,J=8Hz), 8.28(2H,d,J=8Hz), 9.02(1H,br d,J=8Hz), 10.50(1H,br s)

Example 79

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 543 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.42-3.75(2H,m), 4.18(2H,s), 5.41-5.54(1H,m), 6.98-7.85(17H,m), 8.21(2H,d,J=8Hz), 8.66(1H,d,J=2Hz), 9.27(1H,br s)

Example 80

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 510 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 3.16-3.45(2H,m), 3.23(3H,s), 5.46-5.61(1H,m), 5.89(2H,s), 6.48-6.72(3H,m), 6.97(1H,s), 7.07-7.69(8H,m), 8.28(2H,d,J=8Hz), 9.38(1H,br s)

Example 81

The object compound was obtained according to a similar manner to that of Example 1.

mp : 205-206℃

MASS (ESI) (m/z) : 500, 502 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.41-3.63(2H,m), 3.62(3H,s), 5.81-5.97(1H,m), 6.95-7.69(13H,m), 8.49(1H,d,J=5Hz), 9.03(1H,br d,J=8Hz), 10.50(1H,br s)

Example 82

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 556 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 1.41(3H,t,J=7Hz), 3.31(3H,s), 3.48-3.63(2H,m), 3.81(2H,s), 4.03(2H,q,J=7Hz), 5.89-6.05(1H,m), 6.80-7.67(17H,m), 7.80(1H,br d,J=8Hz), 8.52(1H,d,J=5Hz), 9.79(1H,br s)

Example 83

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 495 $(M+H)^+$

^{1}H-NMR ($CDCl_3$,300MHz) δ : 0.70(3H,t,J=7Hz), 1.36-1.58(2H,m), 3.56-3.68(2H,m), 3.84-4.17(2H,m), 5.98-6.11(1H,m), 6.97-7.84(12H,m), 8.25(2H,d,J=8Hz), 8.54(1H,d,J=5Hz), 9.67(1H,br s)

Example 84

The object compound was obtained according to a similar manner to that of Example 1.

mp : 134-135℃

MASS (ESI) (m/z) : 482 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 1.11(3H,t,J=7Hz), 3.50-3.62(2H,m), 4.05-4.38(2H,m), 5.81-5.96(1H,m), 7.13-7.38(5H,m), 7.51(1H,br d,J=8Hz), 7.58-7.75(2H,m), 7.72(2H,d,J=8Hz), 8.28(2H,d,J=8Hz), 8.51(1H,d,J=5Hz), 9.24(1H,br d,J=8Hz),

10.50(1H,br s)

Example 85

The object compound was obtained according to a similar manner to that of Example 1.

mp : 245-246℃

MASS (ESI) (m/z) : 488 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.42-3.66(2H,m), 3.66(3H,s), 5.82-5.98(1H,m), 6.56(1H,t,J=2Hz), 6.95-7.21(3H,m), 7.06(1H,s), 7.25(1H,s), 7.29-7.42(2H,m), 7.55(2H,d,J=8Hz), 7.56-7.69(2H,m), 7.77(1H,d,J=2Hz), 7.91(2H,d,J=8Hz), 8.49(1H,d,J=5Hz), 8.55(1H,d,J=2Hz), 9.05(1H,br d,J=8Hz), 10.50(1H,br s)

Example 86

The object compound was obtained according to a similar manner to that of Example 1.

mp : 199-200℃

MASS (ESI) (m/z) : 502 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 1.07(3H,t,J=7Hz), 3.41-3.68(2H,m), 3.96-4.32(2H,m), 5.84-5.99(1H,m), 6.56(1H,t,J=2Hz), 6.94-7.22(4H,m), 7.26(1H,s), 7.29-7.42(2H,m), 7.52(2H,d,J=8Hz), 7.54-7.70(2H,m), 7.77(1H,d,J=2Hz), 7.92(2H,d,J=8Hz), 8.50(1H,d,J=5Hz), 8.55(1H,d,J=2Hz), 9.10(1H,br d,J=8Hz), 10.50(1H,br s)

Example 87

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 495 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 3.49(1H,dd,J=7 and 14Hz), 3.61(1H,dd,J=5 and 14Hz), 3.75(3H,s), 3.76(3H,s), 5.92(1H,m), 6.82(1H,dd,J=2 and 8Hz), 7.05(1H,s), 7.16(2H,m), 7.27(2H,t,J=5Hz), 7.34(1H,d,J=8Hz), 7.64(1H,d,J=8Hz), 7.75(2H,d,J=8Hz), 8.26(2H,d,J=8Hz), 8.49(1H,d,J=5Hz),

9.02(1H,d,J=8Hz)

Example 88

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 499 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 3.49(1H,dd,J=7 and 15Hz), 3.62(1H,dd,J=5 and 15Hz), 3.73(3H,s), 5.92(1H,m), 7.13-7.19(2H,m), 7.24(1H,d,J=2Hz), 7.27(1H,s), 7.34(1H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.63(1H,m), 7.68(1H,d,J=2Hz), 7.73(2H,d,J=8Hz), 8.25(2H,d,J=8Hz), 8.49(1H,d,J=5Hz), 9.19(1H,d,J=8Hz)

Example 89

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 483 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 3.49(1H,dd,J=7 and 15Hz), 3.61(1H,dd,J=5 and 15Hz), 3.73(3H,s), 5.92(1H,m), 7.02(1H,dt,J=2 and 8Hz), 7.18(1H,m), 7.24(1H,d,J=2Hz), 7.27(1H,s), 7.32-7.40(3H,m), 7.63(1H,m), 7.74(2H,d,J=8Hz), 8.26(2H,d,J=8Hz), 8.49(1H,d,J=5Hz), 9.12(1H,d,J=8Hz)

Example 90

The object compound was obtained according to a similar manner to that of Example 1.

mp : 245°C

MASS (m/z) : 468 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.50(3H,s), 3.32(3H,s), 3.47(1H,dd,J=7 and 14Hz), 3.58(1H,dd,J=5 and 14Hz), 5.88(1H,m), 6.97(1H,s), 7.02(1H,t,J=8Hz), 7.15(2H,m), 7.23(1H,d,J=2Hz), 7.29-7.39(6H,m), 7.59(1H,d,J=8Hz), 7.62(1H,m), 8.49(1H,d,J=5Hz), 9.02(1H,d,J=8Hz)

Example 91

The object compound was obtained according to a similar manner to

that of Example 1.

MASS (m/z) : 496 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.46(3H,s), 3.49(3H,s), 3.60(2H,m), 3.77(2H,t,J=5Hz), 4.14(2H,t,J=5Hz), 5.98(1H,m), 6.94-6.99(4H,m), 7.09-7.12(3H,m), 7.20(2H,d,J=8Hz), 7.35(1H,t,J=8Hz), 7.50(1H,m), 7.65(1H,d,J=8Hz), 7.85(1H,d,J=8Hz), 8.54(1H,d,J=5Hz), 9.44(1H,br s)

Example 92

The object compound was obtained according to a similar manner to that of Example 1.

mp : 173°C (from AcOEt-hexane)

MASS (m/z) : 381 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.23(1H,dd,J=5 and 15Hz), 3.32(1H,dd,J=7 and 15Hz), 3.72(3H,s), 5.10(1H,d,J=13Hz), 5.19(1H,d,J=13Hz), 5.93(1H,m), 6.87(1H,s), 7.12-7.17(1H,m), 7.17(1H,s), 7.26-7.33(5H,m), 7.42(2H,d,J=8Hz), 7.50(2H,d,J=8Hz), 7.63(1H,d,J=8Hz), 8.28(2H,d,J=8Hz), 9.25(1H,s)

Example 93

The object compound was obtained according to a similar manner to that of Example 73.

MASS (m/z) : 432 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 3.23(1H,dd,J=5 and 15Hz), 3.34(1H,dd,J=7 and 15Hz), 3.89(3H,s), 5.72(1H,m), 7.05(1H,t,J=8Hz), 7.20(1H,t,J=8Hz), 7.28(1H,s), 7.43(1H,d,J=8Hz), 7.63(1H,d,J=8Hz), 7.86(2H,d,J=8Hz), 8.31(1H,s), 8.36(2H,d,J=8Hz), 9.33(1H,d,J=8Hz)

Example 94

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 524 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.23(2H,d,J=7Hz), 3.77(3H,s),

4.47(1H,dd,J=7 and 15Hz), 4.66(1H,dd,J=7 and 15Hz),
5.98(1H,m), 6.96(1H,s), 7.08-7.14(3H,m), 7.22-7.29(1H,m),
7.38(1H,d,J=8Hz), 7.48(2H,d,J=8Hz), 7.58(2H,m), 7.67(1H,m),
8.07(1H,d,J=8Hz), 8.26(2H,d,J=8Hz), 8.44(1H,d,J=8Hz),
9.46(1H,s)

Example 95

To a solution of the starting compound (30 mg) in N,N-dimethylformamide were added triethylamine (0.01 ml) and pivaloyl chloride (0.01 ml) at -20°C and the mixture was stirred at the same temperature for 30 minutes. Aniline (6 mg) was added to the mixture and stirring at room temperature was continued for 1 hour. The mixture was poured into water and extracted three times with ethyl acetate. The extract was washed with a sodium hydrogencarbonate solution and dried over magnesium sulfate. Evaporation of the solvent followed by column chromatography (silica gel, chloroform/methanol) gave the object compound (13 mg) as a pale yellow powder.

MASS (m/z) : 509 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.32(2H,d,J=7Hz), 3.77(3H,s),
6.03(1H,m), 6.97(1H,s), 7.07-7.78(13H,m), 8.28(2H,d,J=8Hz),
8.39(1H,br s), 9.36(1H,br s)

Example 96

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 523 (M+1)

^{1}H-NMR (CD_3OD) δ : 3.07(2H,m), 3.86(3H,s), 4.34(2H,s),
5.93(1H,t,J=7Hz), 7.09-7.15(6H,m), 7.28(1H,t,J=8Hz),
7.46(1H,d,J=8Hz), 7.52-7.66(5H,m), 8.33(2H,d,J=8Hz)

Example 97

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 510 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.38(1H,m), 3.53(1H,dd,J=7 and 15Hz),

3.82(3H,s), 6.11(1H,m), 7.01-7.13(4H,m), 7.37-7.44(3H,m),
7.58(1H,d,J=8Hz), 8.65(1H,t,J=8Hz), 8.14(1H,m),
8.22-8.27(4H,m), 9.37(1H,br s), 9.73(1H,br s)

Example 98

The object compound was obtained according to a similar manner to that of Example 74.

MASS (m/z) : 448 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.19(1H,dd,J=5 and 15Hz),
3.28(1H,dd,J=7 and 15Hz), 3.68(3H,s), 3.76(3H,s),
5.95(1H,dd,J=5 and 7Hz), 6.98(1H,s), 7.12-7.15(2H,m),
7.29(1H,t,J=8Hz), 7.37-7.43(1H,m), 7.52(2H,d,J=8Hz),
7.65(1H,d,J=8Hz), 6.71(1H,m), 8.28(2H,d,J=8Hz), 9.56(1H,m)

Example 99

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 433 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.73(1H,dd,J=5 and 15Hz),
3.17(1H,dd,J=7 and 15Hz), 3.76(3H,s), 5.74(1H,m), 6.85(1H,s),
7.02(1H,t,J=8Hz), 7.18(1H,t,J=8Hz), 7.25(1H,s),
7.26(1H,s), 7.40(1H,s), 7.44(1H,d,J=8Hz), 7.60(1H,d,J=8Hz),
7.76(2H,d,J=8Hz), 8.27(2H,d,J=8Hz), 8.97(1H,d,J=8Hz)

Example 100

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 523 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.64(1H,dd,J=5 and 15Hz), 3.13(3H,s),
3.25(1H,dd,J=7 and 15Hz), 3.76(3H,s), 5.83(1H,m),
7.00(1H,t,J=8Hz), 7.16(2H,t,J=8Hz), 7.24-7.62(8H,m),
7.77(2H,d,J=8Hz), 8.27(2H,d,J=8Hz), 8.90(1H,d,J=8Hz)

Example 101

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 539 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.07(1H,dd,J=5 and 15Hz),
3.44(1H,dd,J=7 and 15Hz), 3.75(3H,s), 3.82(3H,s), 5.83(1H,m),
6.85(1H,t,J=8Hz), 6.99-7.05(3H,m), 7.19(1H,t,J=8Hz),
7.27(1H,s), 7.31(1H,s), 7.42(1H,d,J=8Hz), 7.61(1H,d,J=8Hz),
7.78(2H,d,J=8Hz), 7.95(1H,d,J=8Hz), 8.28(2H,d,J=8Hz),
9.04(1H,d,J=8Hz), 9.40(1H,s)

Example 102

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 543 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.02(1H,dd,J=5 and 15Hz),
3.46(1H,dd,J=7 and 15Hz), 3.76(3H,s), 5.88(1H,m),
7.03(1H,t,J=8Hz), 7.18(1H,t,J=8Hz), 7.23-7.26(2H,m),
7.32(2H,d,J=8Hz), 7.42(1H,d,J=8Hz), 7.58-7.62(3H,m),
7.77(2H,d,J=8Hz), 8.27(2H,d,J=8Hz), 9.07(1H,d,J=8Hz)

Example 103

The object compound was obtained according to a similar manner to that of Example 95.

MASS (m/z) : 539 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.97(1H,dd,J=5 and 15Hz),
3.42(1H,dd,J=7 and 15Hz), 3.69(3H,s), 3.76(3H,s), 5.88(1H,m),
6.84(2H,d,J=8Hz), 7.03(1H,t,J=8Hz), 7.18(1H,t,J=8Hz),
7.26(2H,s), 7.42(1H,d,J=8Hz), 7.47(2H,d,J=8Hz),
7.60(1H,d,J=8Hz), 7.76(2H,d,J=8Hz), 8.27(2H,d,J=8Hz),
9.06(1H,d,J=8Hz)

Example 104

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 447 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.54(3H,d,J=6Hz), 2.74(1H,dd,J=5 and 15Hz),
3.17(1H,dd,J=7 and 15Hz), 3.76(3H,s), 5.77(1H,m),

7.02(1H,t,J=8Hz), 7.17(1H,t,J=8Hz), 7.23(1H,s), 7.25(1H,s),
7.42(1H,d,J=8Hz), 7.59(1H,d,J=8Hz), 7.76(2H,d,J=8Hz),
7.90(1H,m), 8.27(2H,d,J=8Hz), 8.97(1H,d,J=8Hz)

Example 105

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 491 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.83(3H,d,J=5Hz), 3.49-3.62(2H,m),
3.63(3H,s), 5.89(1H,q,J=7Hz), 6.57(1H,d,J=8Hz),
7.11-7.18(3H,m), 7.24(1H,dd,J=2 and 8Hz), 7.43(1H,m),
7.48(2H,d,J=8Hz), 7.58(1H,t,J=8Hz), 7.67(1H,m),
8.27(2H,d,J=8Hz), 8.56(1H,d,J=5Hz)

Example 106

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 487 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.81(3H,s), 3.56(2H,m), 3.64(3H,s),
5.90(1H,q,J=7Hz), 6.62(1H,d,J=8Hz), 6.90(1H,m),
6.96-7.02(2H,m), 7.12-7.17(3H,m), 7.43-7.49(3H,m),
7.57(1H,t,J=8Hz), 8.27(2H,d,J=8Hz), 8.53(1H,d,J=5Hz)

Example 107

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 457 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.83(3H,d,J=5Hz), 3.56(2H,m), 3.62(3H,s),
5.91(1H,q,J=7Hz), 6.57(1H,t,J=7Hz), 6.65(1H,d,J=8Hz),
7.12-7.17(3H,m), 7.31(2H,t,J=8Hz), 7.43(2H,d,J=8Hz),
7.47(2H,d,J=8Hz), 7.56(1H,t,J=8Hz), 8.26(2H,d,J=8Hz),
8.53(1H,d,J=5Hz)

Example 108

The object compound was obtained according to a similar manner to that of Preparation 3.

MASS (m/z) : 443 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.57(2H,m), 3.62(3H,s), 5.53(2H,br s),
5.93(1H,q,J=7Hz), 6.65(2H,m), 7.12-7.23(3H,m),
7.43(2H,t,J=8Hz), 7.48(2H,d,J=8Hz), 7.57(1H,t,J=8Hz),
8.27(2H,d,J=8Hz), 8.53(1H,d,J=5Hz)

Example 109

The object compound was obtained according to a similar manner to that of Example 1.

mp : 95-100°C

MASS (m/z) : 467 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.29(3H,s), 3.38-3.52(2H,m),
5.68(1H,q,J=8Hz), 7.01(1H,s), 7.10-7.21(2H,m),
7.21-7.32(2H,m), 7.38-7.50(2H,m), 7.42(2H,d,J=8Hz),
7.62(2H,t,J=8Hz), 8.28(2H,d,J=8Hz), 8.37(1H,s),
8.48(1H,d,J=2Hz), 9.60(1H,s)

Example 110

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS (m/z) : 494 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.41(3H,t,J=8Hz), 3.30(3H,s),
3.48(2H,d,J=8Hz), 4.40(2H,q,J=8Hz), 5.70(1H,q,J=8Hz),
7.00-7.10(3H,m), 7.10-7.20(2H,m), 7.27-7.37(3H,m),
7.41(1H,d,J=8Hz), 7.61(1H,d,J=8Hz), 7.83(1H,d,J=8Hz),
8.07(2H,d,J=8Hz), 8.45(2H,d,J=8Hz), 9.71(1H,s)

Example 111

A solution of the starting compound (500 mg) in anhydrous THF (20 ml) was added dropwise with stirring to a solution of 1N $LiAlH_4$ in THF (2.02 ml) maintained at -78°C. After the addition was complete, the suspension was stirred at -78°C for 30 minutes and then ethyl acetate (30 ml) was added dropwise. The mixture was allowed to warm to about 5°C and then water (30 ml) was added dropwise. The white

solid was filtered and washed with ether, and the filtrate and washing were dried and concentrated to give a yellow oil. The oil was chromatographed on silica gel with chloroform as eluent to give the object compound (360 mg).

amorphous solid

MASS (m/z) : 452 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.20(3H,s), 3.43(2H,d,J=8Hz), 4.71(2H,s), 5.69(1H,q,J=8Hz), 6.98(1H,s), 7.09(2H,d,J=6Hz), 7.10-7.21(4H,m), 7.29(1H,t,J=8Hz), 7.38(2H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.64(1H,d,J=8Hz), 8.07(1H,d,J=8Hz), 8.42(2H,d,J=6Hz), 9.63(1H,s)

Example 112

Oxalyl chloride (0.10 ml) in CH_2Cl_2 (20 ml) was placed in a three-necked flask equipped with two addition funnels and a stirrer. Dimethyl sulfoxide (0.12 ml) in CH_2Cl_2 (10 ml) was placed in one addition funnel, and the other one contained a solution of the starting compound (310 mg) in CH_2Cl_2 (10 ml). The content of the flask was cooled to -60 ℃ and dimethyl sulfoxide was added over a period of 10 minutes. Stirring was continued for 20 minutes, followed by addition of the solution of the starting compound during 10 minutes. After the mixture was stirred at -60℃ for 20 minutes, triethylamine (0.53 ml) was added over a period of 10 minutes. The cooling bath was removed and the suspension was allowed to warm to room temperature. Water (30 ml) was added, the yellow organic layer was separated, and the aqueous layer was extracted with chloroform. The combined organic layer was dried and concentrated to give an orange-yellow liquid. This was chromatographed on silica gel with chloroform as eluent to give the object compound (190 mg).

amorphous solid

MASS (m/z) : 450 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.31(3H,s), 3.46(2H,d,J=8Hz), 5.69(1H,q,J=8Hz), 7.00(1H,s), 7.08(2H,d,J=6Hz),

7.13(1H,t,J=8Hz), 7.19(1H,s), 7.29(1H,t,J=8Hz),
7.34-7.59(3H,m), 7.63(2H,d,J=8Hz), 7.91(2H,d,J=8Hz),
8.49(2H,d,J=8Hz), 9.58(1H,s), 10.20(1H,s)

Example 113

The starting compound (500 mg) was dissolved in methanol (20 ml) to which was added 1N NaOH (10.1 ml) and the mixture was stirred at room temperature for about 6 hours. The solvent was then evaporated and the residue was dissolved in a minimum amount of water. The solution was extracted with chloroform and the aqueous layer was acidified to pH 4 with concentrated HCl to give the object compound as an amorphous solid (320 mg).

MASS (m/z) : 466 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.40-3.53(2H,m), 3.64(3H,s),
5.70(1H,q,J=8Hz), 7.01(1H,t,J=8Hz), 7.17(1H,t,J=8Hz),
7.19(1H,s), 7.22(1H,s), 7.39(1H,d,J=8Hz), 7.41(2H,d,J=6Hz),
7.60(1H,d,J=8Hz), 7.60(2H,d,J=8Hz), 8.00(2H,d,J=8Hz),
8.42(2H,d,J=6Hz), 9.09(1H,d,J=8Hz)

Example 114

The object compound was obtained according to a similar manner to that of Example 1.

mp : 235-238°C

MASS (m/z) : 494 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(3H,t,J=8Hz), 3.59(3H,s),
3.60-3.69(2H,m), 4.39(2H,q,J=8Hz), 6.04(1H,q,J=8Hz),
7.02(1H,s), 7.05-7.18(4H,m), 7.22(1H,d,J=8Hz),
7.30-7.42(3H,m), 7.50(1H,t,J=8Hz), 7.60(1H,d,J=2Hz),
8.00-8.12(3H,m), 8.52(1H,d,J=4Hz), 9.78(1H,s)

Example 115

The object compound was obtained according to a similar manner to that of Example 111.

mp : 124-129°C

MASS (m/z) : 452 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.49(3H,s), 3.59-3.67(2H,m), 4.72(2H,s),
6.00(1H,q,J=8Hz), 6.90(1H,s), 7.02-7.18(4H,m),
7.18-7.30(3H,m), 7.36(1H,s), 7.38(2H,d,J=8Hz),
7.51(1H,t,J=8Hz), 7.61(1H,d,J=8Hz), 8.01(1H,d,J=8Hz),
8.51(1H,d,J=6Hz), 9.59(1H,s)

Example 116

The object compound was obtained according to a similar manner to that of Example 113.

amorphous solid

MASS (m/z) : 466 (M+1)

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 4.20-4.30(1H,m), 4.31(3H,s),
4.37-4.49(1H,m), 6.55(1H,q,J=8Hz), 7.55(1H,t,J=8Hz),
7.65-7.73(2H,m), 7.79(1H,s), 7.81(1H,s), 7.82(1H,d,J=8Hz),
7.94(2H,d,J=8Hz), 7.94(1H,d,J=8Hz), 8.10(1H,d,J=8Hz),
8.15(1H,t,J=8Hz), 8.61(2H,d,J=8Hz), 9.01(1H,d,J=2Hz),
9.77(1H,d,J=8Hz),

Example 117

The object compound was obtained according to a similar manner to that of Example 1.

amorphous solid

MASS (m/z) : 489 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.51(3H,s), 3.68-3.83(2H,m),
6.21(1H,q,J=8Hz), 7.00-7.10(2H,m), 7.14-7.50(10H,m),
7.59(1H,br s), 7.70(1H,br s), 7.90(1H,s), 8.50(1H,d,J=2Hz),
8.80(1H,d,J=8Hz)

Example 118

The object compound was obtained according to a similar manner to that of Example 1.

mp : 141-145°C

MASS (m/z) : 481 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.60(3H,s), 3.30(3H,s), 3.48-3.65(2H,m),
5.70(1H,q,J=8Hz), 7.00(1H,s), 7.10(1H,s), 7.11-7.29(4H,m),

7.30(2H,d,J=8Hz), 7.40(1H,s), 7.46(1H,dd,J=8 and 2Hz),
7.61(1H,t,J=8Hz), 8.08(2H,d,J=8Hz), 8.43(1H,s), 9.67(1H,s)

Example 119

A solution of the starting compound (420 mg) in ethanol (20 ml) - water (2 ml) was heated to 70°C. Powdered iron (484 mg) and one drop of concentrated hydrochloric acid were added. The mixture was stirred at 70°C for 1 hour, then allowed to cool to room temperature. The reaction mixture was filtered, concentrated, made basic with 1N sodium hydroxide solution and extracted three times with chloroform. The organic layer was washed with brine, dried over magnesium sulfate and concentrated. The residue was purified by silica gel column chromatography (chloroform/methanol=10/1) to give the object compound as an amorphous solid (380 mg).

MASS (m/z) : 451 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.59(3H,s), 3.00(3H,s), 3.10-3.20(1H,m),
3.31-3.41(1H,m), 3.61(2H,br s), 5.41-5.53(1H,m),
6.57(2H,d,J=8Hz), 6.81(2H,d,J=8Hz), 7.01(1H,s),
7.09-7.17(2H,m), 7.20(1H,d,J=8Hz), 7.23(1H,t,J=8Hz),
7.39(1H,d,J=8Hz), 7.48(1H,d,J=8Hz), 7.62(1H,d,J=8Hz),
7.80(1H,d,J=8Hz), 8.40(1H,s), 9.51(1H,s)

Example 120

The object compound was obtained according to a similar manner to that of Example 63.

amorphous solid

MASS (m/z) : 523 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.28(3H,t,J=8Hz), 2.50(3H,s), 3.03(3H,s),
3.28-3.49(2H,m), 4.20(2H,q,J=8Hz), 5.61(1H,q,J=8Hz),
6.99(2H,d,J=8Hz), 7.01-7.30(8H,m), 7.37(1H,d,J=8Hz),
7.41(1H,d,J=8Hz), 7.58(1H,d,J=8Hz), 8.38(1H,s), 8.39(1H,s)

Example 121

The object compound was obtained according to a similar manner to that of Example 61.

amorphous solid

MASS (m/z) : 607 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.58(3H,s), 2.98(3H,s), 3.12-3.49(1H,m), 3.39(6H,s), 3.47-3.60(1H,m), 5.52-5.63(1H,m), 7.03(1H,s), 7.09-7.21(8H,m), 7.38(1H,d,J=8Hz), 7.41(1H,dd,J=8 and 2Hz), 7.59(1H,d,J=8Hz), 8.30(1H,d,J=8Hz), 8.40(1H,s)

Example 122

The object compound was obtained according to a similar manner to that of Example 1.

mp : 147-152°C

MASS (m/z) : 447 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.58(3H,s), 3.60-3.70(2H,m), 6.00-6.18(1H,m), 7.02(1H,s), 7.07-7.18(4H,m), 7.19-7.29(1H,m), 7.38(1H,s), 7.39(2H,d,J=8Hz), 7.49(1H,t,J=8Hz), 7.62(1H,d,J=8Hz), 7.68(2H,d,J=8Hz), 8.11(1H,d,J=8Hz), 8.51(1H,d,J=2Hz), 9.85(1H,s)

Example 123

A solution of the starting compound (852 mg) in anhydrous THF (40 ml) was added dropwise with stirring to a solution of 1N $LiAlH_4$ in THF (4.78 ml) maintained at -78°C. After the addition was complete, the suspension was stirred at -78°C for 30 minutes and then ethyl acetate (60 ml) was added dropwise. The mixture was allowed to warm to about 5°C and then water (60 ml) was added dropwise. The white solid was filtered and washed with ether, and the filtrate and washings were dried and concentrated to give a yellow oil. The oil was chromatographed on silica gel with chloroform as eluent to give the object compound (470 mg).

amorphous solid

MASS (m/z) : 451 (M+1)

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 3.38-3.61(2H,m), 3.54(3H,s), 3.90(2H,s), 5.91(1H,t,J=8Hz), 6.97(1H,s), 7.04-7.20(4H,m), 7.20-7.30(4H,m), 7.30-7.43(3H,m), 7.59(1H,t,J=8Hz),

7.62(1H,d,J=8Hz), 8.50(1H,d,J=2Hz)

Example 124

The object compound was obtained according to a similar manner to that of Example 63.

amorphous solid

MASS (m/z) : 523 (M+1)

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 1.27(3H,t,J=8Hz), 3.43-3.52(2H,m), 3.51(3H,s), 4.11(2H,q,J=8Hz), 4.34(2H,s), 5.90(1H,t,J=8Hz), 6.97(1H,s), 7.07-7.30(7H,m), 7.30-7.43(4H,m), 7.59(1H,t,J=8Hz), 7.63(1H,d,J=8Hz), 8.50(1H,d,J=2Hz)

Example 125

The object compound was obtained according to a similar manner to that of Example 61.

amorphous solid

MASS (m/z) : 529 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 2.82(3 x 1/4H,s), 2.96(3 x 3/4H,s), 3.33(3 x 3/4H,s), 3.42(3 x 1/4H,s), 3.48-3.70(2H,m), 4.38(2H,s), 6.00(1H,q,J=8Hz), 6.28(1 x 3/4H,s), 6.40(1 x 1/4H,s), 6.90-7.17(5H,m), 7.17-7.33(5H,m), 7.33-7.57(2H,m), 7.57-7.68(1H,m), 8.38-8.61(2H,m)

Example 126

The object compound was obtained according to a similar manner to that of Preparation 5.

amorphous solid

MASS (m/z) : 493 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.00(3H,s), 3.12(3H,s), 3.55(3H,s), 3.60-3.72(2H,m), 6.09(1H,q,J=8Hz), 7.01(1H,s), 7.02-7.13(4H,m), 7.18-7.32(3H,m), 7.38(1H,d,J=8Hz), 7.40-7.52(3H,m), 7.61(1H,d,J=8Hz), 8.30(1H,d,J=8Hz), 8.51(1H,d,J=8Hz)

Example 127

To a stirred solution of the starting compound (300 mg) and 1-

hydroxybenzotriazole (88 mg) in anhydrous dichloromethane (20 ml) at 5°C was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (124 mg). The mixture was stirred at 5°C for 30 minutes and then NH_3 gas was bubbled for 15 minutes. The mixture was warmed to 25°C and stirred overnight. The mixture was poured into a saturated sodium hydrogencarbonate solution and extracted with chloroform. The organic layer was washed with brine, dried, and concentrated. Silica gel column chromatographic purification (chloroform/methanol=30/1) gave the object compound (120 mg).

mp : 155-160°C

MASS (m/z) : 463 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 3.42-3.57(1H,m), 3.57-3.65(1H,m), 3.70(3H,s), 5.91(1H,q,J=8Hz), 7.01(1H,t,J=8Hz), 7.10(1H,s), 7.16(2H,t,J=8Hz), 7.23(1H,s), 7.30-7.48(3H,m), 7.51(2H,d,J=8Hz), 7.60(2H,t,J=8Hz), 7.92(2H,d,J=8Hz), 8.02(1H,br s), 8.50(1H,d,J=2Hz), 9.08(1H,d,J=8Hz)

Example 128

The object compound was obtained according to a similar manner to that of Preparation 5.

mp : 189-193°C

MASS (m/z) : 479 (M+1)

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 2.70(3H,s), 3.30(2H,d,J=8Hz), 3.31(3H,s), 5.68(1H,t,J=8Hz), 6.80(1H,s), 6.84(1H,t,J=8Hz), 6.90(1H,s), 6.92-7.02(3H,m), 7.10-7.20(3H,m), 7.40(2H,d,J=8Hz), 7.61(2H,d,J=8Hz), 8.22(1H,d,J=2Hz)

Example 129

The object compound was obtained according to a similar manner to that of Example 1 except that a mixture of dichloromethane and dimethylformamide was used instead of dichloromethane.

mp : 233-235°C

MASS (m/z) : 468 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.48-3.60(1H,m), 3.61-3.72(1H,m),
3.77(3H,s), 6.00(1H,q,J=8Hz), 7.01(1H,t,J=8Hz),
7.18(1H,t,J=8Hz), 7.23(1H,s), 7.28(1H,s), 7.40(1H,d,J=8Hz),
7.51(1H,d,J=6Hz), 7.59(1H,d,J=8Hz), 7.78(2H,d,J=8Hz),
8.28(2H,d,J=8Hz), 8.63(1H,d,J=4Hz), 9.09(1H,s),
9.12(1H,d,J=8Hz)

Example 130

The object compound was obtained according to a similar manner to that of Example 1.

mp : 235-237°C

MASS (m/z) : 466 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.40(3H,t,J=8Hz), 3.51(3H,s),
3.58-3.68(2H,m), 3.92-4.08(2H,m), 6.09(1H,q,J=8Hz),
6.73-6.90(3H,m), 7.00(1H,s), 7.01-7.12(4H,m), 7.18-7.30(2H,m),
7.31-7.40(1H,m), 7.45(1H,t,J=8Hz), 7.60(1H,d,J=8Hz),
8.29(1H,d,J=8Hz), 8.50(1H,d,J=2Hz)

Example 131

The object compound was obtained according to a similar manner to that of Example 1.

mp : 255-257°C

MASS (m/z) : 528 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.40-3.52(1H,m), 3.53-3.63(1H,m),
3.58(3H,s), 5.11(3H,s), 5.89(1H,q,J=8Hz), 6.90(1H,s),
7.01(1H,t,J=8Hz), 7.09(2H,d,J=8Hz), 7.18(2H,d,J=8Hz),
7.24(1H,s), 7.30-7.50(9H,m), 7.58-7.68(2H,m),
8.49(1H,d,J=2Hz), 9.01(1H,d,J=8Hz)

Example 132

To a solution of the starting compound (970 mg) and methanol (50 ml) in 70 ml of THF was added Pd/C (10%, 300 mg). The resulting mixture was stirred under hydrogen at 25°C for 16 hours. The catalyst was filtered off, and the filtrate was concentrated to give an oil. The oil was chromatographed on silica gel with chloroform as

eluent to give the object compound (780 mg).

amorphous solid

MASS (m/z) : 438 (M+1)

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 3.48-3.58(2H,m), 3.50(3H,s),
5.88(1H,t,J=8Hz), 6.88(2H,d,J=8Hz), 6.90(1H,s),
7.07-7.19(4H,m), 7.19-7.30(3H,m), 7.41(1H,d,J=8Hz),
7.60-7.70(2H,m), 8.49(1H,d,J=4Hz)

Example 133

Acetic anhydride (52 mg) was added to a stirred solution of the starting compound (150 mg) and pyridine (81 mg) in methylene chloride/N,N-dimethylformamide (10:1, 22 ml) at 5°C. The reaction mixture was allowed to warm to room temperature and stirred overnight. The mixture was concentrated *in vacuo* and the residue was taken up in ethyl acetate and washed with brine. The organic layer was dried and concentrated to give a solid. The solid was chromatographed on silica gel with chloroform as eluent to give the object compound (110 mg).

mp : 227-230°C

MASS (m/z) : 480 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.24(3H,s), 3.41-3.52(1H,m),
3.53-3.63(1H,m), 3.62(3H,s), 5.90(1H,q,J=8Hz), 7.00(1H,s),
7.00(1H,t,J=8Hz), 7.11-7.28(5H,m), 7.32(1H,d,J=8Hz),
7.38(1H,d,J=8Hz), 7.47(2H,d,J=8Hz), 7.59(1H,d,J=8Hz),
7.62(1H,t,J=8Hz), 8.49(1H,d,J=8Hz), 9.01(1H,d,J=8Hz)

Example 134

The object compound was obtained according to a similar manner to that of Example 133.

solid

^{1}H-NMR ($CDCl_3$) δ : 3.46(3H,s), 3.80-4.00(2H,m),
5.92(1H,t,J=8Hz), 6.80(2H,d,J=8Hz), 6.88(1H,s),
7.12-7.29(4H,m), 7.30-7.50(3H,m), 7.55(1H,t,J=8Hz),
7.70(1H,t,J=8Hz), 7.77(1H,d,J=8Hz), 7.80(1H,d,J=8Hz),
8.31(1H,d,J=8Hz), 9.62(1H,s)

Example 135

Trimethylsilyldiazomethane (2.0M hexane solution, 0.34 ml) was added to a stirred solution of the starting compound (150 mg) and N,N-diisopropylethylamine (87 mg) in methanol-acetonitrile (1:9, 10 ml) at room temperature. The mixture was stirred overnight at room temperature, and concentrated *in vacuo*. The residue was taken up in ethyl acetate and washed with brine. The organic layer was dried and concentrated to give a solid. The solid was chromatographed on silica gel with chloroform as eluent to give the object compound (100 mg).

mp : 250°C (dec.)

MASS (m/z) : 452 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.41-3.51(1H,m), 3.52-3.62(1H,m), 3.59(3H,s), 3.79(3H,s), 5.89(1H,q,J=8Hz), 6.90(1H,s), 7.00(2H,d,J=8Hz), 7.02(1H,t,J=8Hz), 7.18(2H,t,J=8Hz), 7.22(1H,s), 7.31(2H,d,J=8Hz), 7.32-7.40(2H,m), 7.58-7.68(2H,m), 8.49(1H,d,J=2Hz), 9.01(1H,d,J=8Hz)

Example 136

The object compound was obtained according to a similar manner to that of Example 1.

mp : 210-215°C

MASS (m/z) : 406 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.78(3H,s), 3.90-4.02(1H,m), 5.01(1H,t,J=8Hz), 5.40(1H,q,J=8Hz), 7.02(1H,t,J=8Hz), 7.19(1H,t,J=8Hz), 7.28(1H,s), 7.29(1H,s), 7.41(1H,d,J=8Hz), 7.60(1H,d,J=8Hz), 7.80(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.81(1H,d,J=8Hz)

Example 137

The object compound was obtained according to a similar manner to that of Example 1 except that a mixture of dichloromethane and dimethylformamide was used instead of dichloromethane.

mp : 115-120°C

MASS (m/z) : 510 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.78(3H,s), 4.74-4.82(1H,m), 4.88-4.95(1H,m), 5.90-6.02(1H,m), 7.02(1H,s), 7.11(1H,t,J=8Hz), 7.28(1H,s), 7.40(3H,t,J=8Hz), 7.51(2H,d,J=8Hz), 7.53(1H,t,J=8Hz), 7.63(1H,d,J=8Hz), 7.81(1H,d,J=8Hz), 7.97(2H,d,J=8Hz), 8.30(2H,d,J=8Hz), 9.40(1H,s)

Example 138

Acetic anhydride (112 mg) was added to a stirred solution of the starting compound (150 mg) and pyridine (75 mg) in methylene chloride/N,N-dimethylformamide (10:1, 22 ml) at 5°C. The reaction mixture was allowed to warm to room temperature and stirred overnight. The mixture was concentrated *in vacuo* and the residue was taken up in ethyl acetate and washed with brine. The organic layer was dried and concentrated to give a solid. The solid was chromatographed on silica gel with chloroform as eluent to give the object compound (165 mg).

mp : 110-115°C

MASS (m/z) : 448 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.00(3H,s), 3.70(3H,s), 4.50-4.60(1H,m), 4.63-4.72(1H,m), 5.68-5.78(1H,m), 7.03(1H,t,J=8Hz), 7.20(1H,t,J=8Hz), 7.28(1H,s), 7.31(1H,s), 7.42(1H,d,J=8Hz), 7.60(1H,d,J=8Hz), 7.79(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 9.05(1H,d,J=8Hz)

Example 139

The object compound was obtained according to a similar manner to that of Example 1.

mp : 220-223°C

MASS (m/z) : 466 (M+1)

^{1}H-NMR ($CDCl_3$+CD_3OD) δ : 3.40-3.60(2H,m), 3.51(3H,s), 5.90(1H,t,J=8Hz), 6.00(2H,s), 6.70-6.80(2H,m), 6.88(1H,d,J=8Hz), 6.91(1H,s), 7.09-7.21(4H,m), 7.29(1H,t,J=8Hz), 7.41(1H,d,J=8Hz), 7.59(1H,t,J=8Hz),

7.69(1H,d,J=8Hz), 8.50(1H,d,J=2Hz)

Example 140

The object compound was obtained according to a similar manner to that of Example 1.

mp : 125-130℃

MASS (m/z) : 418 (M-1)

^{1}H-NMR ($CDCl_3$) δ : 3.31(3H,s), 3.78(3H,s), 3.98(2H,d,J=8Hz), 5.61(1H,q,J=8Hz), 7.02(1H,t,J=8Hz), 7.19(1H,t,J=8Hz), 7.29(1H,s), 7.42(1H,d,J=8Hz), 7.51(1H,d,J=8Hz), 7.79(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.91(1H,d,J=8Hz)

Example 141

The object compound was obtained according to a similar manner to that of Example 1.

mp : 115-120℃

MASS (m/z) : 496 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.71(3H,s), 4.08(2H,d,J=8Hz), 4.58(1H,d,J=10Hz), 4.62(1H,d,J=10Hz), 5.70(1H,q,J=8Hz), 7.02(1H,t,J=8Hz), 7.19(1H,t,J=8Hz), 7.21-7.33(7H,m), 7.42(1H,d,J=8Hz), 7.60(1H,d,J=8Hz), 7.79(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.99(1H,d,J=8Hz)

Example 142

The object compound was obtained according to a similar manner to that of Example 1.

mp : 180℃ (dec.)

MASS (m/z) : 456 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.20-3.42(2H,m), 3.70(3H,s), 5.62(1H,q,J=8Hz), 6.73(1H,s), 7.01(1H,t,J=8Hz), 7.18(1H,t,J=8Hz), 7.28(1H,s), 7.30(1H,s), 7.40(1H,d,J=8Hz), 7.50(1H,s), 7.60(1H,d,J=8Hz), 7.73(2H,d,J=8Hz), 8.28(2H,d,J=8Hz), 9.00(1H,d,J=8Hz)

Example 143

The object compound was obtained according to a similar manner to

that of Example 1.

amorphous solid

MASS (m/z) : 510 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.00-3.12(2H,m), 3.45-3.58(1H,m), 3.77(3H,s), 5.85-5.98(1H,m), 7.02(1H,t,J=8Hz), 7.20(1H,t,J=8Hz), 7.30(2H,s), 7.58(2H,d,J=6Hz), 7.60(1H,d,J=8Hz), 7.78(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 8.40(2H,d,J=6Hz), 9.10(1H,d,J=8Hz)

Example 144

The object compound was obtained according to a similar manner to that of Example 1.

mp : 145-150°C

MASS (m/z) : 501 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 2.90-3.00(1H,m), 3.23-3.40(1H,m), 3.42-3.70(8H,m), 3.80(3H,s), 5.78-5.88(1H,m), 7.01(1H,t,J=8Hz), 7.19(1H,t,J=8Hz), 7.22(1H,s), 7.25(1H,s), 7.41(1H,d,J=8Hz), 7.60(1H,d,J=8Hz), 7.77(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 9.00(1H,d,J=8Hz)

Example 145

The object compound was obtained according to a similar manner to that of Example 1.

mp : 245-250°C

MASS (m/z) : 456.5 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.39-3.51(1H,m), 3.52-3.61(1H,m), 3.60(3H,s), 5.90(1H,q,J=8Hz), 7.01(1H,t,J=8Hz), 7.03(1H,s), 7.16(2H,t,J=8Hz), 7.26(1H,s), 7.30-7.40(3H,m), 7.41-7.53(3H,m), 7.58-7.71(2H,m), 8.50(1H,d,J=2Hz), 9.03(1H,d,J=8Hz)

Example 146

Butyl iodide (120 mg) was added to a stirred solution of the starting compound (190 mg) and potassium carbonate (178 mg) in N,N-dimethylformamide (10 ml) at 5°C. The reaction mixture was allowed

to warm to room temperature and stirred for 4 hours. The mixture was poured into water and extracted with ethyl acetate and washed with brine. The organic layer was dried and concentrated to give a solid.

The solid was chromatographed on silica gel with chloroform as eluent to give the object compound (110 mg).

mp : 236-240°C

MASS (m/z) : 494 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 0.92(3H,t,J=8Hz), 1.38-1.50(2H,m), 1.62-1.73(2H,m), 3.40-3.52(1H,m), 3.52-3.63(1H,m), 3.60(3H,s), 4.00(2H,t,J=8Hz), 5.89(1H,q,J=8Hz), 6.90(1H,s), 6.93-7.05(3H,m), 7.16(2H,t,J=8Hz), 7.24(1H,s), 7.19-7.41(4H,m), 7.57-7.68(2H,m), 8.50(1H,d,J=2Hz), 9.01(1H,d,J=2Hz)

Example 147

The object compound was obtained according to a similar manner to that of Example 1.

mp : 215-220°C

MASS (m/z) : 473 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 3.43-3.70(2H,m), 3.74(3H,s), 5.98(1H,q,J=8Hz), 7.02(1H,t,J=8Hz), 7.10-7.21(3H,m), 7.29(1H,s), 7.39(2H,t,J=8Hz), 7.51-7.71(3H,m), 7.83(1H,d,J=8Hz), 8.00-8.10(2H,m), 8.39(1H,d,J=8Hz), 8.50(1H,d,J=8Hz), 8.90(1H,d,J=2Hz), 9.10(1H,d,J=8Hz)

Example 148

The object compound was obtained according to a similar manner to that of Example 1 except that dimethylformamide was used instead of dichloromethane.

mp : 120-125°C

MASS (m/z) : 553 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.91-3.02(1H,m), 3.38-3.49(1H,m), 3.80(3H,s), 5.89(1H,q,J=8Hz), 5.95(2H,s), 6.81(1H,d,J=8Hz), 6.94(1H,d,J=8Hz), 7.02(1H,t,J=8Hz), 7.20(1H,t,J=8Hz),

7.24(3H,s), 7.41(1H,d,J=8Hz), 7.60(1H,d,J=8Hz),
7.78(2H,d,J=8Hz), 8.29(2H,d,J=8Hz), 9.08(1H,d,J=8Hz)

Example 149

The object compound was obtained according to a similar manner to that of Example 1.

oil

MASS (m/z) : 538 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.21(3H,t,J=8Hz), 3.18-3.28(1H,m),
3.40-3.51(1H,m), 4.20(2H,q,J=8Hz), 5.07(1H,d,J=15Hz),
5.09(1H,d,J=15Hz), 5.90-6.02(1H,m), 6.99(1H,s),
7.09-7.20(2H,m), 7.21-7.45(6H,m), 7.51(2H,d,J=8Hz),
7.61(1H,d,J=8Hz), 7.80(1H,d,J=8Hz), 8.30(2H,d,J=8Hz),
9.40(1H,s)

Example 150

The object compound was obtained according to a similar manner to that of Example 73.

mp : 150-160°C

MASS (m/z) : 448 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.13(3H,t,J=8Hz), 2.88-2.99(1H,m),
3.30-3.40(1H,m), 4.10-4.28(1H,m), 4.28-4.41(1H,m),
5.79(1H,q,J=8Hz), 7.00(1H,t,J=8Hz), 7.19(1H,t,J=8Hz),
7.22(1H,s), 7.27-7.33(1H,m), 7.41(1H,d,J=8Hz),
7.60(1H,d,J=8Hz), 7.79(2H,d,J=8Hz), 8.30(2H,d,J=8Hz),
9.09(1H,d,J=8Hz)

Example 151

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 523 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.22(3H,t,J=7Hz), 3.33(2H,d,J=7Hz),
4.22(2H,q,J=7Hz), 6.10(1H,q,J=7Hz), 7.02-7.12(4H,m),
7.21-7.23(2H,m), 7.37-7.45(5H,m), 7.57(1H,d,J=8Hz),
8.18(1H,m), 8.23(2H,d,J=8Hz), 8.57(1H,br s), 9.83(1H,br s)

Example 152

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 553 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.26(3H,t,J=7Hz), 3.29(2H,d,J=7Hz), 3.73(3H,s), 4.23(2H,q,J=7Hz), 6.05(1H,q,J=7Hz), 6.77(2H,d,J=8Hz), 7.05-7.12(3H,m), 7.33-7.41(5H,m), 7.58(1H,m), 8.23(2H,d,J=8Hz), 8.32(1H,m), 8.42(1H,br s), 9.73(1H,br s)

Example 153

The object compound was obtained according to a similar manner to that of Example 1.

MASS (m/z) : 567 (M+1)

^{1}H-NMR ($CDCl_3$) δ : 1.47(3H,t,J=7Hz), 3.53(2H,d,J=7Hz), 4.46(2H,t,J=7Hz), 6.09(2H,s), 6.29(1H,q,J=7Hz), 6.85(1H,d,J=8Hz), 6.98(1H,d,J=8Hz), 7.31-7.38(2H,m), 7.49(3H,m), 7.59-7.66(3H,m), 7.81(1H,d,J=8Hz), 8.48(2H,d,J=8Hz), 8.88(1H,br s)

Example 154

The object compound was obtained according to a similar manner to that of Example 1.

mp : 125-130°C

MASS (m/z) : 502 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.09(3H,t,J=8Hz), 3.42-3.52(1H,m), 3.54-3.64(1H,m), 4.00-4.11(1H,m), 4.20-4.31(1H,m), 5.91(1H,q,J=8Hz), 7.01(1H,t,J=8Hz), 7.03(1H,s), 7.10-7.20(3H,m), 7.28(1H,s), 7.32-7.40(2H,m), 7.52-7.69(2H,m), 7.53(2H,d,J=8Hz), 7.73(2H,d,J=8Hz), 7.80(1H,s), 8.31(1H,s), 8.50(1H,d,J=4Hz), 9.10(1H,d,J=8Hz)

Example 155

The object compound was obtained according to a similar manner to that of Example 1.

mp : 140-145°C

MASS (m/z) : 480 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.01(3H,t,J=8Hz), 1.37(3H,t,J=8Hz), 3.41-3.51(1H,m), 3.52-3.63(1H,m), 3.89-4.22(2H,m), 4.02(2H,q,J=8Hz), 5.89(1H,q,J=8Hz), 6.88(1H,s), 6.94-7.00(3H,m), 7.17(2H,t,J=8Hz), 7.22-7.36(4H,m), 7.40(1H,d,J=8Hz), 7.58-7.68(2H,m), 8.50(1H,d,J=2Hz), 9.08(1H,d,J=8Hz)

Example 156

The object compound was obtained according to a similar manner to that of Example 1.

mp : 255-260°C

MASS (m/z) : 507 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.10-3.18(4H,m), 3.40-3.51(1H,m), 3.52-3.63(1H,m), 3.59(3H,s), 3.69-3.80(4H,m), 5.88(1H,q,J=8Hz), 6.89(1H,s), 6.95-7.07(3H,m), 7.18(2H,t,J=8Hz), 7.22(1H,s), 7.27(2H,d,J=8Hz), 7.31(1H,d,J=8Hz), 7.39(1H,d,J=8Hz), 7.59(1H,t,J=8Hz), 7.61(1H,t,J=8Hz), 8.49(1H,d,J=2Hz), 9.00(1H,d,J=8Hz)

Example 157

To a suspension of the starting compound (244 mg) in methanol (10 ml) was added 10% hydrogen chloride/methanol (1 ml). The mixture was evaporated and the residue was dried *in vacuo* to give the object compound as a pale yellow amorphous powder (275 mg).

MASS (ESI) (m/z) : 488 (free, M+H)$^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.82-4.05(2H,m), 3.91(3H,s), 6.04-6.18(1H,m), 6.98-7.10(1H,m), 7.15-7.25(1H,m), 7.32-7.45(2H,m), 7.48-7.74(2H,m), 7.78-7.85(1H,m), 7.88(2H,d,J=8Hz), 7.92-8.01(2H,m), 8.04(2H,d,J=8Hz), 8.07-8.18(1H,m), 8.40(1H,s), 8.71(1H,d,J=5Hz), 9.78(1H,br d,J=8Hz), 9.88(1H,s), 10.50(1H,br s)

Example 158

The object compound was obtained according to a similar manner to that of Example 1.

mp : 235-236°C

MASS (ESI) (m/z) : 501 $(M-H)^-$

^{1}H-NMR (DMSO-d_6, 300MHz) δ : 1.08(3H,t,J=7Hz), 3.51-3.62(2H,m), 3.98-4.30(2H,m), 5.80-5.95(1H,m), 7.03(1H,s), 7.12(1H,s), 7.15-7.37(4H,m), 7.46-7.77(7H,m), 7.81(1H,s), 8.32(1H,s), 8.51(1H,d,J=5Hz), 9.16(1H,br d,J=8Hz), 10.50(1H,br s)

Example 159

The object compound was obtained according to a similar manner to that of Example 1.

mp : 255-260°C (dec.)

MASS (ESI) (m/z) : 521 $(M+H)^+$

^{1}H-NMR (DMSO-d_6, 300MHz) δ : 1.04(3H,t,J=7Hz), 3.08-3.19(4H,m), 3.39-3.64(2H,m), 3.67-3.79(4H,m), 3.87-4.23(2H,m), 5.80-5.95(1H,m), 6.81-7.69(13H,m), 8.48(1H,d,J=5Hz), 9.06(1H,br d,J=8Hz), 10.50(1H,br s)

Example 160

The object compound was obtained according to a similar manner to that of Example 1.

MASS (ESI) (m/z) : 516 $(M+H)^+$

^{1}H-NMR (DMSO-d_6, 300MHz) δ : 0.64(3H,t,J=7Hz), 1.31-1.55(2H,m), 3.41-3.67(2H,m), 3.90-4.28(2H,m), 5.86-6.00(1H,m), 6.97-7.21(5H,m), 7.27(1H,s), 7.29-7.42(2H,m), 7.53(2H,d,J=8Hz), 7.55-7.68(2H,m), 7.73(2H,d,J=8Hz), 7.81(1H,s), 8.32(1H,s), 8.49(1H,d,J=5Hz), 9.09(1H,br d,J=8Hz), 10.50(1H,br s)

Example 161

The object compound was obtained according to a similar manner to that of Example 1.

mp : 209-210°C (dec.)

MASS (ESI) (m/z) : 489 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 3.41-3.66(2H,m), 3.68(3H,s), 5.84-5.99(1H,m), 6.96-7.07(1H,m), 7.10(1H,s), 7.11-7.21(2H,m), 7.25(1H,s), 7.30-7.42(2H,m), 7.54-7.69(2H,m), 7.62(2H,d,J=8Hz), 7.93(2H,d,J=8Hz), 8.26(1H,s), 8.49(1H,d,J=5Hz), 9.05(1H,br d,J=8Hz), 9.34(1H,s), 10.50(1H,br s)

Example 162

The object compound was obtained according to a similar manner to that of Example 1.

mp : 227-228°C (dec.)

MASS (ESI) (m/z) : 503 $(M+H)^+$

^{1}H-NMR (DMSO-d_6,300MHz) δ : 1.08(3H,t,J=7Hz), 3.42-3.67(2H,m), 3.99-4.35(2H,m), 5.84-6.00(1H,m), 6.95-7.05(1H,m), 7.05(1H,s), 7.11-7.22(2H,m), 7.26(1H,s), 7.29-7.41(2H,m), 7.54-7.70(4H,m), 7.93(2H,d,J=8Hz), 8.26(1H,s), 8.49(1H,d,J=5Hz), 9.10(1H,br d,J=8Hz), 9.34(1H,s), 10.50(1H,br s)

Example 163

The object compound was obtained according to a similar manner to that of Example 1.

mp : 240-243°C

MASS (m/z) : 505 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.49-2.68(6H,m), 3.13-3.23(4H,m), 3.42-3.51(1H,m), 3.52-3.60(1H,m), 3.58(3H,s), 5.89(1H,q,J=8Hz), 6.85(1H,s), 6.98(2H,d,J=8Hz), 7.01(1H,t,J=8Hz), 7.11-7.29(5H,m), 7.31(1H,d,J=8Hz), 7.39(1H,d,J=8Hz), 7.59(1H,d,J=8Hz), 7.61(1H,t,J=8Hz), 8.49(1H,d,J=2Hz), 9.00(1H,d,J=8Hz)

Example 164

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS (m/z) : 565 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.81(3H,s), 3.26(1H,dd,J=12.0 and 9.0Hz),
3.46(1H,dd,J=12.0 and 6.0Hz), 5.49(1H,m),
6.97-7.06(4H,m), 7.10(2H,d,J=7.5Hz), 7.13-7.30(6H,m),
7.36(1H,d,J=7.5Hz), 7.50(2H,d,J=7.5Hz), 7.48-7.58(1H,m),
7.63(1H,d,J=7.5Hz)

Example 165

The object compound was obtained according to a similar manner to that of Preparation 5.

orange amorphous solid

MASS (m/z) : 453 $(M+H)^+$

^{1}H-NMR ($CDCl_3$-CD_3OD) δ : 3.50-3.60(2H,m), 5.68(1H,t,J=7.0Hz),
7.11(1H,s), 7.11-7.38(5H,m), 7.40(1H,d,J=7.5Hz),
7.61-7.70(2H,m), 7.78-7.89(2H,m), 8.23(2H,d,J=7.5Hz),
8.50(1H,m)

Example 166

The object compound was obtained according to a similar manner to that of Preparation 5.

yellow amorphous solid

MASS (m/z) : 609 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.53-3.67(2H,m), 3.61(3H,s),
5.76-5.86(1H,m), 6.93-7.61(12H,m), 7.10(1H,s),
7.32(2H,d,J=7.5Hz), 7.77(1H,d,J=7.5Hz), 7.91(1H,d,J=7.5Hz),
8.25(2H,d,J=7.5Hz), 8.53(1H,m)

Example 167

The object compound was obtained according to a similar manner to that of Example 1.

yellow amorphous solid

MASS (m/z) : 581 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.09(3H,t,J=7.0Hz),
3.32(1H,dd,J=14.5 and 5.5Hz), 3.45(1H,dd,J=14.5 and 7.5Hz),
3.64(3H,s), 4.16(2H,q,J=7.0Hz), 6.01(1H,m), 6.81(1H,s),
7.03-7.12(2H,m), 7.20-7.59(8H,m), 7.51(2H,d,J=7.5Hz),

8.30(2H,d,J=7.5Hz), 8.51(1H,s), 9.31(1H,br s)

Example 168

The object compound was obtained according to a similar manner to that of Example 73.

off-white solid

mp : 189-191℃

MASS (m/z) : 551 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.10(1H,dd,J=14.5 and 7.5Hz), 3.47(1H,dd,J=14.5 and 7.5Hz), 3.57(3H,s), 5.83(1H,q,J=7.5Hz), 6.97-7.07(2H,m), 7.19(1H,t,J=7.5Hz), 7.25-7.30(3H,m), 7.41(1H,d,J=7.5Hz), 7.59(2H,d,J=7.5Hz), 7.61(1H,d,J=7.5Hz), 7.71(2H,d,J=7.5Hz), 8.30(2H,d,J=7.5Hz), 9.15(1H,d,J=7.5Hz)

Example 169

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow solid

mp : 189-192℃

MASS (m/z) : 656 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 2.78(3H x 4/9,s), 2.86(3H x 5/9,s), 3.00(1H,dd,J=15.0 and 5.5Hz), 3.42(1H,m), 3.58(3H x 4/9,s), 3.61(3H x 5/9,s), 4.32(1H x 4/9,d,J=15.0Hz), 4.43(1H x 5/9,d,J=15.0Hz), 4.58(1H x 5/9,d,J=15.0Hz), 4.97(1H x 4/9,d,J=15.0Hz), 5.90(1H,m), 6.82(1H,m), 6.95-7.04(1H,m), 7.03(1H,t,J=7.5Hz), 7.09-7.35(8H,m), 7.42(1H,d,J=7.5Hz), 7.50-7.63(4H,m), 7.68(1H,d,J=7.5Hz), 8.26(2H,d,J=7.5Hz), 9.10(1H,d,J=7.5Hz)

Example 170

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow solid

mp : 290-291.5℃

MASS (m/z) : 642 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 2.99(1H,dd,J=14.5 and 5.5Hz), 3.49(3H,s), 3.49(1H,m), 4.41(2H,d,J=7.0Hz), 5.84(1H,m), 7.01(1H,t,J=7.5Hz), 7.03(1H,t,J=7.5Hz), 7.15-7.32(9H,m), 7.42(1H,d,J=7.5Hz), 7.53(2H,d,J=7.5Hz), 7.60(1H,d,J=7.5Hz), 7.75(2H,d,J=7.5Hz), 8.29(2H,d,J=7.5Hz), 8.51(1H,t,J=7.0Hz), 9.10(1H,d,J=7.5Hz)

Example 171

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow solid

mp : 208-212℃

MASS (m/z) : 539 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 1.13(3H,t,J=7.0Hz), 3.48(3H,s), 3.68(2H,d,J=7.5Hz), 4.21(2H,q,J=7.0Hz), 6.03(1H,q,J=7.5Hz), 6.98(1H,s), 7.11(2H,d,J=7.5Hz), 7.15(1H,d,J=7.5Hz), 7.27(1H,t,J=7.5Hz), 7.37(1H,d,J=7.5Hz), 7.49(2H,d,J=7.5Hz), 7.53(1H,t,J=7.5Hz), 7.62-7.69(2H,m), 7.30(2H,d,J=7.5Hz), 7.52(1H,m), 9.22(1H,br s)

Example 172

The object compound was obtained according to a similar manner to that of Example 73.

off-white solid

mp : 177-181℃

MASS (m/z) : 509 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.50(3H,s), 3.52-3.62(2H,m), 5.76(1H,m), 7.01(1H,t,J=7.5Hz), 7.12-7.21(2H,m), 7.24(1H,s), 7.38(2H,d,J=7.5Hz), 7.60(1H,d,J=7.5Hz), 7.67(1H,t,J=7.5Hz), 7.68(2H,d,J=7.5Hz), 8.29(2H,d,J=7.5Hz), 8.49(1H,d,J=5.5Hz), 9.17(1H,d,J=7.5Hz)

Example 173

The object compound was obtained according to a similar manner to

that of Example 1.

pale yellow amorphous solid

MASS (m/z) : 586 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.53(3H,s), 3.62(2H,d,J=7.5Hz),
5.96(1H,q,J=7.5Hz), 7.05(1H,s), 7.08(1H,t,J=7.5Hz),
7.12-7.35(6H,m), 7.41(1H,d,J=7.5Hz), 7.53-7.61(4H,m),
7.68(1H,t,J=7.5Hz), 7.69(1H,d,J=7.5Hz), 8.20(1H,d,J=7.5Hz),
8.28(2H,d,J=7.5Hz), 8.62(1H,m), 8.90(1H,s), 9.21(1H,br s)

Example 174

The object compound was obtained according to a similar manner to that of Example 1.

yellow amorphous solid

MASS (m/z) : 456 $(M+H)^+$

^{1}H-NMR ($CDCl_3$-CD_3OD) δ : 3.43(1H,dd,J=14.5 and 7.5Hz),
3.51(1H,dd,J=14.5 and 7.5Hz), 3.64(3H,s), 5.80(1H,t,J=7.5Hz),
6.90(2H,s), 7.07-7.19(3H,m), 7.27(1H,t,J=7.5Hz),
7.42(1H,d,J=7.5Hz), 7.51(2H,d,J=7.5Hz), 7.65(1H,d,J=7.5Hz),
8.30(2H,d,J=7.5Hz)

Example 175

The object compound was obtained according to a similar manner to that of Example 1.

yellow amorphous solid

MASS (m/z) : 512 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.63(1H,dd,J=14.5 and 7.5Hz),
3.70(1H,dd,J=14.5 and 7.5Hz), 3.77(3H,s), 6.07(1H,m),
7.01-7.22(5H,m), 7.44-7.58(1H,m), 7.51(2H,d,J=7.5Hz),
7.90(1H,d,J=7.5Hz), 8.19(1H,dd,J=7.5 and 1.5Hz),
8.30(2H,d,J=7.5Hz), 8.57(1H,d,J=1.5Hz), 9.12(1H,m)

Example 176

The object compound was obtained according to a similar manner to that of Example 1.

yellow solid

mp : 195-196.5℃

MASS (m/z) : 473 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.44(1H,dd,J=14.5 and 7.5Hz), 3.62(1H,dd,J=14.5 and 7.5Hz), 3.77(3H,s), 5.88(1H,q,J=7.5Hz), 7.21(1H,dd,J=7.5 and 4.5Hz), 7.28(1H,s), 7.37(1H,d,J=7.5Hz), 7.47(1H,d,J=7.5Hz), 7.63-7.80(3H,m), 7.77(2H,d,J=7.5Hz), 8.00(1H,d,J=7.5Hz), 8.31(2H,d,J=7.5Hz), 8.52(1H,d,J=4.5Hz), 9.37(1H,d,J=7.5Hz)

Example 177

The object compound was obtained according to a similar manner to that of Example 1.

off-white solid

mp : 243-245.5℃

MASS (m/z) : 563 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.66(3H,s), 7.05(1H,t,J=7.5Hz), 7.11-7.19(4H,m), 7.21(1H,t,J=7.5Hz), 7.29-7.33(2H,m), 7.37-7.47(3H,m), 7.49(2H,d,J=7.5Hz), 7.57(1H,d,J=7.5Hz), 7.64(1H,d,J=7.5Hz), 7.69(2H,d,J=7.5Hz), 8.01(1H,d,J=7.5Hz), 9.90(1H,s)

Example 178

The object compound was obtained according to a similar manner to that of Preparation 2.

pale yellow amorphous solid

MASS (m/z) : 476 $(M-H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.26(3H,s), 2.36(3H,s), 5.02(2H,s), 7.03(1H,d,J=8.5Hz), 7.15-7.36(9H,m), 7.57(2H,d,J=8.5Hz), 7.71(1H,s)

Example 179

The object compound was obtained according to a similar manner to that of Example 1.

off-white solid

mp : 311-319℃

MASS (m/z) : 577 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.43(3H,s), 4.63(2H,s), 7.05-7.13(3H,m), 7.18-7.29(5H,m), 7.31(1H,s), 7.32-7.49(4H,m), 7.43(2H,d,J=8.5Hz), 7.67(1H,d,J=8.5Hz), 7.70(2H,d,J=8.5Hz), 7.98(1H,dd,J=8.5 and 1.5Hz), 9.75(1H,s)

Example 180

The object compound was obtained according to a similar manner to that of Example 1.

off-white solid

mp : 232-234°C

MASS (m/z) : 563 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.67(3H,s), 7.06-7.27(7H,m), 7.39-7.49(4H,m), 7.51-7.58(3H,m), 7.69(2H,d,J=8.5Hz), 7.72(1H,d,J=8.5Hz), 8.54(1H,d,J=8.5Hz)

Example 181

The object compound was obtained according to a similar manner to that of Example 1.

off-white solid

mp : 251-252.5°C

MASS (m/z) : 575 $(M-H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.61(3H,s), 5.35(2H,s), 7.08(1H,t,J=7.5Hz), 7.22(1H,s), 7.23(1H,t,J=7.5Hz), 7.28-7.42(5H,m), 7.45-7.53(4H,m), 7.58(2H,d,J=7.5Hz), 7.65-7.73(3H,m), 8.00(1H,d,J=7.5Hz), 9.59(1H,s)

Example 182

The object compound was obtained according to a similar manner to that of Example 1.

off-white solid

mp : 253-255°C

MASS (m/z) : 547 $(M+H)^+$

^{1}H-NMR ($CDCl_3$-CD_3OD) δ : 3.70(3H,s), 6.48(1H,s), 7.12(1H,t,J=7.5Hz), 7.18(1H,s), 7.26-7.35(1H,m),

7.33(2H,d,J=7.5Hz), 7.46(1H,d,J=7.5Hz), 7.50-7.63(8H,m), 7.67-7.73(2H,m), 8.61(1H,d,J=7.5Hz)

Example 183

The object compound was obtained according to a similar manner to that of Preparation 5.

off-white amorphous solid

MASS (m/z) : 345 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.71(3H,br s), 4.77(2H,br s), 5.20(2H,br s), 6.80(1H,s), 7.01(1H,m), 7.09(1H,t,J=7.5Hz), 7.21-7.68(9H,m), 9.28(1H,br s)

Example 184

The object compound was obtained according to a similar manner to that of Example 1.

off-white amorphous solid

MASS (m/z) : 421 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 4.77(2H,br s), 5.11(2H,br s), 5.42(2H,br s), 6.91(1H,s), 6.91-7.18(3H,m), 7.21-7.60(13H,m), 9.07(1H,br s)

Example 185

The object compound was obtained according to a similar manner to that of Preparation 5 except that dimethylformamide was used instead of dichloromethane.

off-white solid

mp : 198-200°C

MASS (m/z) : 241 $(M+H)^+$

^{1}H-NMR (DMSO-d_6) δ : 3.57(3H,s), 6.83(1H,s), 6.90-7.22(4H,m), 7.43(1H x 4/7,s), 7.47(1H x 3/7,s), 7.52-7.66(1H,m)

Example 186

The object compound was obtained according to a similar manner to that of Example 1.

yellowish brown amorphous solid

MASS (m/z) : 467 $(M+H)^+$

^{1}H-NMR ($CDCl_3$-CD_3OD) δ : 3.54(2H,t,J=7.0Hz), 3.72(3H,s),

5.90(1H,t,J=7.0Hz), 7.06-7.43(7H,m), 7.59(1H,t,J=7.5Hz), 7.66(1H,d,J=7.5Hz), 7.81(2H,d,J=7.5Hz), 8.22(2H,d,J=8.5Hz), 8.50(1H,d,J=4.5Hz)

Example 187

The object compound was obtained according to a similar manner to that of Example 1.

off-white solid

mp : 130-132°C

MASS (m/z) : 423 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.68(2H,d,J=7.5Hz), 3.69(3H,s), 6.07(1H,q,J=7.5Hz), 7.08(1H,d,J=1.0Hz), 7.10-7.18(4H,m), 7.21(2H,d,J=5.5Hz), 7.26(1H,t,J=7.5Hz), 7.40(1H,d,J=7.5Hz), 7.55(1H,t,J=7.5Hz), 7.65(1H,d,J=7.5Hz), 8.16(1H,d,J=7.5Hz), 8.52(1H,d,J=4.5Hz), 8.64(2H,d,J=5.5Hz), 9.62(1H,s)

Example 188

The object compound was obtained according to a similar manner to that of Example 1.

pale yellow amorphous solid

MASS (m/z) : 500 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 3.09(3H,s), 3.42(1H,dd,J=13.0 and 9.0Hz), 3.53(1H,dd,J=13.0 and 7.0Hz), 5.58(1H,m), 7.11-7.19(2H,m), 7.22-7.48(9H,m), 7.71(1H,d,J=7.5Hz), 7.75(1H,d,J=7.5Hz), 7.90(1H,s), 7.98(1H,d,J=5.5Hz), 8.99(1H,d,J=7.5Hz), 9.06(1H,d,J=5.5Hz)

Example 189

The object compound was obtained according to a similar manner to that of Example 1.

colorless solid

mp : 224-228°C

MASS (m/z) : 497 $(M+H)^+$

^{1}H-NMR ($CDCl_3$) δ : 2.80(3H,s), 3.33(1H,dd,J=13.5 and 9.0Hz), 3.52(1H,dd,J=13.5 and 6.0Hz), 5.57(1H,m), 7.05(1H,d,J=1.0Hz),

7.10-7.31(12H,m), 7.37-7.45(4H,m), 7.50(2H,d,J=7.5Hz),
7.63(1H,d,J=7.5Hz), 7.69(1H,d,J=7.5Hz), 9.27(1H,s)

Example 190

The object compound was obtained according to a similar manner to that of Example 1.

mp : 200-210°C

MASS : 520 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.21(3H,s), 2.41-2.49(4H,m),
3.11-3.20(4H,m), 3.40-3.51(1H,m), 3.52-3.61(1H,m), 3.59(3H,s),
5.88(1H,q,J=8Hz), 6.83(1H,s), 6.92-7.07(3H,m),
7.13(2H,t,J=8Hz), 7.20(1H,s), 7.21-7.28(2H,m),
7.31(1H,d,J=8Hz), 7.39(1H,d,J=8Hz), 7.60(1H,t,J=8Hz),
7.61(1H,t,J=8Hz), 8.49(1H,d,J=4Hz), 9.00(1H,d,J=8Hz)

Example 191

The object compound was obtained according to a similar manner to that of Example 1.

mp : 145-150°C

MASS : 506 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.43-3.64(2H,m), 3.69(3H,s),
5.91(1H,q,J=8Hz), 7.02(1H,t,J=8Hz), 7.08(1H,s), 7.11(1H,s),
7.19(1H,t,J=8Hz), 7.26(1H,s), 7.31-7.41(3H,m),
7.58(2H,d,J=8Hz), 7.63(1H,t,J=8Hz), 7.72(2H,d,J=8Hz),
7.80(1H,s), 8.31(1H,s), 8.50(1H,d,J=4Hz), 9.11(1H,d,J=8Hz)

Example 192

The object compound was obtained according to a similar manner to that of Example 1.

mp : 145-152°C

MASS : 518 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.41-3.52(1H,m), 3.52-3.63(1H,m),
3.63(3H,s), 3.71(3H,s), 5.90(1H,q,J=8Hz), 6.81(1H,d,J=8Hz),
7.08(1H,s), 7.09(1H,s), 7.11(1H,s), 7.12-7.20(2H,m),
7.29(1H,d,J=8Hz), 7.32(1H,d,J=8Hz), 7.58(2H,d,J=8Hz),

7.62(1H,t,J=8Hz), 7.71(2H,d,J=8Hz), 7.80(1H,s), 8.31(1H,s),
8.50(1H,d,J=4Hz), 9.00(1H,d,J=8Hz)

Example 193

The object compound was obtained according to a similar manner to that of Example 1.

mp : 155-160°C

MASS : 522 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.43-3.54(1H,m), 3.56-3.67(1H,m),
3.71(3H,s), 5.90(1H,q,J=8Hz), 7.08(1H,s), 7.11(1H,s),
7.14-7.20(2H,m), 7.28(1H,s), 7.35(1H,d,J=8Hz),
7.40(1H,d,J=8Hz), 7.58(2H,d,J=8Hz), 7.60-7.70(2H,m),
7.72(2H,d,J=8Hz), 7.80(1H,s), 8.30(1H,s), 8.49(1H,d,J=4Hz),
9.18(1H,d,J=8Hz)

Example 194

The object compound was obtained according to a similar manner to that of Example 1.

mp : 175-180°C

MASS : 574 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.90-3.00(1H,m), 3.37-3.49(1H,m),
3.70(3H,s), 5.82-5.91(1H,m), 5.93(2H,s), 6.82(1H,d,J=8Hz),
6.98(1H,d,J=8Hz), 7.01(1H,t,J=8Hz), 7.09(1H,s), 7.11(1H,s),
7.20(1H,t,J=8Hz), 7.29(2H,d,J=4Hz), 7.42(1H,d,J=8Hz),
7.60(1H,d,J=8Hz), 7.61(2H,d,J=8Hz), 7.72(2H,d,J=8Hz),
7.80(1H,s), 8.31(1H,s), 9.03(1H,d,J=8Hz)

Example 195

The object compound was obtained according to a similar manner to that of Example 1.

mp : 225-230°C

MASS : 498 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.43-3.53(1H,m), 3.56-3.67(1H,m),
3.70(3H,s), 5.91(1H,q,J=8Hz), 7.01(1H,t,J=8Hz), 7.07(1H,s),
7.11-7.20(2H,m), 7.28(1H,s), 7.30-7.41(3H,m), 7.42-7.58(4H,m),

7.60(2H,t,J=8Hz), 7.64-7.79(4H,m), 8.50(1H,d,J=2Hz),
9.07(1H,d,J=8Hz)

Example 196

The object compound was obtained according to a similar manner to that of Example 1.

mp : 165-170°C

MASS : 560 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 2.90-3.00(1H,m), 3.31(3H,s),
3.38-3.49(1H,m), 3.70(3H,s), 5.89(1H,q,J=8Hz),
6.86(2H,d,J=8Hz), 7.01(1H,t,J=8Hz), 7.06(1H,s), 7.11(1H,s),
7.19(1H,t,J=8Hz), 7.29(1H,s), 7.41(1H,d,J=8Hz),
7.49(2H,d,J=8Hz), 7.58-7.62(3H,m), 7.72(2H,d,J=8Hz),
7.80(1H,s), 8.31(1H,s), 9.02(1H,d,J=8Hz), 11.62(1H,s)

Example 197

The object compound was obtained according to a similar manner to that of Example 1.

mp : 110-115°C

MASS : 500 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 2.31(3H,s), 3.42-3.53(1H,m),
3.54-3.62(1H,m), 3.69(3H,s), 5.90(1H,q,J=8Hz),
7.00(1H,d,J=8Hz), 7.05(1H,s), 7.10-7.20(3H,m),
7.28(1H,d,J=8Hz), 7.31(1H,d,J=8Hz), 7.38(1H,s),
7.58(2H,d,J=8Hz), 7.7.62(1H,t,J=8Hz), 7.71(2H,d,J=8Hz),
7.79(1H,s), 8.30(1H,s), 8.50(1H,d,J=2Hz), 9.00(1H,d,J=8Hz)

Example 198

The object compound was obtained according to a similar manner to that of Example 1.

mp : 140-145°C

MASS : 516 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.40(3H,d,J=4Hz), 1.41(3H,d,J=4Hz),
3.49(2H,t,J=8Hz), 4.53-4.69(1H,m), 5.99(1H,q,J=4Hz),
6.91(1H,s), 7.01(1H,t,J=8Hz), 7.12(1H,s), 7.16-7.22(2H,m),

7.30(1H,s), 7.31-7.40(2H,m), 7.49(2H,d,J=8Hz),
7.56-7.70(2H,m), 7.73(2H,d,J=8Hz), 7.81(1H,s), 8.31(1H,s),
8.51(1H,d,J=8Hz), 9.02(1H,d,J=8Hz)

Example 199

The object compound was obtained according to a similar manner to that of Example 1.

mp : 135-140°C

MASS : 520 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.00(3H,t,J=8Hz), 3.43-3.53(1H,m),
3.55-3.65(1H,m), 4.00-4.14(1H,m), 4.18-4.31(1H,m),
5.92(1H,q,J=8Hz), 6.99-7.10(1H,m), 7.05(1H,s), 7.11(1H,s),
7.13-7.21(1H,m), 7.27(1H,s), 7.31(1H,s), 7.32-7.41(2H,m),
7.57(2H,d,J=8Hz), 7.65(1H,t,J=8Hz), 7.73(2H,d,J=8Hz),
7.81(1H,s), 8.31(1H,s), 8.50(1H,d,J=2Hz), 9.19(1H,d,J=8Hz)

Example 200

The object compound was obtained according to a similar manner to that of Example 1.

mp : 130-135°C

MASS : 536 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.09(3H,t,J=8Hz), 3.42-3.52(1H,m),
3.53-3.63(1H,m), 4.00-4.15(1H,m), 4.18-4.31(1H,m),
5.91(1H,q,J=8Hz), 7.02(1H,s), 7.10-7.20(3H,m),
7.27(1H,s), 7.32(1H,d,J=8Hz), 7.40(1H,d,J=8Hz),
7.53(2H,d,J=8Hz), 7.64(1H,t,J=8Hz), 7.69(1H,s),
7.72(2H,d,J=8Hz), 7.80(1H,s), 8.31(1H,s), 8.50(1H,d,J=4Hz),
9.21(1H,d,J=8Hz)

Example 201

The object compound was obtained according to a similar manner to that of Example 1.

mp : 170-175°C

MASS : 532 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 0.62(3H,t,J=8Hz), 1.30-1.52(2H,m),

3.42-3.53(1H,m), 3.54-3.68(1H,m), 3.91-4.08(1H,m),
4.10-4.28(1H,m), 5.92(1H,q,J=8Hz), 6.99-7.09(1H,m),
7.01(1H,s), 7.11(1H,s), 7.12-7.20(1H,m), 7.26(1H,s),
7.30-7.41(3H,m), 7.51(2H,d,J=8Hz), 7.62(1H,t,J=8Hz),
7.73(2H,d,J=8Hz), 7.81(1H,s), 8.32(1H,s), 8.50(1H,d,J=2Hz),
9.17(1H,d,J=8Hz)

Example 202

The object compound was obtained according to a similar manner to that of Example 1.

mp : 136-138℃

MASS : 550 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.60(3H,t,J=8Hz), 1.32-1.52(2H,m),
3.42-3.52(1H,m), 3.55-3.68(1H,m), 3.90-4.08(1H,m),
4.11-4.25(1H,m), 5.91(1H,q,J=8Hz), 7.01(1H,s), 7.11(1H,s),
7.17(2H,dd,J=8Hz and 2Hz), 7.23(1H,s), 7.31(1H,d,J=8Hz),
7.40(1H,d,J=8Hz), 7.53(2H,d,J=8Hz), 7.62(1H,t,J=8Hz),
7.70(1H,s), 7.73(2H,d,J=8Hz), 7.80(1H,s), 8.32(1H,s),
8.50(1H,d,J=2Hz), 9.20(1H,d,J=8Hz)

Example 203

The object compound was obtained according to a similar manner to that of Example 1.

mp : 148-152℃

MASS : 550 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.40(6H,t,J=8Hz), 3.42-3.52(2H,m),
4.51-4.68(1H,m), 5.99(1H,q,J=8Hz), 6.91(1H,s), 7.11(1H,s),
7.19(2H,t,J=8Hz), 7.30(1H,s), 7.31(1H,d,J=8Hz),
7.39(1H,d,J=8Hz), 7.50(2H,d,J=8Hz), 7.63(1H,t,J=8Hz),
7.70(1H,s), 7.73(2H,d,J=8Hz), 7.81(1H,s), 8.31(1H,s),
8.50(1H,d,J=4Hz), 9.17(1H,d,J=8Hz)

Example 204

The object compound was obtained according to a similar manner to that of Example 1.

mp : 140-145℃

MASS : 534 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.38(6H,t,J=7Hz), 3.43-3.53(2H,m),
4.52-4.64(1H,m), 5.95(1H,q,J=8Hz), 6.91(1H,s),
7.01(1H,t,J=8Hz), 7.12(1H,s), 7.17(2H,t,J=6Hz), 7.20(1H,s),
7.32-7.42(3H,m), 7.47(2H,d,J=8Hz), 7.62(1H,t,J=8Hz),
7.72(2H,d,J=8Hz), 7.81(1H,s), 8.50(1H,d,J=4Hz),
9.11(1H,d,J=8Hz)

Example 205

The object compound was obtained according to a similar manner to that of Example 1.

mp : 240-245℃

MASS : 530 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.63(3H,t,J=8Hz), 1.00-1.13(2H,m),
1.30-1.50(2H,m), 3.41-3.51(1H,m), 3.58-3.68(1H,m),
3.91-4.08(1H,m), 4.18-4.30(1H,m), 5.92(1H,q,J=8Hz),
7.01(1H,t,J=8Hz), 7.03(1H,s), 7.11(1H,s), 7.12-7.20(2H,m),
7.27(1H,s), 7.31(1H,d,J=8Hz), 7.39(1H,d,J=8Hz),
7.52(2H,d,J=8Hz), 7.53-7.69(2H,m), 7.72(2H,d,J=8Hz),
7.80(1H,s), 8.30(1H,s), 8.49(1H,d,J=2Hz), 9.09(1H,d,J=8Hz)

Example 206

The object compound was obtained according to a similar manner to that of Example 1.

mp : 235-240℃

MASS : 565 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.63(3H,t,J=8Hz), 1.00-1.11(2H,m),
1.30-1.50(2H,m), 3.40-3.56(1H,m), 3.58-3.70(1H,m),
3.91-4.08(1H,m), 4.18-4.30(1H,m), 5.93(1H,q,J=8Hz),
7.07(1H,t,J=6Hz), 7.11-7.22(3H,m), 7.28(1H,s),
7.32(1H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.58(2H,d,J=8Hz),
7.67(1H,t,J=8Hz), 7.69(1H,s), 7.74(2H,d,J=8Hz), 7.82(1H,s),
8.31-8.45(1H,m), 8.50(1H,d,J=2Hz), 9.21(1H,d,J=8Hz)

Example 207

The object compound was obtained according to a similar manner to that of Example 1.

mp : 235-240°C

MASS : 546 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 0.63(3H,t,J=8Hz), 0.98-1.11(2H,m), 1.30-1.48(2H,m), 3.40-3.51(1H,m), 3.58-3.69(1H,m), 3.90-4.08(1H,m), 4.17-4.30(1H,m), 5.92(1H,q,J=8Hz), 6.98-7.09(1H,m), 7.02(1H,s), 7.11(1H,s), 7.13-7.20(1H,m), 7.28(1H,s), 7.30-7.42(3H,m), 7.52(2H,d,J=8Hz), 7.62(1H,t,J=8Hz), 7.73(2H,d,J=8Hz), 7.81(1H,s), 8.32(1H,s), 8.49(1H,d,J=2Hz), 9.16(1H,d,J=8Hz)

Example 208

The object compound was obtained according to a similar manner to that of Example 1.

mp : 235-240°C

MASS : 544 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.61(3H,t,J=8Hz), 0.97-1.00(4H,m), 1.31-1.50(2H,m), 3.41-3.52(1H,m), 3.59-3.70(1H,m), 3.90-4.08(1H,m), 4.18-4.30(1H,m), 5.93(1H,q,J=8Hz), 7.00(1H,d,J=8Hz), 7.02(1H,s), 7.10-7.20(3H,m), 7.28(1H,s), 7.32(1H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.52(2H,d,J=8Hz), 7.57-7.70(2H,m), 7.72(2H,d,J=8Hz), 7.81(1H,s), 8.31(1H,s), 8.50(1H,d,J=2Hz), 9.00(1H,d,J=8Hz)

Example 209

The object compound was obtained according to a similar manner to that of Example 1.

mp : 220-225°C

MASS : 562 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.60(3H,t,J=8Hz), 0.92-1.10(4H,m), 1.36-1.50(2H,m), 3.40-3.51(1H,m), 3.58-3.70(1H,m), 3.91-4.08(1H,m), 4.12-4.30(1H,m), 5.92(1H,q,J=8Hz),

6.99-7.09(1H,m), 7.00(1H,s), 7.10(1H,s), 7.19(1H,t,J=8Hz),
7.28(1H,s), 7.30-7.40(3H,m), 7.53(2H,d,J=8Hz),
7.63(1H,t,J=8Hz), 7.73(2H,d,J=8Hz), 7.82(1H,s), 8.32(1H,s),
8.50(1H,d,J=2Hz), 9.18(1H,d,J=8Hz)

Example 210

The object compound was obtained according to a similar manner to that of Example 1.

mp : 53-56°C

MASS (m/z) : 500 (M^++1,bp)

^{1}H-NMR ($CDCl_3$) δ : 3.67(3H,s),
3.76(2H,ABX,J=16Hz, 15Hz and 7.5Hz),
6.10(1H,dd,J=7.5Hz and 7.5Hz), 7.10(1H,s), 7.12(1H,t,J=7.5Hz),
7.19-7.22(2H,m), 7.30(1H,s), 7.40-7.48(4H,m),
7.55(1H,ddd,J=7.5Hz, 7.5Hz and 2Hz),
7.64(1H,ddd,J=7.5Hz, 7.5Hz and 2Hz),
7.79(1H,ddd,J=7.5Hz, 7.5Hz and 2Hz), 7.88(1H,d,J=7.5Hz),
7.90(1H,s), 8.18(1H,d,J=7.5Hz), 8.27(2H,AB,J=8Hz and 7.5Hz),
8.57(1H,d,J=2Hz), 9.08(1H,d,J=7.5Hz)

Example 211

The object compound was obtained according to a similar manner to that of Example 1.

mp : 100-105°C

MASS : 566 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 3.42-3.53(1H,m), 3.54-3.61(1H,m),
3.68(3H,s), 5.90(1H,q,J=8Hz), 7.08(1H,s), 7.11(1H,s),
7.18(1H,t,J=6Hz), 7.27(1H,s), 7.29(1H,d,J=8Hz),
7.31-7.39(2H,m), 7.55(2H,d,J=8Hz), 7.63(1H,t,J=8Hz),
7.72(2H,d,J=8Hz), 7.81(2H,d,J=8Hz), 8.31(1H,s),
8.50(1H,d,J=2Hz), 9.19(1H,d,J=8Hz)

Example 212

The object compound was obtained according to a similar manner to that of Example 1.

mp : 105-110°C

MASS : 594 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 0.61(3H,t,J=8Hz), 1.32-1.52(2H,m), 3.41-3.53(1H,m), 3.57-3.63(1H,m), 3.90-4.05(1H,m), 4.12-4.28(1H,m), 5.92(1H,q,J=8Hz), 7.01(1H,s), 7.11(1H,s), 7.18(1H,t,J=6Hz), 7.24-7.40(4H,m), 7.53(2H,d,J=8Hz), 7.62(1H,t,J=8Hz), 7.72(2H,d,J=8Hz), 7.82(2H,d,J=8Hz), 8.31(1H,s), 8.50(1H,d,J=2Hz), 9.21(1H,d,J=8Hz)

Example 213

The object compound was obtained according to a similar manner to that of Example 1.

mp : 145-150°C

MASS : 580 (M+1)

^{1}H-NMR (DMSO-d_6) δ : 1.05(3H,t,J=8Hz), 3.41-3.52(1H,m), 3.42-3.63(1H,m), 3.99-4.12(1H,m), 4.15-4.30(1H,m), 5.91(1H,q,J=8Hz), 7.02(1H,s), 7.11(1H,s), 7.19(1H,t,J=6Hz), 7.23-7.40(4H,m), 7.55(2H,d,J=8Hz), 7.64(1H,t,J=8Hz), 7.72(2H,d,J=8Hz), 7.81(2H,d,J=8Hz), 8.31(1H,s), 8.50(1H,d,J=2Hz), 9.21(1H,d,J=8Hz)

Example 214

The object compound was obtained according to a similar manner to that of Example 1.

mp : 155-160°C

MASS : 512 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 0.97-1.02(4H,m), 3.27-3.40(2H,m), 3.41-3.49(1H,m), 3.50-3.60(1H,m), 6.11(1H,q,J=8Hz), 6.98-7.09(1H,m), 7.02(1H,s), 7.09-7.23(3H,m), 7.29(1H,s), 7.31(1H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.59-7.78(5H,m), 7.81(1H,s), 8.32(1H,s), 8.51(1H,d,J=8Hz), 9.00(1H,d,J=8Hz)

Example 215

The object compound was obtained according to a similar manner to that of Example 1.

mp : 208-218°C

MASS : 547 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 0.75-0.89(2H,m), 1.75(2H,d,J=8Hz), 3.10-3.20(1H,m), 3.38-3.69(2H,m), 6.00-6.19(2H,m), 6.25-6.38(1H,m), 7.11-7.24(3H,m), 7.31(1H,s), 7.35-7.41(2H,m), 7.47(2H,d,J=8Hz), 7.66-7.79(4H,m), 7.86(1H,s), 8.36(1H,s), 8.52(1H,d,J=4Hz), 9.18(1H,d,J=8Hz)

Example 216

The object compound was obtained according to a similar manner to that of Example 1.

mp : 100-105°C

MASS : 486 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 3.43-3.63(2H,m), 3.64(3H,s), 5.88(1H,q,J=8Hz), 6.48(1H,s), 7.02(1H,s), 7.11(1H,s), 7.18(1H,dd,J=8Hz and 4Hz), 7.33(1H,d,J=8Hz), 7.49(1H,t,J=4Hz), 7.51-7.58(3H,m), 7.58(1H,s), 7.63(1H,t,J=8Hz), 7.70(1H,s), 7.73(1H,s), 7.80(1H,s), 7.98(1H,s), 8.31(1H,s), 8.50(1H,d,J=4Hz), 8.92(1H,d,J=8Hz)

Example 217

The object compound was obtained according to a similar manner to that of Example 1.

mp : 115-120°C

MASS : 486 (M-1)

^{1}H-NMR (DMSO-d_6) δ : 1.57-1.72(2H,m), 2.20-2.48(4H,m), 3.40-3.53(2H,m), 5.79-5.91(1H,m), 6.00(1H,q,J=8Hz), 6.91(1H,s), 7.02(1H,t,J=8Hz), 7.10-7.22(3H,m), 7.30(1H,s), 7.31(1H,d,J=8Hz), 7.40(1H,d,J=8Hz), 7.49(2H,d,J=8Hz), 7.61(2H,d,J=8Hz), 7.72(2H,d,J=8Hz), 7.81(1H,s), 8.32(1H,s), 8.52(1H,d,J=4Hz), 9.01(1H,d,J=8Hz)

Example 218

The object compound was obtained according to a similar manner to that of Example 1.

mp : 55-75°C

^{1}H-NMR (DMSO-d_6) δ : 3.45-3.65(2H,m), 3.65(3H,s),
5.89(1H,q,J=6Hz), 7.08(1H,s), 7.14(1H,s),
7.20(1H,dd,J=8Hz and 6Hz), 7.30-7.38(2H,m), 7.48(1H,t,J=8Hz),
7.59(2H,d,J=8Hz), 7.61-7.71(3H,m) 7.75(2H,d,J=8Hz),
7.78-7.85(2H,m), 8.32(1H,s), 8.51(1H,d,J=4Hz),
9.28(1H,d,J=8Hz)

Example 219

The object compound was obtained according to a similar manner to that of Example 1.

mp : 146-150°C

ESI-MS(M+1) : 488

^{1}H-NMR (DMSO-d_6) δ : 3.42-3.67(2H,m), 3.68(3H,s),
5.92(1H,q,J=6Hz), 6.97-7.05(1H,m), 7.08(1H,s),
7.10-7.21(3H,m), 7.25(1H,s), 7.30-7.42(2H,m), 7.50-7.68(4H,m),
7.72(2H,d,J=8Hz), 7.80(1H,s) 8.32(1H,s), 8.50(1H,d,J=2Hz),
9.07(1H,d,J=8Hz)

Example 220

The object compound was obtained according to a similar manner to that of Example 1.

mp : 96-155°C

ESI-MS(M+1) : 488

^{1}H-NMR ($CDCl_3$) δ : 3.30(3H,s), 3.45-3.55(2H,m),
5.72(1H,q,J=6Hz), 7.05-7.50(12H,m), 7.65(1H,d,J=8Hz),
7.85-7.97(2H,m), 8.48(2H,d,J=8Hz), 9.61(1H,s)

Example 221

The object compound was obtained according to a similar manner to that of Example 1.

mp : 155-207°C

ESI-MS(M+1) : 517

^{1}H-NMR ($CDCl_3$) δ : 3.70(3H,s), 4.00-4.15(2H,m),
4.54(2H,d,J=4Hz), 5.80(1H,q,J=6Hz), 7.10-7.35(10H,m),

7.38-7.50(5H,m), 7.65(1H,d,J=8Hz), 7.91(1H,s),
8.33(1H,d,J=8Hz), 9.77(1H,s)

Example 222

The object compound was obtained according to a similar manner to that of Example 1.

mp : 199-201°C

^{1}H-NMR ($CDCl_3$) δ : 2.15(3H,s), 2.40-2.78(4H,m), 3.85(3H,s),
5.74(1H,t,J=6Hz), 7.09-7.37(6H,m), 7.44(1H,d,J=8Hz),
7.50(4H,s), 7.68(1H,d,J=8Hz), 7.93(1H,s)

Example 223

The object compound was obtained according to a similar manner to that of Example 1.

mp : 240-242°C

ESI-MS(M+1) : 517

^{1}H-NMR ($CDCl_3$) δ : 0.70(3H,t,J=6Hz), 1.40-1.65(2H,m),
3.70(2H,d,J=6Hz), 3.86-4.12(2H,m), 6.09(1H,q,J=6Hz),
7.04(1H,s), 7.08-7.30(5H,m), 7.40(2H,d,J=8Hz),
7.52(1H,d,J=8Hz), 7.65(1H,d,J=8Hz), 7.73(2H,d,J=8Hz),
8.13(1H,s), 8.18(1H,d,J=8Hz), 8.55(1H,d,J=4Hz), 8.59(1H,s),
9.90(1H,s)

Example 224

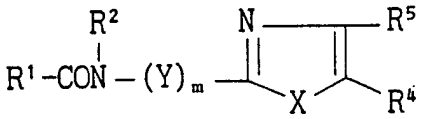
The object compound was obtained according to a similar manner to that of Example 1.

mp : 238-241°C

^{1}H-NMR ($CDCl_3$) δ : 0.72(3H,t,J=6Hz), 1.40-1.62(2H,m),
3.62(2H,d,J=6Hz), 3.82-4.15(2H,m), 6.04(1H,q,J=6Hz),
7.02(1H,s), 7.04(1H,s), 7.08-7.17(3H,m), 7.24(1H,s),
7.32(1H,s), 7.39(1H,s), 7.42(4H,d,J=8Hz), 7.52(1H,t,J=8Hz),
7.65(1H,d,J=8Hz), 7.80-7.89(1H,m), 7.90(1H,s),
8.55(1H,d,J=4Hz)

CLAIMS

1. A compound of the formula



(I)

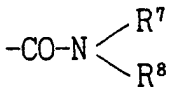
wherein

R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro, benzofuranyl, phenyl which may have one or two suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl, pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halogen, trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl, morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy, quinolyl or 3,4-methylenedioxyphenyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



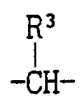
in which R^7 and R^8 are the same or different and each is

hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

$-CH=CH-CH=CH-$

Y is a group of the formula

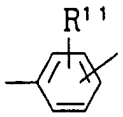


in which R^3 is hydrogen or a group of the formula

$-(CH_2)_n-R^6$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

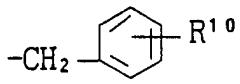
R^2 and R^3 in combination form a group of the formula



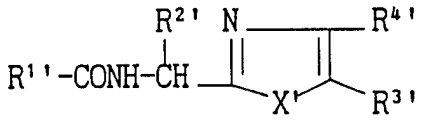
m is 0 or 1; and

X is S or NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula

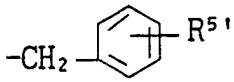


in which R^{10} is hydrogen, lower alkyl or lower alkoxy;
or a pharmaceutically acceptable salt thereof,
provided that the compound shown below is excluded:
a compound of the formula

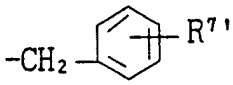


(A)

wherein
$R^{1'}$ is indolyl or benzofuranyl;
$R^{2'}$ is hydrogen, lower alkylthio(lower)alkyl or a group of the formula

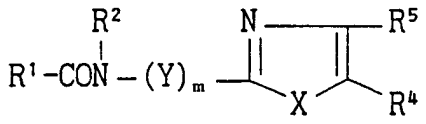


in which $R^{5'}$ is hydrogen, lower alkoxy or halogen;
$R^{3'}$ is hydrogen, quinolyl or phenyl which may have a suitable substituent selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen;
$R^{4'}$ is hydrogen or optionally esterified carboxy; and
X' is S or $NR^{6'}$
in which $R^{6'}$ is hydrogen, lower alkyl or a group of the formula



in which $R^{7'}$ is lower alkyl or lower alkoxy,
and a pharmaceutically acceptable salt thereof.

2. A compound of the formula



(I)

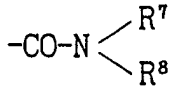
wherein

R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro, benzofuranyl, phenyl which may have one or two suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl, pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is phenyl or pyridyl, each of which has suitable substituent(s) selected from the group consisting of trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl, morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy, or 3,4-methylenedioxyphenyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

-CH=CH-CH=CH-

Y is a group of the formula

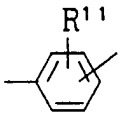


in which R^3 is hydrogen or a group of the formula

$-(CH_2)_n-R^6$

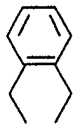
in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

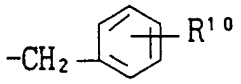
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;
or a pharmaceutically acceptable salt thereof.

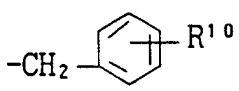
3. The compound of claim 2, wherein
R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro or benzofuranyl;
R^2 is hydrogen;
R^4 is phenyl which may have suitable substituent(s) selected from the group consisting of trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl, morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy;
R^5 is hydrogen;
Y is a group of the formula



in which R^3 is hydrogen or a group of the formula

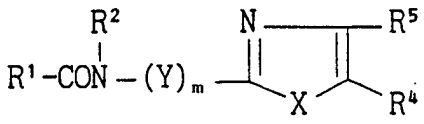
$-(CH_2)_n-R^6$

in which R^6 is pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, and
n is an integer of 0 to 3;
m is 0 or 1; and
X is NR^9
in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy.

4. A compound of the formula



(I)

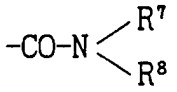
wherein

R^1 is indolyl which has a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro, phenyl which may have one or two suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl, pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen or quinolyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

-CH=CH-CH=CH-

Y is a group of the formula



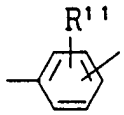
in which R^3 is hydrogen or a group of the formula

$-(CH_2)_n-R^6$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and

n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

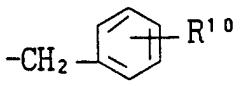
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

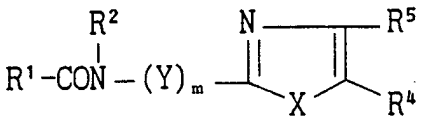
in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a pharmaceutically acceptable salt thereof.

5. A compound of the formula



(I)

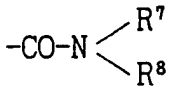
wherein

R^1 is indolyl or benzofuranyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen or quinolyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

$-CH=CH-CH=CH-$

Y is a group of the formula



in which R^3 is a group of the formula

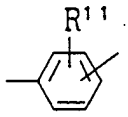
$-(CH_2)_n-R^6$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, phenyl which has a suitable substituent selected from the group consisting of amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl,

pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and

n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

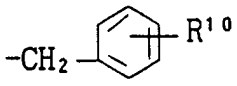
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

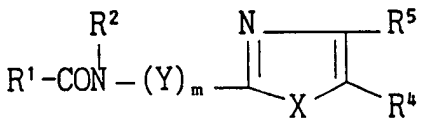
in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a pharmaceutically acceptable salt thereof.

6. A process for preparing a compound of the formula



(I)

wherein

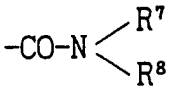
R^1 is indolyl which may have a suitable substituent selected from the group consisting of lower alkyl, phenyl, halogen, lower alkoxy, and nitro, benzofuranyl, phenyl which may have one or two suitable substituent(s) selected from the group consisting of amino, acylamino, lower alkylamino, halogen, lower alkoxy and nitro, lower alkyl, quinoxalinyl, quinolyl, pyrrolyl,

pyrimidinyl having benzofuranyl, benzimidazolyl, benzothienyl, benzothiazolyl, benzoxazolyl, indolinyl, anilino, phenylcarbamoyl or imidazolyl which may have one or two suitable substituent(s) selected from the group consisting of phenyl, lower alkyl and indolyl;

R^2 is hydrogen or phenyl(lower)alkyl;

R^4 is hydrogen, phenyl or pyridyl, each of which may have suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halogen, trihalomethyl, nitro, cyano, imidazolyl, optionally protected hydroxy, acyl, amino, acylamino, diacylamino, di(lower)alkylamino, amino(lower)alkyl, acylamino(lower)alkyl, pyrazolyl, morpholinyl, piperidyl, triazolyl, lower alkoxy(lower)alkoxy, hydroxy(lower)alkyl, lower alkylpiperazinyl, phenyl and carboxy, quinolyl or 3,4-methylenedioxyphenyl;

R^5 is hydrogen, imidazolyl, phenyl, nitrophenyl, phenyl(lower)alkyl, optionally esterified carboxy or a group of the formula



in which R^7 and R^8 are the same or different and each is hydrogen, phenyl, phenyl(lower)alkyl, lower alkyl or lower alkoxy; or

R^4 and R^5 in combination form a group of the formula

$-CH=CH-CH=CH-$

Y is a group of the formula



in which R^3 is hydrogen or a group of the formula

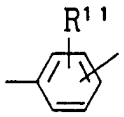
$-(CH_2)_n-R^6$

in which R^6 is optionally protected hydroxy, acyl, carboxy, acylamino, lower alkoxy, phenyl(lower)alkoxy, lower alkylthio, phenyl which may have a suitable

substituent selected from the group consisting of lower alkoxy, halogen, amino, acylamino, diacylamino and nitro, pyridyl which may have a suitable substituent selected from the group consisting of lower alkoxy and halogen, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-(lower)-alkylindolyl or 3,4-methylenedioxyphenyl, and

n is an integer of 0 to 3,

or a group of the formula



in which R^{11} is phenyl, phenoxy or phenyl(lower)alkoxy; or

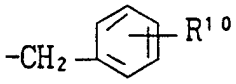
R^2 and R^3 in combination form a group of the formula



m is 0 or 1; and

X is S or NR^9

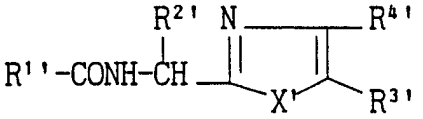
in which R^9 is hydrogen, lower alkyl, cyclo(lower)alkyl or a group of the formula



in which R^{10} is hydrogen, lower alkyl or lower alkoxy;

or a salt thereof, provided that the compound shown below is excluded:

a compound of the formula

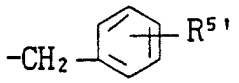


(A)

wherein

$R^{1'}$ is indolyl or benzofuranyl;

$R^{2'}$ is hydrogen, lower alkylthio(lower)alkyl or a group of the formula



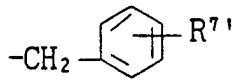
in which $R^{5'}$ is hydrogen, lower alkoxy or halogen;

$R^{3'}$ is hydrogen, quinolyl or phenyl which may have a suitable substituent selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio and halogen;

$R^{4'}$ is hydrogen or optionally esterified carboxy; and

X' is S or $NR^{6'}$

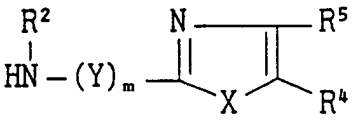
in which $R^{6'}$ is hydrogen, lower alkyl or a group of the formula



in which $R^{7'}$ is lower alkyl or lower alkoxy,

and a salt thereof, which comprises

(1) reacting a compound of the formula

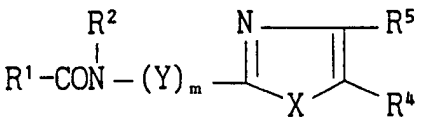


(II)

wherein R^2, R^4, R^5, X, Y and m are each as defined above, or its reactive derivative at the amino group, or a salt thereof, with a compound of the formula

$$R^1\text{-}COOH \qquad \text{(III)}$$

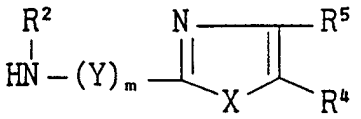
wherein R^1 is as defined above, or its reactive derivative at the carboxy group, or a salt thereof to give a compound of the formula



(I)

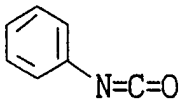
wherein R^1, R^2, R^4, R^5, X, Y and m are each as defined above, or a salt thereof, or

(2) reacting a compound of the formula



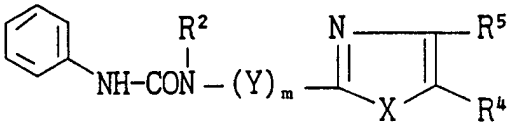
(II)

wherein R^2, R^4, R^5, X, Y and m are each as defined above, or a salt thereof with a compound of the formula



(IV)

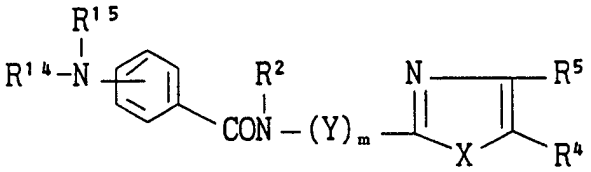
to give a compound of the formula



(I)-1

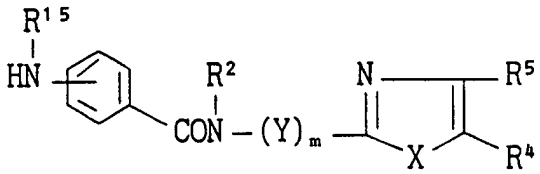
wherein R^2, R^4, R^5, X, Y and m are each as defined above, or a salt thereof, or

(3) subjecting a compound of the formula



(V)

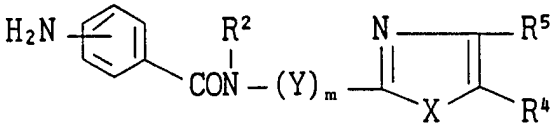
wherein R^2, R^4, R^5, X, Y and m are each as defined above, R^{14} is amino protective group, and R^{15} is hydrogen or lower alkyl, or a salt thereof to elimination reaction of the amino protective group to give a compound of the formula



(I)-2

wherein R^2, R^4, R^5, R^{15}, X, Y and m are each as defined above, or a salt thereof, or

(4) reacting a compound of the formula



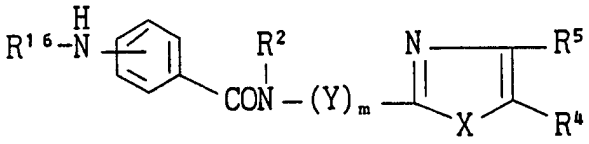
(I)-3

wherein R^2, R^4, R^5, X, Y and m are each as defined above, or its

reactive derivative at the amino group, or a salt thereof, with a compound of the formula

$$R^{16}\text{-OH} \qquad \text{(VI)}$$

wherein R^{16} is acyl, or its reactive derivative at the carboxy group, or a salt thereof to give a compound of the formula



(I)-4

wherein R^2, R^4, R^5, R^{16}, X, Y and m are each as defined above, or a salt thereof.

7. A pharmaceutical composition comprising the compound of Claim 1 or a pharmaceutically acceptable salt thereof in admixture with a pharmaceutically acceptable carrier.

8. Use of the compound of Claim 1 or a pharmaceutically acceptable salt thereof as a medicament.

9. Use of the compound of Claim 1 or a pharmaceutically acceptable salt thereof as a medicament for prophylactic or therapeutic treatment of NO-mediated diseases.