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Amine Derivative having NPY Y5 receptor antagonist activity and use thereof

Field of the Invention

[0001]

A compound for this invention has NPY Y5 receptor antagonistic activity and useful as an anorectic or anti-obesity composition.

Background Art

[0002]

Obesity is classified as primary obesity (simple obesity) and secondary obesity (symptomatic obesity) according to its cause. The cause of primary obesity is thought to include the excess energy intake (e.g., overeating), energy under consumption (e.g., lack of exercise) and lower heat production. Currently, over 90 % of obesity is primary obesity. When this primary obesity is developed and the condition is kept, it causes various health problems. On the other hand, secondary obesity results from some underlying disease. The Examples of the secondary obesity include endocrine obesity, hypothalamic obesity, hereditary obesity, obesity caused by a medicament and the like. Obesity triggers lifestyle-related diseases and obese people is susceptible to complications such as diabetes, hypertension, hyperlipemia, coronary atherosclerosis (angina or myocardial infarction), gout, cholelithiasis, fatty liver, infertility, osteoarthritis and the like.

The basic treatment for obesity is a combination of diet therapy and exercise therapy. However, this has a limitation and drug therapy is expected to be effective especially for morbid obesity.

Y5 receptor, which is a subtype of Neuropeptide Y (hereinafter referred to as NPY) receptor, at least involves in the feeding behavior and its antagonist is expected as an anti-obesity agent (Non-patent Document 1).

[0003]

Amine derivatives having sulfonyl group and similar structures to compounds for this invention and exhibiting NPY Y5 receptor antagonistic activity are disclosed in Patent Document 1, 2, 3, 4 and the like. Amide derivatives having sulfonyl group and exhibiting NPY Y5 receptor antagonistic

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activity are disclosed in Patent Document 5, 8, 9, 10 and 11. Derivatives having sulfonyl group and exhibiting NPY Y5 receptor antagonistic activity are disclosed in Patent Document 12. The structures of these compounds are different from those of the compounds for this invention.

[0004]

Furthermore, although compounds having similar structures to compounds for this invention are disclosed in Patent Document 6, 7, 13, 14 and the like, the activities of their compounds are quite different from those of the compounds for this invention. These documents do not disclose that their compounds are useful as an anorectic or anti-obesity composition and do not suggest this invention.

[Non-patent Document 1] Peptides, Vol.18, 445(1997)
[Patent Document 1] WO01/002379
[Patent Document 2] WO00/064880
[Patent Document 3] WO99/055667
[Patent Document 4] WO00/068197
[Patent Document 5] WO01/037826
[Patent Document 6] WO2006/014482
[Patent Document 7] WO2005/097738
[Patent Document 8] WO97/20823
[Patent Document 9] US2006/293341
[Patent Document 10] WO2007/002126
[Patent Document 11] WO2006/001318
[Patent Document 12] WO2005/080348
[Patent Document 13] US2007/060598
[Patent Document 14] WO2005/121107

Disclosure of Invention

Problems to be solved by the Invention

[0005]

The object of this invention is to provide excellent anorectic or anti-obesity compositions.

Means for Solving the Problem

[0006]

The present inventors have intensively studied to synthesize the following

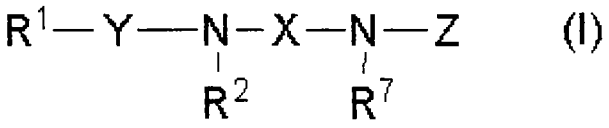
excellent novel compounds having NPY Y5 receptor antagonistic activity. Patent Document 5 disclosed amide derivatives having sulfonyl group and exhibiting NPY Y5 receptor antagonistic activity. However, the present inventors found that transportability through the blood-brain barrier of compounds which the amide is substituted with the amine is much higher than those of the unsubstituted compounds. Furthermore, the inventors found that compounds for this invention have less the induction of a drug-metabolizing enzyme compared to compounds disclosed in Patent Document 1 or 2. It was confirmed that these novel compounds suppress food intake or body weight gain by verification tests for suppression of food intake, body weight gain and the like to achieve this invention. The inventors found that a compound for this invention has high metabolic stability and water solubility. Furthermore, compounds for this invention are less toxic and thought to be safe enough as a medicament.

[0007]

This invention includes the followings.

(1) An anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 1]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

Y is -S(O)n- wherein n is 1 or 2, or -CO-,

R^2 is hydrogen or optionally substituted lower alkyl,

R^1 and R^2 taken together may form lower alkylene,

R^7 is hydrogen or optionally substituted lower alkyl,

X is optionally substituted lower alkylene,

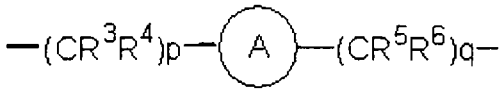
optionally substituted lower alkenylene,

optionally substituted -CO-lower alkylene,

optionally substituted -CO-lower alkenylene or

a group of the formula:

[Formula 2]



wherein

R^3, R^4, R^5 and R^6 are each independently hydrogen or optionally substituted lower alkyl,

a group of the formula:

[Formula 3]



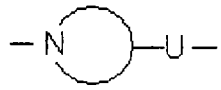
is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted arylene or optionally substituted heterocyclediyl,

p and q are each independently an integer between 0 and 2, and

either p or q is not 0,

$-NR^2-X-$ may be a group of the formula:

[Formula 4]



wherein a group of the formula:

[Formula 5]



is piperidinediyl, piperazinediyl, pyridinediyl, pyrazinediyl, pyrrolidinediyl orpyrroledіyl, and U is lower alkylene or lower alkenylene,

Z is optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino, optionally substituted lower alkoxy, optionally substituted carbocyclyl, optionally substituted heterocyclyl, and

provided that Z is not fused heterocyclyl consisting of three rings or optionally substituted thiazolyl or optionally substituted quinazolinyl.

(2) The anorectic or anti-obesity composition of (1) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein R1 is lower alkyl.

(3) The anorectic or anti-obesity composition of (1) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Y is $-S(O)_2-$.

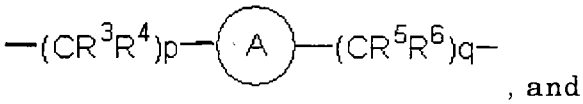
(4) The anorectic or anti-obesity composition of (1) comprising a compound,

pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl. (5) The anorectic or anti-obesity composition of (1) comprising a compound, pharmaceutically acceptable salt or solvate thereof,

wherein

X is a group of the formula:

[Formula 6]



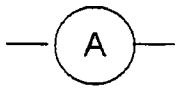
, and

R^1 is optionally substituted C2 to C10 alkyl.

(6) The anorectic or anti-obesity composition of (5) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted heterocyclyl.

(7) The anorectic or anti-obesity composition of (5) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein a group of the formula:

[Formula 7]



is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene or optionally substituted piperidinylene.

(8) The anorectic or anti-obesity composition of (5) comprising a compound, pharmaceutically acceptable salt or solvate thereof,

wherein

a group of the formula:

[Formula 8]



is optionally substituted cyclohexylene or optionally substituted piperidinylene, p and q are each independently 0 or 1, and either p or q is not 0.

(9) The anorectic or anti-obesity composition of (7) or (8) comprising the compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted lower alkyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyrazolyl, optionally substituted isoxazolyl, optionally substituted oxadiazolyl, optionally substituted pyridazinyl,

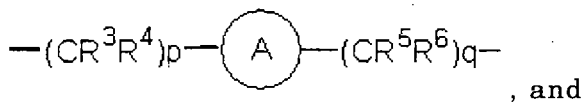
optionally substituted pyrazinyl, optionally substituted pyrimidinyl or optionally substituted fused heterocycle consisting of two rings.

(10) The anorectic or anti-obesity composition of (1) comprising a compound, pharmaceutically acceptable salt or solvate thereof,

wherein

X is a group of the formula:

[Formula 9]



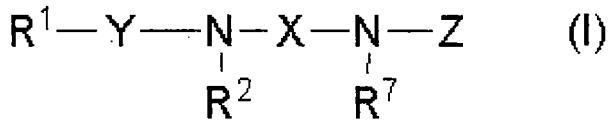
, and

p+q is 1 or 2.

(11) The anorectic or anti-obesity composition of (10) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein p+q is 1.

(12) An anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 10]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

Y is $-S(O)_2-$,

R^2 is hydrogen or optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:

[Formula 11]

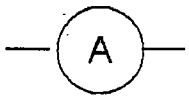


wherein

R^5 and R^6 are each independently hydrogen,

a group of the formula:

[Formula 12]



is optionally substituted cycloalkylene, p is 0, and

q is 1 or 2,

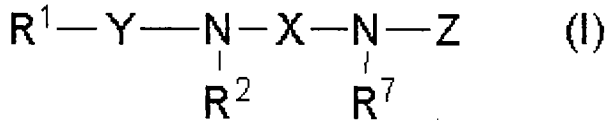
Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl, and provided that a compound wherein Z is fused heterocyclyl consisting of three rings is excluded.

(13) The anorectic or anti-obesity composition of (12) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted phenyl, optionally substituted indanyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrimidinyl, optionally substituted pyrazolyl, optionally substituted isoxazolyl, optionally substituted oxadiazolyl or optionally substituted fused heterocycle consisting of two rings.

(14) The anorectic or anti-obesity composition of (12) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzoxazolyl, optionally substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzimidazolyl, optionally substituted thiazolopyridyl, optionally substituted isoxazolinonyl, optionally substituted oxazolinonyl, optionally substituted benzoxadinonyl or optionally substituted benzoxyazepinonyl.

(15) An anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 13]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

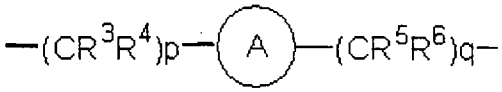
Y is $-S(O)_2-$,

R^2 is hydrogen or optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:

[Formula 14]



wherein R^3 and R^4 are each independently hydrogen,

a group of the formula:

[Formula 15]



is optionally substituted cycloalkylene,

p is 1 or 2, and

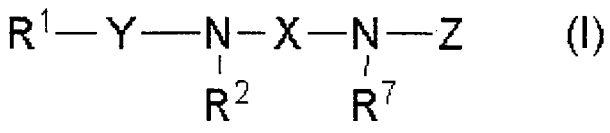
q is 0,

Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl, and provided that a compound wherein Z is fused heterocyclyl consisting of three rings, optionally substituted thiazolyl or optionally substituted quinazolinyl is excluded.

(16) The anorectic or anti-obesity composition of (15) comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl or optionally substituted oxazolopyridyl.

(17) An anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 16]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

Y is $-S(O)_2-$,

R^2 is hydrogen or optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:

[Formula 17]



wherein R^3 and R^4 are each independently hydrogen,

a group of the formula:

[Formula 18]



is optionally substituted cycloalkylene,

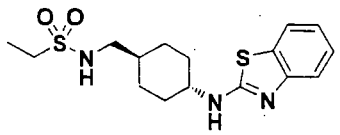
p is 1 or 2, and

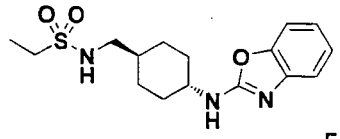
q is 0, and

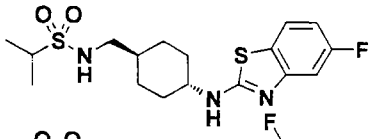
Z is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl or optionally substituted oxazolopyridyl.

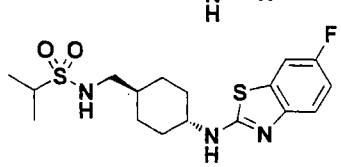
(18) A compound of the formula :

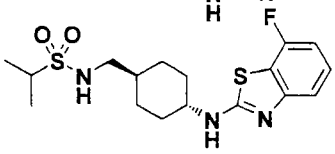
[Formula 19]

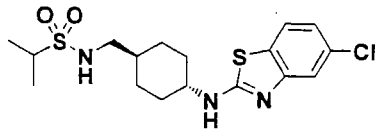
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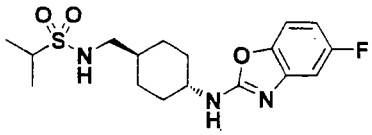
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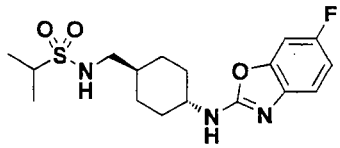
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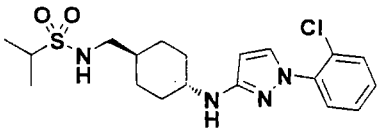
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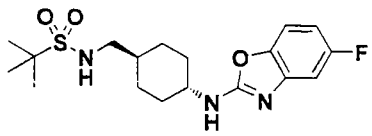
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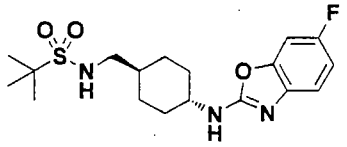
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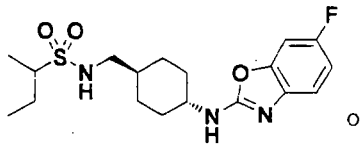
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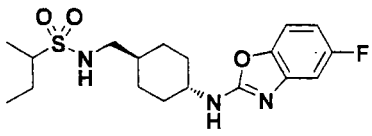
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Ij-160  or

Ij-161 

a pharmaceutically acceptable salt or solvate thereof.

(19) A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of (18).

(20) A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of (18) and exhibiting NPY Y5 receptor antagonistic activity.

(21) An anorectic or anti-obesity composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of (18).

(22) A method for suppression of appetite by administering the compound, pharmaceutically acceptable salt or solvate thereof of (18).

(23) A method for treatment or prevention of obesity by administering the compound, pharmaceutically acceptable salt or solvate thereof of (18).

(24) Use of the compound, pharmaceutically acceptable salt or solvate thereof of (18) for manufacture of an anorectic or anti-obesity composition.

Effect of the Invention

[0008]

Compounds for this invention exhibit NPY Y5 receptor antagonistic activity and are very useful as a medicine, especially as an anorectic or anti-obesity composition for preventing and/or treating feeding disorder, obesity or hyperorexia.

Brief Description of Drawings

[0009]

[Figure 1] Compound Ii-45 suppresses Body Weight Gain

[Figure 2] Compound Ij-112 suppresses Body Weight Gain

Best Mode for Carrying Out the Invention

[0010]

Terms used in the present description are explained below. Each term has the same meaning alone or together with other terms in this description.

[0011]

"Halogen" includes fluorine, chlorine, bromine and iodine. Especially preferred is fluorine or chlorine.

[0012]

The protective group in "optionally protected hydroxyl" or "optionally protected hydroxyl(lower alkyl)" includes all of hydroxy protecting groups usually used. Examples are acyl such as acetyl, trichloroacetyl, benzoyl and the like, lower alkoxycarbonyl such as t-butoxycarbonyl and the like, lower alkylsulfonyl such as methane sulfonyl and the like, lower alkoxy(lower alkyl) such as methoxymethyl and the like, and trialkylsilyl such as t-butyldimethylsilyl and the like.

[0013]

"Lower alkyl" includes C1 to C10 straight or branched alkyl. Examples are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-buthyl, tert-butyl, n-pentyl, isopentyl, neopentyl, hexyl, isohexyl, n-heptyl, isoheptyl, n-octyl, isooctyl, n-nonyl, n-decyl and the like.

"Lower alkyl" of R^1 is preferably C2 to C10, more preferably C2 to C6 alkyl and most preferably ethyl, isopropyl or t-butyl.

[0014]

"Lower alkyl" in other cases is preferably C1 to C6 and more preferably C1

to C4 alkyl.

[0015]

The examples of substituents of "optionally substituted lower alkyl" of Z are, (1) halogen; (2) cyano;

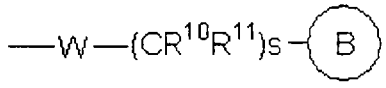
(3) the following groups (i) to (xvi), which are optionally substituted with one or more substituents selected from "Substituent group ß" defined below,

(i) hydroxy, (ii) lower alkoxy, (iii) mercapto, (iv) lower alkylthio, (v) acyl, (vi) acyloxy, (vii) carboxy, (viii) lower alkoxycarbonyl, (ix) imino, (x) carbamoyl, (xi) thiocarbamoyl, (xii) lower alkylcarbamoyl, (xiii) lower alkylthiocarbamoyl, (xiv) amino, (xv) lower alkylamino or (xvi) heterocyclylcarbonyl;

or

(4) a group of the formula:

[Formula 19]



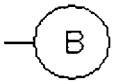
wherein R^{10} and R^{11} are each independently hydrogen or lower alkyl and when this group has two or more of R^{10} and/or R^{11}, each R^{10} and/or R^{11} may be different,

W is single bond, O, S or NR^{12},

R^{12} is hydrogen, lower alkyl or phenyl,

a group of the formula:

[Formula 20]



is cycloalkyl, bicycloalkyl, cycloalkenyl, aryl or heterocyclyl, each of which is optionally substituted with one or more of substituent(s) selected from "Substituent group α" defined below and

s is an integer of 0 to 4.

[0016]

"Substituent group α" is a group consisting of (1) halogen; (2) oxo; (3) cyano; (4) nitro; (5) imino optionally substituted with lower alkyl or hydroxy;

(6) the following groups (i) to (xxi), which are optionally substituted with one or more of group(s) selected from Substituent group ß,

(i) hydroxy, (ii) lower alkyl, (iii) lower alkenyl, (iv) lower alkoxy, (v) carboxy, (vi) lower alkoxycarbonyl, (vii) acyl, (viii) acyloxy, (ix) imino, (x) mercapto, (xi) lower

alkylthio, (xii) carbamoyl, (xiii) lower alkylcarbamoyl, (xiv) cycloalkylcarbamoyl, (xv) thiocarbamoyl, (xvi) lower alkylthiocarbamoyl, (xvii) lower alkylsulfinyl, (xviii) lower alkylsulfonyl, (xix) sulfamoyl, (xx) lower alkylsulfamoyl and (xxi) cycloalkylsulfamoyl;

(7) the following groups (i) to (v), which are optionally substituted with Substituent group β, lower alkyl, lower alkoxy(lower alkyl), optionally protected hydroxy(lower alkyl), halogeno(lower alkyl), lower alkylsulfonyl and/or arylsulfonyl,

(i) cycloalkyl, (ii) cycloalkenyl, (iii)cycloalkyloxy, (iv) amino and (v) alkylenedioxy;

and

(8) the following groups (i) to (xii), which are optionally substituted with Substituent group β, lower alkyl, halogeno(lower alkyl) and/or oxo,

(i) phenyl, (ii) naphthyl, (iii) phenoxy, (iv) phenyl(lower alkoxy), (v) phenylthio, (vi) phenyl(lower alkylthio), (vii) phenylazo, (viii) heterocyclyl, (ix) heterocyclyloxy, (x) heterocyclylthio, (xi) heterocyclylcarbonyl and (xii) heterocyclylsulfonyl.

[0017]

The preferable examples of Substituent group α as substituents for Ring B are halogen; nitro; hydroxy;

optionally substituted lower alkyl wherein the substituent(s) is halogen, cyano, phenyl, carboxy and/or lower alkoxycarbonyl;

lower alkenyl; lower alkoxycarbonyl(lower alkenyl);

optionally substituted lower alkoxy wherein the substituent(s) is halogen, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, lower alkylamino and/or cyano;

acyl; hydroxyimino; lower alkylthio; lower alkylsulfinyl; sulfamoyl;

optionally substituted amino wherein the substituent(s) is lower alkyl, optionally protected hydroxy(lower alkyl), phenyl and/or acyl;

alkylenedioxy; cyanophenyl; phenyl substituted heterocycle; biphenylyl; phenoxy; phenylazo optionally substituted with lower alkyl; or

optionally substituted heterocyclyl wherein the substituent(s) is optionally protected hydroxy, mercapto, halogen, lower alkyl, cycloalkyl, lower alkoxycarbonyl, amino, lower alkoxycarbonyl amino, carbamoyl, oxo, phenyl, lower alkoxyphenyl or heterocyclyl. More preferable examples are halogen; lower alkyl optionally substituted with halogen; or lower alkoxy optionally

substituted with halogen.

[0018]

"Substituent group β" is a group consisting of halogen, optionally protected hydroxy, mercapto, lower alkoxy, lower alkenyl, amino, lower alkylamino, lower alkoxycarbonylamino, lower alkylthio, acyl, carboxy, lower alkoxycarbonyl, carbamoyl, cyano, cycloalkyl, phenyl, phenoxy, lower alkylphenyl, lower alkoxyphenyl, halogenophenyl, naphthyl and heterocyclyl.

[0019]

Examples of the substituent(s) for "optionally substituted lower alkyl" of any other than Z (e.g., R^1) are one or more substituent(s) selected from Substituent group β. The lower alkyl may be substituted with these substituents at any possible position(s).

[0020]

The lower alkyl part in "lower alkoxy", "lower alkoxycarbonyl", "lower alkoxycarbonyl(lower alkyl)", "lower alkylphenyl", "lower alkoxyphenyl", "lower alkylcarbamoyl", "lower alkylthiocarbamoyl", "lower alkylamino", "halogeno(lower alkyl)", "hydroxy(lower alkyl)", "phenyl(lower alkoxy)", "lower alkylthio", "phenyl(lower alkylthio)", "lower alkoxycarbonylamino", "lower alkoxycarbonyl(lower alkenyl)", "lower alkylsulfinyl", "lower alkylsulfonyl", "aryl(lower alkoxycarbonyl)", "lower alkylbenzoyl" or "lower alkoxybenzoyl" is the same as defined in the above "lower alkyl".

[0021]

Examples of the substituent(s) for "optionally substituted lower alkoxy" are one or more substituent(s) selected from Substituent group β. Preferable examples are phenyl, lower alkylphenyl, lower alkoxyphenyl, naphthyl and heterocyclyl.

[0022]

"Cycloalkyl" includes C3 to C8 and preferably C5 to C6 cyclic alkyl. Examples are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl and the like.

[0023]

Examples of the substituent(s) for "optionally substituted cycloalkyl" are one or more substituent(s) selected from Substituent group α and the cycloalkyl may be substituted with these substituents at any possible position(s).

[0024]

"Bicycloalkyl" includes a group which is formed by excluding one hydrogen

atom from C5 to C8 aliphatic cycle containing two rings which possess two or more of atoms in common. Examples are bicyclo[2.1.0]pentyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.2]octyl, bicyclo[3.2.1]octyl and the like.

[0025]

"Lower alkenyl" includes C2 to C10, preferably C2 to C8 and more preferably C3 to C6 straight or branched alkenyl having one or more double bond(s) at any possible position(s). Examples are vinyl, propenyl, isopropenyl, butenyl, isobutenyl, prenyl, butadienyl, pentenyl, isopentenyl, pentadienyl, hexenyl, isohexenyl, hexadienyl, heptenyl, octenyl, nonenyl, decenyl and the like.

[0026]

The "lower alkenyl" part in "lower alkoxycarbonyl(lower alkenyl)" is the same as the above "lower alkenyl".

[0027]

Examples of the substituent(s) for "optionally substituted lower alkenyl" are halogen, lower alkoxy, lower alkenyl, amino, lower alkylamino, lower alkoxycarbonylamino, lower alkylthio, acyl, carboxy, lower alkoxycarbonyl, carbamoyl, cyano, cycloalkyl, phenyl, lower alkylphenyl, lower alkoxyphenyl, naphthyl and/or heterocyclyl.

[0028]

"Acyl" includes (1) C1 to C10, preferably C1 to C6 and more preferably C1 to C4 straight or branched alkylcarbonyl or alkenylcarbonyl, (2) C4 to C9 and preferably C4 to C7 cycloalkylcarbonyl and (3) C7 to C11 arylcarbonyl. Examples are formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, pivaloyl, hexanoyl, acryloyl, propioloyl, methacryloyl, crotonoyl, cyclopropylcarbonyl, cyclohexylcarbonyl, cyclooctylcarbonyl, benzoyl and the like.

[0029]

The "acyl" part in "acyloxy" is same as above.

[0030]

"Cycloalkenyl" includes a group having one or more double bond(s) at any possible position(s) in the above cycloalkyl. Examples are cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl and the like.

[0031]

Examples of substituent(s) for "optionally substituted cycloalkenyl" are one or more substituent(s) selected from Substituent group B.

[0032]

Examples of the substituent(s) for "optionally substituted amino" are

Substituent(s) group β, optionally substituted benzoyl and/or optionally substituted heterocyclylcarbonyl wherein the substituent(s) is hydroxy, lower alkyl, lower alkoxy and/or lower alkylthio.

[0033]

"Aryl" includes a monocyclic or polycyclic aromatic carbocyclyl. Examples are phenyl, naphthyl, anthryl, phenanthryl and the like. It also includes aryl fused with other non-aromatic carbocyclyl. Examples are indanyl, indenyl, biphenylyl, acenaphthyl, tetrahydronaphthyl, fluorenyl and the like. Phenyl is preferable.

[0034]

The aryl part in "aryl lower alkoxycarbonyl" is same as above.

"Optionally substituted aryl" or "optionally substituted phenyl" of Z includes the above "aryl" or "phenyl" respectively, which is optionally substituted with Substituent group α or lower alkyl optionally substituted with one or more group(s) selected from Substituent group α.

[0035]

Examples of the substituent(s) for "optionally substituted aryl" and "optionally substituted phenyl" of any other than Z are one or more group(s) selected from Substituent group β.

[0036]

"Carbocyclyl" includes the above "cycloalkyl", "cycloalkenyl", "bicycloalkyl" and "aryl".

[0037]

"Non-aromatic carbocyclyl" includes the above "cycloalkyl", "cycloalkenyl" and "bicycloalkyl".

[0038]

"Optionally substituted carbocyclyl" includes the above "optionally substituted cycloalkyl", "optionally substituted cycloalkenyl", "optionally substituted bicycloalkyl" and "optionally substituted aryl".

[0039]

"Heterocyclyl" includes a heterocyclic group containing one or more heteroatom(s) arbitrarily selected from O, S and N. Examples are 5- or 6-membered heteroaryl such as pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazolyl, triazinyl, tetrazolyl, isooxazolyl, oxazolyl, oxadiazolyl, isothiazolyl, thiazolyl, thiadiazolyl, furyl, thienyl and the like; fused heterocyclyl consisting of two rings such as indolyl, isoindolyl, indazolyl,

indolizinyl, indolinyl, isoindolinyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, pteridinyl, benzopyranyl, benzimidazolyl, benzisoxazolyl, benzoxazolyl benzoxadiazolyl, benzisothiazolyl, benzothiazolyl, benzothiadiazolyl, benzofuryl, isobenzofuryl, benzothienyl, benzotriazolyl, imidazopyridyl, triazoropyridyl, imidazothiazolyl, pyrazinopyridazinyl, tetrahydroquinolyl, tetrahydrobenzothienyl, oxazolopyridyl, thiazolopyridyl (e.g., thiazolo[5,4-b]pyridine-2-yl, thiazolo[5,4-c]pyridine-2-yl, thiazolo[4,5-b]pyridine-2-yl, thiazolo[4,5-c]pyridine-2-yl and the like), benzoxazolinonyl, benzisoxazolinonyl, benzoxazinonyl, benzoxyazepinonyl, oxazolopyridinonyl, benzodioxolyl and the like; fused heterocyclyl consisting of three rings such as carbazolyl, acridinyl, xanthenyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, dibenzofuryl and the like; and non-aromatic heterocyclyl such as dioxanyl, thiiranyl, oxiranyl, oxathiolanyl, azetidinyl, thianyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, morpholinyl, morpholino, thiomorpholinyl, thiomorpholino, dihydropyridyl, tetrahydrofuryl, tetrahydropyranyl, tetrahydrothiazolyl, tetrahydroisothiazolyl and the like.

[0040]

"Fused heterocyclyl" fused with a ring other than a heterocycle (e.g., benzothiazolyl and the like) may attach with the other group(s) at any possible position.

[0041]

The substituent(s) for "optionally substituted heterocyclyl" or "optionally substituted fused heterocyclyl consisting of two rings" are the same as those for the above "optionally substituted aryl".

[0042]

The heterocyclyl part in "heterocyclylcarbonyl", "heterocyclyloxy", "heterocyclylthio" or "heterocyclyl substituted phenyl" is the same as the above "heterocyclyl".

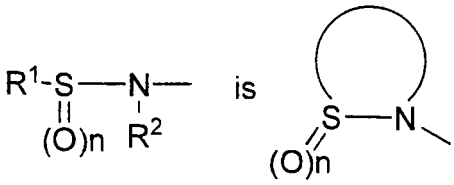
[0043]

"Lower alkylene" includes a bivalent group comprising 1 to 6 of methylene, preferably 2 to 6 of methylene and more preferably 3 to 6 of methylene. Examples are methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene and the like. Tetramethylene is especially preferable.

[0044]

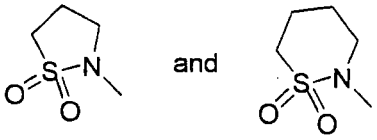
"R^1 and R^2 taken together may form lower alkylene" includes the case

[Formula 21]



Preferable examples are

[Formula 22]



[0045]

The lower alkylene part in "lower alkylenedioxy" is the same as the above "lower alkylene". Methylenedioxy or ethylenedioxy is preferable.

[0046]

"Lower alkenylene" includes a bivalent group comprising 2 to 6 of methylene, preferably 3 to 6 of methylene and more preferably 4 to 5 of methylene and including at least one double bond.

[0047]

"Cycloalkylene" includes a bivalent group which is formed by excluding one hydrogen atom from the above "cycloalkyl". As cycloalkylene of X is 1, 4-cyclohexanediyl is preferable.

[0048]

The term "cycloalkenylene" includes a group containing at least one double bond in the above cycloalkylene.

[0049]

"Bicycloalkylene" includes a group which is formed by excluding one hydrogen atom from the above "bicycloalkyl". Examples are bicyclo[2. 1. 0]pentylene, bicyclo[2. 2. 1]heptylene, bicyclo[2. 2. 2]octylene, bicyclo[3. 2. 1]octylene and the like.

[0050]

"Heterocyclediyl" includes a bivalent group which is formed by excluding one hydrogen atom from the above "heterocyclyl". Piperidinediyl, piperazinediyl, pyridinediyl, pyrimidinediyl, pyrazinediyl, pyrrolidinediyl or

pyrrolediyl is preferable. Piperidinediyl is more preferable.

[0051]

"Arylene" includes a bivalent group which is formed by excluding one hydrogen atom from the above "aryl". Phenylene is preferable.

[0052]

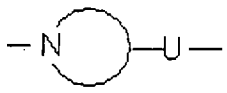
"Heteroarylene" includes aromatic groups in the above "heterocyclediyl". Examples are pyrrolediyl, imidazolediyl, pyrazolediyl, pyridinediyl, pyridazinediyl, pyrimidinediyl, pyrazinediyl, triazolediyl, triazinediyl, isoxazolediyl, oxazolediyl, oxadiazolediyl, isothiazolediyl, thiazolediyl, thiadiazolediyl, furandiyl, thiophenediyl and the like.

[0053]

Examples of substituent(s) for "optionally substituted lower alkylene", "optionally substituted lower alkenylene", "optionally substituted cycloalkylene", "optionally substituted cyclohexylene", "optionally substituted bicycloalkylene", "optionally substituted cycloalkenylene", "optionally substituted phenylene", "optionally substituted heterocyclyldiyl" and "optionally substituted piperidinylene" are one or more group(s) selected from Substituents group β. Preferred is Halogen, hydroxy, lower alkyl, halogeno(lower)alkyl, lower alkoxy, amino, lower alkylamino, acyl, carboxy, lower alkoxycarbonyl or the like. These substituent(s) may attach to any possible position(s).

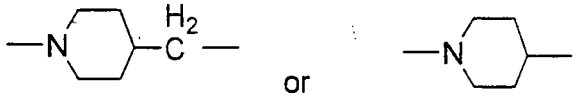
When -NR2-X- is a group of the formula:

[Formula 23]



U is preferably methylene or ethylene. More preferred is a group of the formula:

[Formula 24]

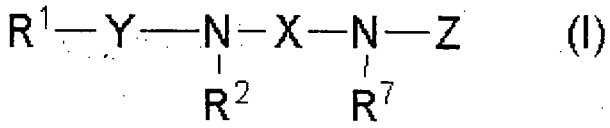


[0054]

The following compounds are preferable as a compound for this invention.

A compound of the formula (I):

[Formula 25]



(I)

wherein

R^1 is lower alkyl,

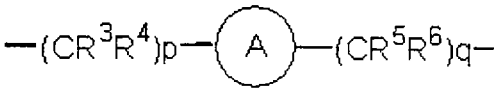
Y is $-S(O)_2-$,

R^2 is hydrogen,

R^7 is hydrogen,

X is a group of the formula:

[Formula 26]



wherein

R^3 and R^4 are each independently hydrogen,

a group of the formula:

[Formula 27]



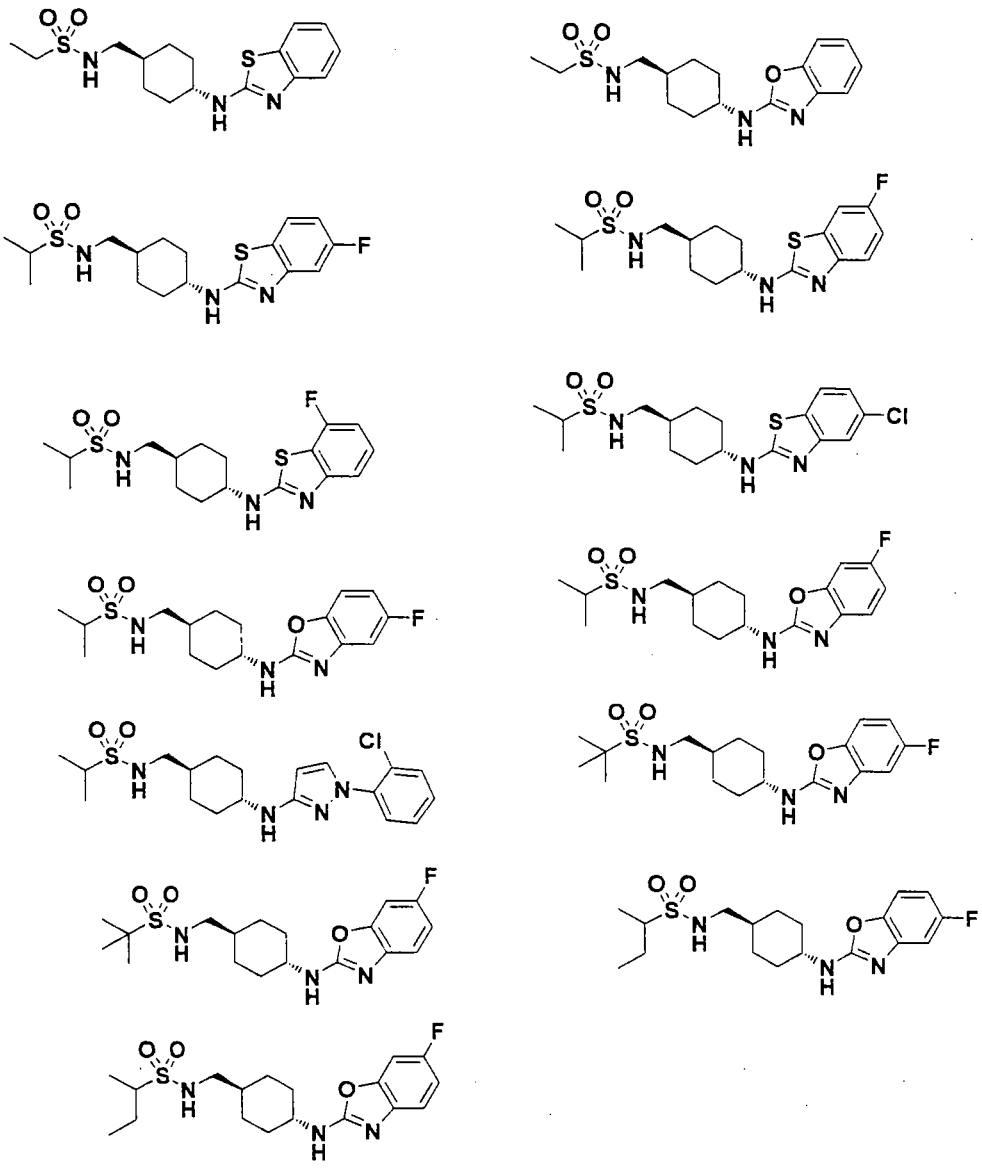
is cycloalkylene, p is 1, and

q is 0, and

Z is optionally substituted pyrazolyl, optionally substituted benzothiazolyl or optionally substituted benzoxazolyl.

The following compounds are more preferable.

[Formula 28]



[0055]

The above compounds have a good character especially that they show effect of suppressing body weight gain at low doses.

[0056]

The compounds for this invention include any formable and pharmaceutically acceptable salts thereof. Examples of "the pharmaceutically acceptable salt" are salts with mineral acids such as hydrochloric acid, sulfuric acid, nitric acid, phosphoric acid and the like; salts with organic acids such as para-toluenesulfonic acid, methanesulfonic acid, oxalic acid, citric acid and the like; salts with organic bases such as ammonium, trimethylammonium, triethylammonium and the like; salts with alkaline metals such as sodium,

potassium and the like; and salts with alkaline earth metals such as calcium, magnesium and the like.

[0057]

The compounds for this invention include solvates thereof. Hydrate is preferable and arbitrary numbers of water molecules may coordinate to the compound for this invention.

[0058]

When Compound (I) for this invention has an asymmetric carbon atom, it includes racemates, all of enantiomers and all of stereoisomers such as diastereomer, epimer, enantiomer thereof and the like. When Compound (I) for this invention having one or more double bond(s) forms an E isomer or Z isomer, Compound (I) includes both isomers. When X is cycloalkylene, Compound (I) includes both of cis isomer and trans isomer.

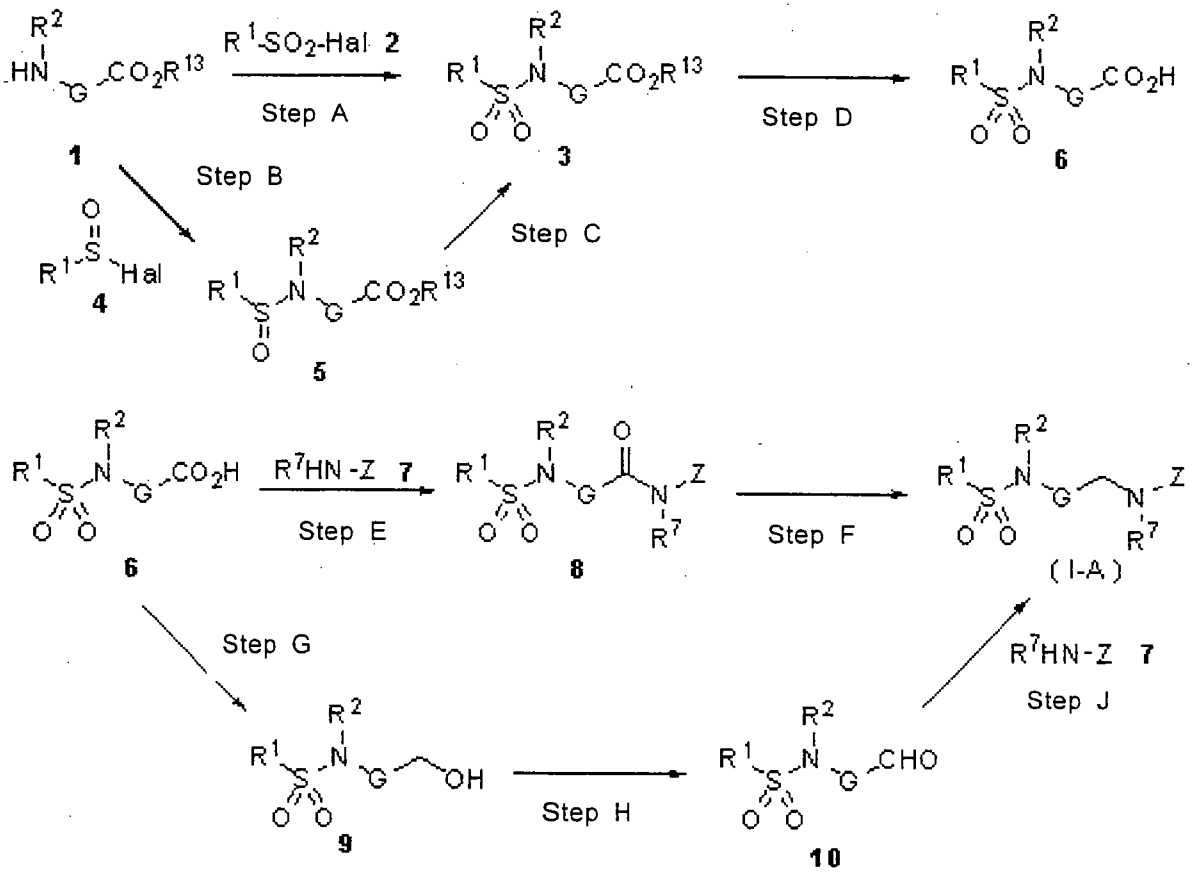
[0059]

For example, Compound (I) for this invention can be synthesized by the following methods. Hereinafter, X will be described as $-CH_2-G-$ or $-G-CH_2-$.

[0060]

[Compounds wherein Y is S(O)n]

[Formula 29]



In the above scheme, Hal is halogen, -G-CH_2- is the same as -X- in the formula (I), R^{13} is lower alkyl and the other symbols have the same meanings as above.

Step A

Compound 1 is reacted with Sulfonyl Halide 2 having the desired substituent R^1 in a suitable solvent within the range of 0 °C to 50 °C for several minutes to several hours to give Compound 3 wherein n is 2. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, mixtures thereof and the like.

Step B

Compound 5 wherein n is 1 can be synthesized by reacting Compound 1 and Sulfinyl Halide 4 having substituent R^1. The conditions for the reaction are the same as those of the above Step A.

Step C

Compound 5 obtained in Step B is oxidized by the usual method to give Compound 3 wherein n is 2. Examples of an oxidizer are m-chloroperbenzoic acid, peracetic acid, hydrogen peroxide, trifluoroperacetic acid, sodium periodate, sodium hypochlorite, potassium permanganate and the like. The reaction may be carried out within the range of 0 °C to 50 °C. Examples of solvents are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water, methanol, ethanol, isopropanol, mixtures thereof and the like.

Step D

Compound 3 obtained from Step A or C is treated with base in a suitable solvent to give Compound 6. Examples of the base are barium hydroxide, sodium hydroxide, potassium hydroxide, hydrazine, lithium salt of propanethiol and the like. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetone, acetonitrile, methanol, ethanol, propanol, water, mixed solvents thereof and the like. The reaction may be carried out within the range of 0 °C to 100 °C for several minutes to tens of hours.

Step E

Compound 6 obtained form Step D is reacted with Amino Compound 7 having the desired substituent Z and R^7 in a suitable solvent within the range of 0 °C to 50 °C for several minutes to several hours to give Compound 8. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, mixed solvents thereof and the like. An activator such as thionyl chloride, acid halide, acid anhydride, activated ester and the like can be used, if necessary.

Step F

The obtained Compound 8 is treated with a suitable reducing agent in a suitable solvent to give Compound (I-A). Examples of the reducing agent are sodium borohydride, lithium boron hydride, lithium aluminum hydride and the like. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane,

acetonitrile, methanol, ethanol, propanol, acetic acid, mixed solvents thereof and the like. The reaction may be carried out within the range of 0 °C to 100 °C for several minutes to tens of hours.

Step G

Compound 6 obtained from Step D is treated with a reducing agent in a suitable solvent to give Compound 9. Examples of the reducing agent are sodium borohydride, lithium boron hydride, lithium aluminum hydride, diborane and the like. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetonitrile, methanol, ethanol, propanol, mixed solvents thereof and the like. The reaction may be carried out within the range of 0 °C to 100 °C for several minutes to tens of hours. Compound 9 can be obtained through the intermediate such as acid halide, acid anhydride, activated ester and the like, if necessary.

Step H

Compound 9 obtained from Step G is oxidized by the usual method to give Compound 10. Examples of an oxidizer are m-chloroperbenzoic acid, peracetic acid, hydrogen peroxide, pertrifluoroacetic acid, sodium periodate, sodium hypochlorite, potassium permanganate, Dess-Martin periodinane, dimethylsulfoxide/oxalyl chloride (Swern oxidation), ruthenium-catalyst and the like. The reaction may be carried out within the range of -80 °C to 50 °C. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water, methanol, ethanol, isopropanol, mixed solvents thereof and the like.

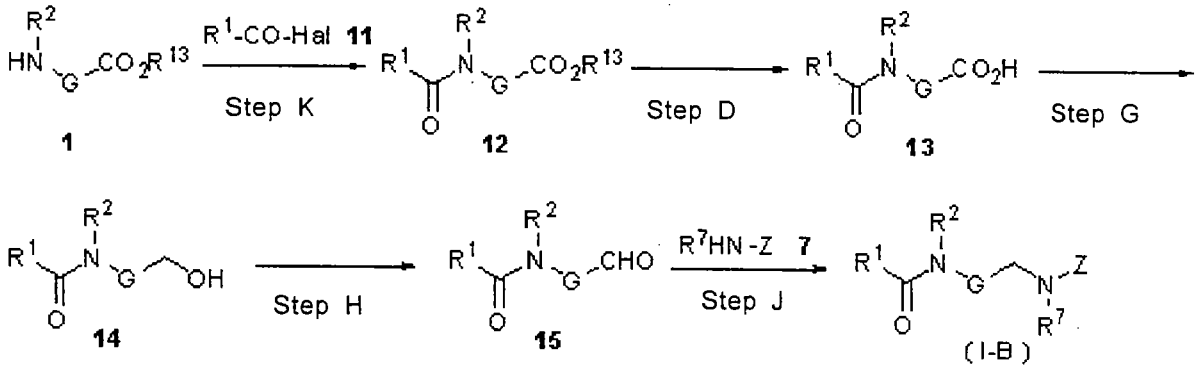
Step J

The obtained Compound 10 and Amino Compound 7 having the desired substituent Z and R^7 are subjected to reductive amination reaction by a ordinary method to give Compound (I-A). Examples of the reducing agent are sodium borohydride, triacetoxy sodium borohydride, cyano sodium borohydride and the like. The reaction may be carried out within the range of 0 °C to 50 °C. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetonitrile, methanol, ethanol, propanol, acetic acid, hydrochloric acid, mixed solvents thereof and the like.

[0061]

[Compounds wherein Y is CO]

[Formula 30]



In the above scheme, each symbol has the same meaning as above and -G-CH_2- is the same as -X- in the formula (I).

Step K

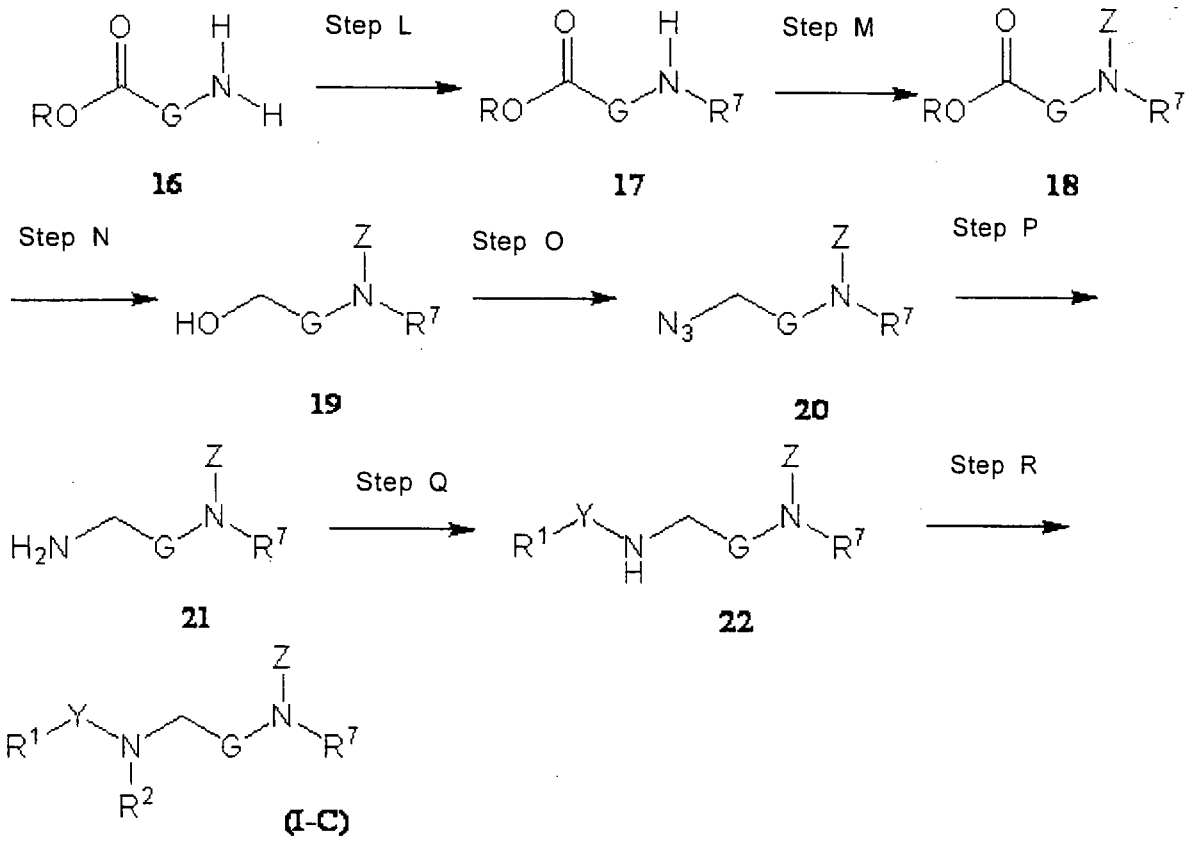
Compound 1 is reacted with Acyl Halide 11 having the desired substituent R^1 in a suitable solvent within the range of -20 °C to 50 °C for several minutes to several hours to give Compound 12. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, mixed solvents thereof and the like.

Step D, G, H and J

The obtained Compound 12 is subjected to the similar method to the above Step D, G, H and J to give Compound (I-B) for this invention.

[0062]

[Formula 31]



In the above scheme, each symbol has the same meaning as above, $-CH_2-G-$ is the same as -X- in the formula (I) and R is alkyl.

Step L

This is the step to introduce substituent R^7 into Compound 16. For example, Compound 16 is reacted with R^7X^1 wherein X^1 is halogen under the presence of a base to give Compound 17. Examples of the solvent are tetrahydrofuran and dimethylformamide. The reaction may be carried out at room temperature. Examples of the base are triethylamine, pyridine, dimethylamino pyridine and the like. This step is not necessary for the compounds wherein R^7 is hydrogen in the formula (I-C).

Step M

This is the step to introduce substituent Z into Compound 17. For example, Compound 17 is reacted with ZX^1 wherein X^1 is halogen under the presence of a base to give Compound 18. Examples of the solvent are methanol, ethanol, isopropanol, dimethylformamide and the like. The reaction may be carried out at room temperature or under heating. For example, it can be

carried out in a sealed tube by a microwave reactor. Examples of the base are N,N-diisopropyl ethyl amine and the like.

Step N

This is the step to reduce Compound 18 to give Compound 19. An example of reducing agent is lithium aluminum hydride. Examples of the solvent are tetrahydrofuran and the like. The reaction may be carried out at room temperature.

Step O

This is the step to give Compound 20 by azidation of Compound 19. For example, methanesulfonyl chloride is reacted with Compound 19 by using triethylamine as a base to give mesylate. Chloroform can be used as the solvent for the mesylation. Sodium azide is reacted with the obtained compound and azidation is carried out in dimethylformamide or the like at room temperature or under heating to give Compound 20.

Step P

This is the step to reduce Compound 20 to give Compound 21. It can be carried out by catalytic reduction. Examples of the catalyst are 10 % palladium carbon and the like. Examples of the solvent are ethanol and the like.

Step Q

This is the step to a compound of the formula: R^1-Y-X^1 wherein X^1 is halogen or the like, and Y is S, SO, SO_2 or CO is reacted with Compound 21 to give Compound 22. Examples of a compound of the formula: R^1-Y-X^1 are various sulfonyl chloride, sulfinyl chloride, acyl chloride and the like. Examples of the solvent are tetrahydrofuran, dimethylformamide and the like. The reaction may be carried out at room temperature or under heating. The reaction is preferably carried out under a base. Examples of the base are pyridine, triethylamine and the like. A compound wherein R^2 is hydrogen in the formula (I-C) do not need the subsequent Step R and Compound 22 is a final target compound. This reaction can be carried out with a compound of the formula: R^1-Y-X^1 wherein Y is S or SO to give Compound 22, and then the oxidation can be carried out to transform to a compound wherein Y is SO_2 used for the next step.

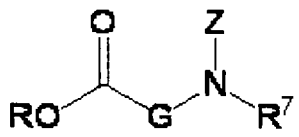
Step R

This is the step to introduce substituent R^2 into Compound 22. R^2X^1 wherein X^1 is halogen or the like is reacted with Compound 22 under the presence of a base to give Compound (I-C). Examples of base are sodium hydride and the like. Examples of the solvent are dimethylformamide and the like.

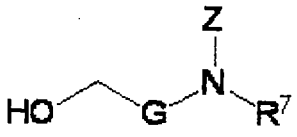
[0063]

The following intermediates are useful in the above steps.

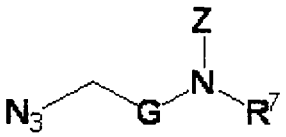
[Formula 32]



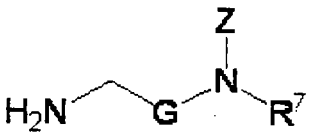
18



19



20



21

wherein

R is optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

G is 1,4-cycloalkylene, and

Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

R is preferably lower alkyl and more preferably methyl and ethyl. Ethyl is especially preferable.

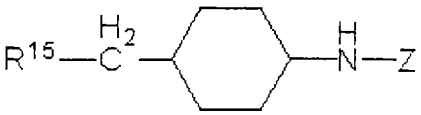
Preferable R^7 is hydrogen.

Preferable Z is optionally substituted heterocyclyl.

The following compounds are especially preferable.

A compound of the formula:

[Formula 33]



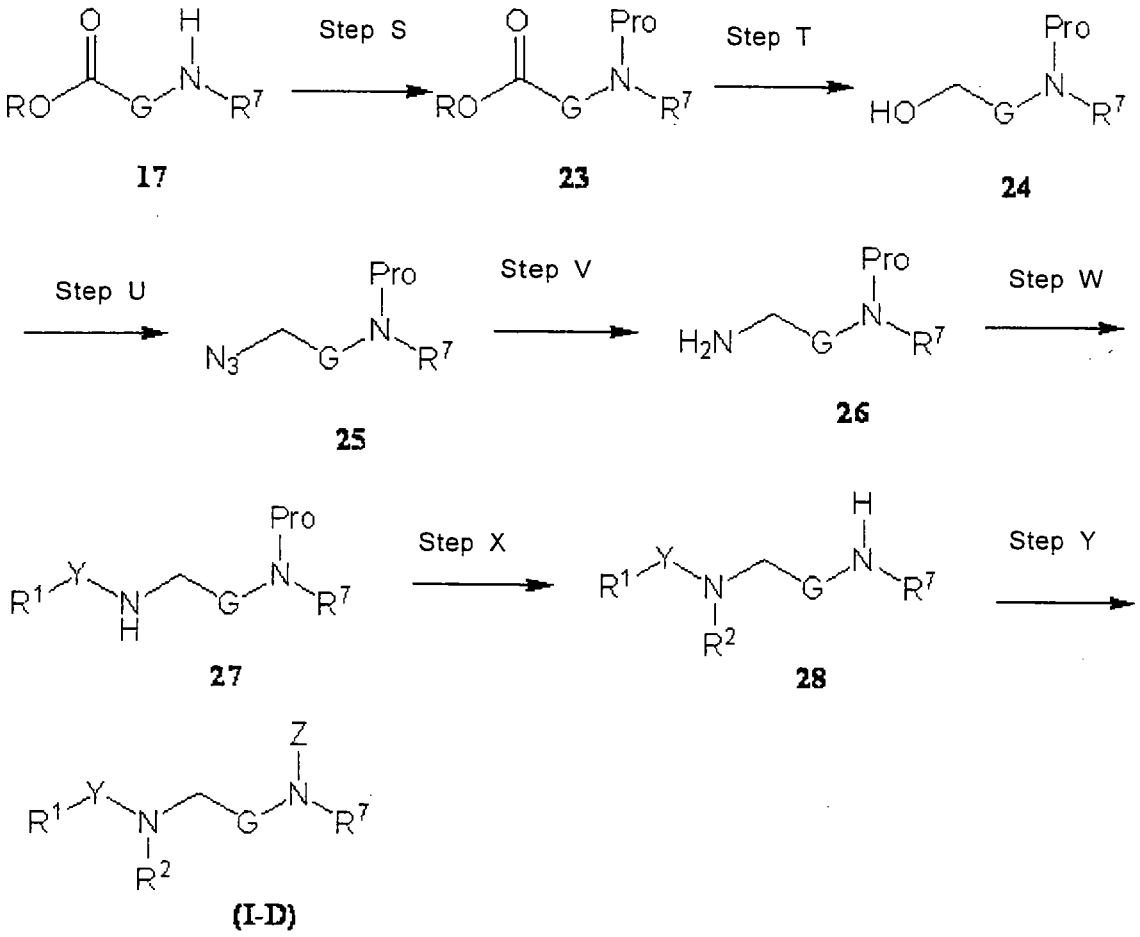
wherein

R^{15} is NH_2 or OH, and

Z is optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzoxazolyl, optionally substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl optionally substituted isoxazolinonyl, optionally substituted oxazolinonyl, optionally substituted benzoxazinonyl or optionally substituted benzoxyazepinonyl.

[0064]

[Formula 34]



In the above scheme, each symbol has the same meaning as above, -CH_2-G- is the same as -X- in the formula (I), R is alkyl and Pro is an amino protecting group.

Step S

This is the step to introduce a protecting group into Compound 17. As a protecting group, the protecting group described in Protective Groups in Organic Synthesis (Theodra W. Greene) or the like can be used. The amino protecting groups which can be removed under the acid condition are preferable. Examples are benzyloxycarbonyl, tert-butyloxycarbonyl and the like. For example, $ProX^1$ wherein X^1 is halogen or the like and Pro is benzyloxycarbonyl, tert-butyloxycarbonyl or the like and Pro-O-Pro wherein Pro is benzyloxycarbonyl, tert-butyloxycarbonyl or the like are reacted under the presence of the base to give Compound 23. Examples of the solvent are tetrahydrofuran and dimethylformamide. The reaction may be carried out at room temperature. Examples of the base are triethylamine, pyridine, dimethyl amino pyridine and the like. The reaction also can be carried out with a compound wherein R^7 is hydrogen.

Step T

This is the step to reduce Compound 23 to give Compound 24. Lithium aluminum hydride can be used as the reducing agent. Examples of the solvent are tetrahydrofuran and the like. The reaction may be carried out at room temperature.

Step U

This is the step to give Compound 25 by azidation of Compound 24. For example, methanesulfonyl chloride is reacted with Compound 24 by using triethylamine as a base to give mesylate. Chloroform can be used as the solvent for the mesylation. Sodium azide is reacted with the obtained compound and azidation is carried out in dimethylformamide or the like at room temperature or under heating to give Compound 25.

Step V

This is the step to reduce Compound 25 to give Compound 26. Compound 25 is reduced with triphenylphosphine and water to give Compound 26. The reaction may be carried out under heating. An example of the solvent is tetrahydrofuran. Except for the reduction method with triphenylphosphine, the catalytic reduction can be used. For the catalytic reduction, 10 % palladium carbon or the like can be used as catalyst. Examples of the solvent are ethanol and the like. The reduction method can be suitably selected depending on the

used protecting group.

Step W

This is the step to react a compound of the formula: R^1-Y-X^1 wherein X^1 is halogen or the like, Y is S, SO, SO_2 or CO with Compound 26 to give Compound 27. Examples of the compound of the formula: R^1-Y-X^1 wherein X^1 is halogen or the like are various sulfonyl chloride, sulfinyl chloride and acyl chloride. Examples of the solvent are tetrahydrofuran, dimethylamide and the like. The reaction may carry out at room temperature or under heating. The reaction is preferably carried out under a base. Examples of the base are pyridine, triethylamine and the like. This reaction can be carried out with a compound of the formula: R^1-Y-X^1 wherein Y is S or SO to give Compound 27, and then the oxidation can be carried out to transform to a compound wherein Y is SO_2 used for the next step.

Step X

This is the step to remove the protecting group of Compound 27. The method for removing the protecting group can be used by selecting various conditions depending on the protecting group. For example, tert-butyloxycarbonyl can be removed with acid. Benzyloxycarbonyl can be removed by catalytic reduction or the like.

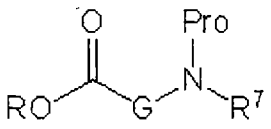
Step Y

This is the step to introduce substituent Z into Compound 28. For example, ZX^1 wherein X^1 is halogen is reacted under the presence of the base to give Compound (I-D). Examples of the solvent are methanol, ethanol, isopropanol, dimethylformamide and the like. The reaction may carry out at room temperature or under heating. For example, it can be carried out in a sealed tube by a microwave reactor. Examples of the base are N,N-diisopropyl ethyl amine and the like.

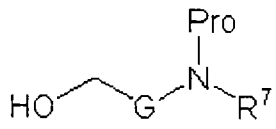
In the above steps, the following intermediates are useful.

A compound of the formula:

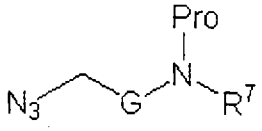
[Formula 35]



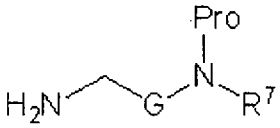
23



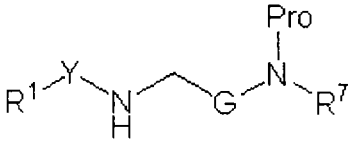
24



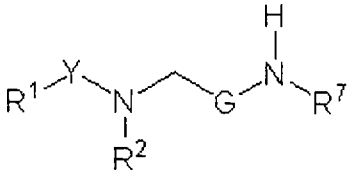
25



26



27



28

wherein

R is optionally substituted lower alkyl,

Pro is a protecting group,

R^7 is hydrogen or optionally substituted lower alkyl,

G is 1,4-cycloalkylene,

Y is SO_2 or SO,

R^1 is optionally substituted lower alkyl, and

R^2 is hydrogen or optionally substituted lower alkyl.

R is preferably lower alkyl and more preferably methyl and ethyl. Ethyl is especially preferable.

Preferable Pro is amino protecting group which can be removed under the acid condition. Examples of Pro are the formula: -(C=O)-O-R, wherein R is optionally substituted lower alkyl or optionally substituted lower alkenyl. Tert-butyloxycarbonyl is especially preferable.

Preferable R^7 is hydrogen.

Preferable Y is SO_2.

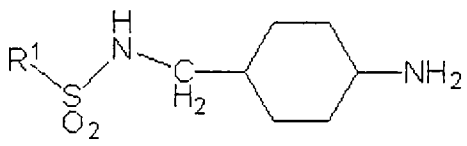
R^1 is preferably lower alkyl and more preferably isopropyl, ethyl and tert-butyl. Tert-butyl is especially preferable.

Preferable R^2 is hydrogen.

The following compounds are especially preferable.

A compound of the formula:

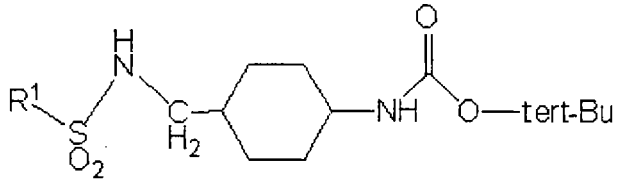
[Formula 36]



wherein R^1 is ethyl or tert-butyl.

A compound of the formula:

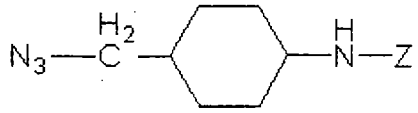
[Formula 37]



wherein R^1 is ethyl, isopropyl or tert-butyl.

A compound of the formula :

[Formula 38]



wherein Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

[0065]

All of the compounds for this invention have an NPY Y5 antagonistic activity and the following compounds are especially preferable.

[0066]

In the formula (I),

a compound wherein R^1 is optionally substituted lower alkyl (hereinafter referred to as "R^1 is R1-1"),

a compound wherein R^1 is C1 to C10 alkyl optionally substituted with halogen (hereinafter referred to as "R^1 is R1-2"),

a compound wherein R^1 is isopropyl or t-butyl (hereinafter referred to as "R^1 is R1-3"),

a compound wherein R^2 is hydrogen or C1 to C3 alkyl (hereinafter referred to as "R^2 is R2-1"),

a compound wherein R^2 is hydrogen (hereinafter referred to as "R^2 is R2-2"),

a compound wherein X is optionally substituted lower alkylene, optionally substituted lower alkenylene or a group of the formula:

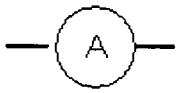
[Formula 39]



,

wherein a group of the formula:

[Formula 40]



is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted phenylene or optionally substituted heterocyclediyl (hereinafter referred to as "X is X-1"), a compound wherein X is C2 to C6 alkylene, C3 to C6 alkenylene or a group of the formula:

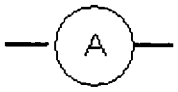
[Formula 41]



,

wherein a group of the formula:

[Formula 42]



is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted phenylene, optionally substituted piperidinylene, optionally substituted thiophenediyl or optionally substituted furandiyl (hereinafter referred to as "X is X-2"), a compound wherein X is C2 to C6 alkylene or a group of the formula:

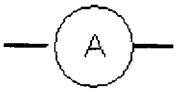
[Formula 43]



,

wherein a group of the formula:

[Formula 44]



wherein is optionally substituted cycloalkylene, optionally substituted phenylene, optionally substituted piperidinylene, optionally substituted thiophenediyl or

optionally substituted furandiyl (hereinafter referred to as "X is X-3"),
a compound wherein X is (i) C2 to C6 alkylene or (ii) cycloalkylene or phenylene, each of which is optionally substituted with halogen, hydroxy, lower alkyl or halogeno(lower alkyl) (hereinafter referred to as "X is X-4"),
a compound wherein X is C2 to C6 alkylene or to C5 to C6 cycloalkylene (hereinafter referred to as "X is X-5"),
a compound wherein X is C3 to C6 alkylene or 1,4-cyclohexylene (hereinafter referred to as "X is X-6"),

a compound wherein Y is -SO- (hereinafter referred to as "Y is Y-1"),
a compound wherein Y is $-SO_2-$ (hereinafter referred to as "Y is Y-2"),
a compound wherein Y is -CO- (hereinafter referred to as "Y is Y-3"),

a compound wherein Z is optionally substituted lower alkyl, optionally substituted carbocyclyl or optionally substituted heterocyclyl (hereinafter referred to as "Z is Z-1"),

a compound wherein Z is $-(CR^8 R^9)_r-W-(CR^{10}R^{11})_s-V$
wherein R^8, R^9, R^{10} and R^{11} are each independently hydrogen or lower alkyl and when Z has two or more of R^8, R^9, R^{10} and/or R^{11}, each of R^8, R^9, R^{10} and R^{11} may be different,
W is single bond, O, S or NR^{12},
R^{12} is hydrogen, lower alkyl or phenyl,
V is hydrogen, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted aryl or optionally substituted heterocyclyl,
r is an integer of 1 to 4 and
s is an integer of 0 to 4
(hereinafter referred to as " Z is Z-2"),

a compound wherein Z is $-(CH_2)_r-W-(CH_2)_s-V$
wherein W is single bond, O, S or NR^{12},
R^{12} is hydrogen or lower alkyl,
V is optionally substituted aryl or optionally substituted heterocyclyl
wherein the substituent(s) is halogen, hydroxy, lower alkyl, halogeno(lower alkyl), lower alkoxy, lower alkenyl, amino, lower alkylamino, acyl, carboxy, lower

alkoxycarbonyl, phenyl or monocyclic heteroaryl,
r is an integer of 1 to 4 and
s is an integer of 0 to 4
(hereinafter referred to as "Z is Z-3"),

a compound wherein Z is $-(CH_2)r-W-(CH_2)s-V$
wherein W is single bond, O, S, NH or NMe,
V is optionally substituted phenyl or optionally substituted heteroaryl
wherein the substituent(s) is halogen, lower alkyl, halogeno(lower alkyl), lower alkoxy, amino or lower alkylamino,
r is an integer of 1 to 3 and
s is an integer of 0 or 1
(hereinafter referred to as "Z is Z-4"),

a compound wherein Z is optionally substituted carbocyclyl,
wherein the substituent(s) is halogen; hydroxy;
optionally substituted lower alkyl wherein the substituents is halogen, hydroxy, carboxy, lower alkoxycarbonyl, cyano and/or phenyl;
lower alkenyl optionally substituted with lower alkoxycarbonyl;
optionally substituted lower alkoxy wherein the substituents is halogen, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, lower alkylamino, cycloalkyl, cyano and /or heterocyclyl;
cycloalkyl; cycloalkyloxy; acyl; lower alkylthio; carbamoyl; lower alkylcarbamoyl; cycloalkylcarbamoyl; hydroxy imino;
optionally substituted amino wherein the substituents is lower alkyl, optionally protected hydroxy(lower alkyl), lower alkoxy(lower alkyl), acyl, lower alkylsulfonyl, arylsulfonyl and/or phenyl;
phenyl optionally substituted with halogen, cyano, phenyl and/or heterocyclyl;
lower alkylsulfinyl; lower alkylsulfamoyl; cycloalkylsulfamoyl;
nitro; cyano; alkylenedioxy; phenylazo optionally substituted with lower alkyl;
phenoxy; oxo;
optionally substituted heterocyclyl wherein the substituents is optionally protected hydroxy, mercapto, halogen, lower alkyl, cycloalkyl, lower alkoxycarbonyl, acyl, amino, lower alkoxycarbonylamino, carbamoyl, oxo, phenyl, lower alkoxyphenyl, halogenophenyl, heterocyclyl and/or oxo;
heterocyclylsulfonyl optionally substituted with lower alkyl; heterocyclyloxy;

heterocyclylcarbonyl optionally substituted with lower alkyl
(hereinafter referred to as "Z is Z-5"),

a compound wherein Z is optionally substituted phenyl
wherein the substituent(s) is halogen; hydroxy; lower alkyl optionally substituted with halogen, hydroxy, lower alkoxycarbonyl, cyano and/or phenyl; lower alkoxycarbonyl(lower alkenyl); lower alkoxy optionally substituted with halogen, lower alkoxy, lower alkoxycarbonyl, cycloalkyl and/or heterocyclyl; cycloalkyl; cycloalkyloxy; acyl; lower alkylthio; carbamoyl; lower alkycarbamoyl; amino optionally substituted with lower alkyl, hydroxy(lower alkyl), acyl, lower alkylsulfonyl and/or phenyl; phenyl optionally substituted with halogen, cyano, phenyl and/or heterocyclyl;
lower alkyl sulfamoyl; cycloalkylsulfamoyl; nitro; alkylenedioxy; phenylazo optionally substituted with lower alkyl; phenoxy; oxo;
heterocyclyl optionally substituted with hydroxy, halogen, lower alkyl, lower alkoxycarbonyl, amino, carbamoyl, phenyl, halogenophenyl, heterocyclyl and/or oxo; heterocyclyloxy; and/or heterocyclylsulfonyl optionally substituted with lower alkyl
(hereinafter referred to as "Z is Z-6"),

a compound wherein Z is optionally substituted phenyl
wherein the substituent(s) is halogen; lower alkyl optionally substituted with halogen, hydroxy, lower alkoxycarbonyl and/or phenyl; lower alkoxy optionally substituted with halogen and/or cycloalkyl; cycloalkyl; cycloalkyloxy; acyl; lower alkylthio; lower alkylcarbamoyl; amino optionally substituted with lower alkyl, hydroxy(lower alkyl), acyl and/or phenyl; phenyl optionally substituted with piperidyl; cycloalkylsulfamoyl; alkylenedioxy; phenoxy;
morpholinyl or morpholino, each of which is optionally substituted with lower alkyl; piperidyl optionally substituted with hydroxy, lower alkyl, lower alkoxycarbonyl, phenyl, halogenophenyl and/or oxo; pyrrolidinyl optionally substituted with hydroxy, carbamoyl and/or oxo;
piperazinyl optionally substituted with phenyl or pyrimidinyl; dihydropyridyl; pyrrolyl; pyrrolinyl; imidazolyl optionally substituted with halogen and/or lower alkyl; pyrazolyl; thienyl; thiadiazolyl; furyl; oxazolyl; isoxazolyl; tetrazolyl optionally substituted with lower alkyl and/or phenyl; indolinyl; indolyl; tetrahydroquinolyl; benzothiazolyl optionally substituted with lower alkyl;

tetrahydroisothiazolyl optionally substituted with oxo; benzopyranyl optionally substituted with oxo; tetrahydropyranyloxy; tetrahydrofuryloxy; morpholinosulfonyl optionally substituted with lower alkyl; and/or piperidylsulfonyl optionally substituted with lower alkyl
(hereinafter referred to as "Z is Z-7"),

a compound wherein Z is optionally substituted phenyl
wherein the substituent(s) is halogen, lower alkyl, halogeno(lower alkyl), lower alkoxy, cycloalkyloxy, lower alkylcarbamoyl, phenyl, lower alkyl morpholino and/or tetrahydropyranyloxy
(hereinafter referred to as "Z is Z-8"),

a compound wherein Z is optionally substituted heterocyclyl
wherein the substituent(s) is halogen, hydroxy, lower alkyl, halogeno(lower alkyl), lower alkoxy, mercapto, lower alkylthio, acyl, carboxy, lower alkoxycarbonyl, amino, lower alkylamino, phenyl, naphthyl, phenylthio optionally substituted with halogen, phenoxy optionally substituted with halogen, oxo and/or heterocyclyl optionally substituted with lower alkyl
(hereinafter referred to as "Z is Z-9"),

a compound wherein Z is thienyl, pyrazolyl, thiazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, indolyl, isoindolyl, indolinyl, isoindolinyl, indazolyl, benzopyranyl, benzoxazolyl, benzothienyl, benzothiazolyl, benzothiazolinyl, benzothiadiazolyl, benzimidazolyl, quinolyl, isoquinolyl, dihydrobenzofuryl, carbazolyl, acridinyl, dibenzofuryl or thiazolopyridyl, each of which is optionally substituted with the substituent(s) selected from the group of lower alkyl; halogeno(lower alkyl); lower alkoxy; lower alkoxycarbonyl; acyl; lower alkoxycarbonyl(lower alkyl); mercapto; phenyl, naphthyl, phenylthio or phenoxy, each of which is optionally substituted with halogen; furyl; nitro; oxo; and morpholino optionally substituted with lower alkyl
(hereinafter referred to as "Z is Z-10"),

a compound wherein Z is thienyl, thiazolyl, thiadiazolyl, pyridyl, pyrazinyl, indolyl, isoindolinyl, benzopyranyl, quinolyl, carbazolyl, dibenzofuryl, benzopyranyl, benzothienyl or benzothiazolyl, each of which is optionally substituted with one or more substituent(s) selected from the group of lower

alkyl, halogeno(lower alkyl), lower alkoxy, lower alkoxycarbonyl, acyl, phenyl, naphthyl, phenylthio, lower alkyl morpholino and oxo
(hereinafter referred to as "Z is Z-11"),

a compound wherein R1 is R1-2, R2 is R2-2, n is 2 and a combination of X, Y and Z, i.e., (X, Y, Z), is any one of the followings.
(X,Y,Z)=(X-3,Y-2,Z-1),(X-3,Y-2,Z-2),(X-3,Y-2,Z-3),(X-3,Y-2,Z-4),(X-3,Y-2,Z-5),(X-3,Y-2,Z-6),(X-3,Y-2,Z-7),(X-3,Y-2,Z-8),(X-3,Y-2,Z-9),(X-3,Y-2,Z-10),(X-3,Y-2,Z-11),
(X-3,Y-3,Z-1),(X-3,Y-3,Z-2),(X-3,Y-3,Z-3),(X-3,Y-3,Z-4),(X-3,Y-3,Z-5),(X-3,Y-3,Z-6),(X-3,Y-3,Z-7),(X-3,Y-3,Z-8),(X-3,Y-3,Z-9),(X-3,Y-3,Z-10),(X-3,Y-3,Z-11),
(X-4,Y-2,Z-1),(X-4,Y-2,Z-2),(X-4,Y-2,Z-3),(X-4,Y-2,Z-4),(X-4,Y-2,Z-5),(X-4,Y-2,Z-6),(X-4,Y-2,Z-7),(X-4,Y-2,Z-8),(X-4,Y-2,Z-9),(X-4,Y-2,Z-10),(X-4,Y-2,Z-11),
(X-4,Y-3,Z-1),(X-4,Y-3,Z-2),(X-4,Y-3,Z-3),(X-4,Y-3,Z-4),(X-4,Y-3,Z-5),(X-4,Y-3,Z-6),(X-4,Y-3,Z-7),(X-4,Y-3,Z-8),(X-4,Y-3,Z-9),(X-4,Y-3,Z-10),(X-4,Y-3,Z-11),
(X-5,Y-2,Z-1),(X-5,Y-2,Z-2),(X-5,Y-2,Z-3),(X-5,Y-2,Z-4),(X-5,Y-2,Z-5),(X-5,Y-2,Z-6),(X-5,Y-2,Z-7),(X-5,Y-2,Z-8),(X-5,Y-2,Z-9),(X-5,Y-2,Z-10),(X-5,Y-2,Z-11),
(X-5,Y-3,Z-1),(X-5,Y-3,Z-2),(X-5,Y-3,Z-3),(X-5,Y-3,Z-4),(X-5,Y-3,Z-5),(X-5,Y-3,Z-6),(X-5,Y-3,Z-7),(X-5,Y-3,Z-8),(X-5,Y-3,Z-9),(X-5,Y-3,Z-10)or (X-5,Y-3,Z-11)
the pharmaceutically acceptable salt or solvate thereof.

[0067]

The anorectic or anti-obesity composition of this invention is especially useful for preventing and/or treating obesity and suppressing food intake. Moreover, the composition is effective for preventing and/or treating the diseases in which obesity acts as a risk factor, for example, diabetes, hypertension, hyperlipemia, atherosclerosis, acute coronary syndrome and the like.

Furthermore, a compound for this invention has not only NPY Y5 receptor antagonistic activity but also any or all good characters as a medicine selected from the followings.

a) weak CYP enzyme inhibition.

b) less induction of a drug-metabolizing enzyme.

c) good drug disposition such as high bioavailability.

d) low toxicity of anemia-inducing activity or the like.

e) high metabolic stability.

f) high selectivity for Y5 receptor.

g) high water solubility.

h) high transportability through the blood-brain barrier.

[0068]

In addition, a compound for this invention has a low affinity for NPY Y1 and Y2 receptors, and has a high selectivity for NPY Y5 receptor. NPY causes a sustained vasoconstrictive action in the periphery and this action is mainly via Y1 receptor. Since Y5 receptor is not involved in this action at all, the compound has a low risk of inducing side effects based on the peripheral vasoconstriction, and is expected to be suitably used as a safe medicine.

[0069]

The compound for this invention shows an anti-obesity effect by suppressing food intake. Therefore, it is one of the features of the present antagonist not to induce side effects such as dyspepsia caused by an anti-obesity agent which inhibits digestion and absorption, or central nervous system side-effects such as an antidepressant effect due to a serotonin transporter inhibitor that shows an anti-obesity effect.

[0070]

An anorectic or anti-obesity composition of this invention can be administered orally or parenterally. In the case of oral administration, it may be in any usual form such as tablets, granules, powders, capsules, pills, solutions, syrups, buccal tablets, sublingual tablets and the like. When the composition is parenterally administered, any usual form is preferable, for example, injections (e.g., intravenous, intramuscular and the like), suppositories, endermic agents, inhalations and the like. Oral administration is especially preferable because the compounds for this invention show a high oral absorbability.

[0071]

A pharmaceutical composition may be manufactured by mixing an effective amount of a compound for this invention with various pharmaceutical additives suitable for the administration form, such as excipients, binders, moistening agents, disintegrants, lubricants and diluents. When the composition is of an injection, an active ingredient together with a suitable carrier can be sterilized to give a pharmaceutical composition.

[0072]

Examples of the excipients include lactose, saccharose, glucose, starch, calcium carbonate, crystalline cellulose and the like. Examples of the binders include methylcellulose, carboxymethylcellulose, hydroxypropylcellulose, gelatin, polyvinylpyrrolidone and the like. Examples of the disintegrants include

carboxymethylcellulose, sodium carboxymethylcellulose, starch, sodium alginate, agar, sodium lauryl sulfate and the like. Examples of the lubricants include talc, magnesium stearate and macrogol, and the like. Cacao oil, macrogol, methylcellulose or the like may be used as base materials of suppositories. When the composition is manufactured as solutions, emulsified injections or suspended injections, solubilizing agent, suspending agents, emulsifiers, stabilizers, preservatives, isotonic agents and the like which are usually used may be added. For oral administration, sweetening agents, flavors and the like which are usually used may be added.

[0073]

Although the dosage of a compound of this invention as an anorectic or anti-obesity composition should be determined in consideration of the patient's age and body weight, the type and degree of diseases, the administration route and the like, a usual oral dosage for an adult is 0.05 to 100 mg/kg/day and preferable is 0.1 to 10 mg/kg/day. For parenteral administration, although the dosage highly varies with administration routes, a usual dosage is 0.005 to 10 mg/kg/day and preferably 0.01 to 1 mg/kg/day. The dosage may be administered in one to several divisions per day.

[0074]

This invention is further explained by the following Examples, which are not intended to limit the scope of this invention.

The abbreviations used in the present description stand for the following meanings.

Me: methyl

Et: ethyl

i-Pr: isopropyl

DMSO: dimethylsulfoxide

Pd-C: palladium carbon

THF: tetrahydrofuran

DMF: N,N-dimethylformamide

mCPBA: meta-Chloroperoxybenzoic acid

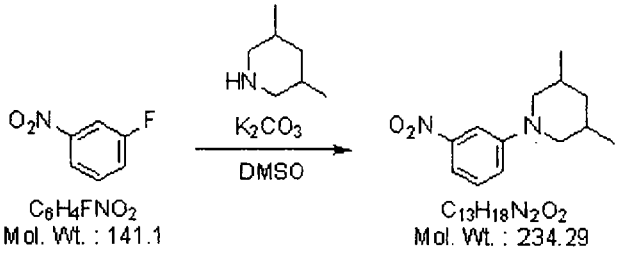
Example

[0075]

Example 1 Synthesis of Compound (Ii-1)

Step 1

[Formula 45]

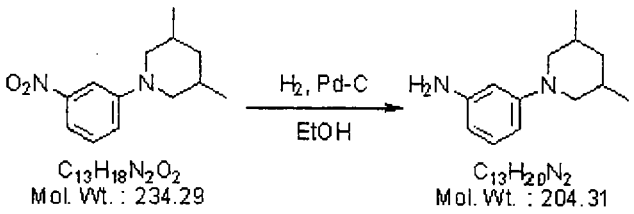


3-Fluoronitrobenzene (2.00 g, 14.2 mmol) was dissolved in dimethylsulfoxide (15 ml). 3,5-Dimethylpiperidine (3.21 g, 28.4 mmol) and potassium carbonate (3.92 g, 28.4 mmol) were added thereto and the mixture was stirred for 3 hours at 150 °C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure. Ethyl acetate and hexane were added to the residue. The precipitated crystals were collected with filtration to give the desired substituted nitrobenzene (2.05 g, 62 % yield).

^{1}H-NMR ($CDCl_3$) δppm: 0.76 (q, 1H, J = 12.0 Hz), 0.96 (d, 6H, J = 6.3 Hz), 1.70-1.91 (m, 3H), 2.32 (t, 2H, J = 12.0 Hz), 3.62-3.72 (m, 2H), 7.17-7.25 (m, 1H), 7.34 (t, 1H, J = 8.1 Hz), 7.59 (d, 1H, J = 8.1 Hz), 7.71 (s, 1H).

Step 2

[Formula 46]



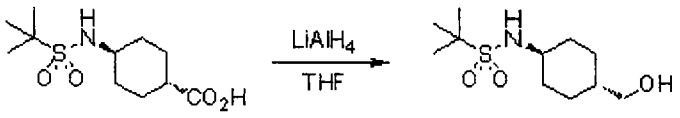
The compound obtained in Step 1 (2.05 g, 8.75 mmol) was dissolved in ethanol (25 ml) and 10 % Pd-C (0.20 g) was added thereto to carry out the hydrogenation reaction for 12 hours. Pd-C was removed by celite filtration and the filtrate was condensed under reduced pressure. The residue was purified by silica gel chromatography to give the desired Aniline (1.62 g, 90 % yield).

^{1}H-NMR ($CDCl_3$) δppm: 0.69 (q, 1H, J = 12.0 Hz), 0.92 (d, 6H, J = 6.3 Hz), 1.75-1.98 (m, 3H), 2.22 (t, 2H, J = 12.0 Hz), 3.53-3.62 (m, 2H), 6.21 (d, 1H, J = 7.5 Hz),

6.38 (s, 1H), 6.42 (d, 1H, J = 8.1 Hz), 7.04 (t, 1H, J = 8.1 Hz).

Step 3

[Formula 47]



$C_{11}H_{21}NO_4S$
Mol. Wt. : 263.35

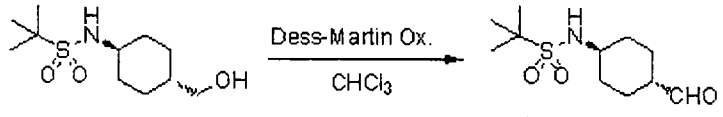
$C_{11}H_{23}NO_3S$
Mol. Wt. : 249.37

Carboxylic acid (the synthesis method was described in WO01/037826) (5.04 g, 19.1 mmol) was suspended in tetrahydrofuran (50 ml). Lithium aluminum hydride (0.726 g, 19.1 mmol) was added thereto under ice-cooling and the mixture was stirred at room temperature for 1 hour. The reactant was stirred under ice-cooling and water (1.5 mL) was carefully added dropwise. After that, the mixture was stirred at room temperature for 5 minutes and the generated deposit was removed by filtration. The filtrate was condensed under reduced pressure. Ethyl acetate and hexane were added to the residue. The precipitated crystals were collected with filtration to give the desired Alcohol (3.15 g, 66 % yield).

^{1}H-NMR (DMSO-d6) δppm: 0.88 (q, 2H, J = 11.6 Hz), 1.25 (s, 9H), 1.15-1.30 (m, 3H), 1.67-1.76 (m, 2H), 1.83-1.92 (m, 2H), 2.97 (m, 1H), 3.13-3.20 (m, 2H), 4.35 (t, 1H, J = 5.2 Hz), 6.71 (d, 1H, J = 8.8 Hz).

Step 4

[Formula 48]



$C_{11}H_{23}NO_3S$
Mol. Wt. : 249.37

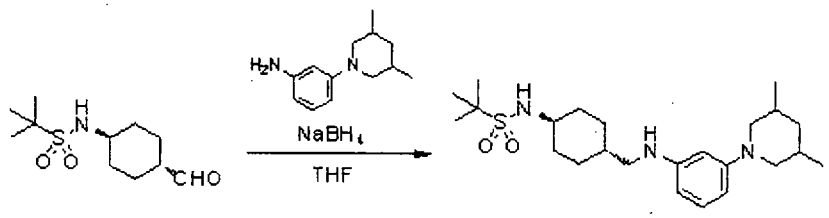
$C_{11}H_{21}NO_3S$
Mol. Wt. : 247.35

The compound obtained in Step 3 (500 mg, 2.01 mmol) was dissolved in chloroform (5 ml) and Dess-Martin periodinane (893 mg, 2.11 mmol) was added thereto. The mixture was stirred at room temperature for 1 hour. The deposit was removed by filtration and the filtrate was condensed under reduced pressure. The residue was purified by silica gel chromatography to give the desired Aldehyde (385 mg, 77 % yield).

^{1}H-NMR (DMSO-d6) δppm: 1.26 (s, 9H), 1.13-1.38 (m, 4H), 1.85-1.98 (m, 4H), 2.16 (m, 1H), 3.01 (m, 1H), 6.80 (d, 1H, J = 8.0 Hz), 9.54 (s, 1H).

Step 5

[Formula 49]



$C_{11}H_{21}NO_3S$
Mol. Wt. : 247.35

$C_{24}H_{41}N_3O_2S$
Mol. Wt. : 435.67

Aniline obtained in Step 2 (107 mg, 0.523 mmol) was dissolved in tetrahydrofuran (3 ml). Aldehyde obtained in Step 4 (130 mg, 0.523 mmol) was added thereto and the mixture was stirred at room temperature for 1 hour. To the reactant was added sodium borohydride (23.7mg, 0.628 mmol) and the mixture was stirred at room temperature for 3 hours. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give the desired compound (99.3 mg, yield 43 %).

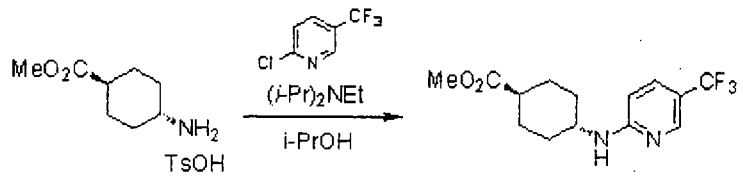
^{1}H-NMR (DMSO-d6) δppm: 0.64 (q, 1H, J = 11.6 Hz), 0.87 (d, 6H, J = 6.0 Hz), 0.92-1.08 (m, 2H), 1.25 (s, 9H), 1.15-1.32 (m, 2H), 1.41 (m, 1H), 1.58-1.95 (m, 7H), 2.08 (t, 2H, J = 11.6 Hz), 2.75-2.82 (m, 2H), 3.00 (m, 1H), 3.48-3.55 (m, 2H), 5.31 (m, 1H), 5.94 (d, 1H, J = 8.5 Hz), 6.08-6.13 (m, 2H), 6.71 (d, 1H, J = 8.5 Hz), 6.85 (t, 1H, J = 8.5 Hz). Melting point: 161 to 162 °C

[0076]

Example 2 Synthesis of Compound (Ij-1)

Step 1

[Formula 50]



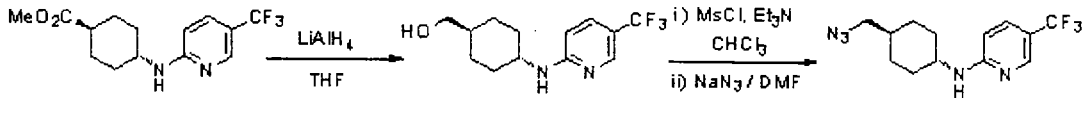
$C_{11}H_{21}NO_4S$
Mol. Wt. : 263.35

$C_{14}H_{17}F_3N_2O_2$
Mol. Wt. : 302.29

Amine (1.20 g, 3.64 mmol) and 2-chloro-5-trifluoromethylpyridine (727 mg, 4.01 mmol) was suspended in isopropanol (4 ml) and N, N-diisopropyl ethyl amine (1.87 ml, 10.9 mmol) was added thereto. After the mixture was in sealed tubes, the reaction was carried out by a microwave reactor for 1 hour at 160 °C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give the desired Ester (222 mg, 20 % yield).

Step 2

[Formula 51]



$C_{14}H_{17}F_3N_2O_2$
Mol. Wt. : 302.29

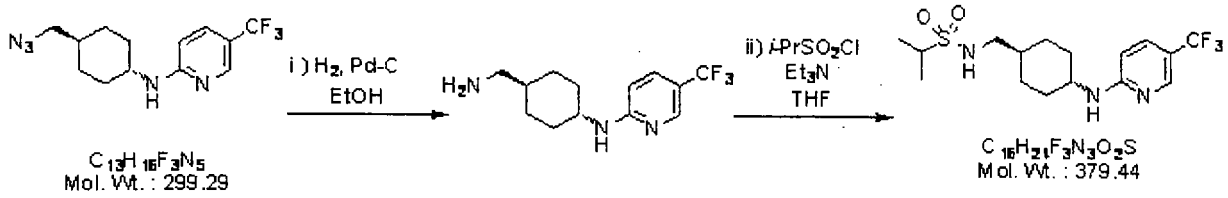
$C_{13}H_{17}F_3N_2O$
Mol. Wt. : 274.28

$C_{13}H_{16}F_3N_5$
Mol. Wt. : 299.29

Ester obtained in Step 1 (207 mg, 0.685 mmol) was dissolved in tetrahydrofuran (3 ml). Lithium aluminum hydride (31.1 mg, 0.822 mmol) was added thereto under ice-cooling and the mixture was stirred at room temperature for 0.5 hour. The reactant was poured into iced water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure to give alcohol. The obtained alcohol was dissolved in chloroform (3 ml). Triethylamine (0.28 ml, 2.04 mmol) was added thereto and methanesulfonyl chloride (0.12 ml, 1.64 mmol) was added dropwise under ice-cooling. The mixture was stirred at room temperature for 1 hour. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure to give mesylate. The obtained mesylate was dissolved in dimethylformamide (3 ml) and sodium azide (221 mg, 3.40 mmol) was added thereto. The mixture was stirred for 3 hours at 100 °C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure. The residue was purified by silica gel chromatography to give the desired Azide (178 mg, 87 % yield).

Step 3

[Formula 52]



Azide (178 mg, 0.595 mmol) obtained in Step 2 was dissolved in ethanol (3 ml) and 10 % Pd-C (30 mg) was added thereto to carry out the hydrogenation reaction for 4 hours. Pd-C was removed by celite filtration and the filtrate was condensed under reduced pressure to give amine.

The obtained amine was dissolved in tetrahydrofuran (3 ml) and triethylamine (0.28 ml, 0.714 mmol) was added thereto. Isopropyl sulfonyl chloride (0.10 ml, 1.64 mmol) was added dropwise under ice-cooling and the mixture was stirred for 1 hour. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure. The residue was purified by silica gel chromatography to give the desired compound (64.8 mg, 29 % yield).

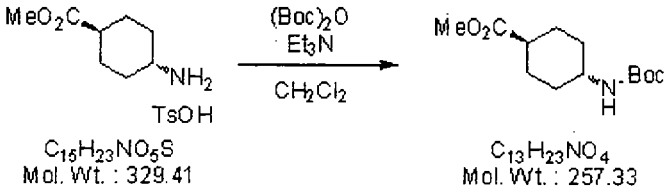
^{1}H-NMR (DMSO-d_6) δ: 0.92-1.06 (m, 2 H), 1.10-1.25 (m, 2H,), 1.22 (d, 6H, J = 6.4 Hz), 1.38 (m, 1H), 1.76-1.84 (m, 2H), 1.93-2.02 (m, 2H), 2.81 (t, 2H, J = 6.0 Hz), 3.08-3.19 (m, 1H), 3.69 (m, 1H), 6.53 (d, 1H, J = 8.8 Hz), 6.95 (t, 1H, J = 5.6 Hz), 7.16 (d, 1H, J = 7.6 Hz), 7.58 (d, 1H, J = 8.8 Hz), 8.26 (s, 1H) Melting point:155-156 °C

[0077]

Example 3 Synthesis of Compound (Ij-62)

Step 1

[Formula 53]



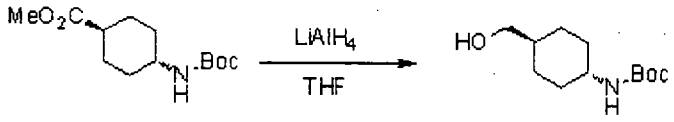
Amine (132 g, 401 mmol) was suspended in dichloromethane (1000 ml)

under ice-cooling. Triethylamine (123 ml, 882 mmol) and $(Boc)_2O$ (101 ml, 440 mmol) were sequentially added thereto and stirred for 10 minutes. After that, the mixture was stirred at room temperature for 2 hours and the solvent was removed. The residue was poured into aqueous citric acid (citric acid monohydrate 50 g in water 400 ml) to become pH4 and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure to quantitatively give the target compound.

^{1}H-NMR (DMSO-d6) δppm: 1.06-1.25 (m, 2H), 1.25-1.43 (m, 2H), 1.37 (s, 9H), 1.75-1.94 (m, 4H), 2.19 (tt, 1H, J = 11.7, 3.9 Hz), 3.07-3.24 (m, 1H), 3.58 (s, 3H), 6.74 (d, 1H, J = 6.6 Hz).

Step 2

[Formula 54]



$C_{13}H_{23}NO_4$
Mol. Wt. : 257.33

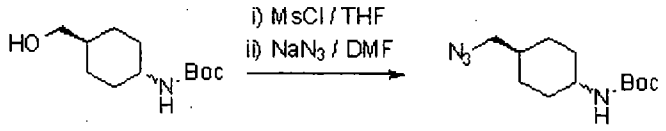
$C_{12}H_{23}NO_3$
Mol. Wt. : 229.32

Lithium aluminum hydride (18.3 g, 483 mmol) was suspended in tetrahydrofuran (800 ml) and ester in tetrahydrofuran (300 ml) obtained in Step 1 was slowly added thereto under ice-cooling with stirring over 1 hour. The mixture was reacted under ice-cooling for 10 minutes and at room temperature for 2.5 hours. The reactant was ice-cooled and the mixture of water and tetrahydrofuran (1:1, 36 ml), 2 N aqueous sodium hydroxide (18 ml) and water (18 ml) were sequentially added thereto. The mixture was stirred for 20 minutes and at room temperature for 1.5 hours. The deposit was removed by filtration and the filtrate was condensed under reduced pressure. Ethyl acetate and hexane were added to the residue. The precipitated crystals were collected with filtration to give the desired Alcohol (79.5 g, 87 % yield)(through Step 1 to 2).

^{1}H-NMR (DMSO-d6) δppm: 0.78-1.00 (m, 2H), 1.00-1.32 (m, 3H), 1.37 (s, 9H), 1.65-1.84 (m, 4H), 3.04-3.24 (m, 3H), 4.32-4.42 (m, 1H), 6.66 (d, 1H, J = 7.8 Hz).

Step 3

[Formula 55]



$C_{12}H_{23}NO_3$
Mol. Wt. : 229.32

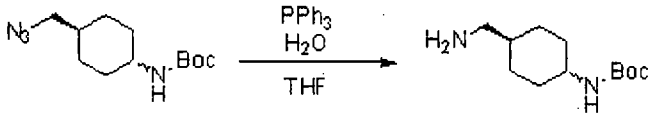
$C_{12}H_{22}N_4O_2$
Mol. Wt. : 254.33

Alcohol (79.5 g, 347 mmol) was dissolved in tetrahydrofuran (800 ml). Triethylamine (72.5 ml, 520 mmol) and methanesulfonyl chloride (32.2 ml, 416 mmol) were sequentially added thereto under ice-cooling with stirring and the mixture was reacted for 1.5 hour. The reactant was poured into aqueous citric acid (citric acid monohydrate 30 g in water 500 ml) to become pH 4 and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure. The crystal deposited in the removal process was collected by filtration and washed with hexane to give mesylate (100 g). The obtained mesylate was dissolved in dimethylformamide (100 ml) and sodium azide (63.7 g, 980 mmol) was added thereto and reacted at 80 °C for 2 hours. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure to quantitatively give the desired Azide (the crude weight is 85.4 g).

^{1}H-NMR (DMSO-d6) δppm: 0.90-1.21 (m, 4H), 1.32-1.50 (m, 1H), 1.37 (s, 9H), 1.65-1.84 (m, 4H), 3.06-3.24 (m, 3H), 6.71 (d, 1H, J = 8.1 Hz).

Step 4

[Formula 56]



$C_{12}H_{22}N_4O_2$
Mol. Wt. : 254.33

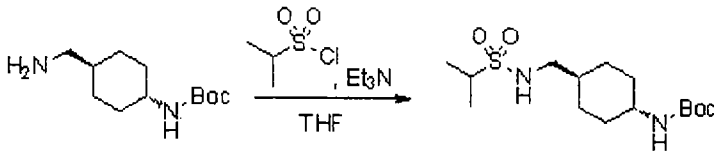
$C_{12}H_{24}N_2O_2$
Mol. Wt. : 228.33

Azide obtained in Step 3 was dissolved in tetrahydrofuran (900 ml) at room temperature. Triphenylphosphine (103 g, 392 mmol) and water (90 ml) were sequentially added thereto and reacted at 80 °C for 1.5 hours. The solvent (770 ml) was removed and water (300 ml), ethyl acetate (400 ml) and 2 N hydrochloric

acid (150 ml) were sequentially added thereto to become pH 2.5 and liquid-liquid extraction was carried out. The organic layer was backextracted with 2 N hydrochloric acid. After washing with ethyl acetate, the aqueous layer was alkalinized and extracted repeatedly with ethyl acetate and chloroform. The organic layers were combined and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure and hexane was added to the residue. The precipitated crystals were collected with filtration and washed with hexane to give the desired Amine (41.7 g, 53 % yield) (through Step 3 to 4).
^{1}H-NMR (DMSO-d6) δppm: 0.77-0.96 (m, 2H), 1.00-1.18 (m, 3H), 1.37 (s, 9H), 1.67-1.82 (m, 4H), 2.30-2.38 (m, 2H), 2.90-3.60 (m, 2H), 3.05-3.22 (m, 1H), 6.66 (d, 1H, J = 7.2 Hz).

Step 5

[Formula 57]



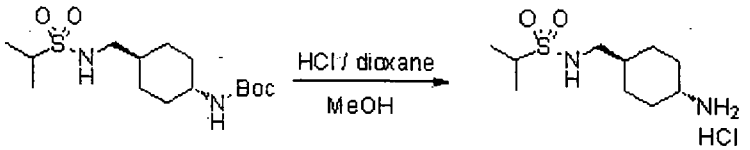
$C_{12}H_{24}N_2O_2$
Mol. Wt.: 228.33

$C_{15}H_{30}N_2O_4S$
Mol. Wt.: 334.47

Amine (37.5 g, 164 mmol) was suspended in tetrahydrofuran (400 ml). Triethylamine (91.7 ml, 656 mmol) and isopropyl sulfonyl chloride (32.2 ml, 416 mmol) were slowly and sequentially added thereto within the range of -55 °C to -40 °C with stirring. The mixture was stirred for 6 hours with gradually warming to 0 °C. The reactant was poured into the ice-cooled dilute aqueous acid and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure and isopropyl ether was added to the residue. The precipitated crystals were collected with filtration and washed with isopropyl ether to give the desired Sulfonamide (43.1 g, 79 % yield).
^{1}H-NMR (DMSO-d6) δppm: 0.79-0.98 (m, 2H), 1.00-1.36 (m, 3H), 1.20 (d, 6H, J = 6.6 Hz), 1.37 (s, 9H), 1.70-1.84 (m, 4H), 2.72-2.80 (m, 2H), 3.04-3.22 (m, 2H), 6.68 (d, 1H, J = 8.1 Hz), 6.94 (t, 1H, J = 6.0 Hz).

Step 6

[Formula 58]



$C_{15}H_{30}N_2O_4S$
Mol. Wt. : 334.47

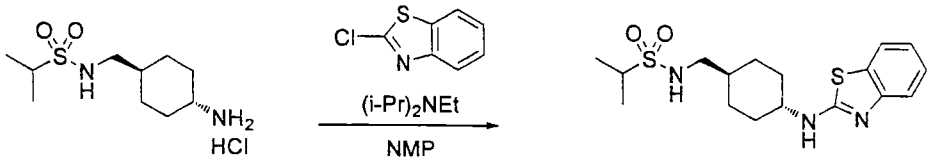
$C_{10}H_{23}ClN_2O_2S$
Mol. Wt. : 270.82

Boc-protected amine (43.0 g, 128 mmol) was suspended in methanol (200 ml) and 4 N hydrochloric acid in dioxane (96 ml, 384 mmol) was added thereto under ice-cooling with stirring for 20 minutes and at room temperature for 3 hours. The reactant was ice-cooled and isopropyl ether (220 ml) was added thereto. After stirring for 30 minutes, the precipitated crystals were collected with filtration and washed with isopropyl ether to give the desired Amine hydrochloride (30.8 g, 89 % yield).

^{1}H-NMR (DMSO-d6) δppm: 0.85-1.02 (m, 2H), 1.20 (d, 6H, J = 6.6 Hz), 1.20-1.40 (m, 3H), 1.75-1.84 (m, 2H), 1.90-2.00 (m, 2H), 2.73-2.82 (m, 2H), 2.83-2.97 (m, 1H), 3.08-3.20 (m, 1H), 7.01 (t, 1H, J = 5.7 Hz), 8.01 (s, 3H).

Step 7

[Formula 59]



$C_{10}H_{23}ClN_2O_2S$
Mol. Wt. : 270.82

$C_{17}H_{25}N_3O_2S_2$
Mol. Wt. : 367.53

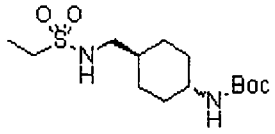
Amine hydrochloride (1.4 g, 5.16 mmol) and 2-chlorobenzothiazole (2.63 g, 15.5 mmol) were suspended in N-methyl pyrrolidone (15 ml) and N,N-diisopropylethyl amine (4.50 ml, 25.8 mmol) was added thereto. After the mixture was divided into two reaction vials, the reaction were carried out by a microwave reactor for 30 minutes at 220 °C. The reactants from the two vials were poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give the desired Compound (Ij-62) (1.5 g, 79 % yield).

[0078]

In Step 5, ethanesulfonyl chloride instead of isopropyl sulfonyl chloride

was reacted to give the following compound wherein R^1 is ethyl.

[Formula 60]



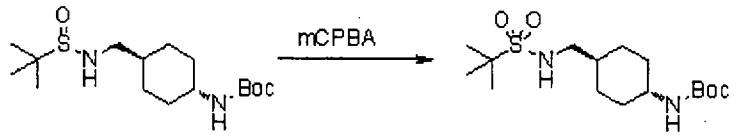
$C_{14}H_{28}N_2O_4S$
Mol. Wt. : 320.45

^{1}H-NMR (DMSO-d6) δppm: 0.80-0.98 (m, 2H), 1.02-1.18 (m, 2H), 1.17 (t, 3H, J = 7.2 Hz), 1.22-1.34 (m, 1H), 1.37 (s, 9H), 1.68-1.82 (m, 4H), 2.68-2.78 (m, 2H), 2.96 (q, 2H, J = 7.2 Hz), 3.04-3.22 (m, 1H), 6.68 (d, 1H, J = 8.1 Hz), 6.94 (t, 1H, J = 6.0 Hz).

[0079]

In Step 5, tert-butyl sulfinylchloride instead of isopropyl sulfonyl chloride was reacted and the oxidation with mCPBA was carried out to give the following compound wherein R^1 is tert-butyl (WO2001037826, Example 3).

[Formula 61]



$C_{16}H_{32}N_2O_4S$
Mol. Wt. : 348.5

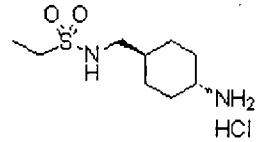
^{1}H-NMR (DMSO-d6) δppm: 0.79-1.00 (m, 2H), 1.01-1.20 (m, 2H), 1.22-1.34 (m, 1H), 1.25 (s, 9H), 1.37 (s, 9H), 1.70-1.86 (m, 4H), 2.81-2.90 (m, 2H), 3.04-3.22 (m, 1H), 6.68 (d, 1H, J = 8.1 Hz), 6.83 (t, 1H, J = 6.0 Hz).

[0080]

The following compounds wherein R^1 is ethyl or tert-butyl were obtained in Step 6 by using the above compound.

A compound wherein R^1 is ethyl.

[Formula 62]

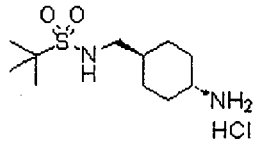


$C_9H_{21}ClN_2O_2S$
Mol. Wt. : 256.79

H-NMR (DMSO-d6) δppm: 0.84-1.02 (m, 2H), 1.18 (t, 3H, J = 7.5 Hz), 1.20-1.40 (m, 3H), 1.74-1.82 (m, 2H), 1.90-2.00 (m, 2H), 2.72-2.80 (m, 2H), 2.83-2.96 (m, 1H), 2.97 (q, 2H, J = 7.5 Hz), 7.04 (t, 1H, J = 6.0 Hz), 8.03 (s, 3H).

A compound wherein R^1 is tert-butyl.

[Formula 63]



$C_{11}H_{25}ClN_2O_2S$
Mol. Wt.: 284.85

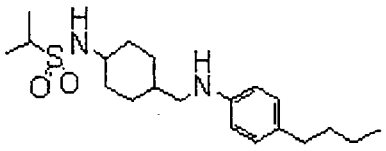
H-NMR (DMSO-d6) δppm: 0.84-1.04 (m, 2H), 1.16-1.38 (m, 3H), 1.26 (s, 9H), 1.74-1.84 (m, 2H), 1.92-2.02 (m, 2H), 2.82-2.98 (m, 3H), 6.90 (d, 1H, J = 6.0 Hz), 8.01 (s, 3H).

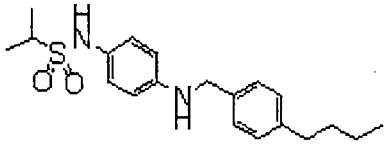
[0081]

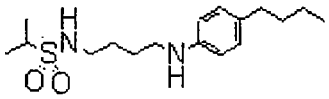
The following compounds synthesized in similar methods also include this invention.

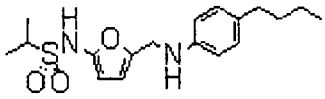
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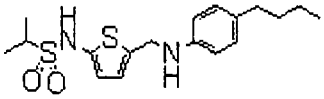
[Formula 64]

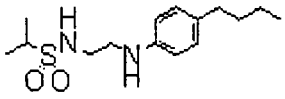
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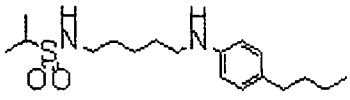
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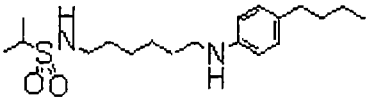
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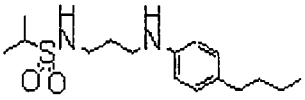
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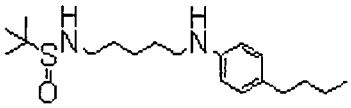
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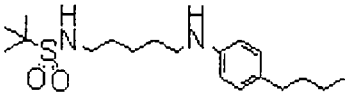
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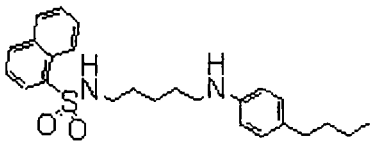
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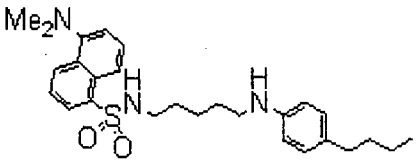
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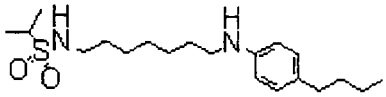
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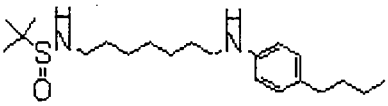
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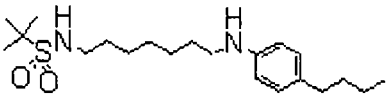
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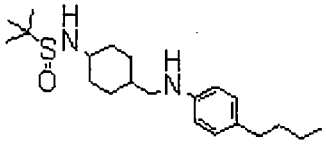
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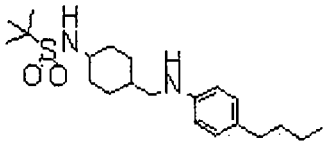
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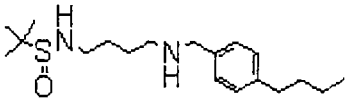
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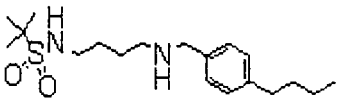
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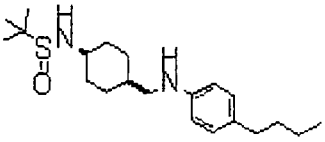
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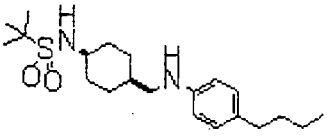
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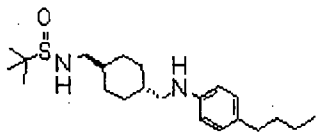
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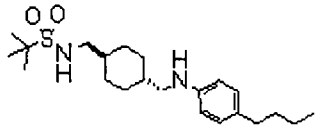
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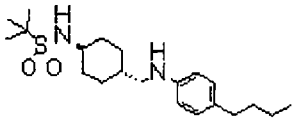
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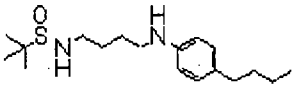
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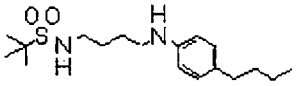
[Formula 65]

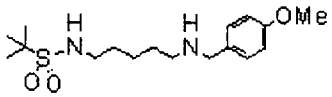
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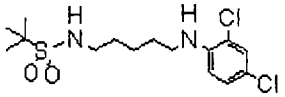
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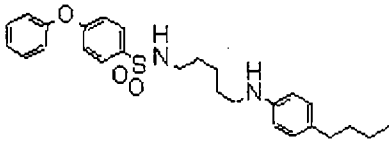
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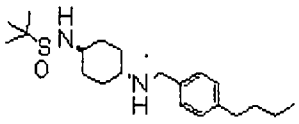
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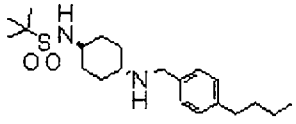
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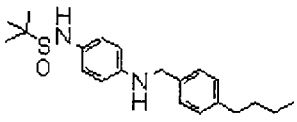
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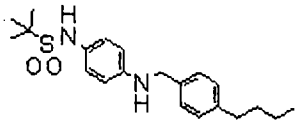
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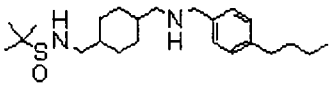
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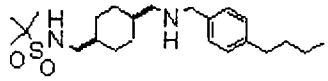
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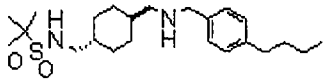
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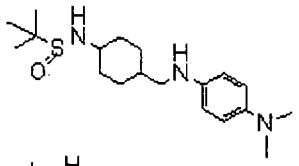
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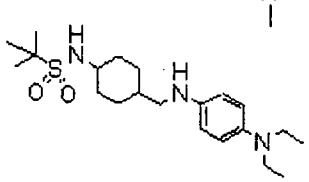
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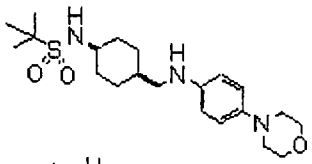
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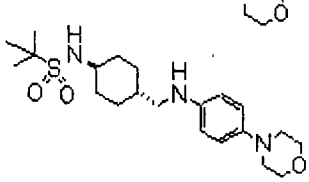
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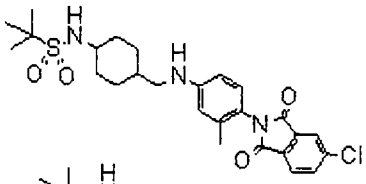
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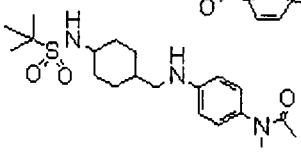
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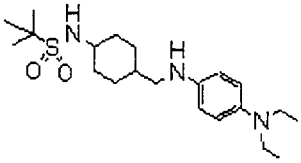
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I-40 

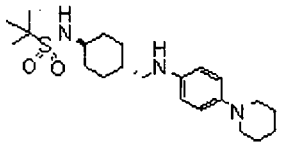
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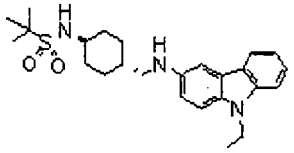
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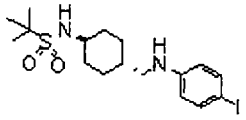
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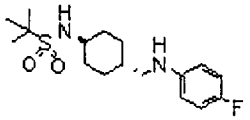
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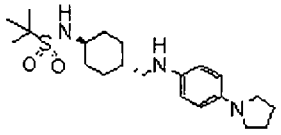
[Formula 66]

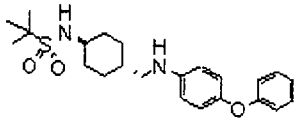
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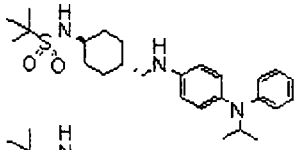
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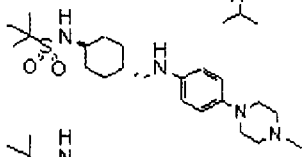
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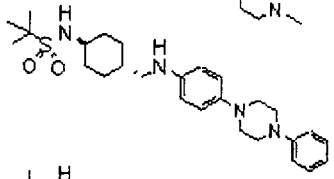
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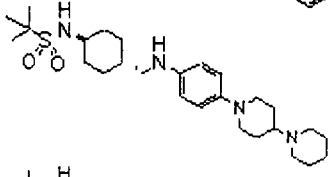
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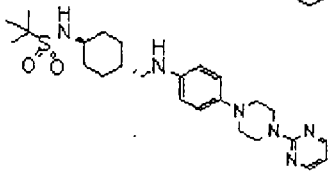
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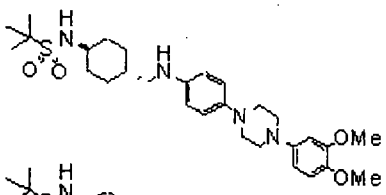
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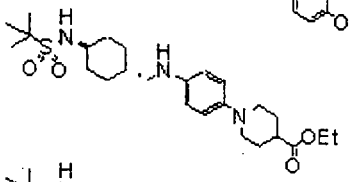
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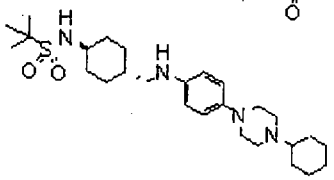
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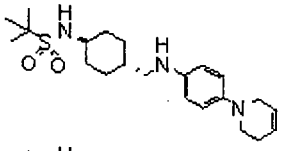
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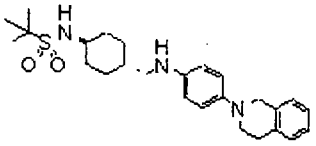
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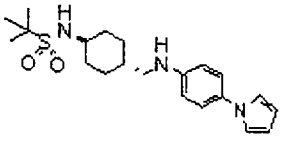
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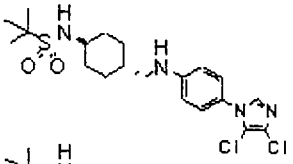
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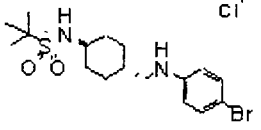
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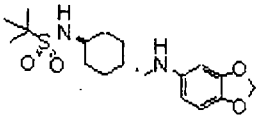
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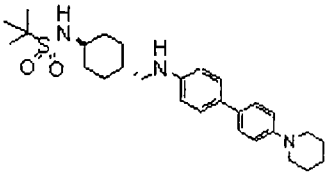
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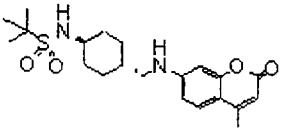
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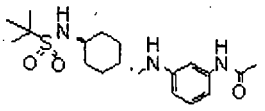
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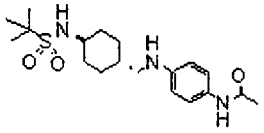
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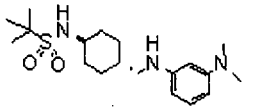
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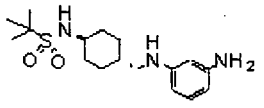
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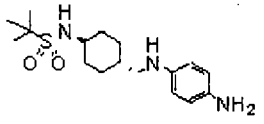
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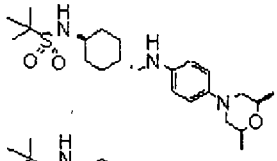
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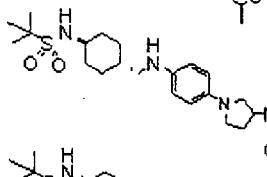
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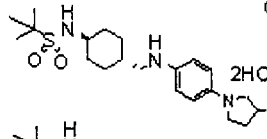
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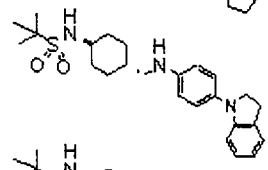
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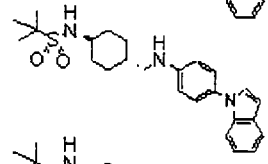
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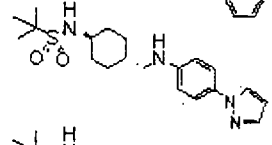
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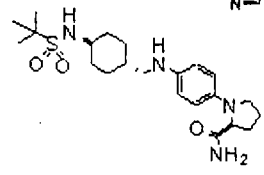
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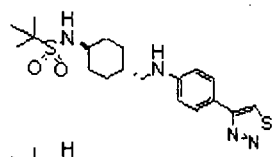
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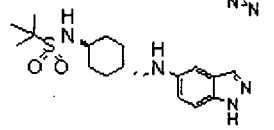
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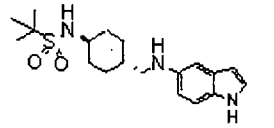
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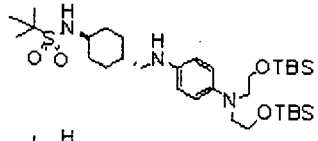
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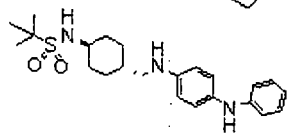
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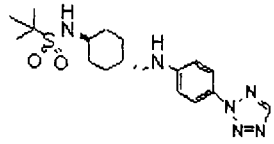
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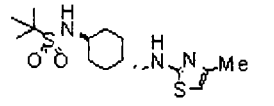
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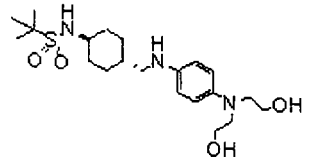
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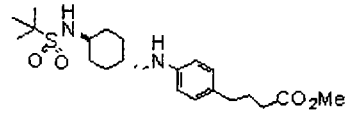
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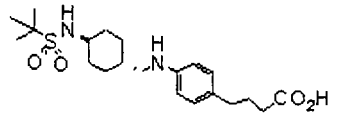
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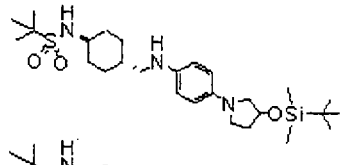
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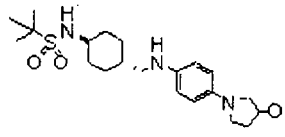
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I-86 

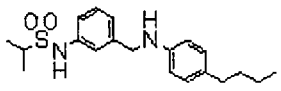
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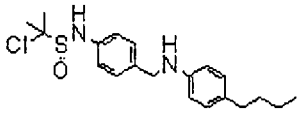
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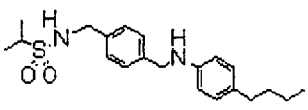
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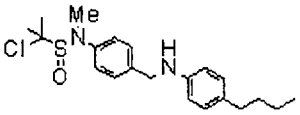
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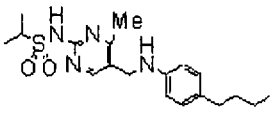
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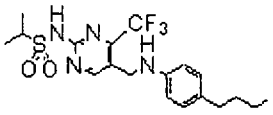
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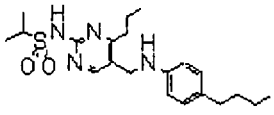
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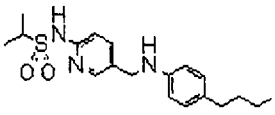
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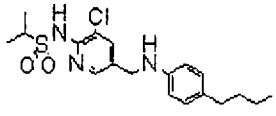
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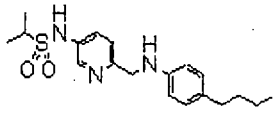
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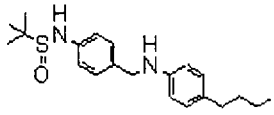
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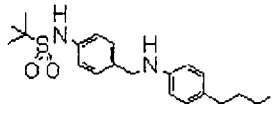
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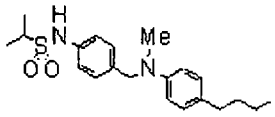
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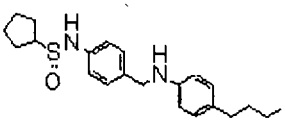
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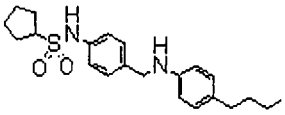
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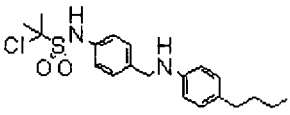
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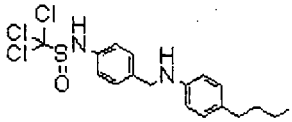
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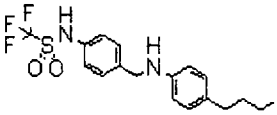
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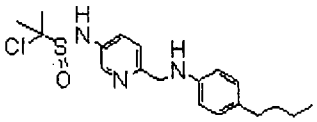
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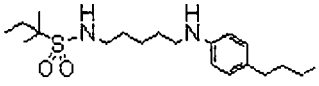
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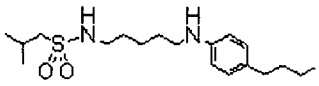
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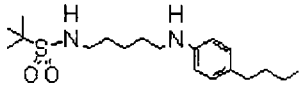
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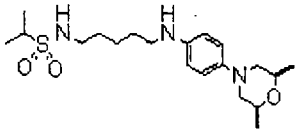
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I-109 

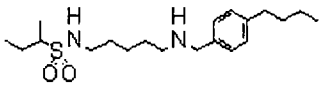
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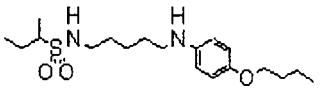
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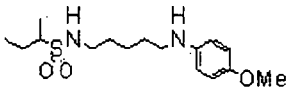
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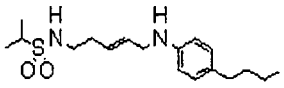
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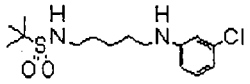
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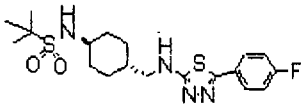
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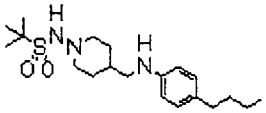
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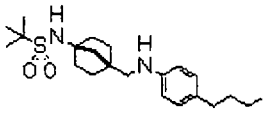
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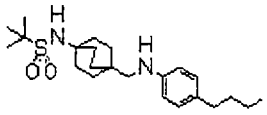
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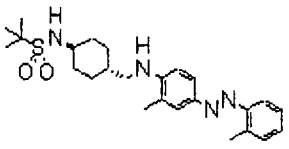
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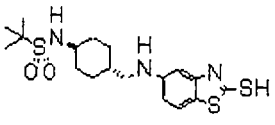
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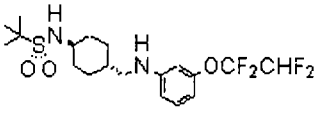
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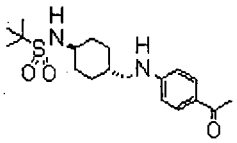
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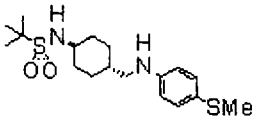
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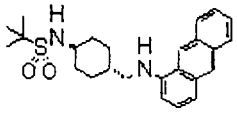
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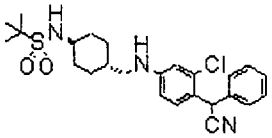
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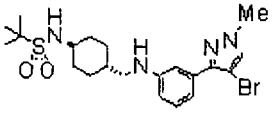
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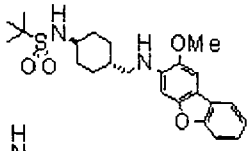
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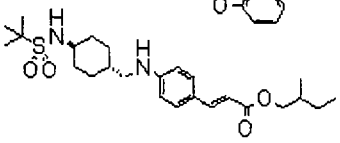
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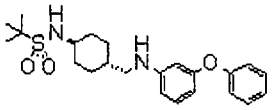
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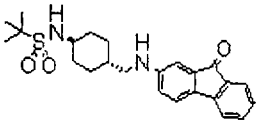
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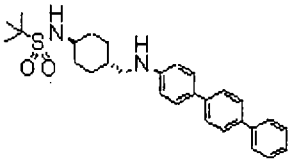
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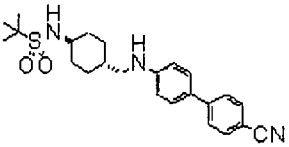
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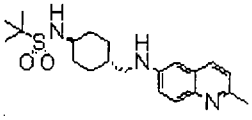
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I-134 

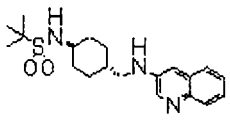
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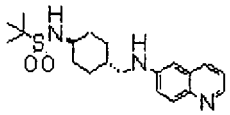
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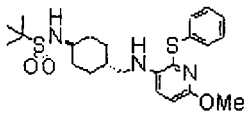
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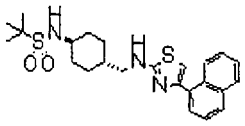
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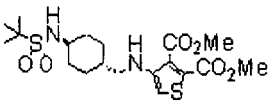
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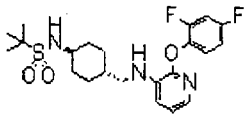
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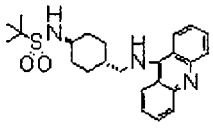
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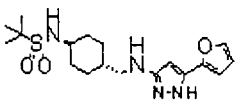
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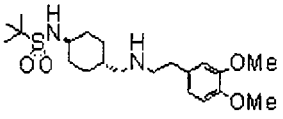
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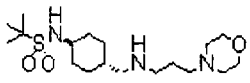
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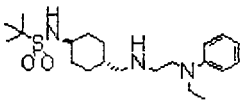
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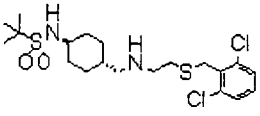
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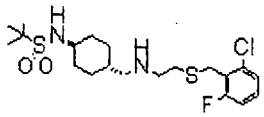
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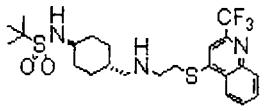
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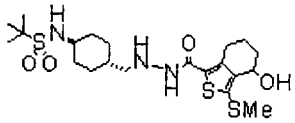
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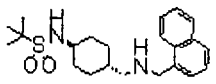
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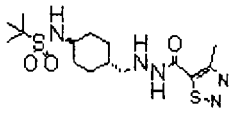
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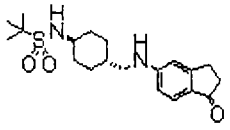
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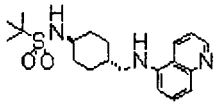
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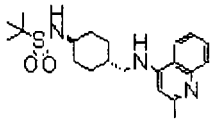
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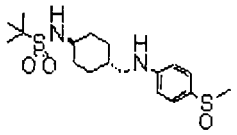
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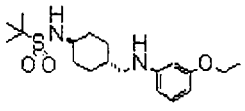
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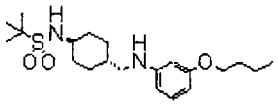
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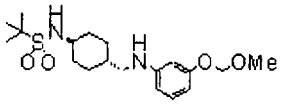
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I-158 

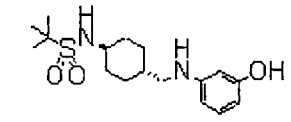
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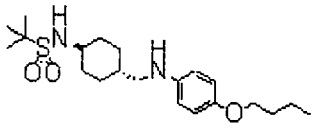
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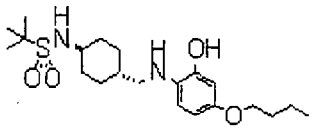
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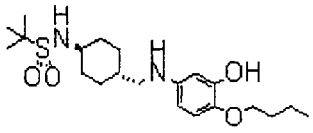
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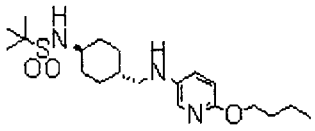
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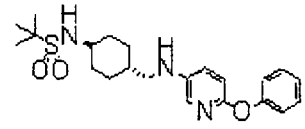
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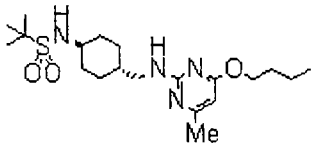
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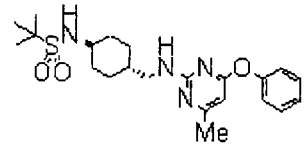
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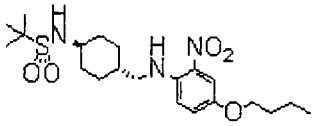
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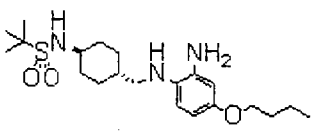
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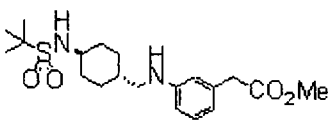
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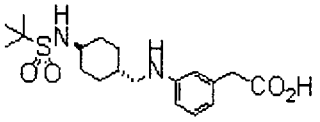
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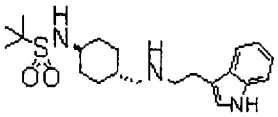
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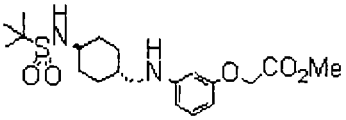
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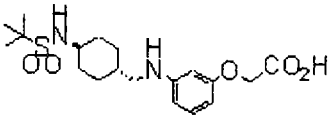
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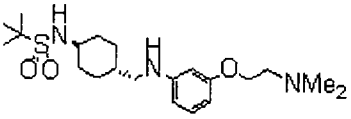
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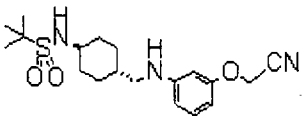
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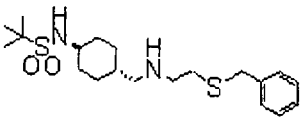
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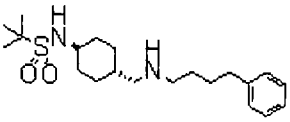
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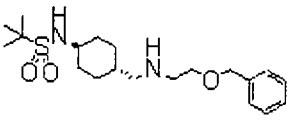
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I-178 

I-179 

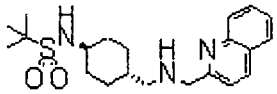
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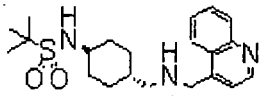
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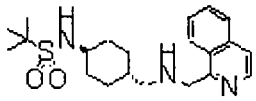
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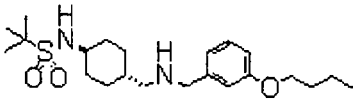
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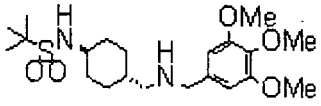
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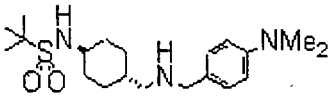
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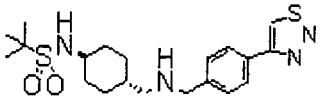
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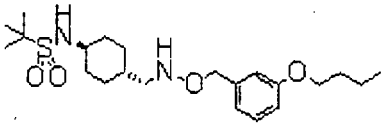
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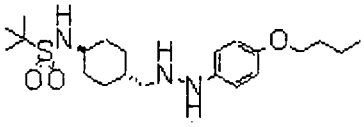
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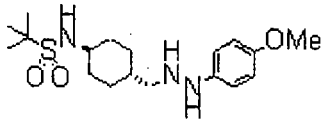
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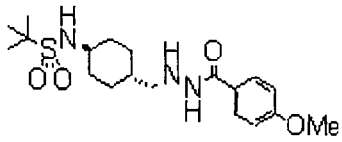
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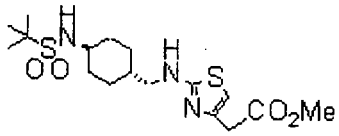
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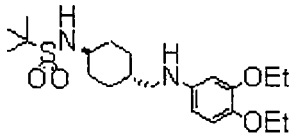
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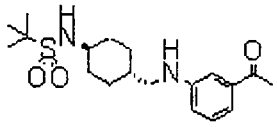
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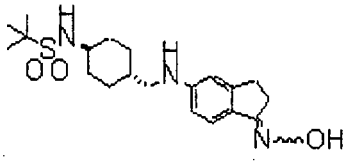
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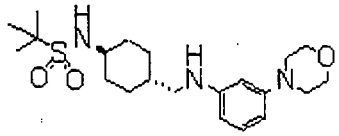
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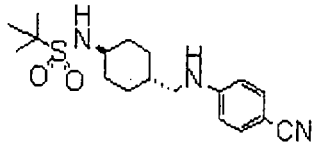
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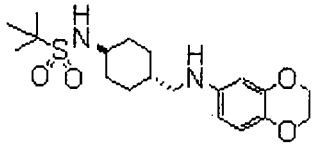
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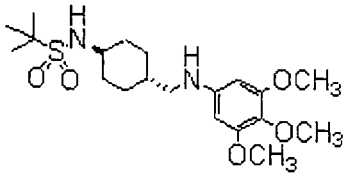
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I-198 

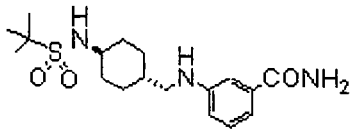
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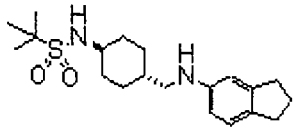
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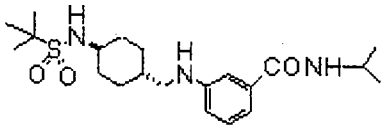
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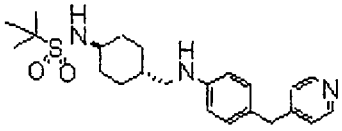
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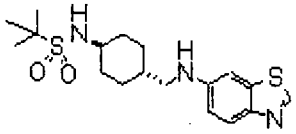
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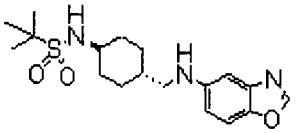
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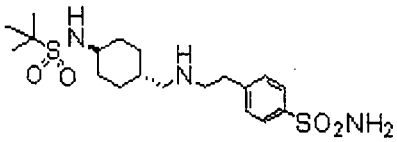
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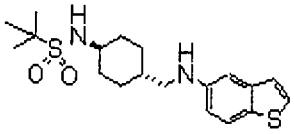
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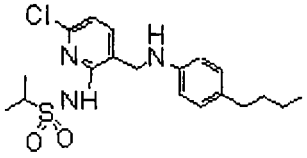
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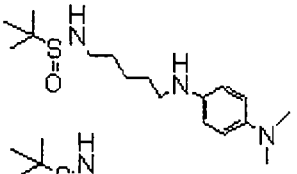
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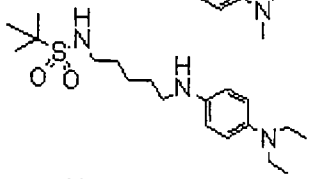
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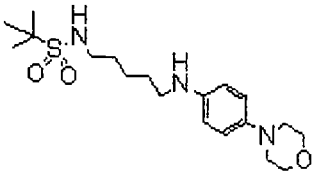
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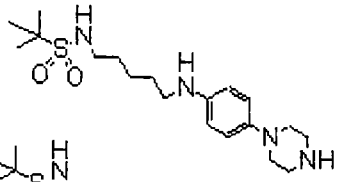
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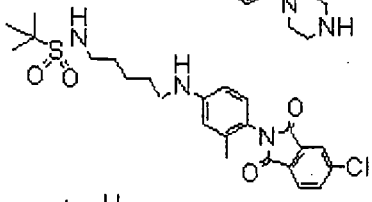
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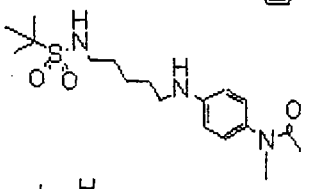
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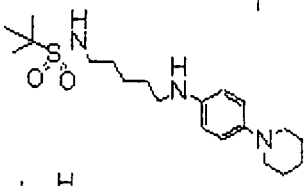
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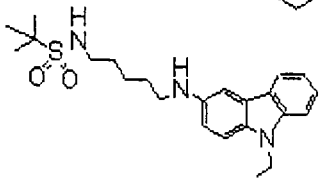
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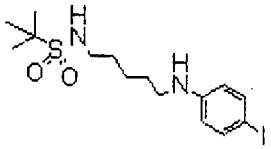
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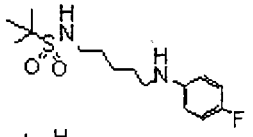
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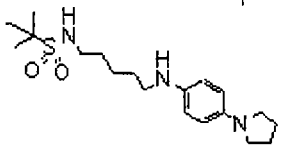
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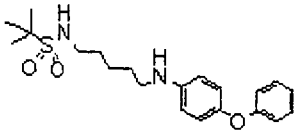
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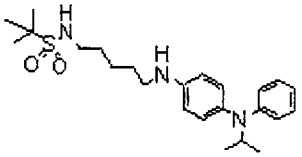
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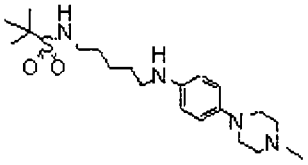
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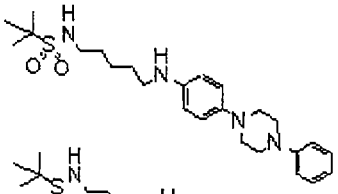
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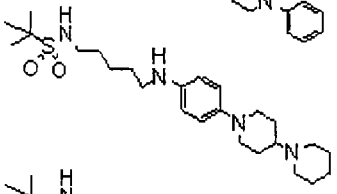
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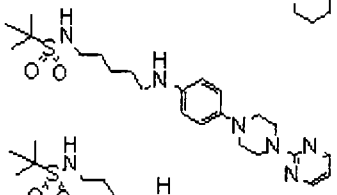
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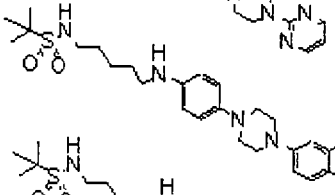
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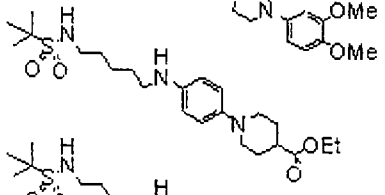
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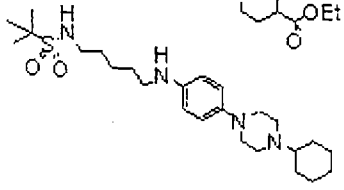
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I-233 

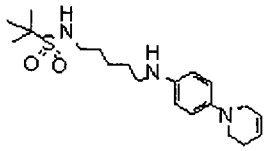
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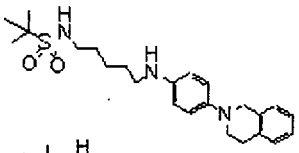
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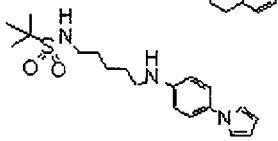
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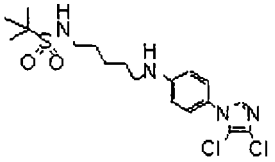
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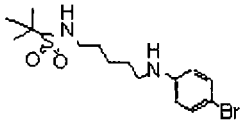
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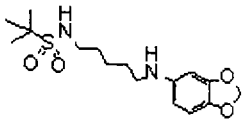
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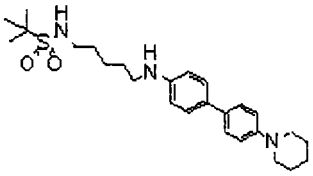
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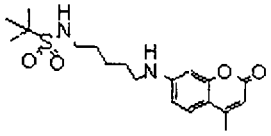
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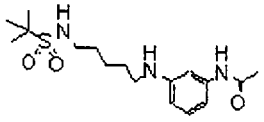
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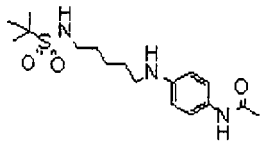
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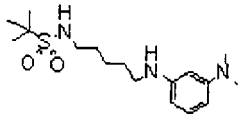
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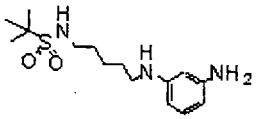
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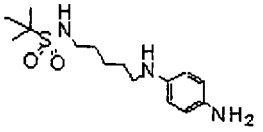
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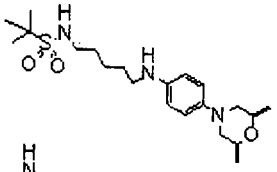
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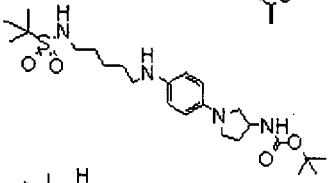
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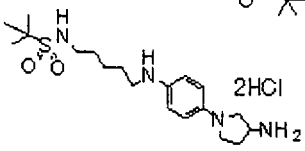
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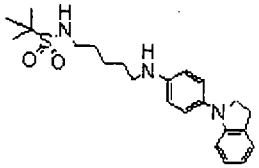
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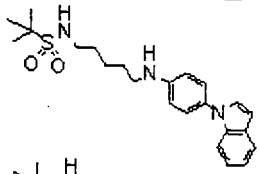
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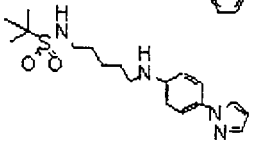
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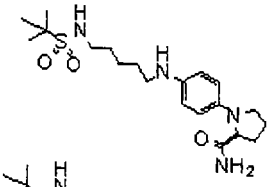
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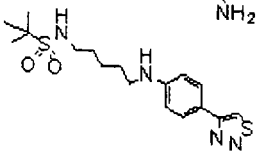
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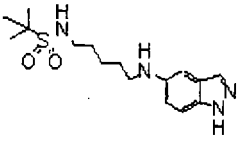
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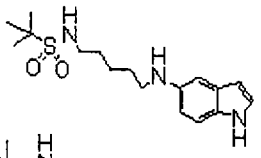
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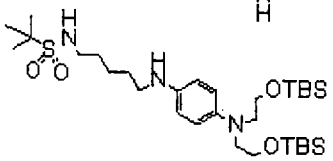
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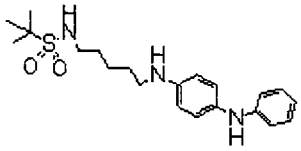
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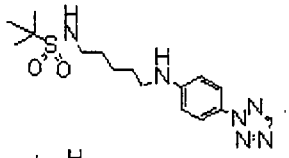
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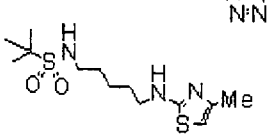
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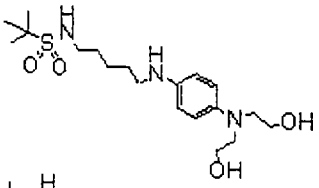
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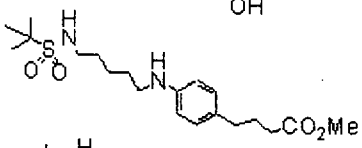
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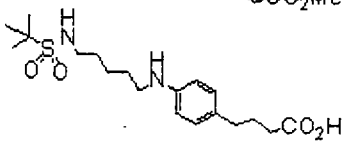
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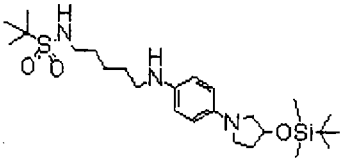
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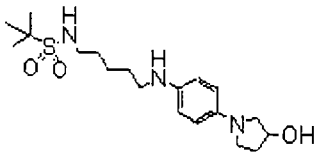
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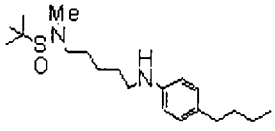
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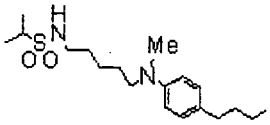
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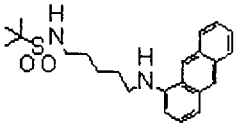
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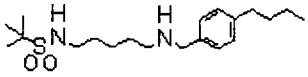
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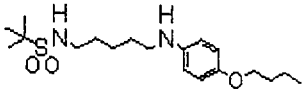
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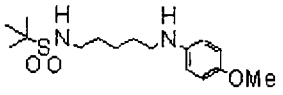
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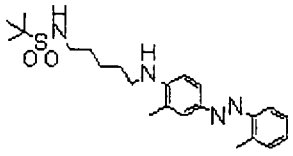
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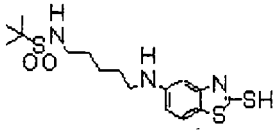
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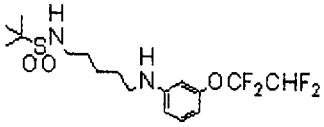
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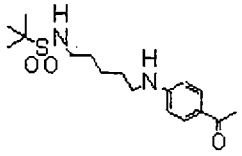
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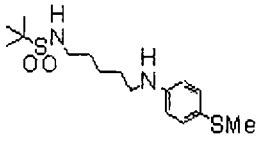
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I-276 

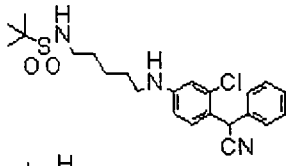
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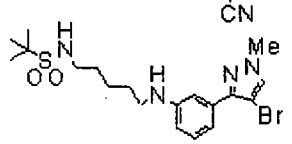
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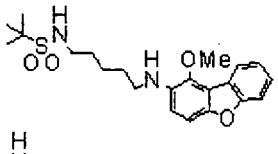
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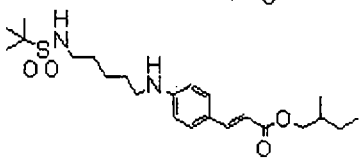
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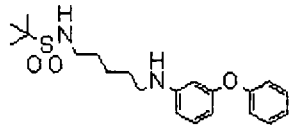
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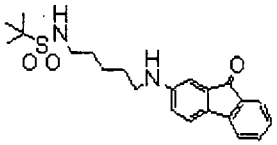
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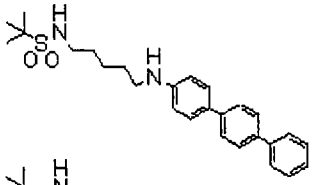
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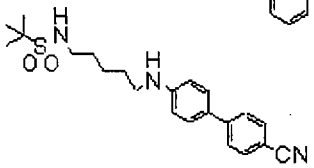
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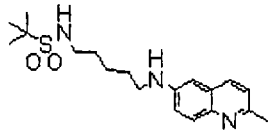
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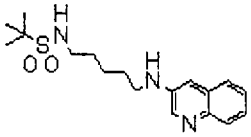
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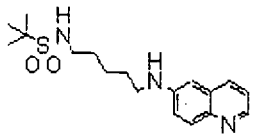
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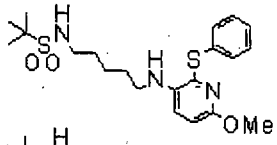
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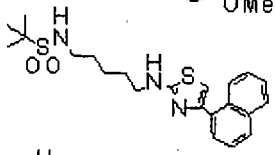
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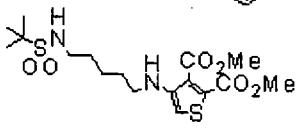
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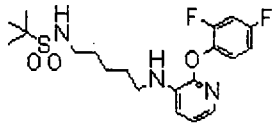
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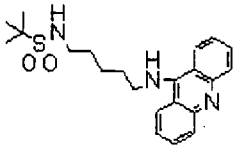
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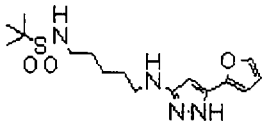
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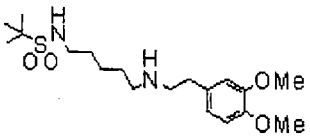
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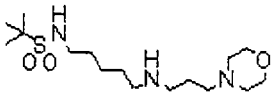
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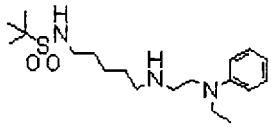
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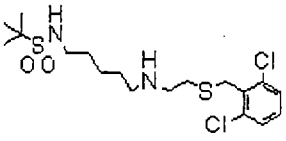
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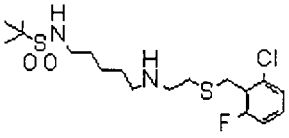
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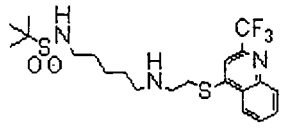
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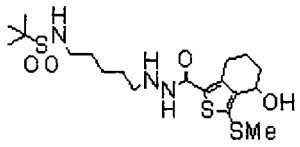
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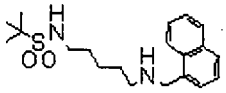
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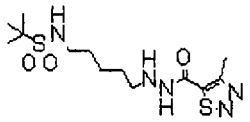
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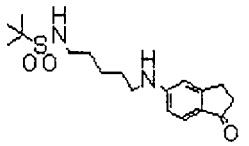
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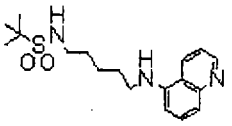
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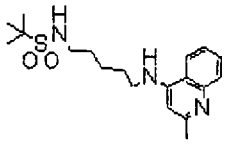
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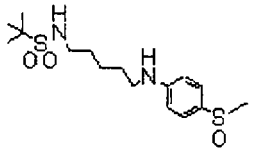
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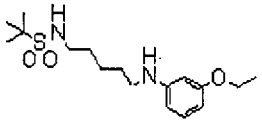
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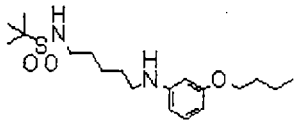
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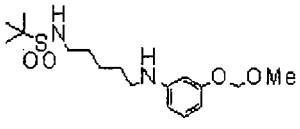
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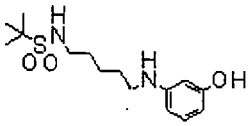
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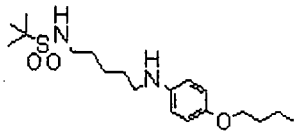
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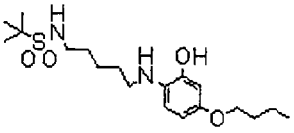
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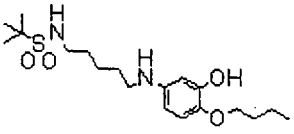
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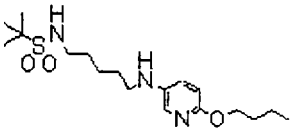
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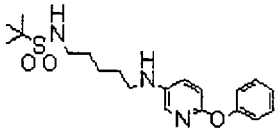
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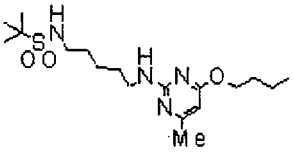
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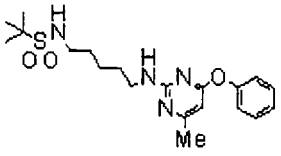
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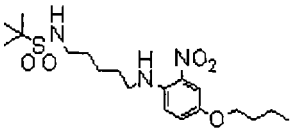
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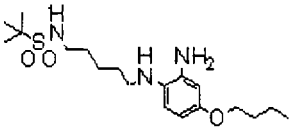
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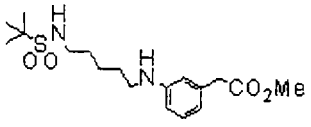
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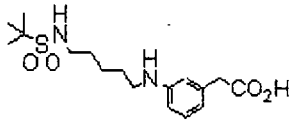
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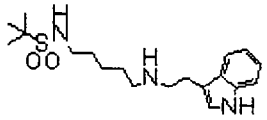
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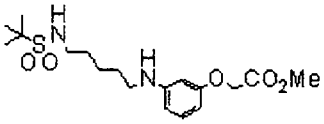
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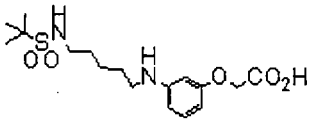
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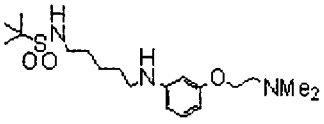
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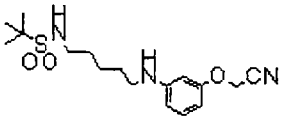
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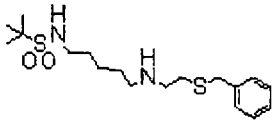
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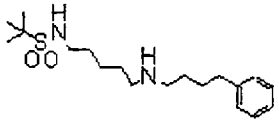
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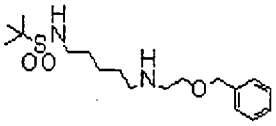
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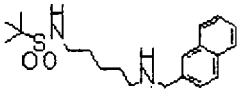
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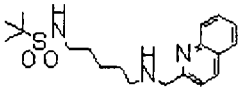
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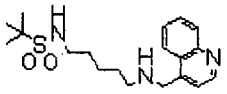
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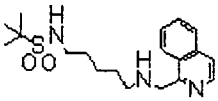
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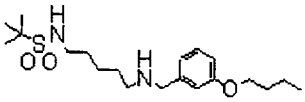
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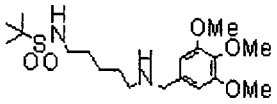
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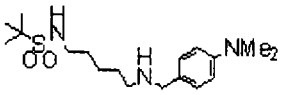
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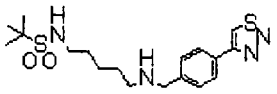
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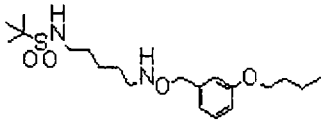
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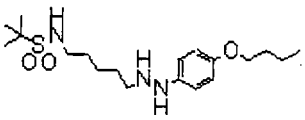
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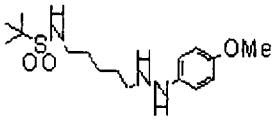
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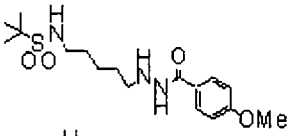
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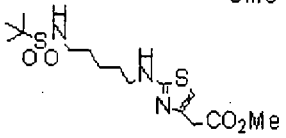
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I-343 

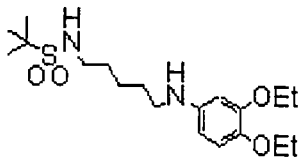
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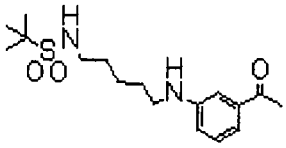
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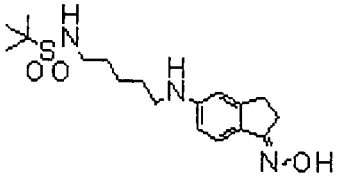
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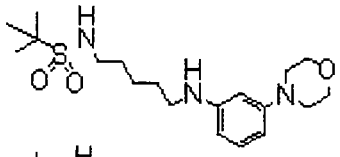
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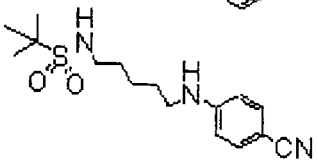
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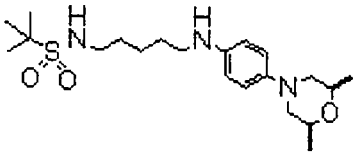
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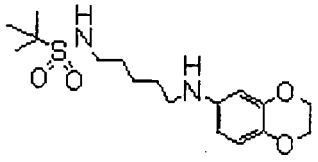
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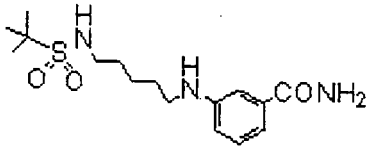
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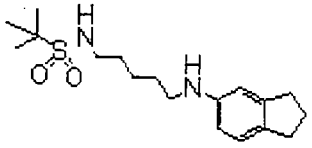
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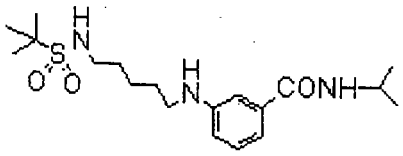
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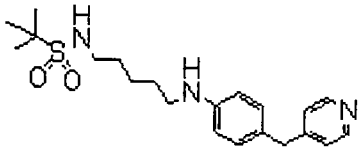
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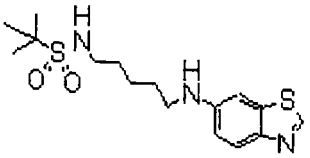
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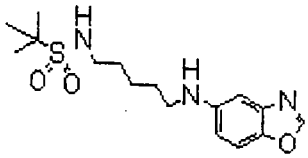
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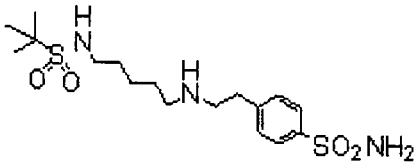
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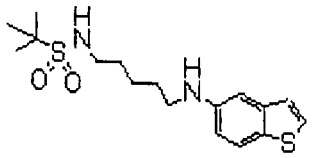
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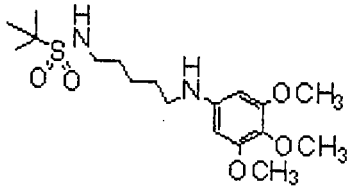
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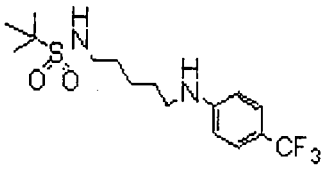
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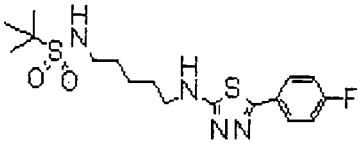
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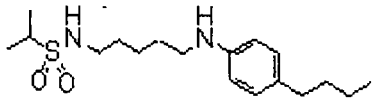
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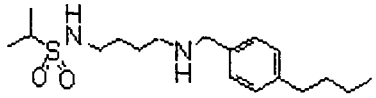
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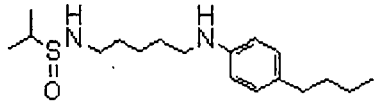
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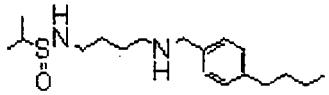
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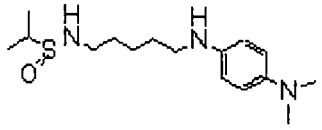
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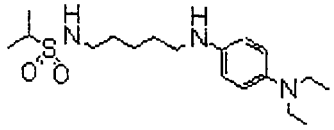
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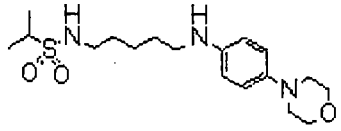
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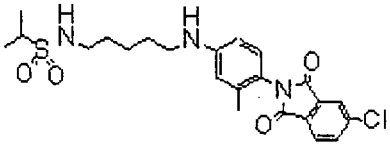
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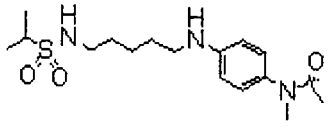
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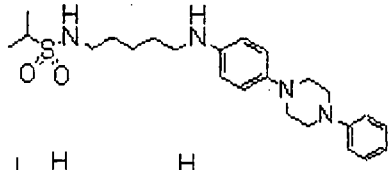
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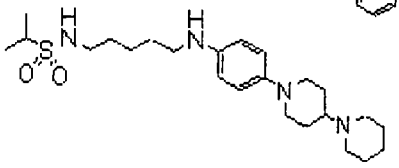
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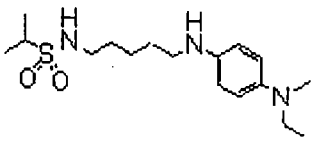
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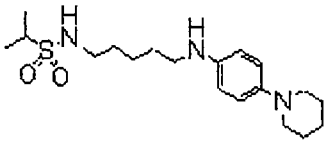
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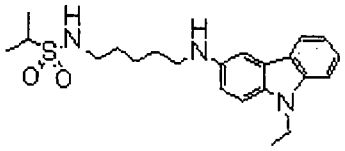
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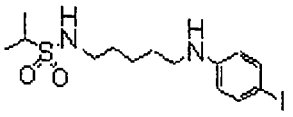
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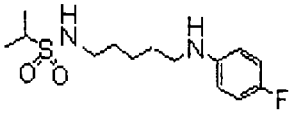
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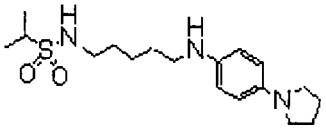
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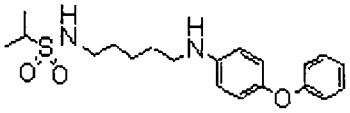
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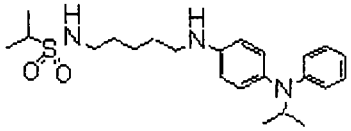
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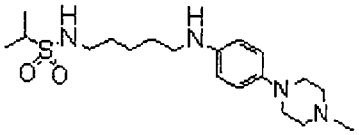
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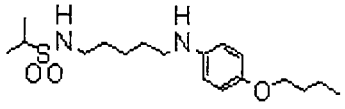
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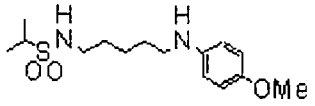
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I-383 

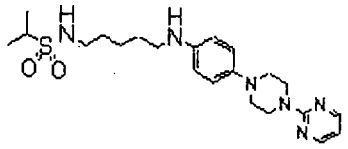
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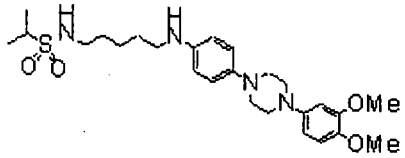
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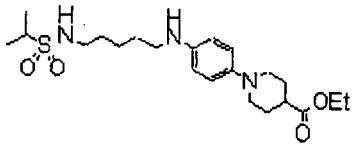
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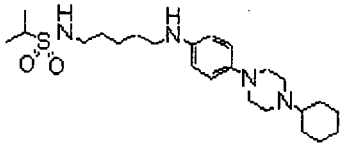
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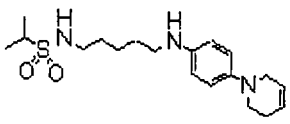
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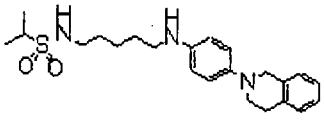
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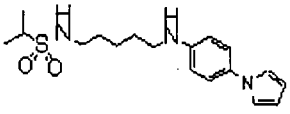
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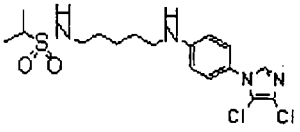
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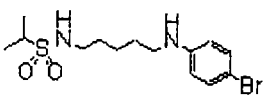
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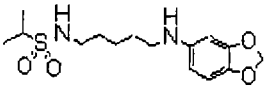
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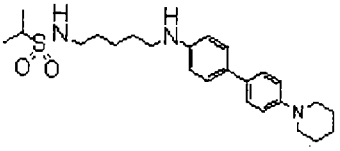
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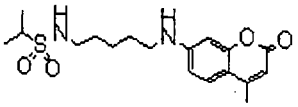
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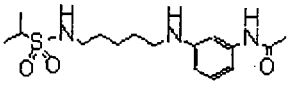
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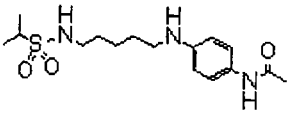
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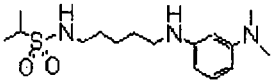
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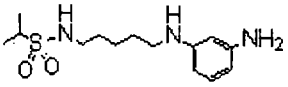
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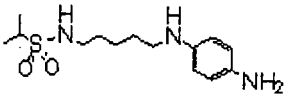
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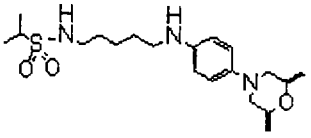
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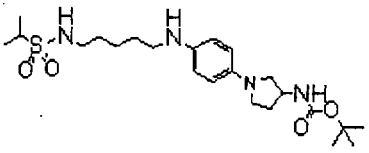
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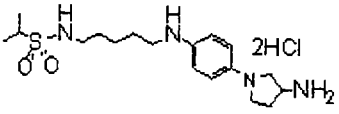
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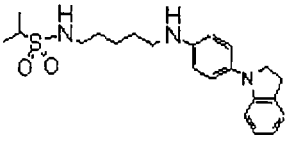
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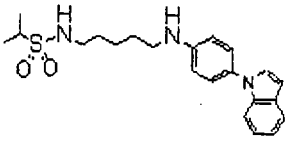
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I-405 

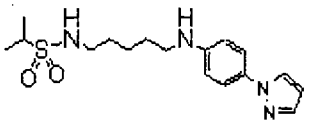
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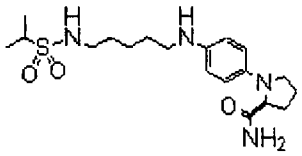
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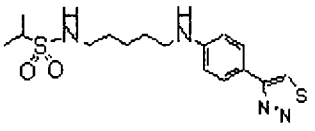
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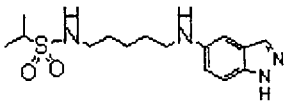
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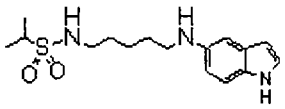
[Formula 83]

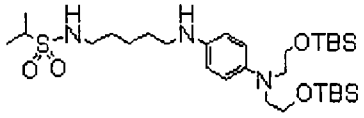
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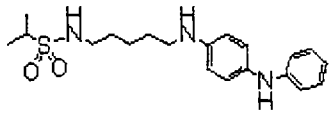
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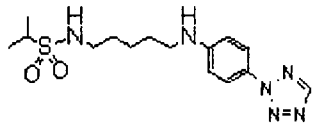
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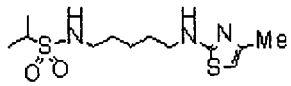
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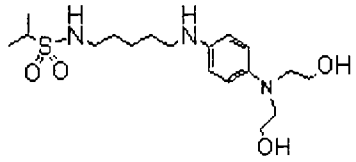
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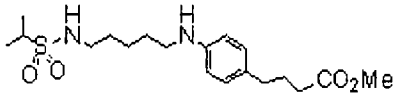
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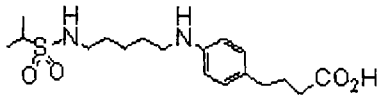
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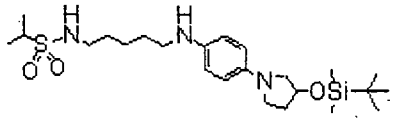
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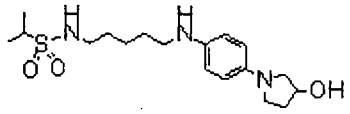
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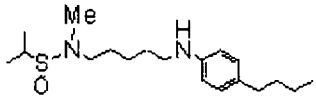
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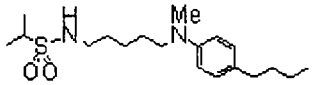
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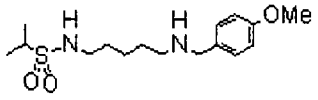
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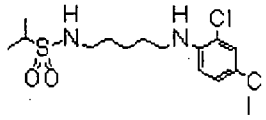
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I-423 

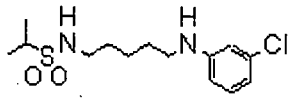
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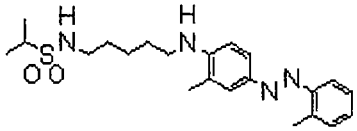
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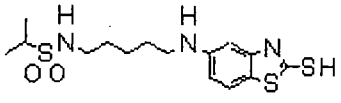
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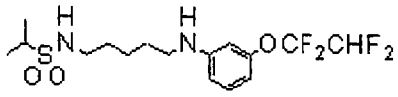
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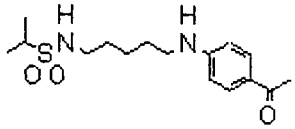
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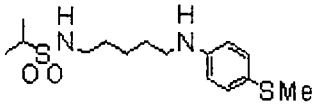
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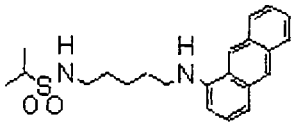
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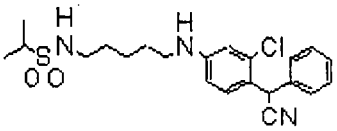
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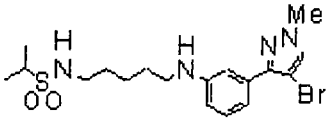
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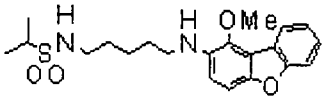
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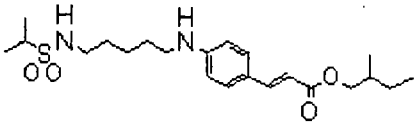
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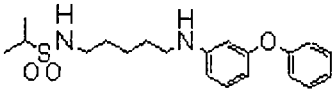
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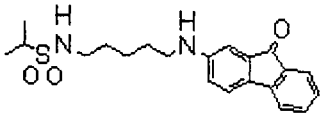
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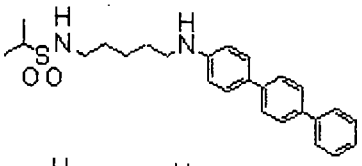
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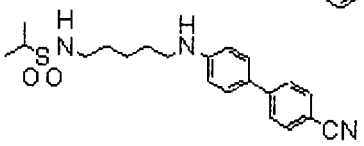
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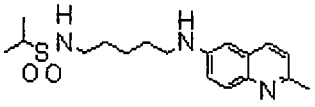
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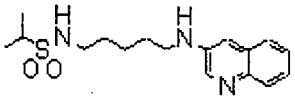
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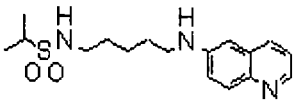
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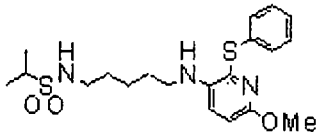
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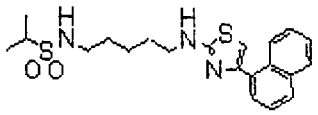
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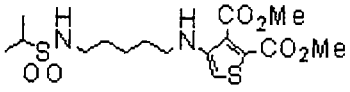
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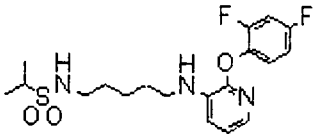
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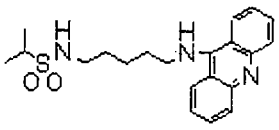
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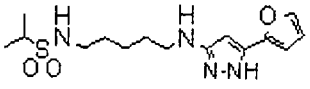
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I-451 

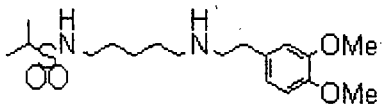
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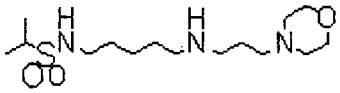
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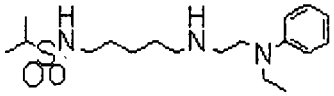
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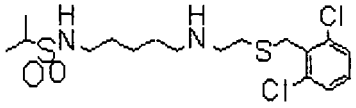
I-455 

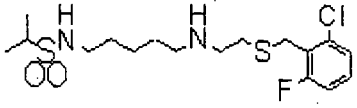
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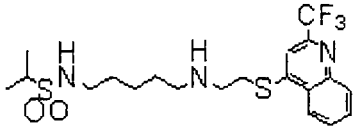
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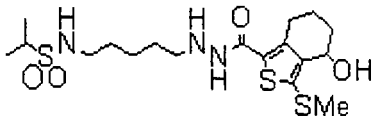
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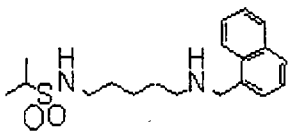
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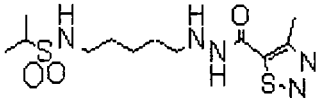
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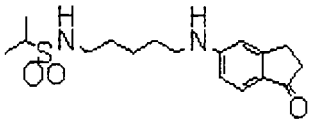
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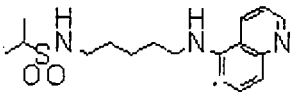
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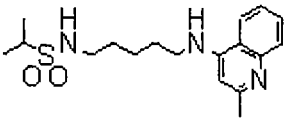
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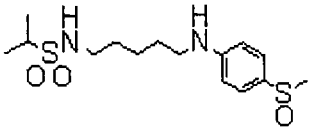
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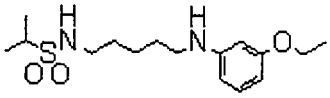
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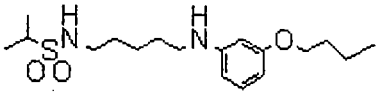
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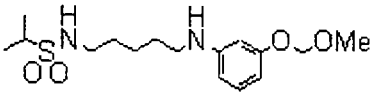
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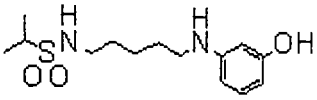
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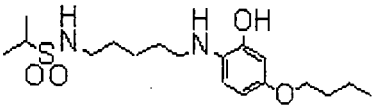
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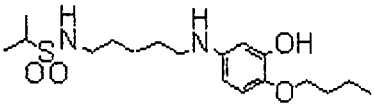
I-469 

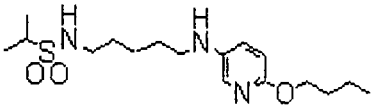
I-470 

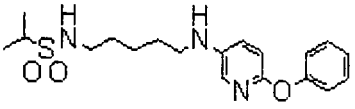
I-471 

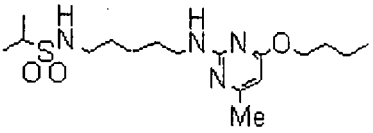
I-472 

I-473 

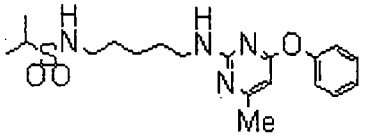
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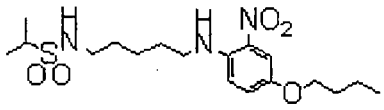
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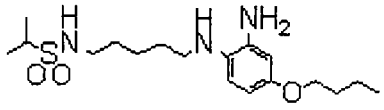
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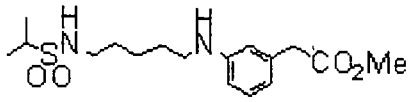
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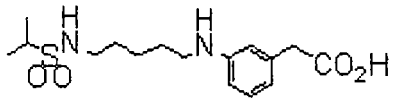
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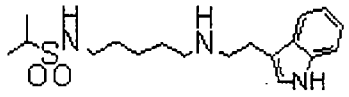
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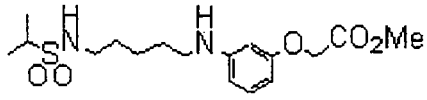
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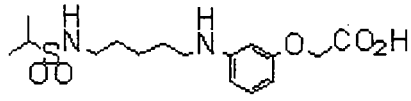
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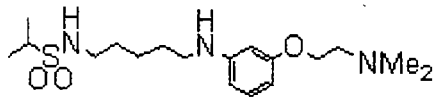
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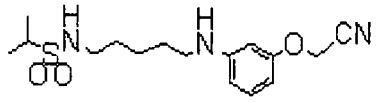
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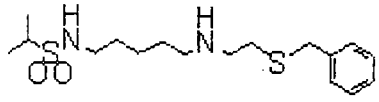
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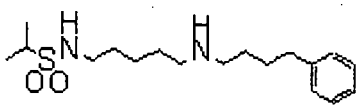
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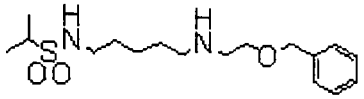
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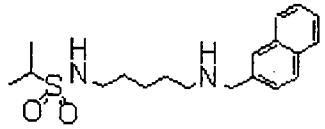
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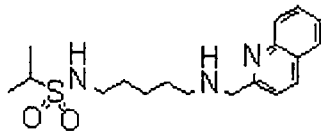
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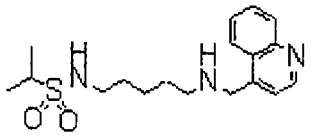
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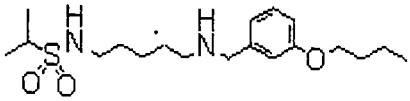
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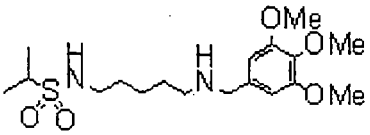
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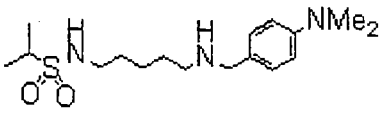
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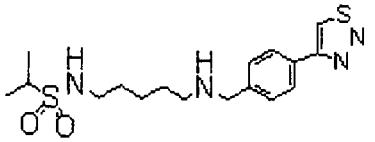
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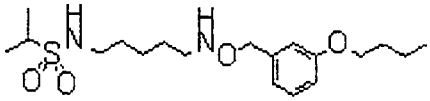
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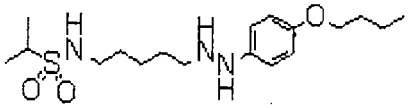
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I-495 

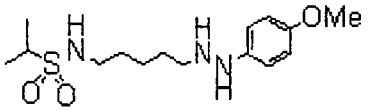
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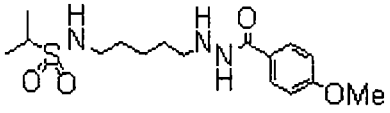
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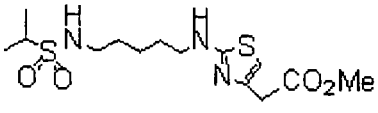
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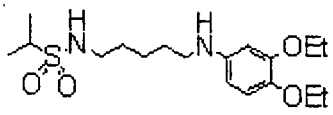
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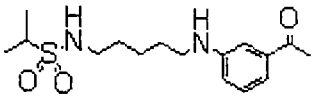
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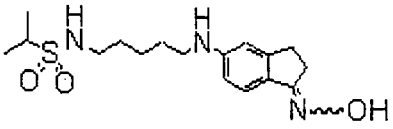
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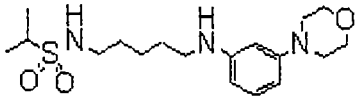
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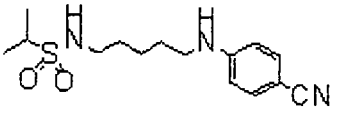
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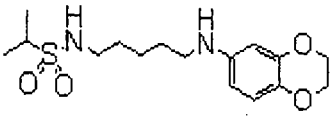
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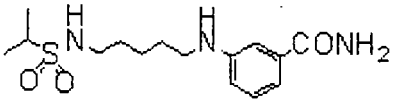
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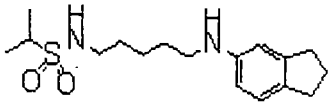
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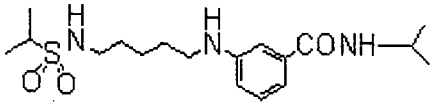
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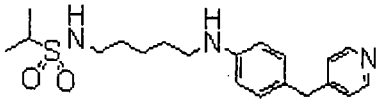
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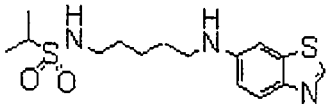
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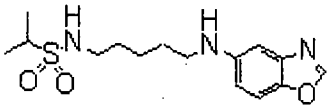
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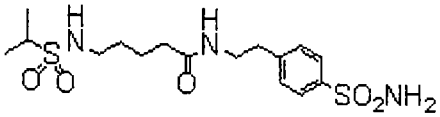
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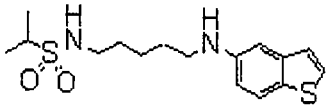
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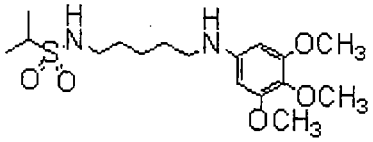
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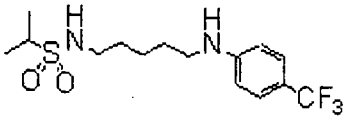
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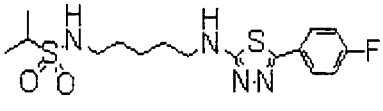
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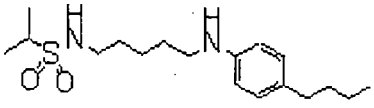
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I-516 

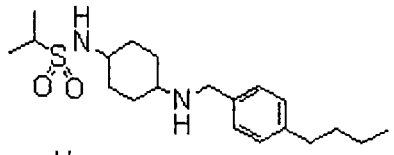
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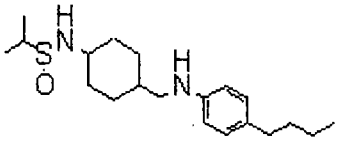
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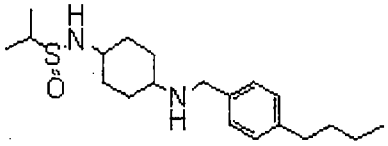
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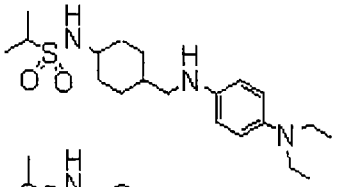
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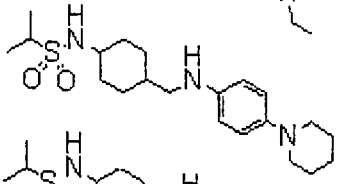
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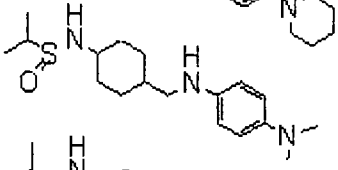
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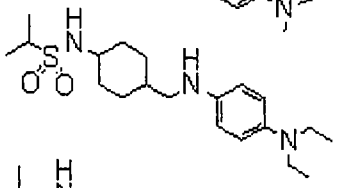
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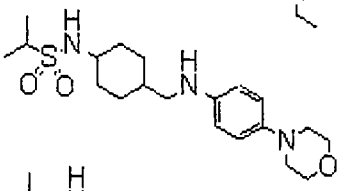
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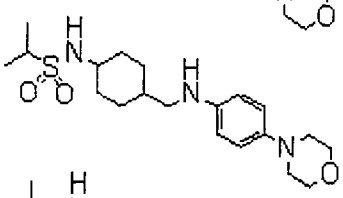
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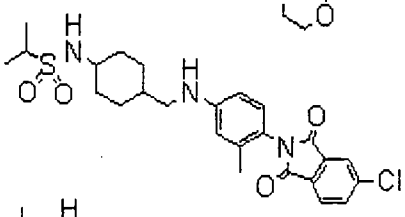
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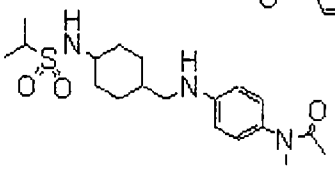
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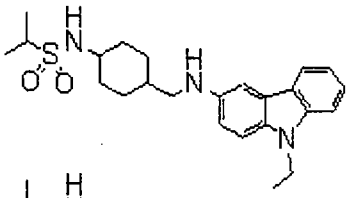
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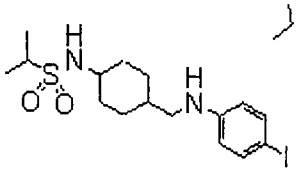
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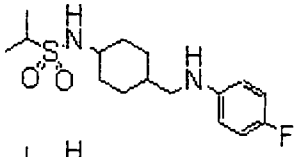
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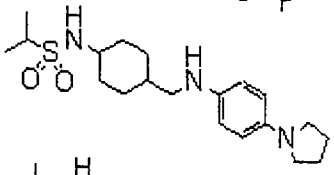
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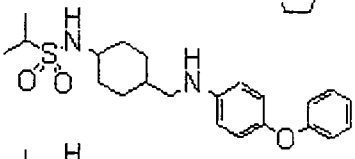
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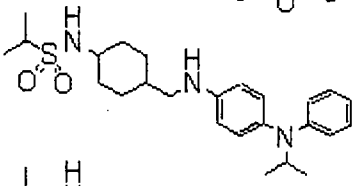
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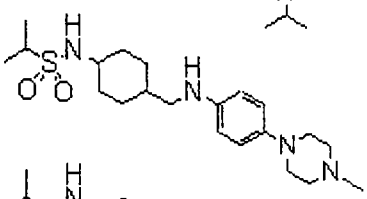
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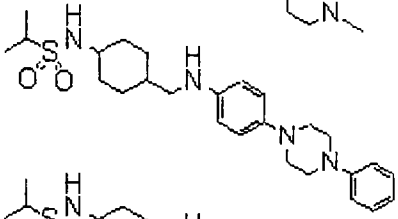
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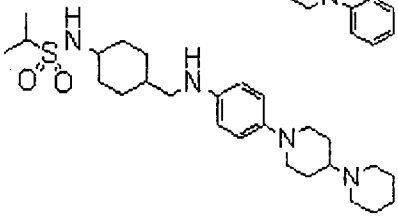
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I-536 

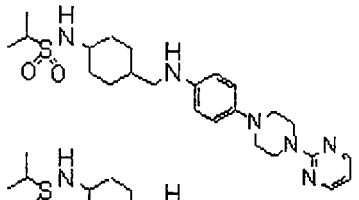
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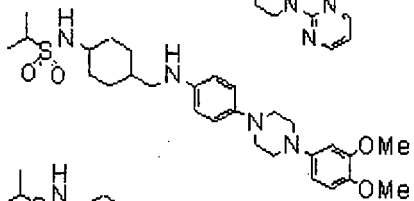
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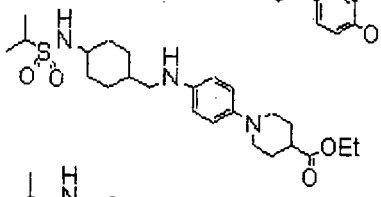
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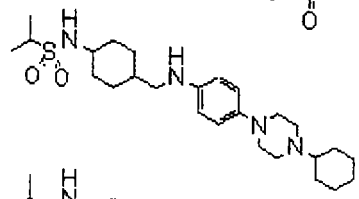
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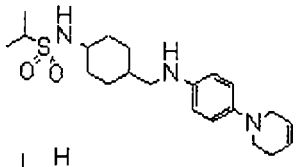
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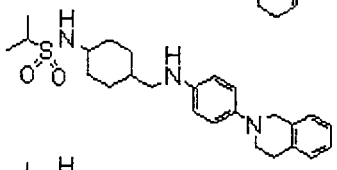
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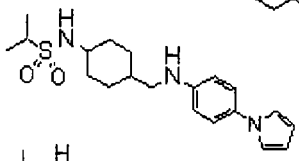
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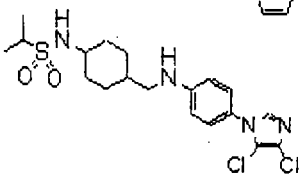
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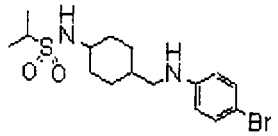
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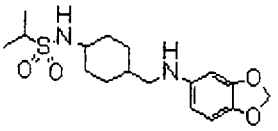
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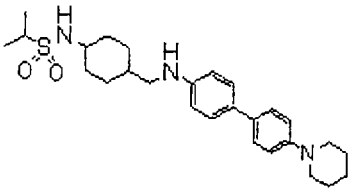
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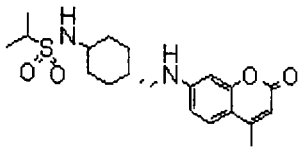
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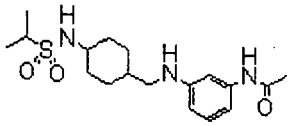
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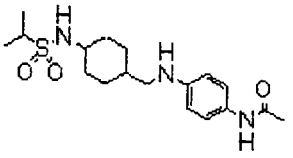
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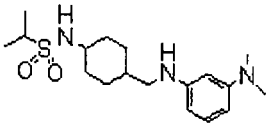
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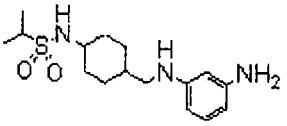
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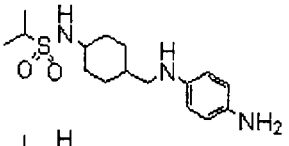
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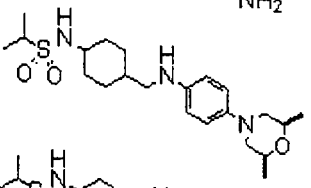
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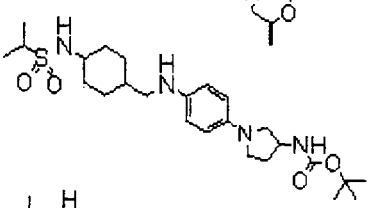
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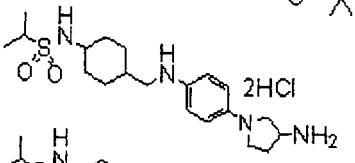
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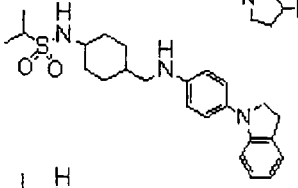
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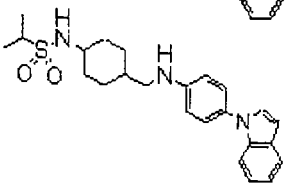
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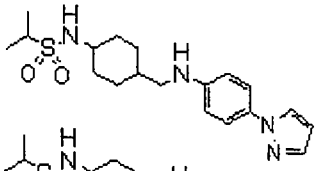
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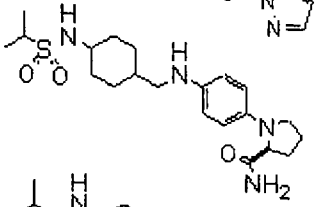
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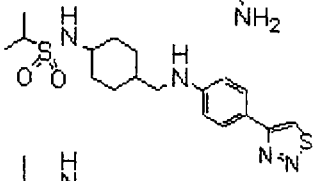
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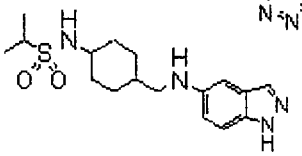
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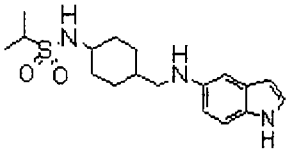
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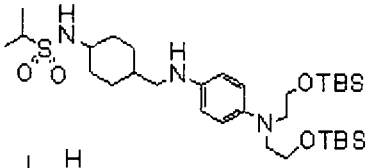
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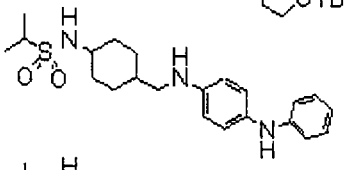
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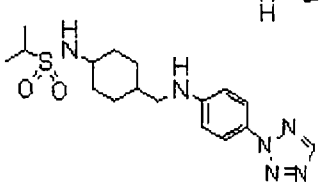
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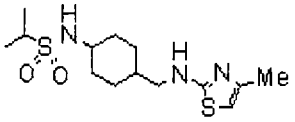
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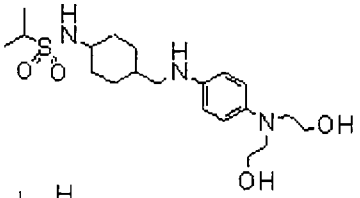
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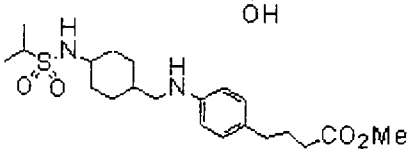
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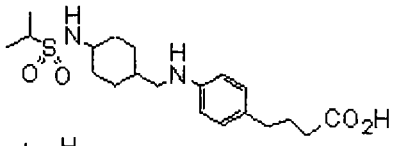
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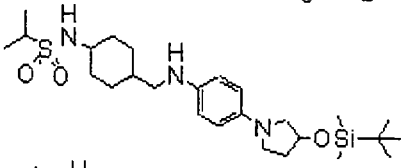
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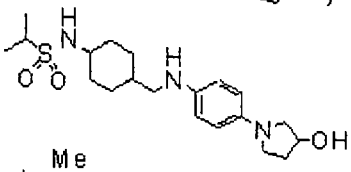
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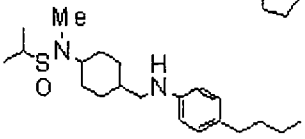
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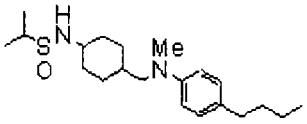
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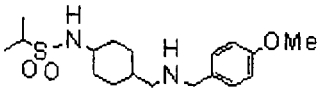
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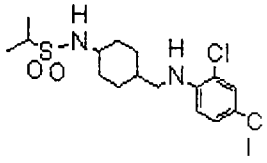
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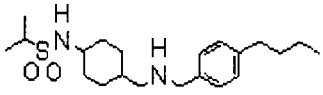
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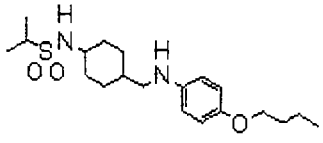
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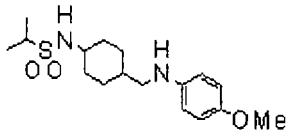
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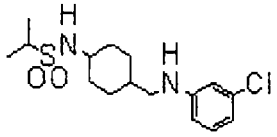
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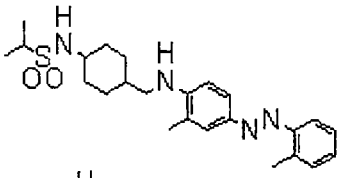
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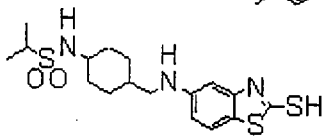
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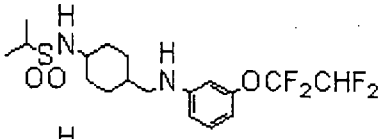
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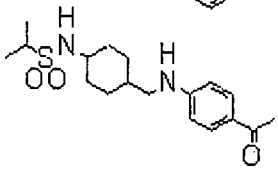
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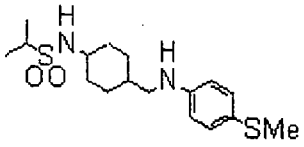
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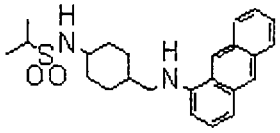
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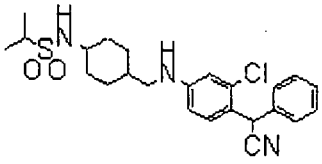
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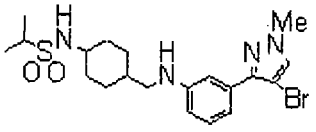
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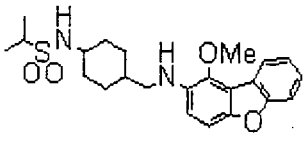
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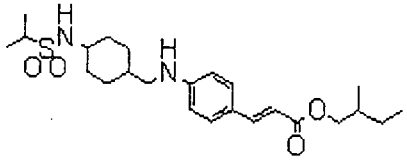
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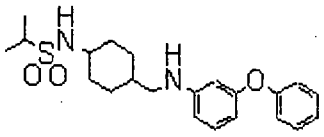
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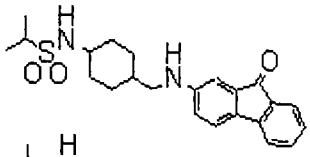
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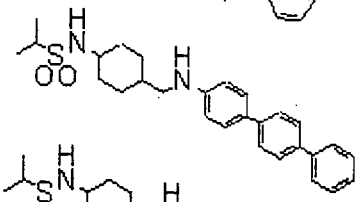
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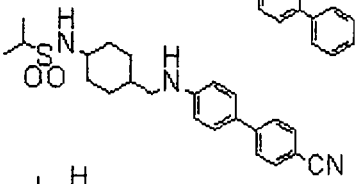
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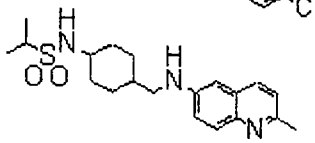
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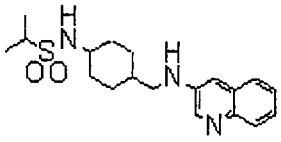
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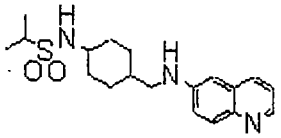
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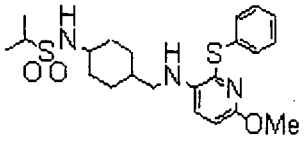
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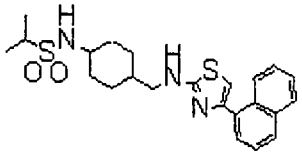
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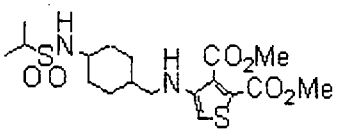
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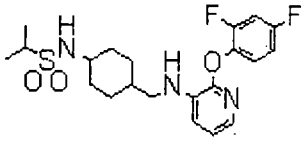
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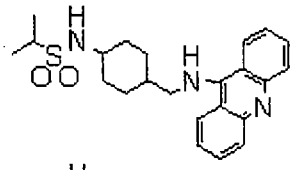
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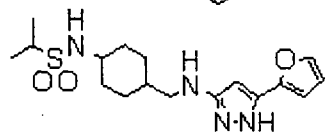
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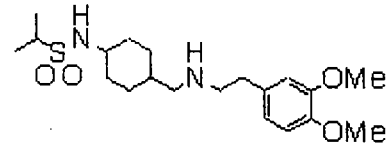
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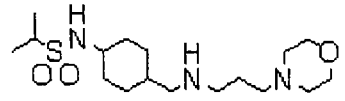
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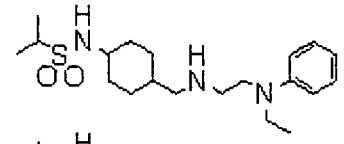
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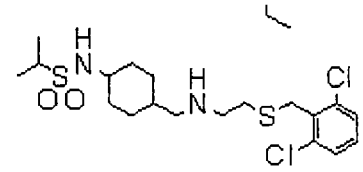
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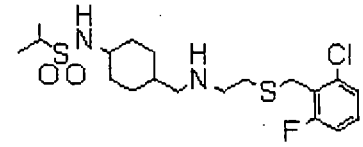
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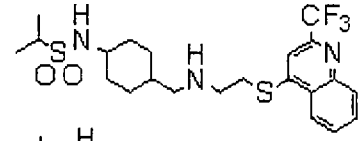
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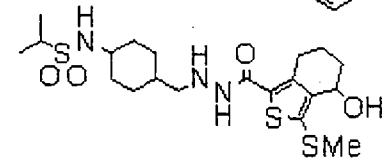
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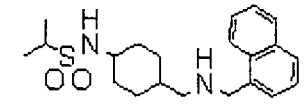
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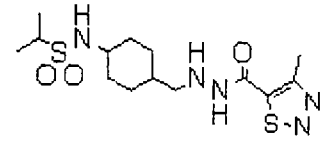
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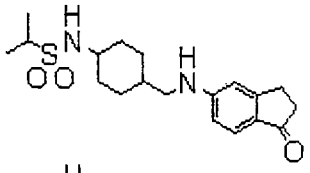
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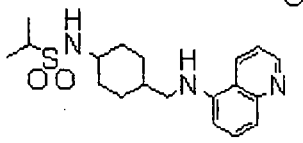
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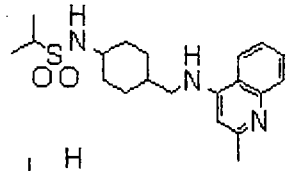
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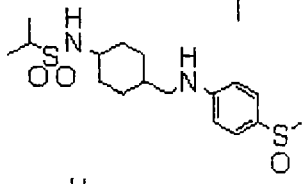
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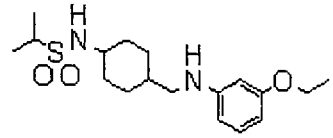
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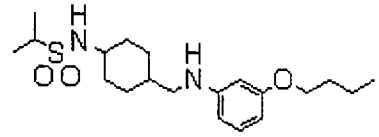
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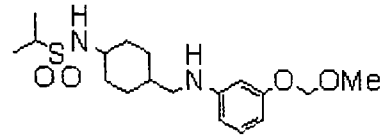
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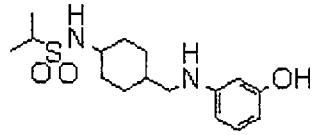
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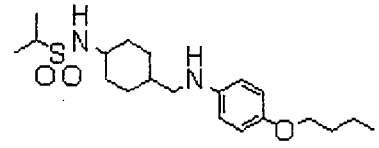
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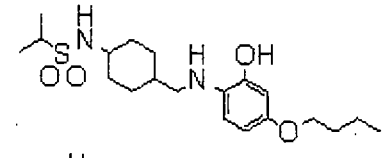
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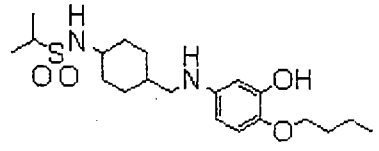
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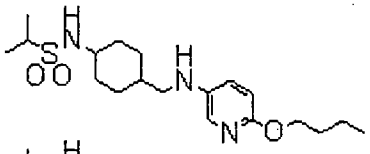
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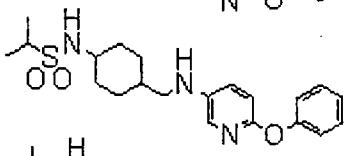
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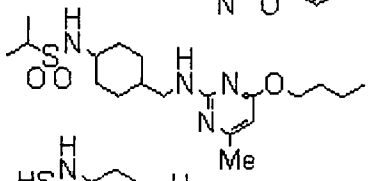
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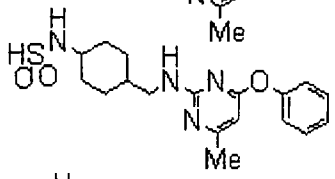
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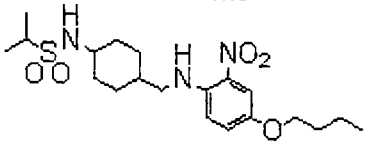
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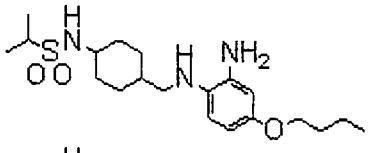
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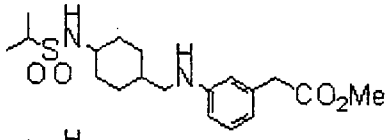
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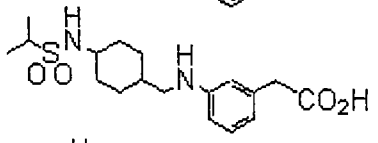
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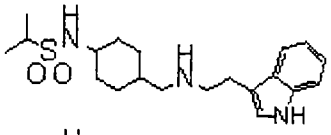
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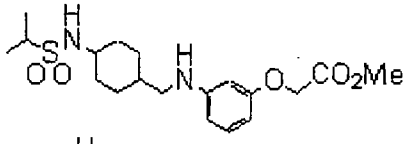
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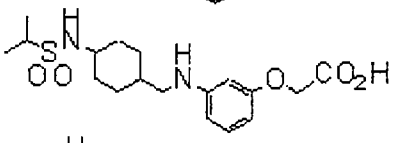
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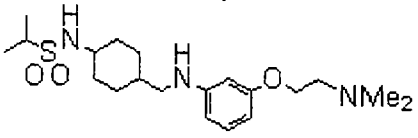
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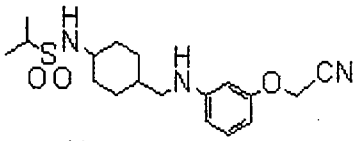
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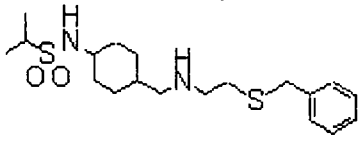
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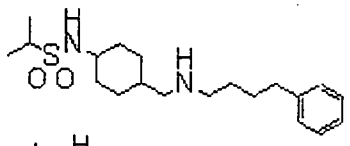
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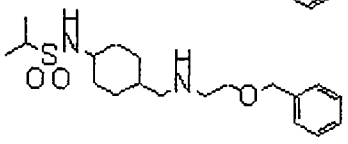
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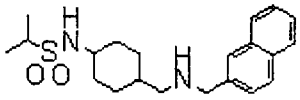
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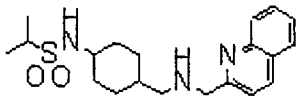
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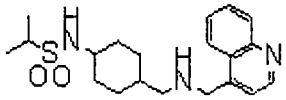
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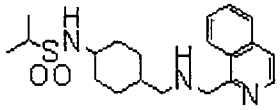
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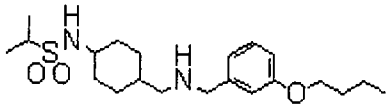
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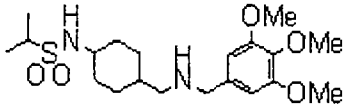
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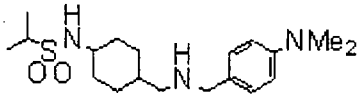
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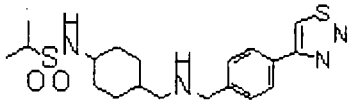
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I-651 

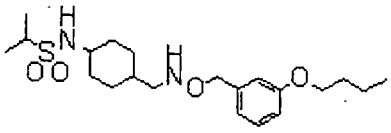
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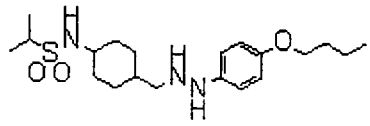
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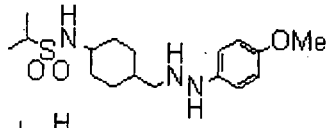
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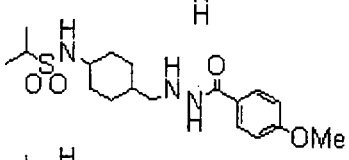
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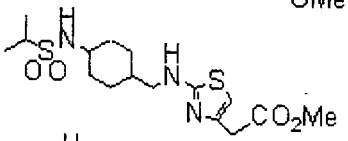
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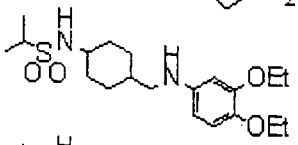
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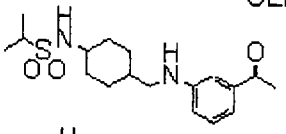
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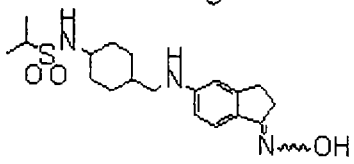
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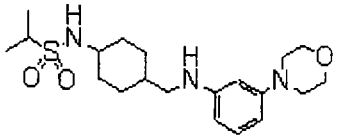
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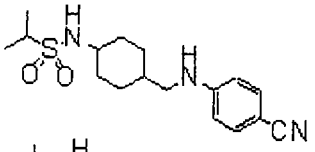
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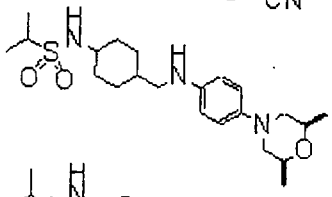
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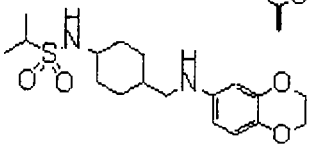
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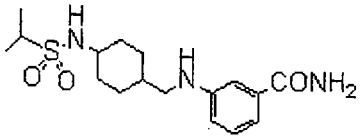
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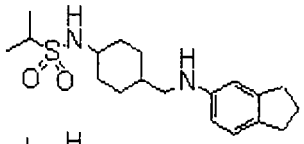
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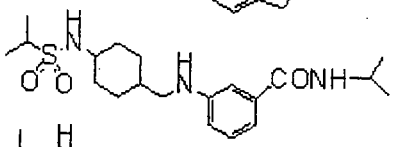
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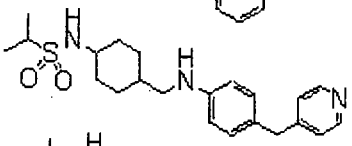
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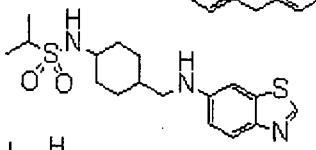
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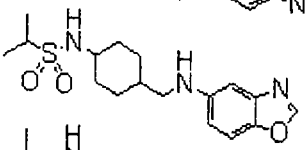
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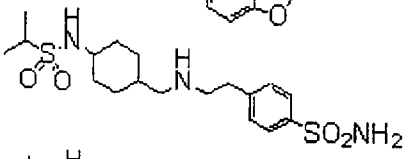
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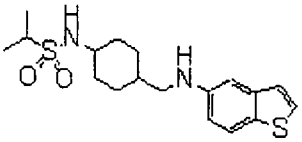
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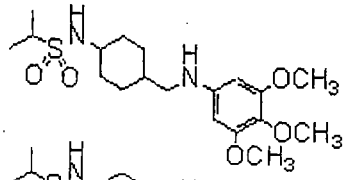
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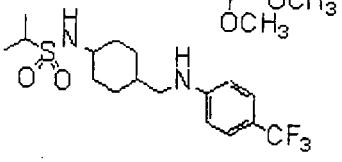
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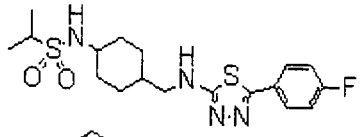
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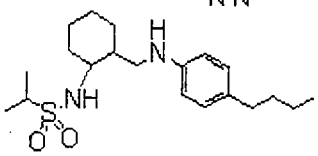
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I-675 

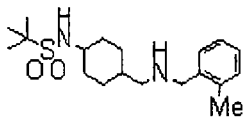
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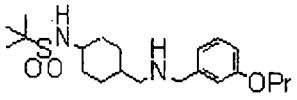
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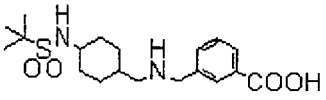
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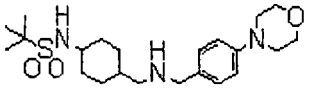
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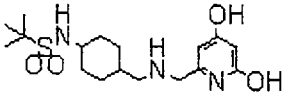
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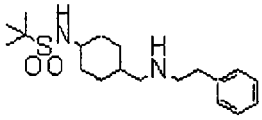
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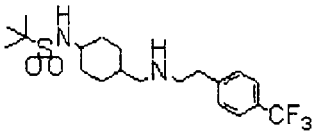
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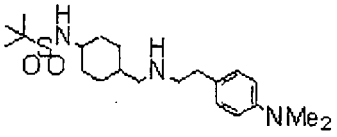
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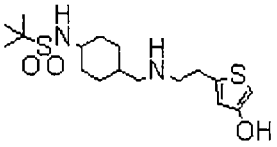
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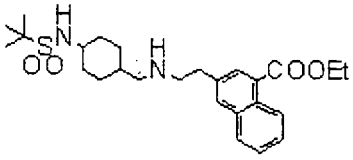
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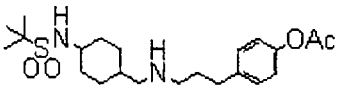
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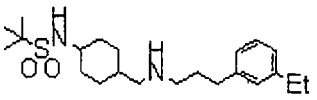
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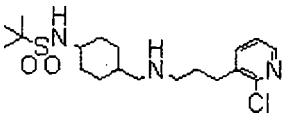
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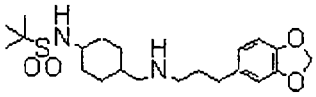
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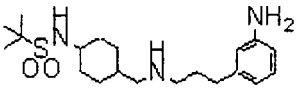
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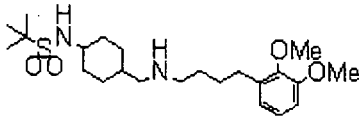
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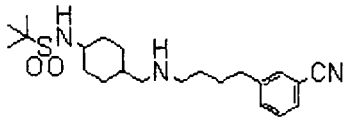
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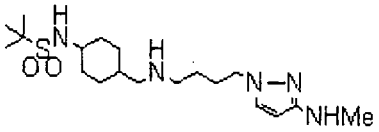
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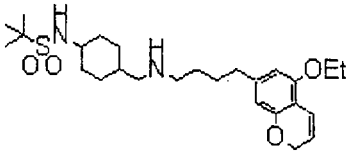
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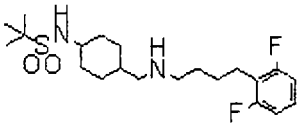
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I-695 

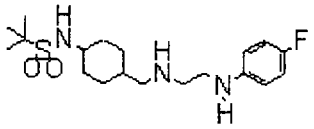
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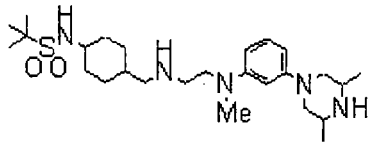
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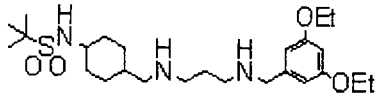
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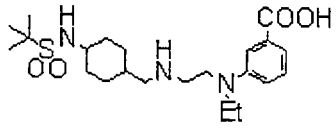
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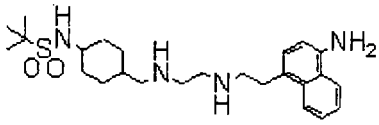
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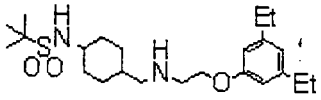
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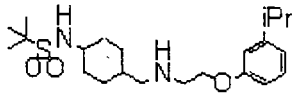
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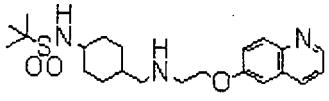
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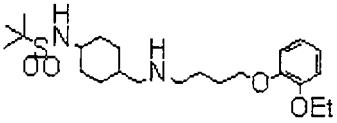
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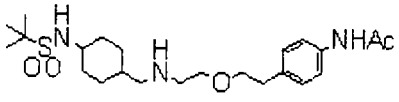
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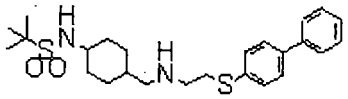
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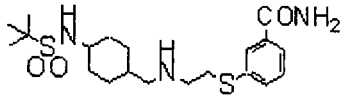
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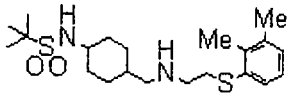
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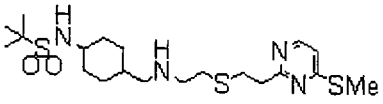
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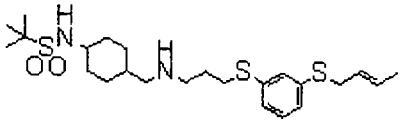
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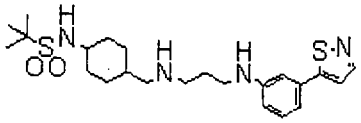
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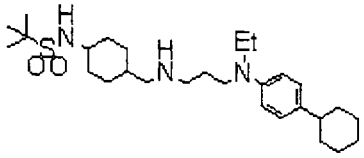
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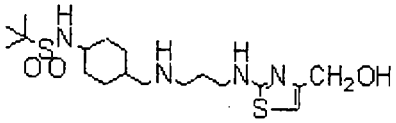
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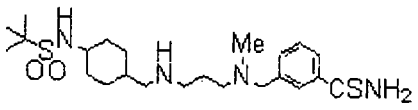
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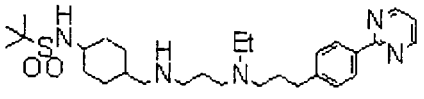
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I-715 

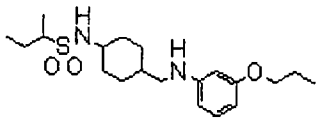
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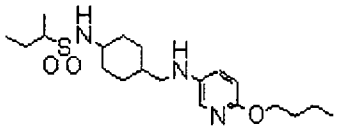
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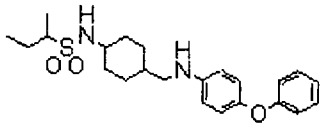
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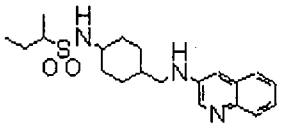
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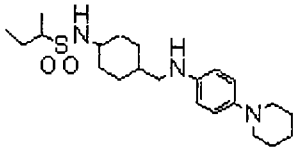
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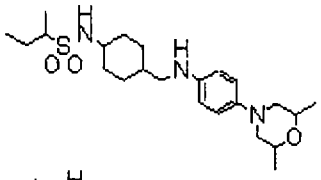
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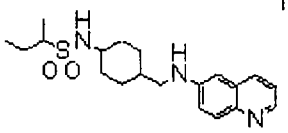
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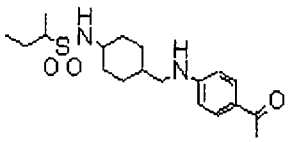
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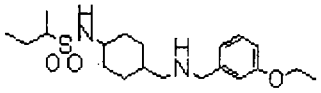
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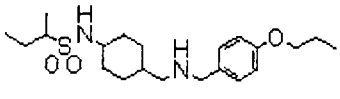
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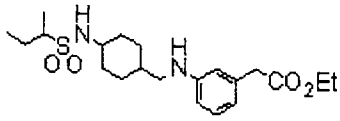
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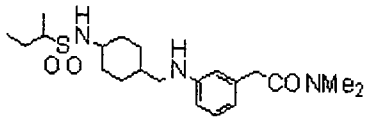
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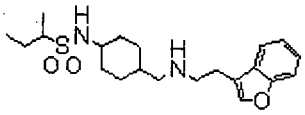
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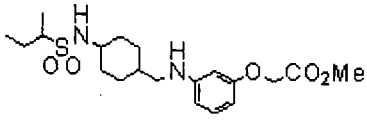
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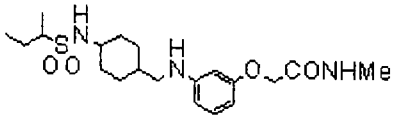
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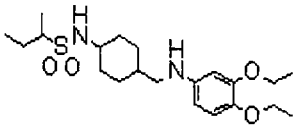
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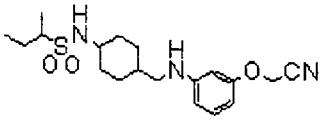
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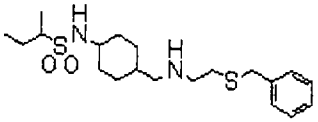
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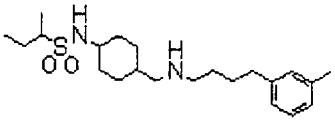
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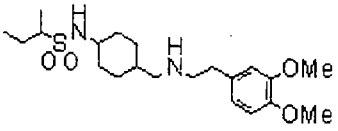
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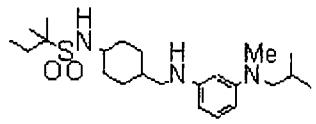
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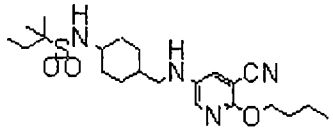
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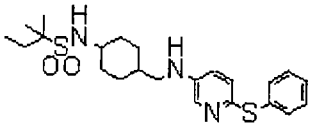
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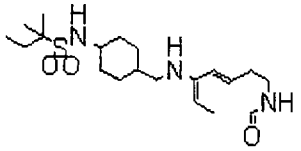
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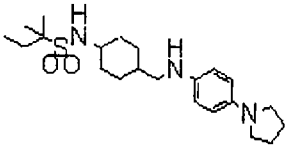
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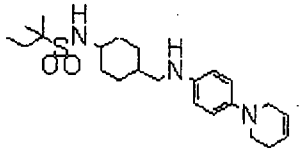
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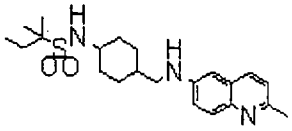
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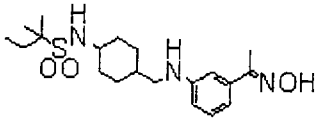
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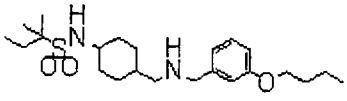
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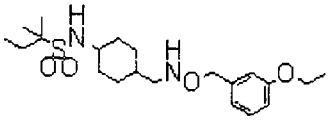
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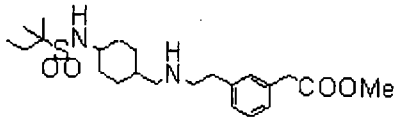
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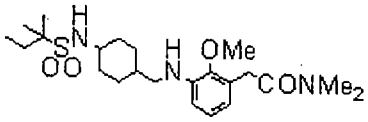
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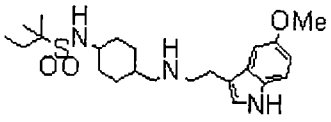
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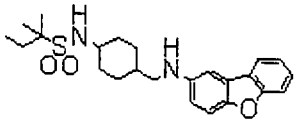
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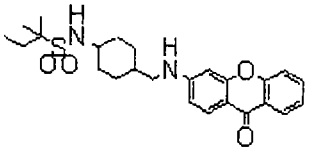
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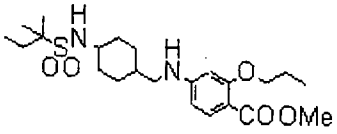
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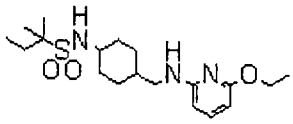
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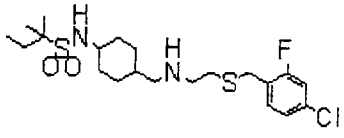
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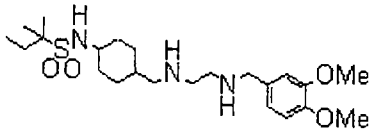
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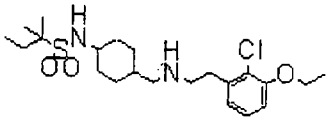
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I-755 

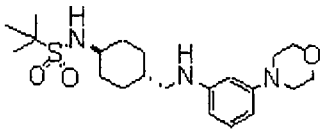
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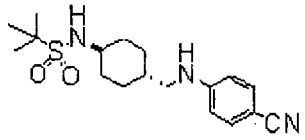
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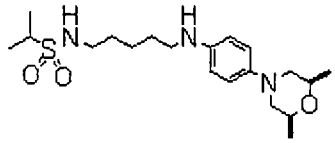
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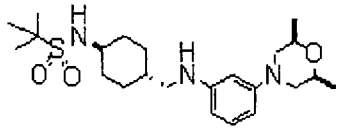
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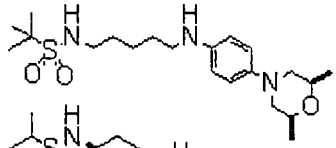
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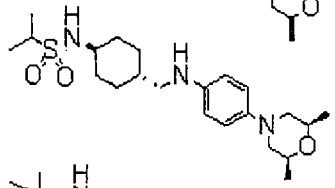
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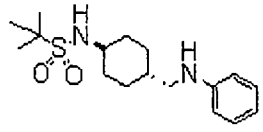
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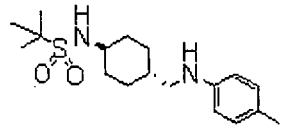
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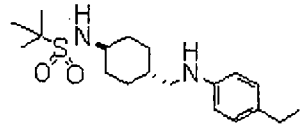
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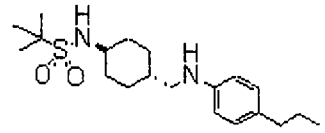
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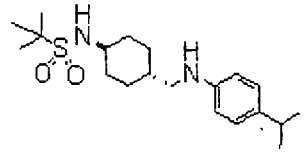
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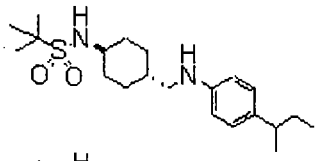
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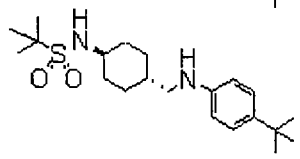
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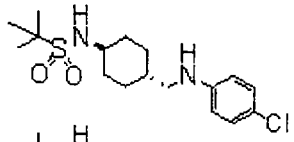
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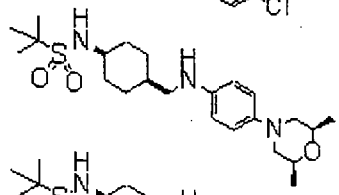
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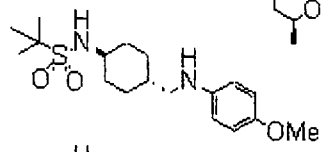
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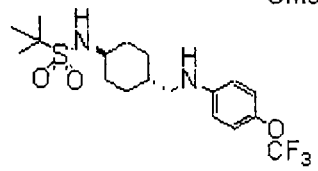
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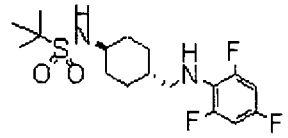
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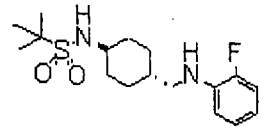
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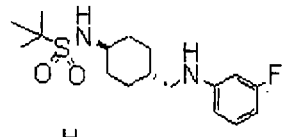
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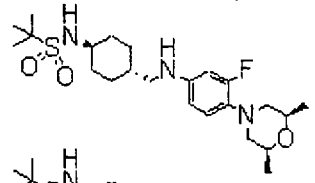
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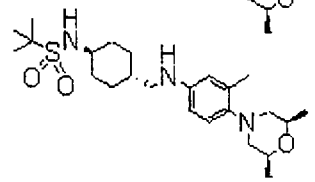
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Ia-18 

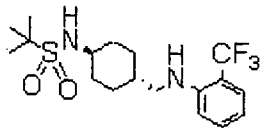
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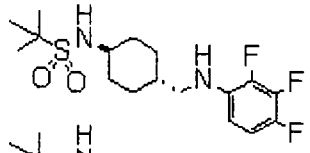
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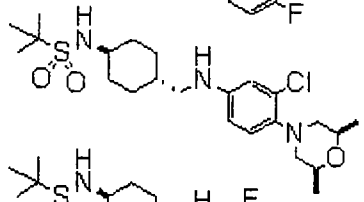
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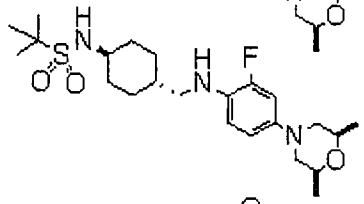
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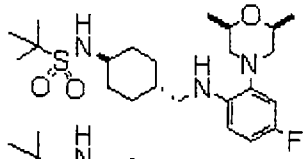
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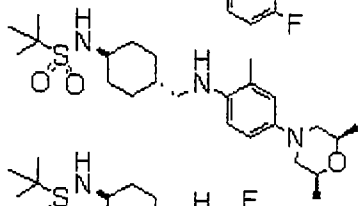
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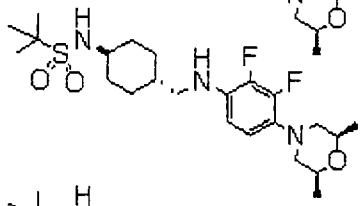
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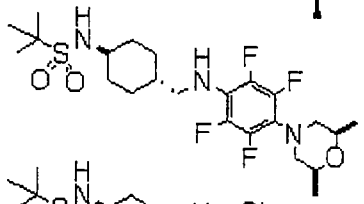
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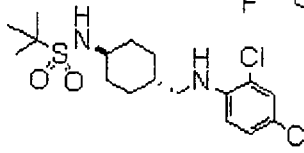
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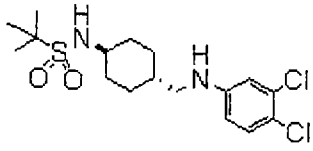
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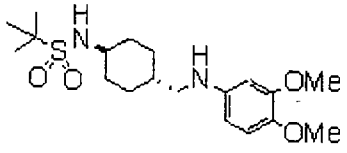
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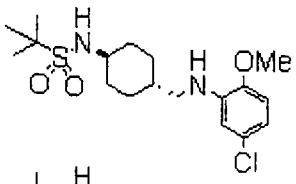
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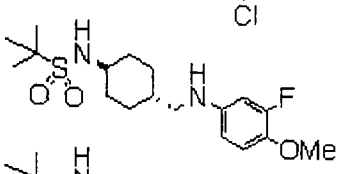
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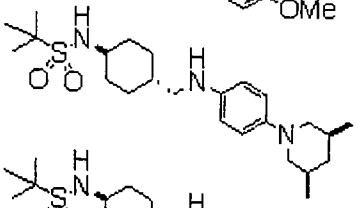
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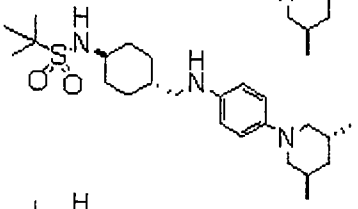
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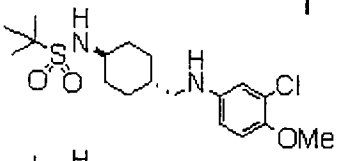
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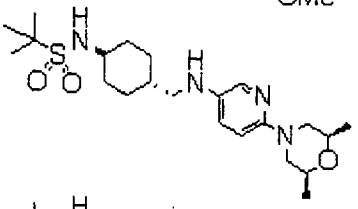
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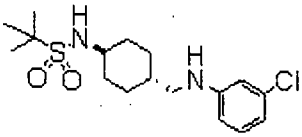
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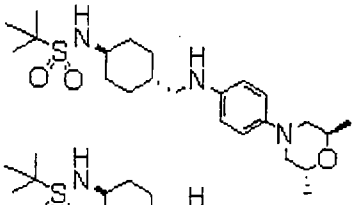
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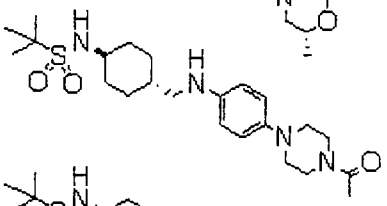
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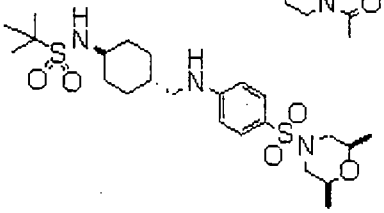
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Ia-40 

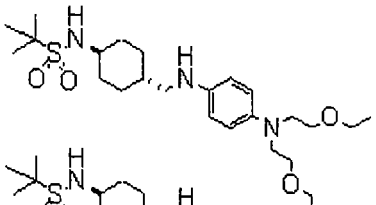
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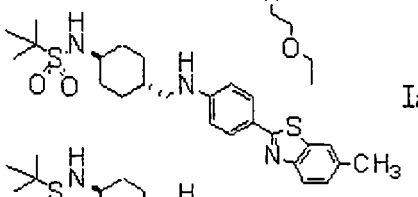
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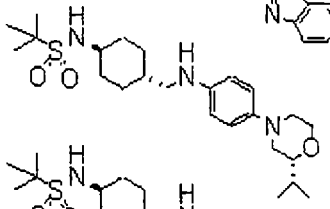
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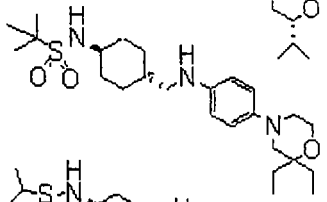
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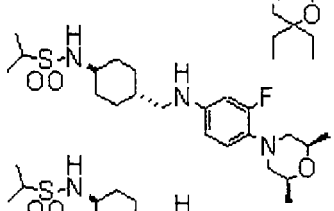
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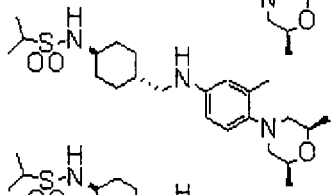
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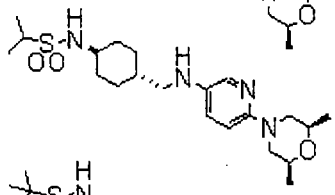
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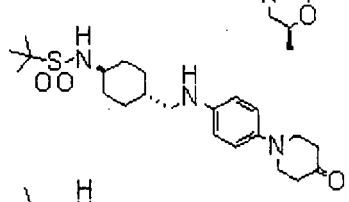
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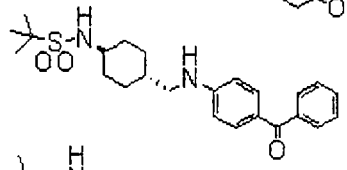
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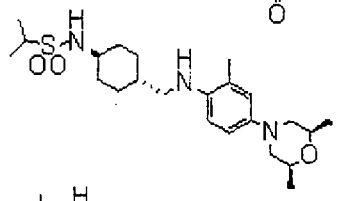
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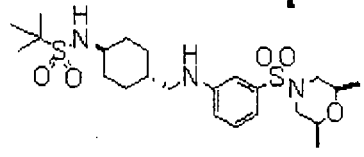
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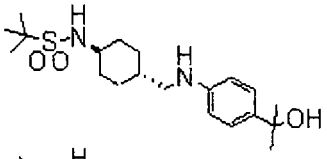
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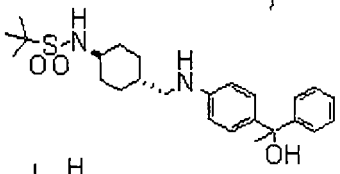
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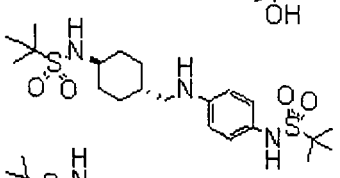
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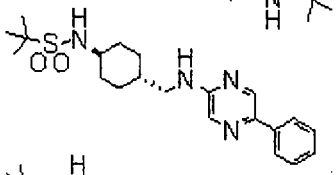
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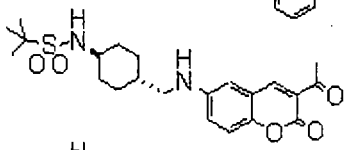
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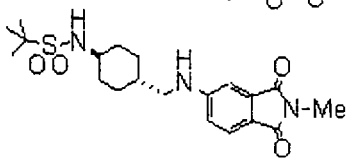
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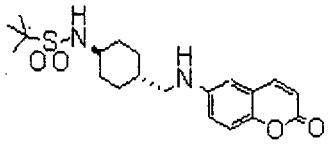
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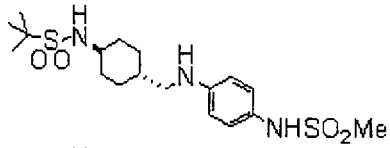
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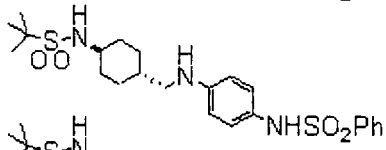
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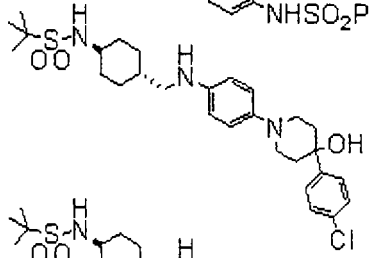
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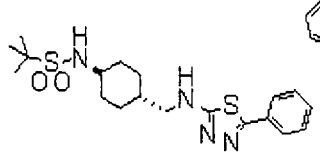
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Ia-62 

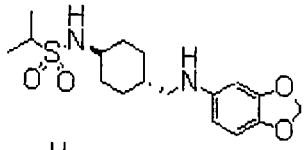
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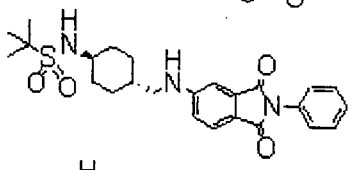
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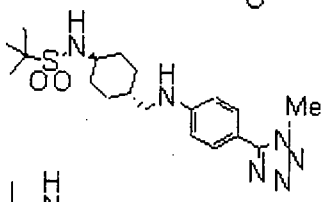
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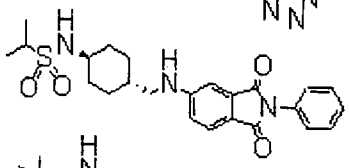
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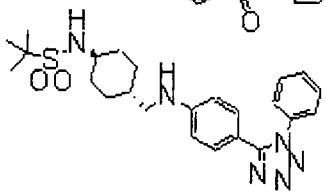
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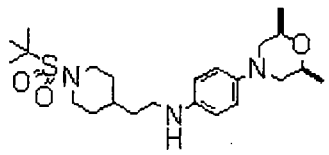
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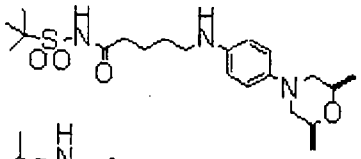
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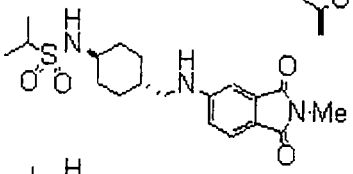
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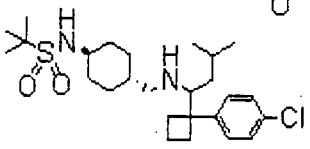
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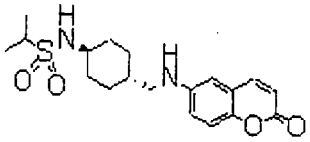
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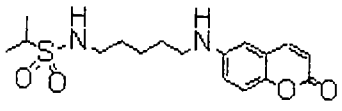
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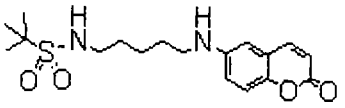
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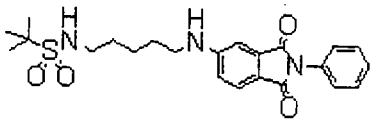
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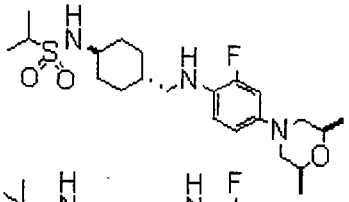
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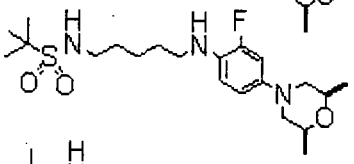
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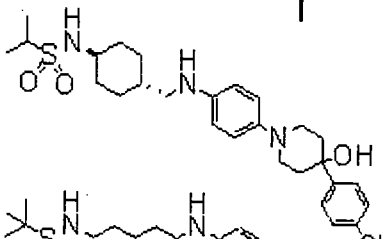
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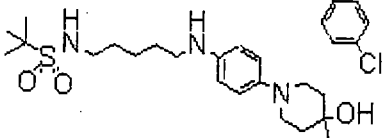
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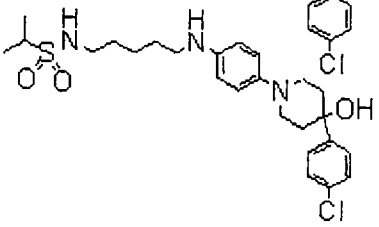
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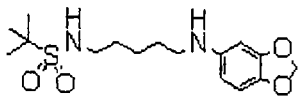
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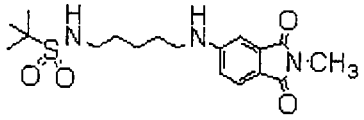
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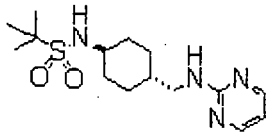
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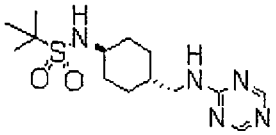
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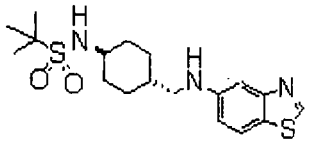
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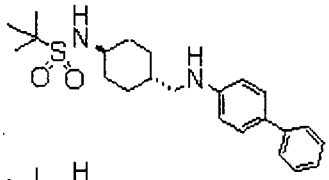
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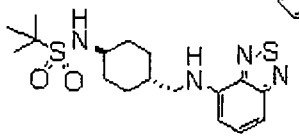
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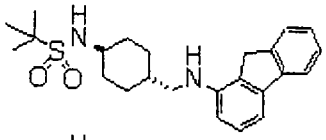
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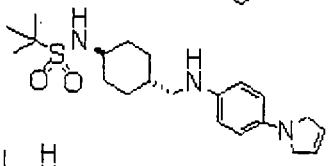
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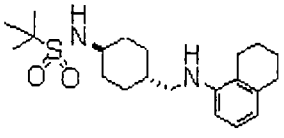
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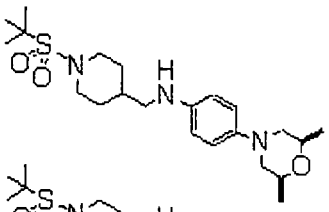
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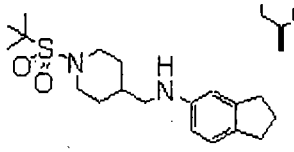
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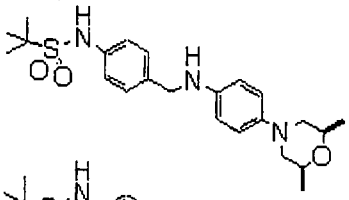
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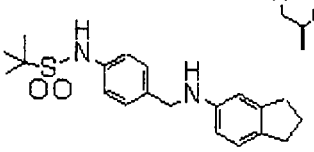
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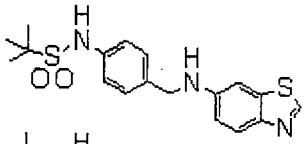
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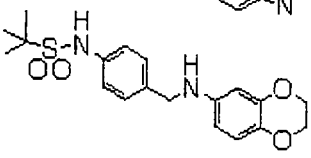
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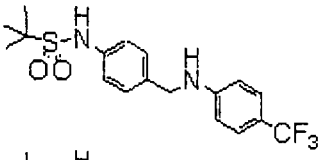
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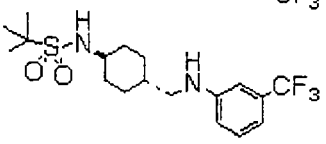
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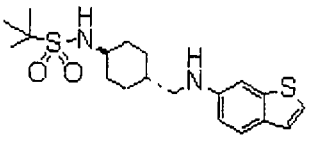
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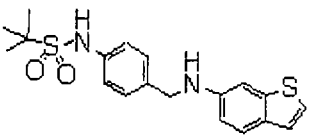
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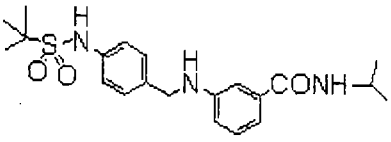
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Ia-128 

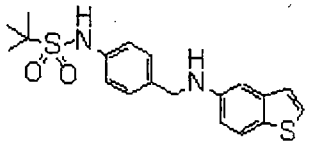
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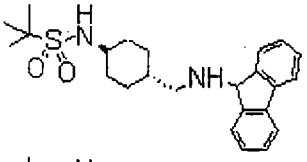
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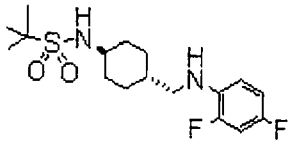
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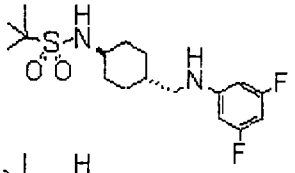
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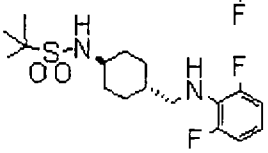
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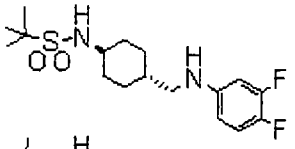
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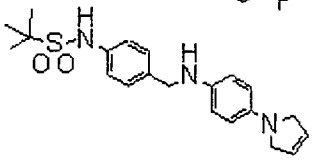
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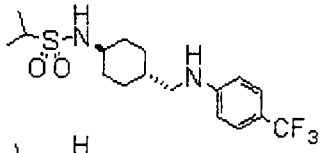
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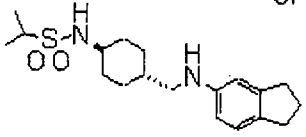
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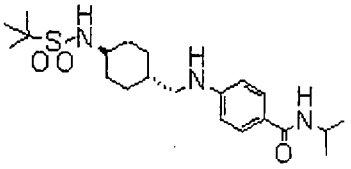
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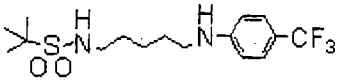
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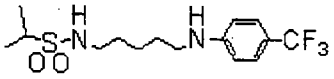
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Ia-140 

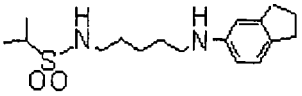
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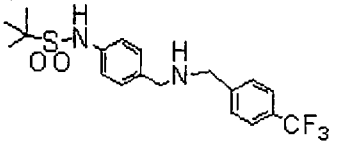
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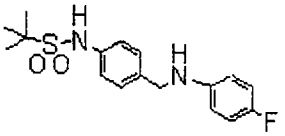
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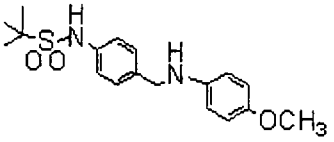
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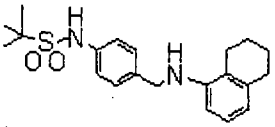
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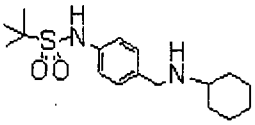
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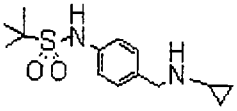
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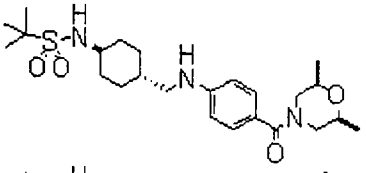
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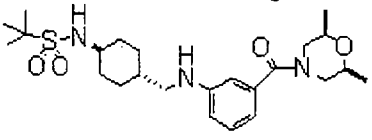
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Ia-150 

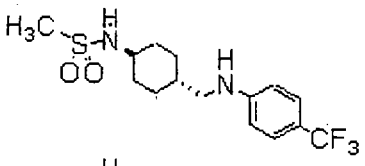
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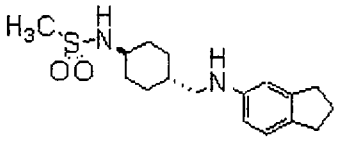
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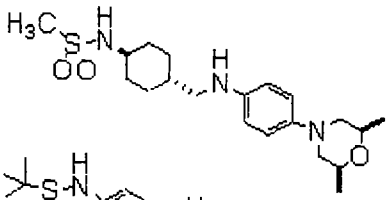
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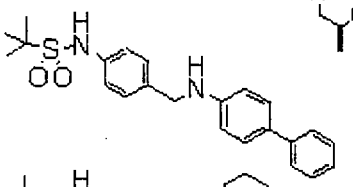
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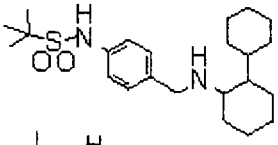
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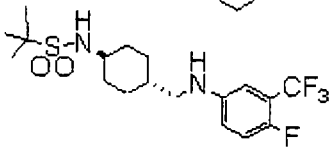
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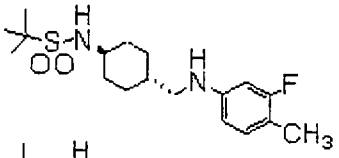
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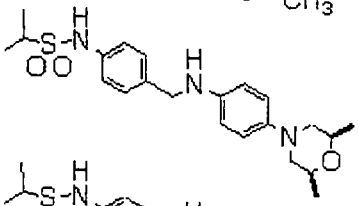
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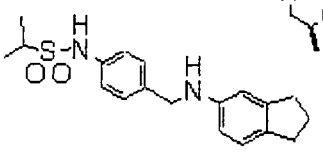
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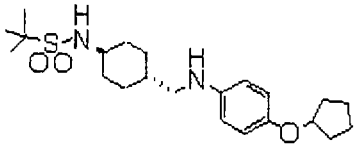
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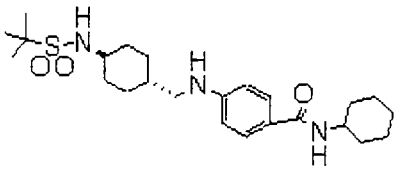
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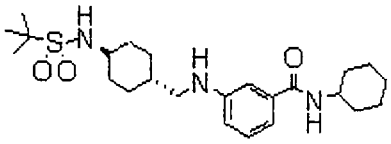
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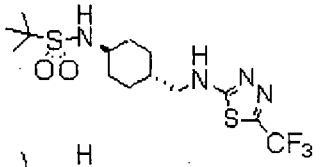
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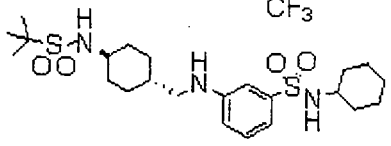
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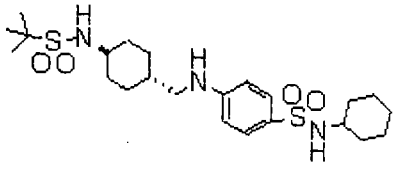
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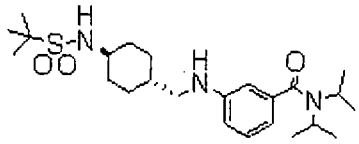
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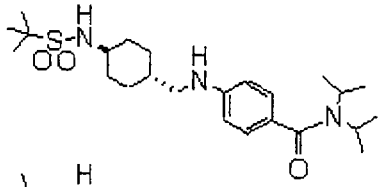
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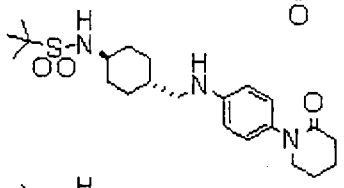
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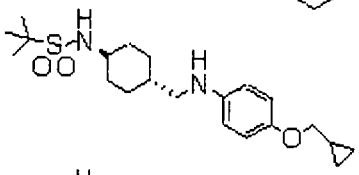
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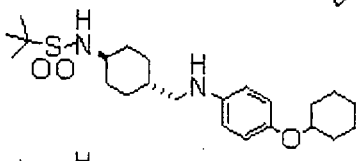
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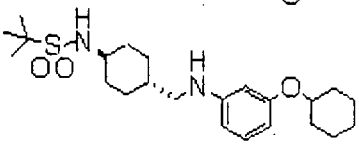
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Ia-172 

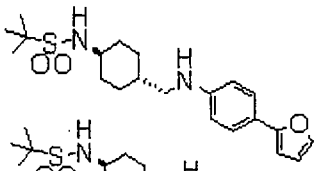
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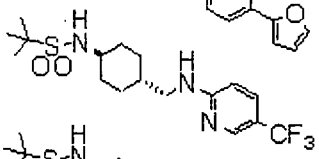
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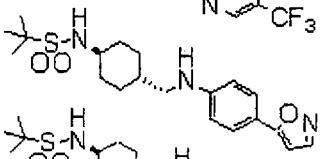
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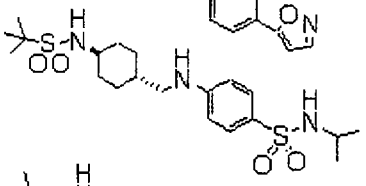
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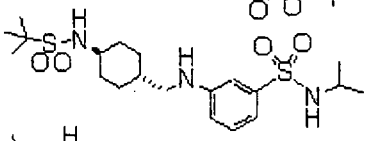
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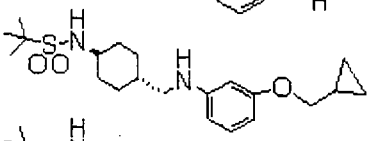
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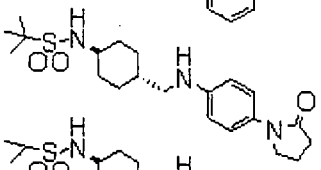
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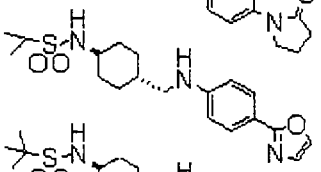
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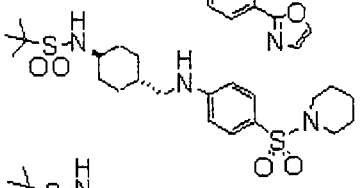
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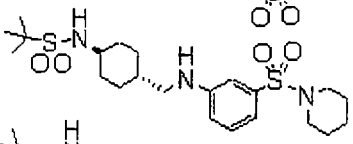
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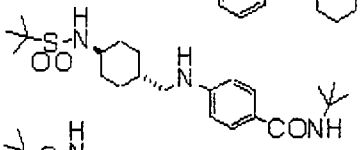
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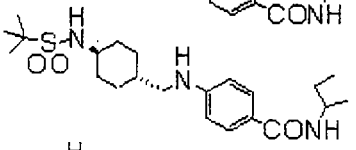
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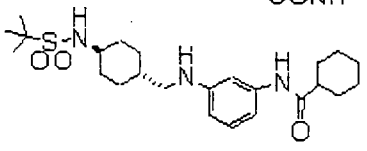
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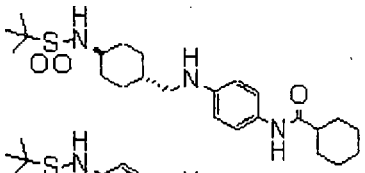
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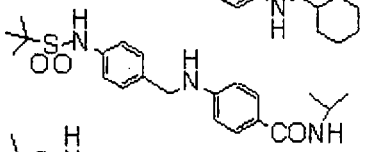
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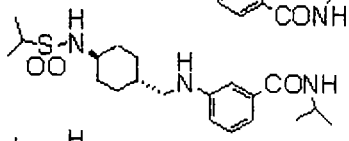
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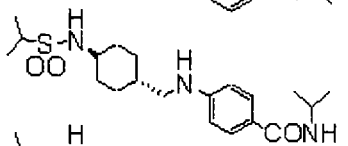
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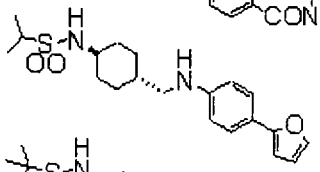
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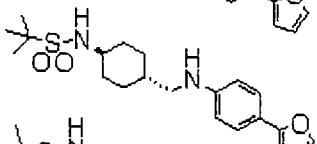
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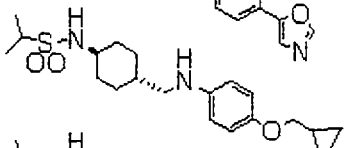
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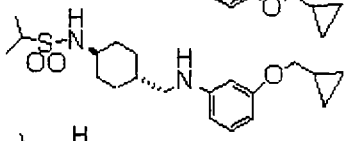
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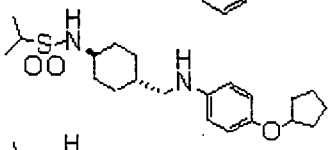
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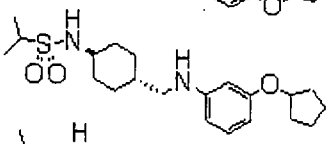
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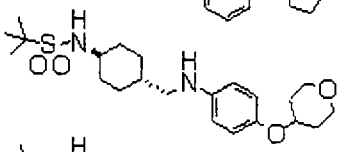
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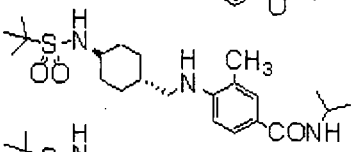
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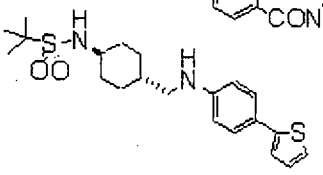
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Ia-198 

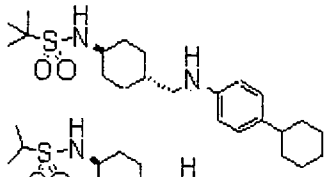
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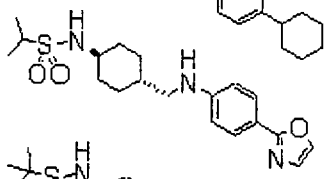
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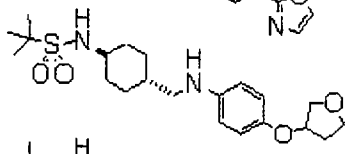
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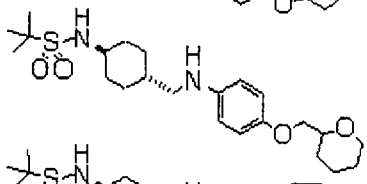
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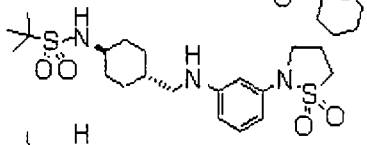
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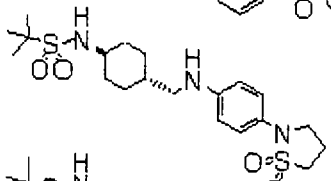
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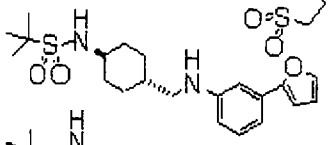
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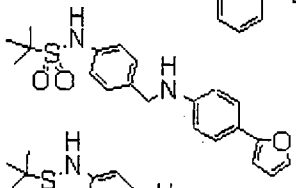
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Ia-206 

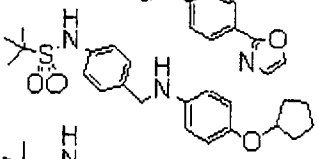
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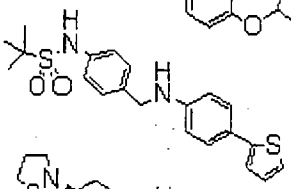
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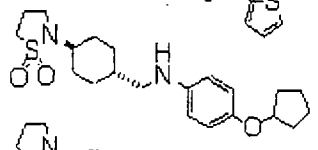
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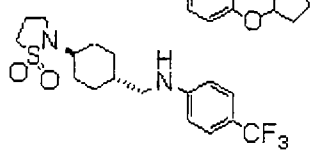
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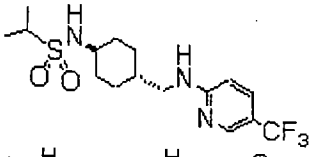
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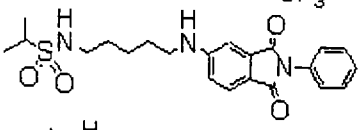
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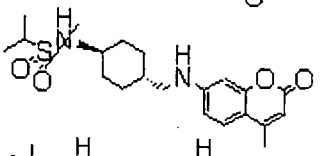
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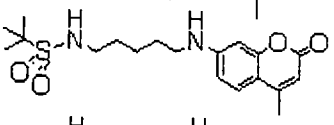
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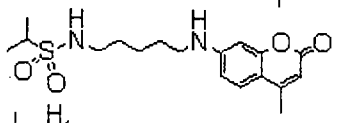
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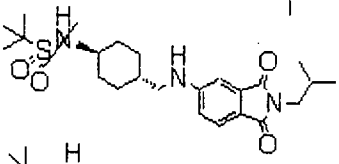
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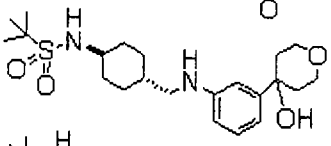
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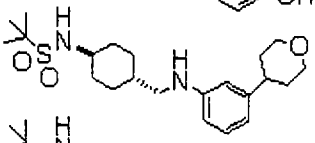
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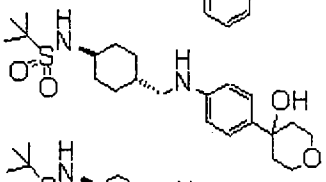
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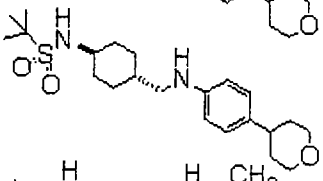
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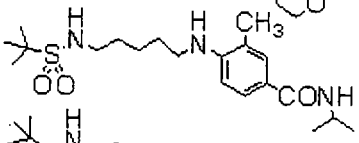
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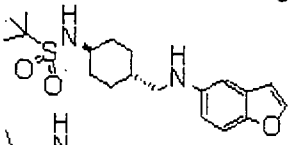
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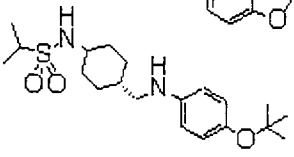
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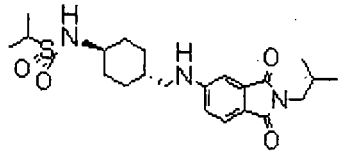
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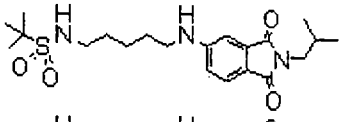
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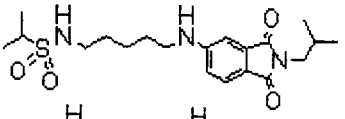
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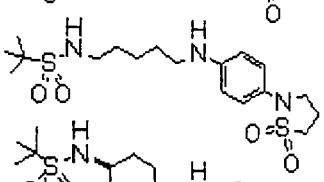
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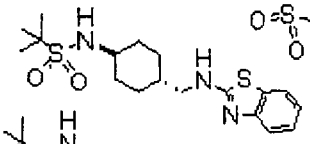
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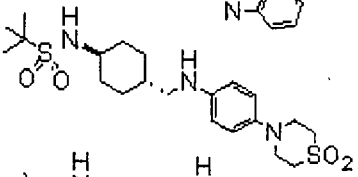
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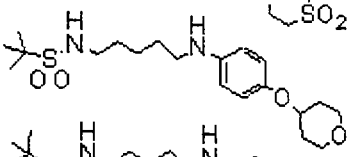
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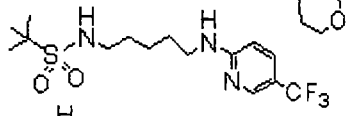
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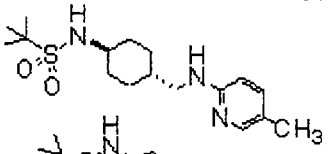
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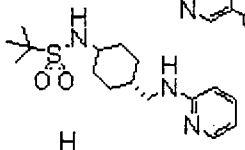
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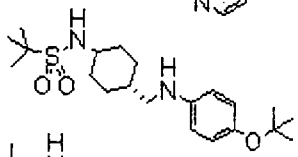
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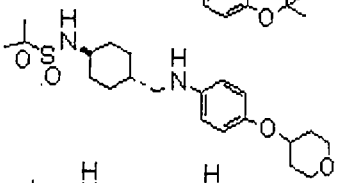
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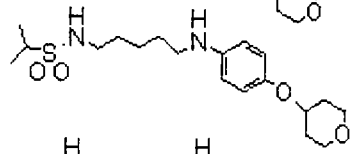
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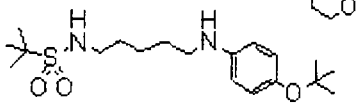
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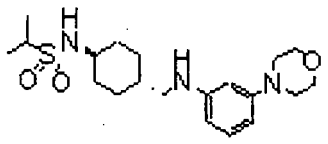
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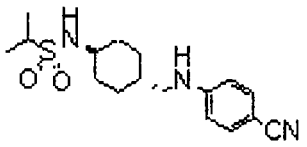
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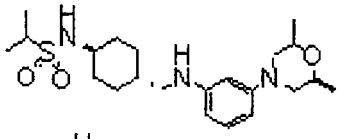
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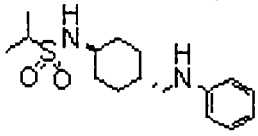
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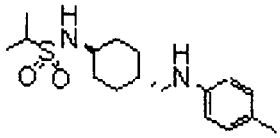
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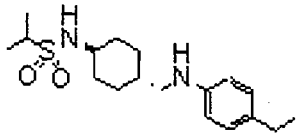
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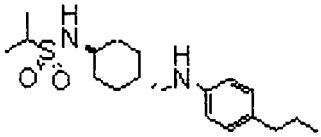
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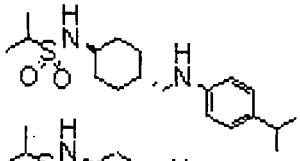
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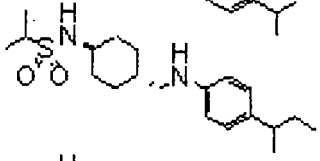
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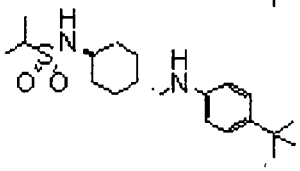
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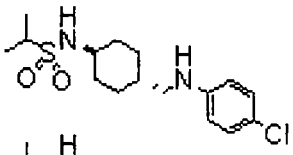
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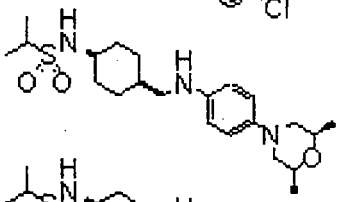
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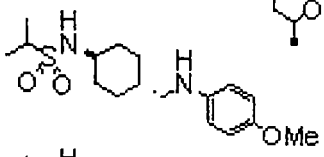
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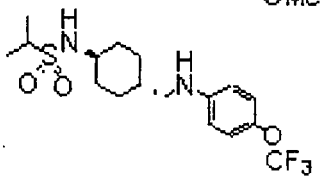
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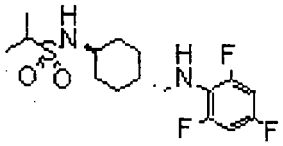
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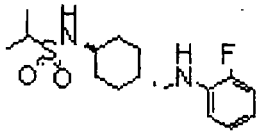
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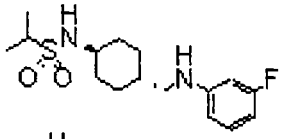
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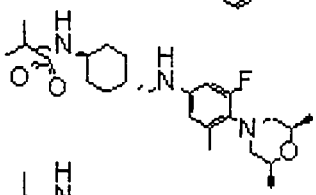
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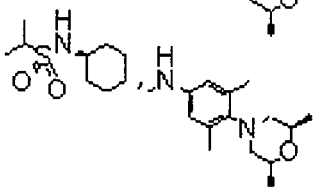
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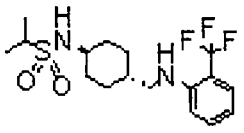
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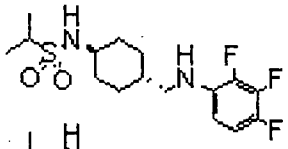
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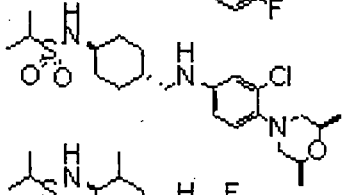
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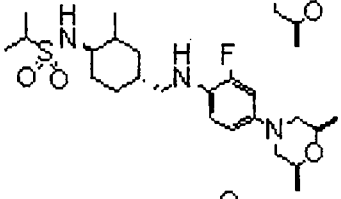
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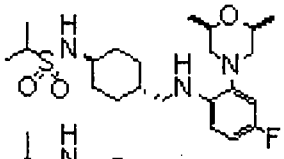
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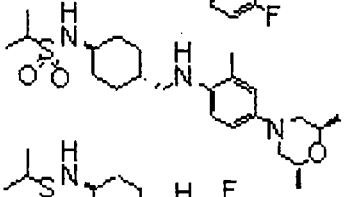
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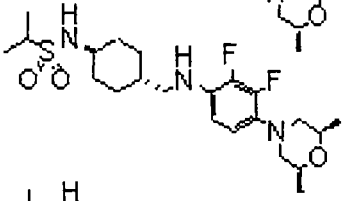
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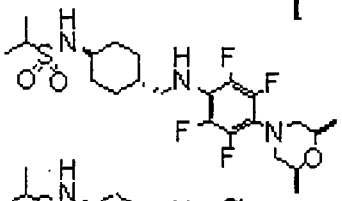
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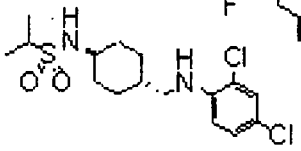
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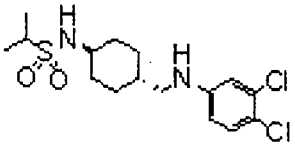
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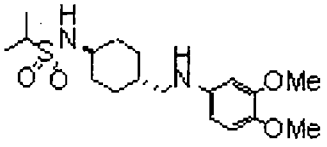
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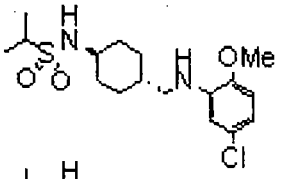
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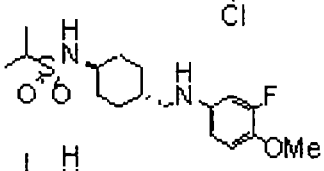
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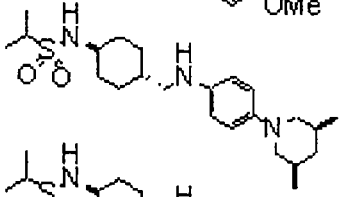
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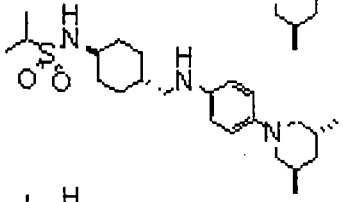
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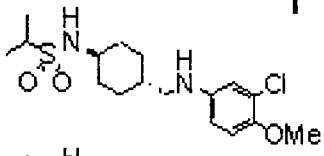
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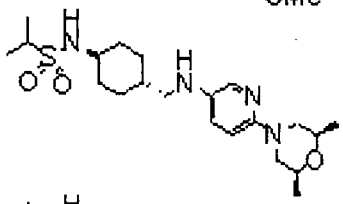
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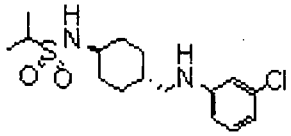
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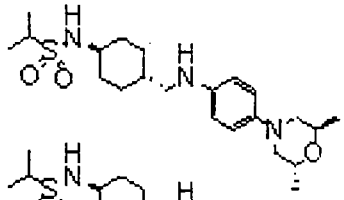
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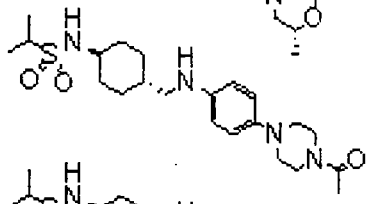
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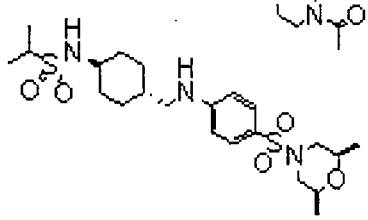
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Ib-40 

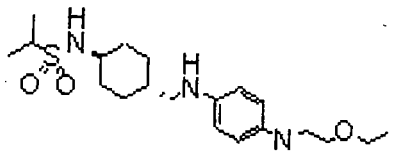
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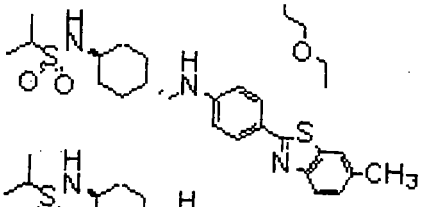
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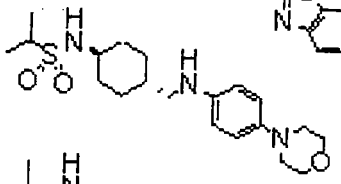
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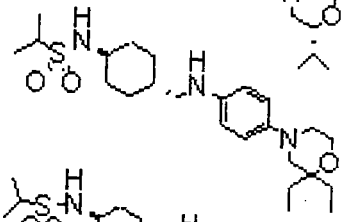
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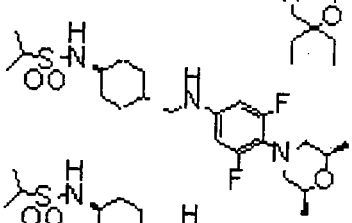
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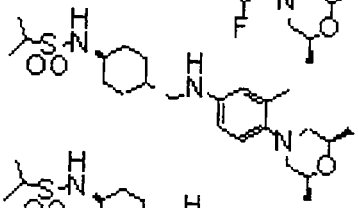
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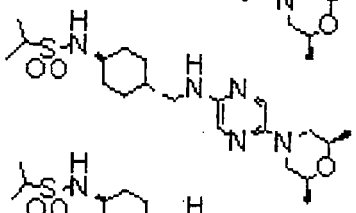
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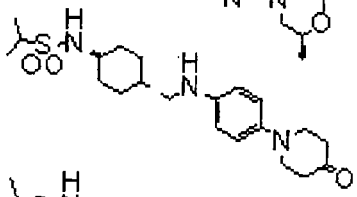
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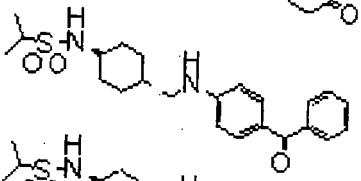
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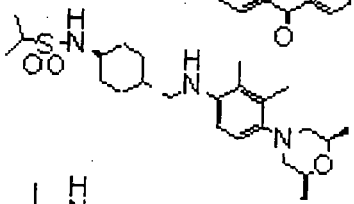
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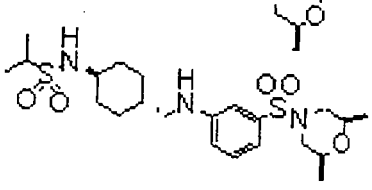
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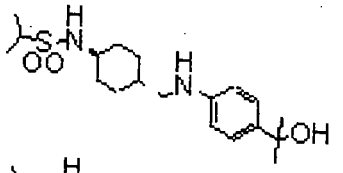
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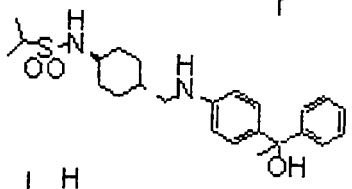
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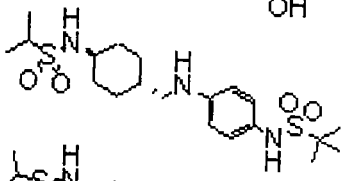
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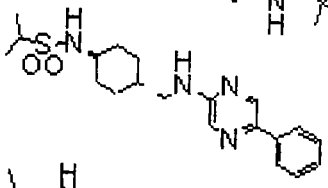
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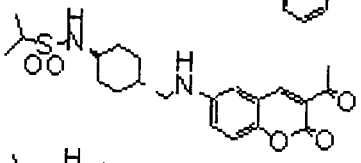
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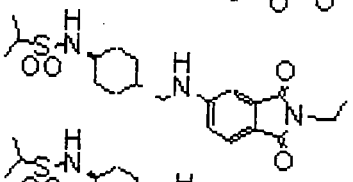
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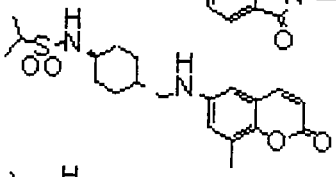
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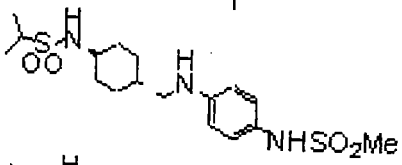
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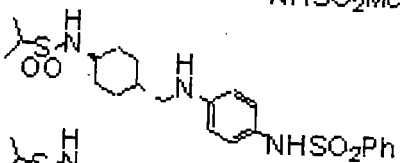
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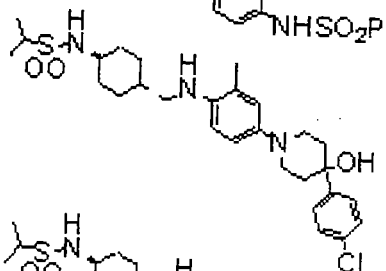
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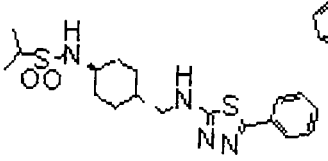
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Ib-62 

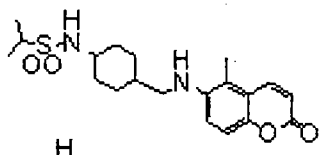
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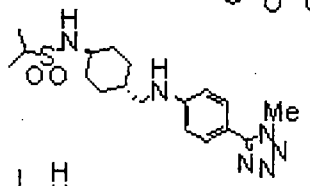
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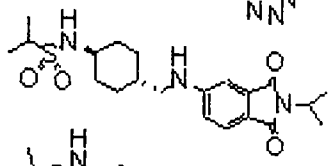
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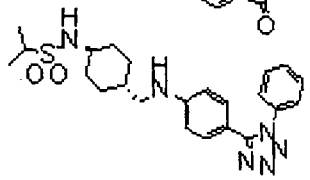
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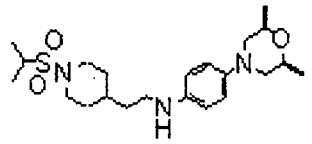
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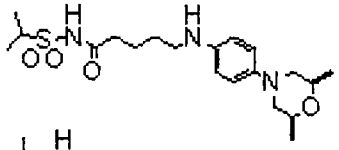
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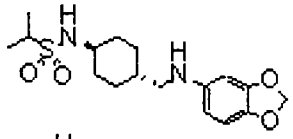
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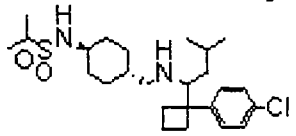
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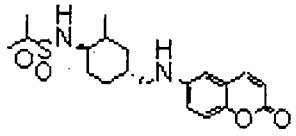
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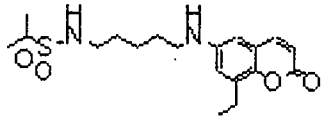
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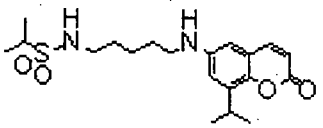
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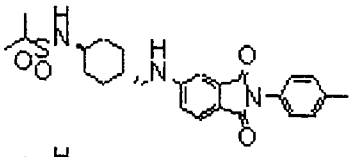
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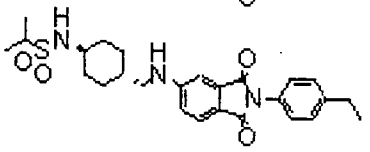
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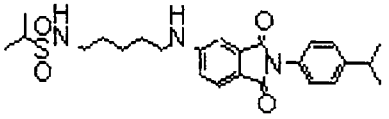
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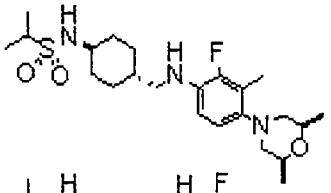
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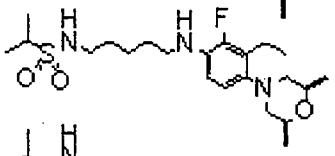
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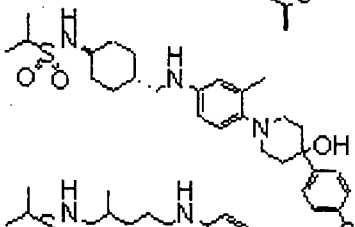
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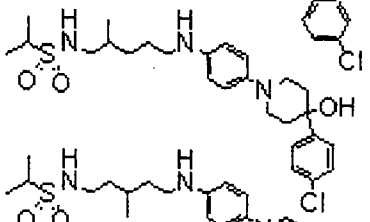
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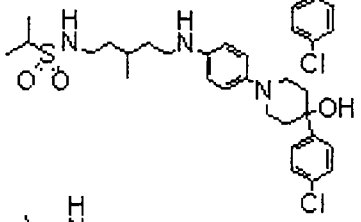
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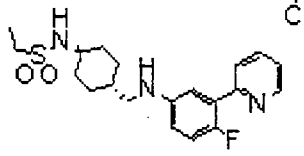
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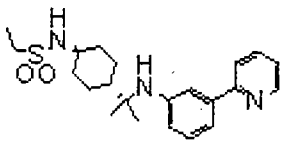
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Ib-84 

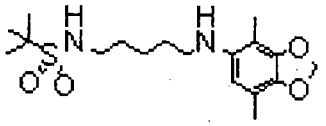
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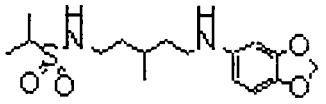
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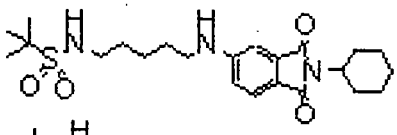
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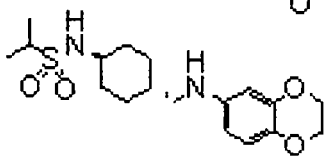
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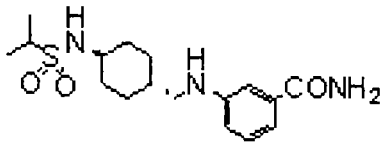
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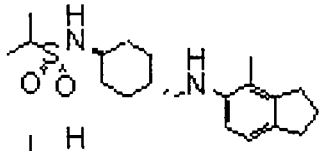
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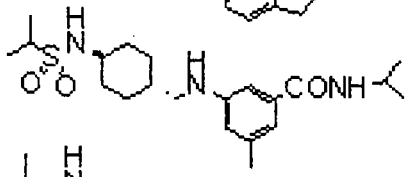
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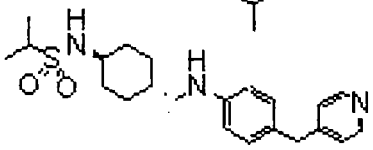
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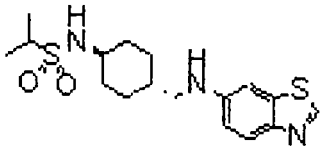
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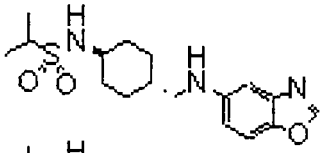
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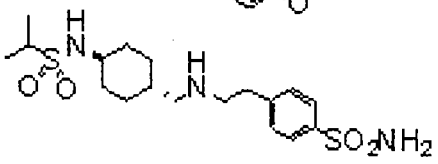
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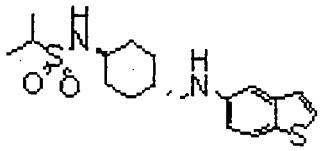
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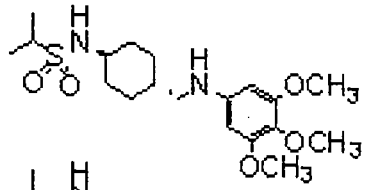
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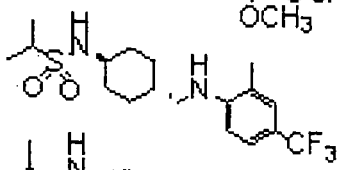
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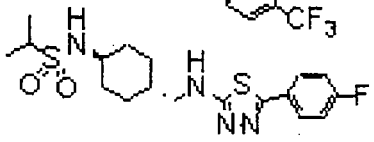
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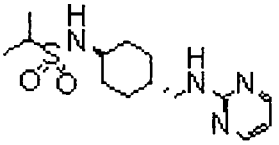
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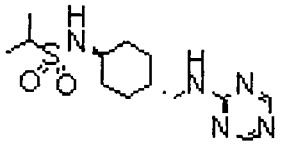
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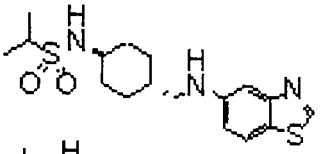
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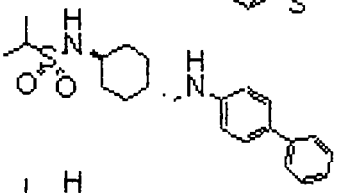
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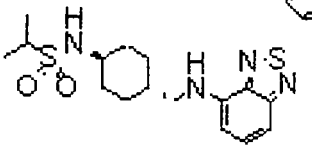
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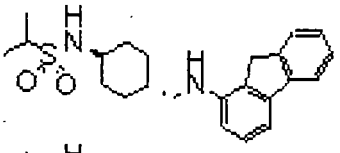
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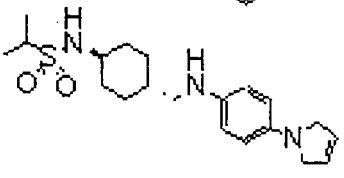
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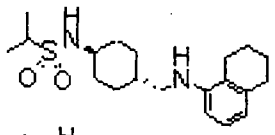
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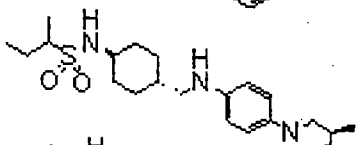
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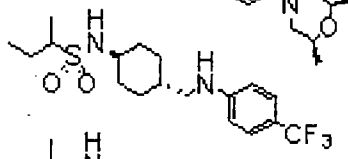
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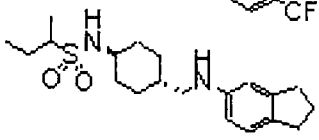
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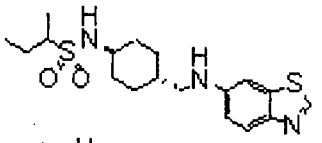
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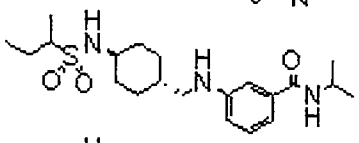
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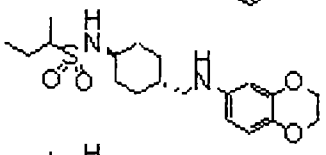
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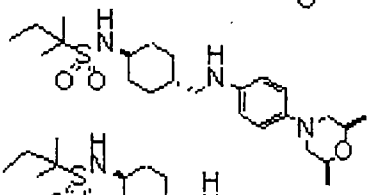
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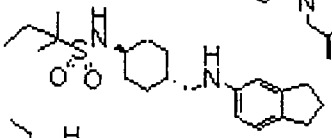
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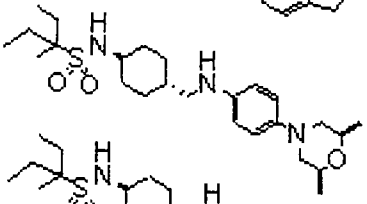
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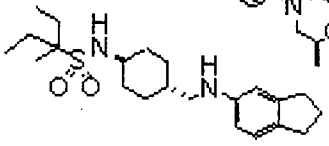
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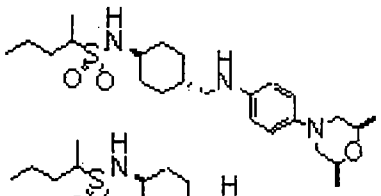
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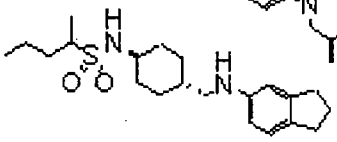
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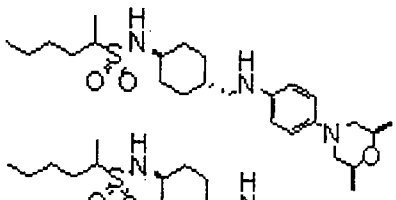
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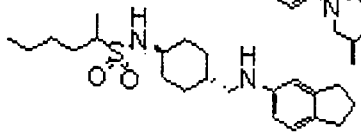
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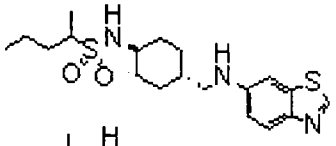
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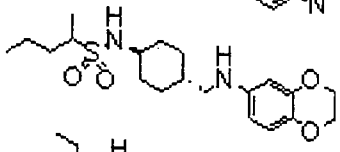
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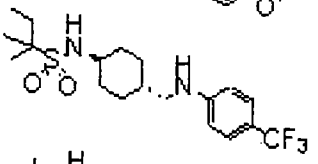
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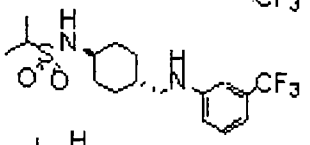
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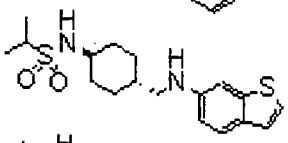
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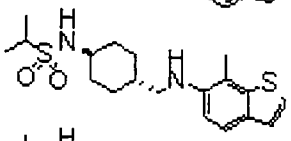
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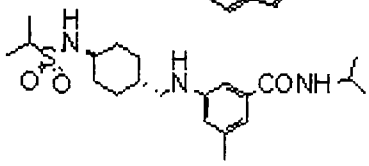
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Ib-128 

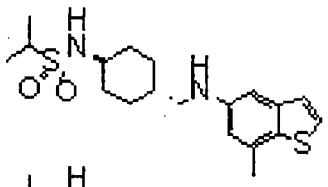
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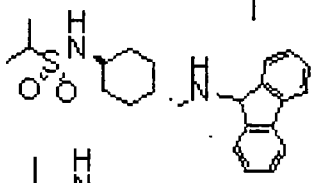
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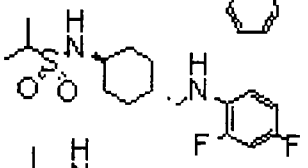
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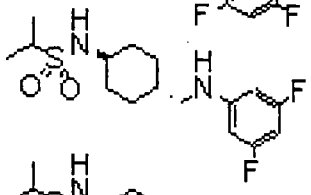
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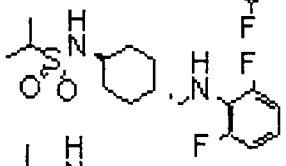
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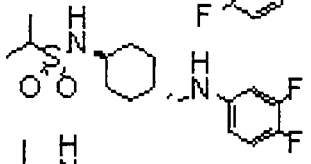
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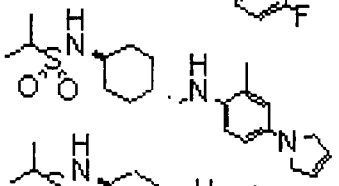
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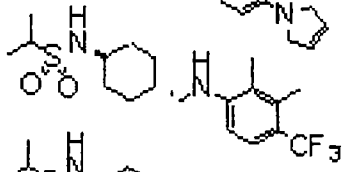
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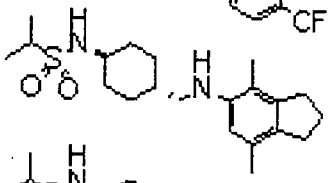
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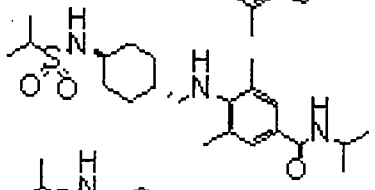
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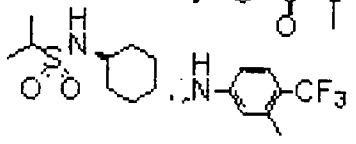
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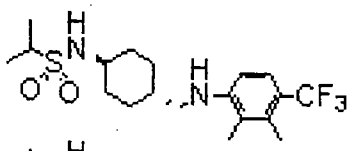
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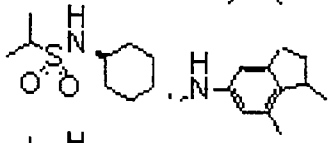
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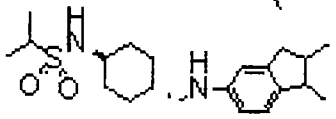
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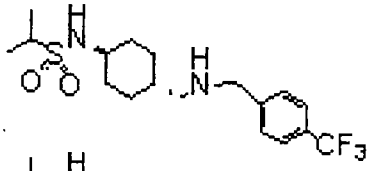
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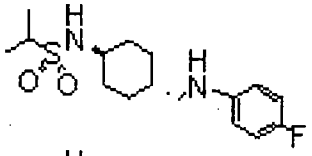
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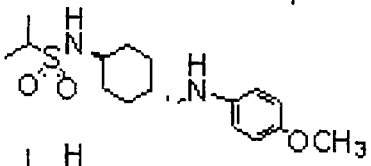
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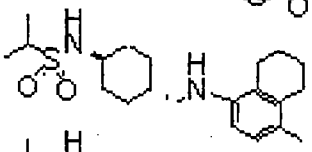
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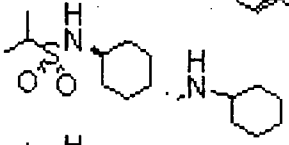
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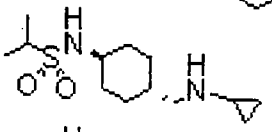
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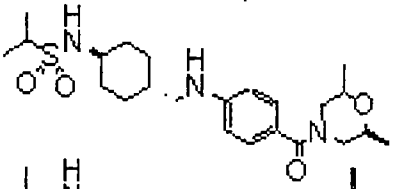
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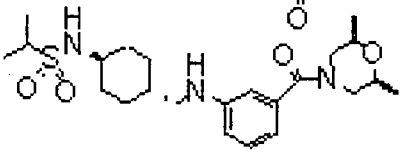
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Ib-150 

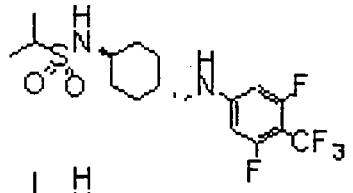
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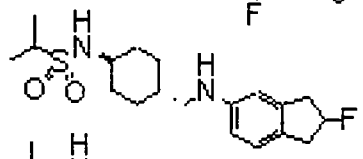
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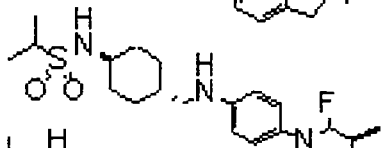
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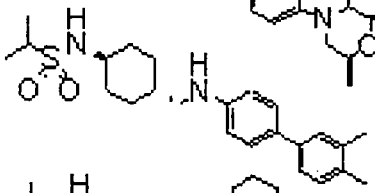
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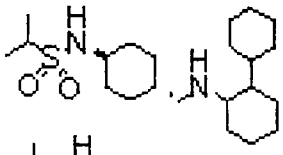
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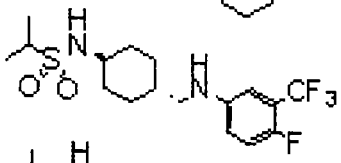
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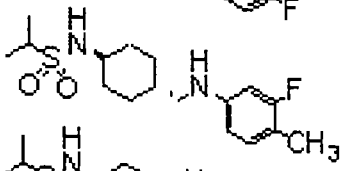
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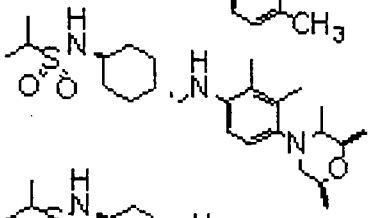
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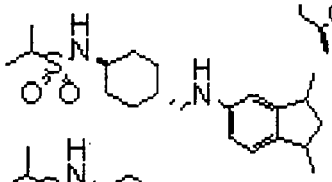
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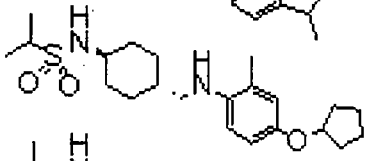
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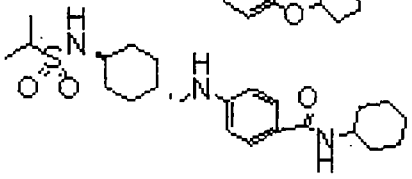
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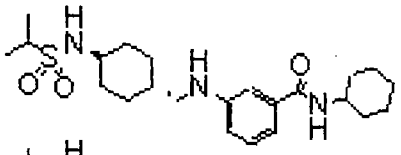
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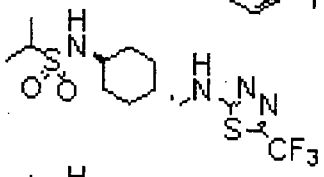
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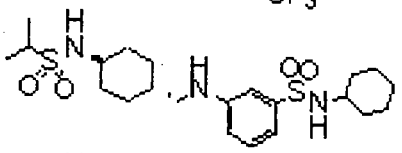
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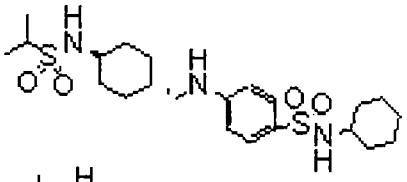
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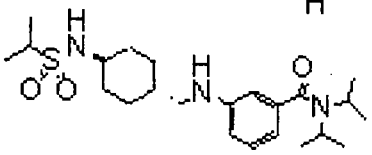
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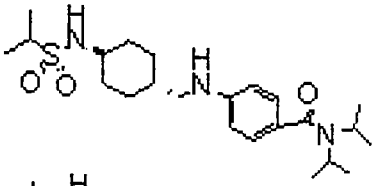
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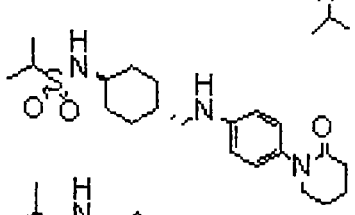
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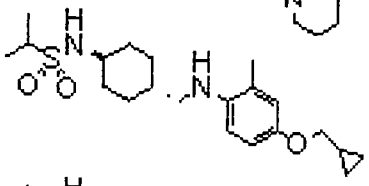
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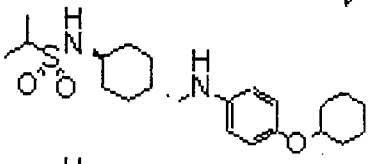
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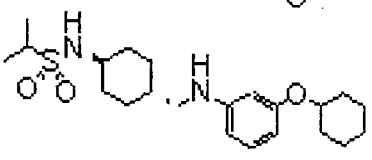
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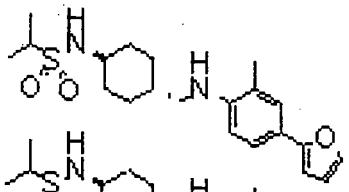
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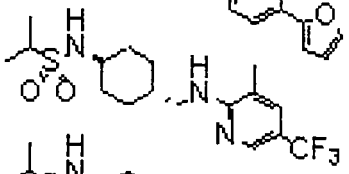
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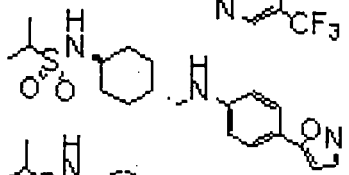
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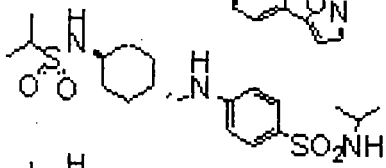
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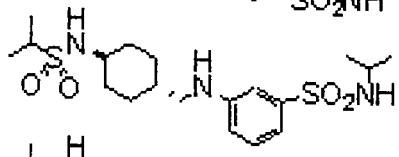
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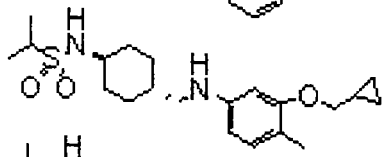
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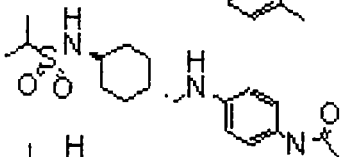
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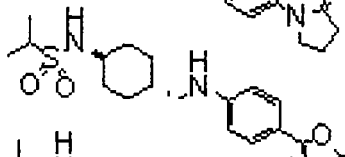
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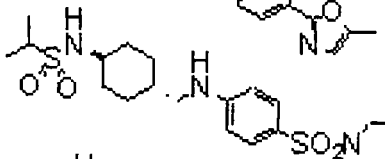
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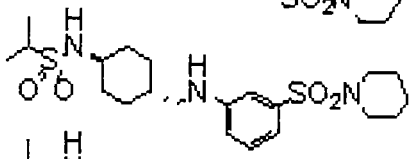
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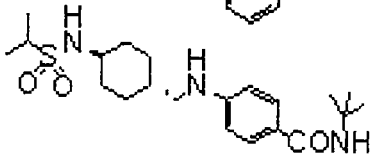
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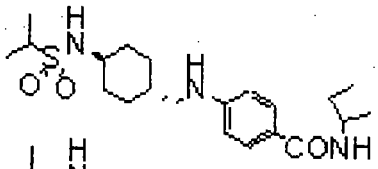
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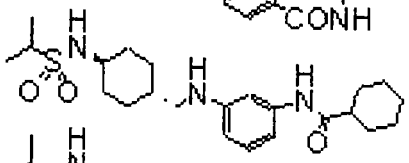
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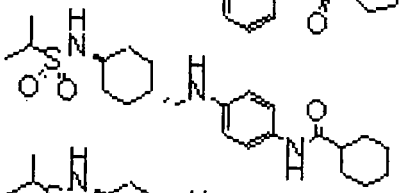
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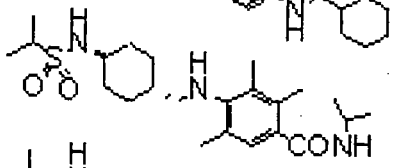
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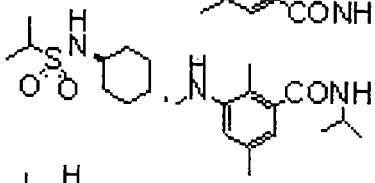
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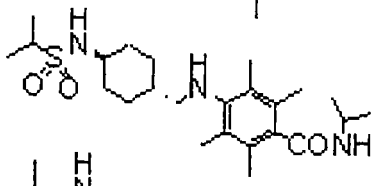
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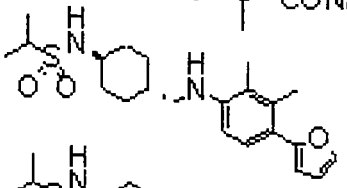
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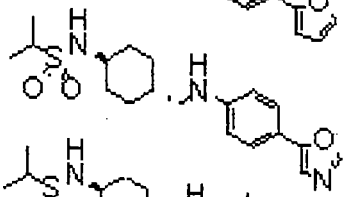
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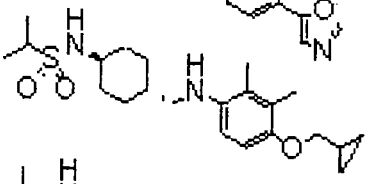
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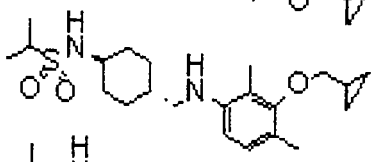
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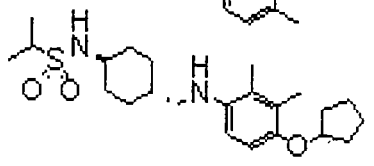
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Ib-194 

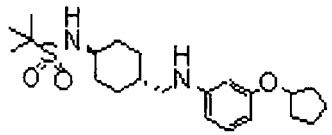
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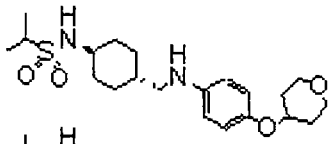
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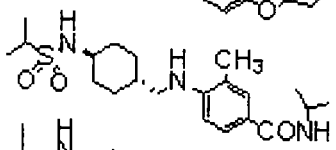
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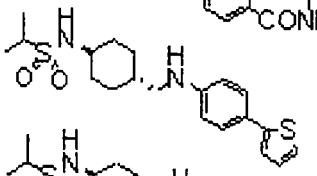
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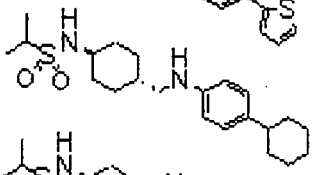
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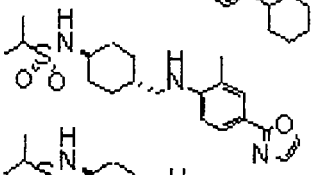
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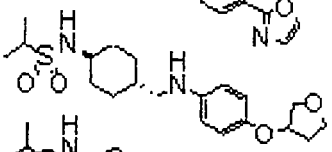
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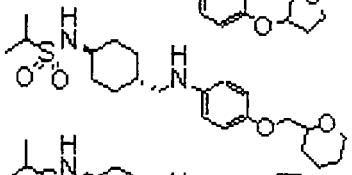
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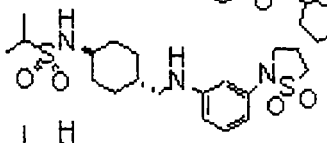
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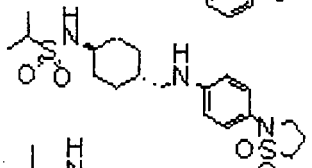
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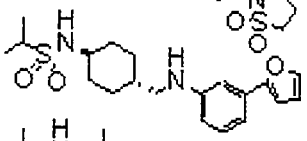
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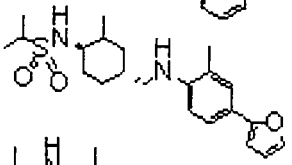
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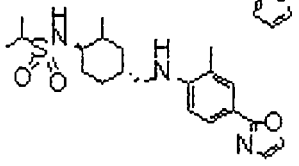
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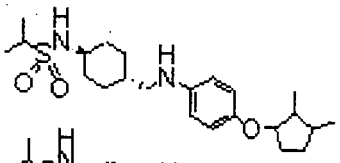
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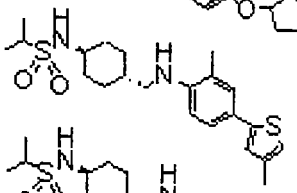
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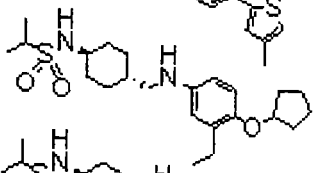
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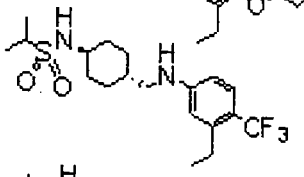
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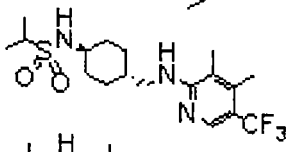
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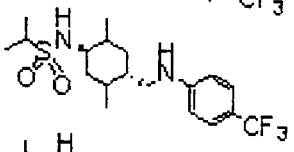
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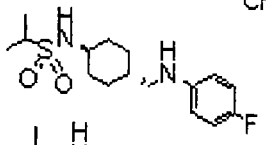
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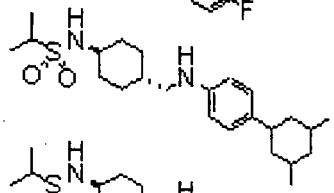
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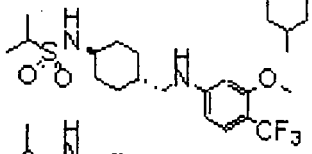
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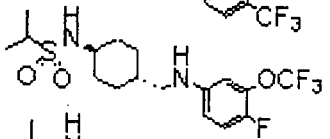
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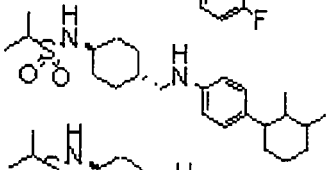
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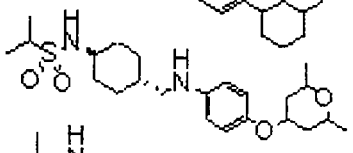
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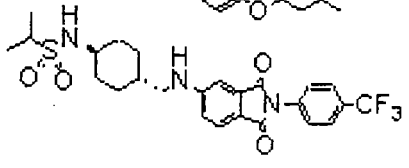
Ib-221 

Ib-222 

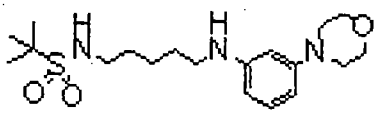
Ib-223 

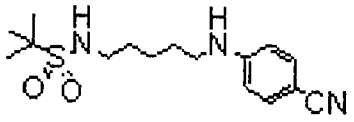
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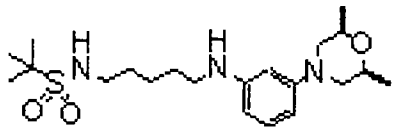
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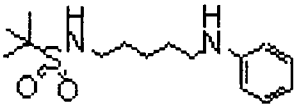
Ib-226 

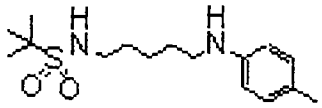
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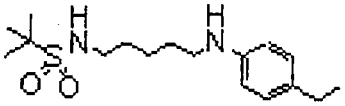
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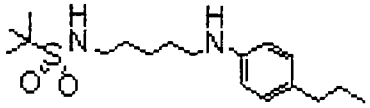
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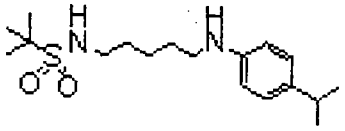
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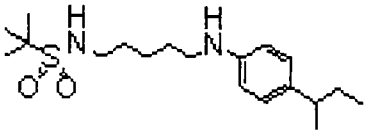
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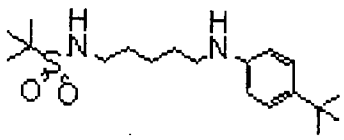
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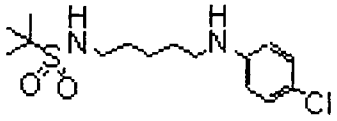
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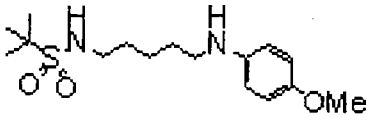
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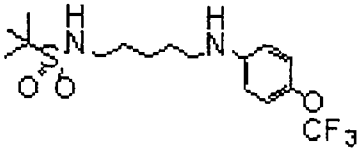
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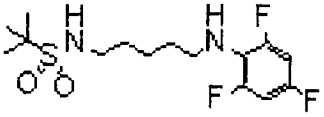
Ic-12 

Ic-13 

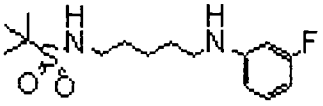
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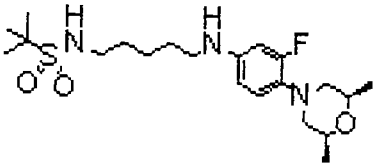
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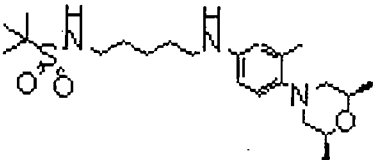
Ic-17 

Ic-18 

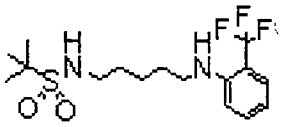
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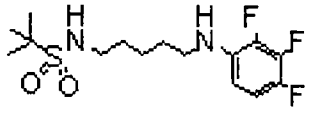
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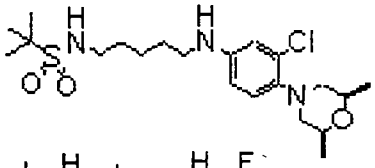
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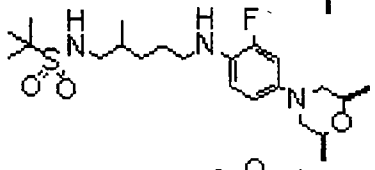
Ic-22 

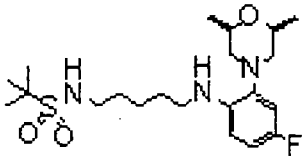
[Formula 120]

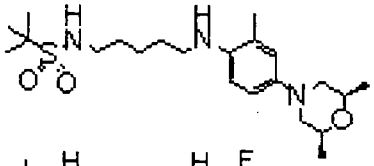
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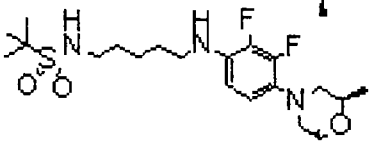
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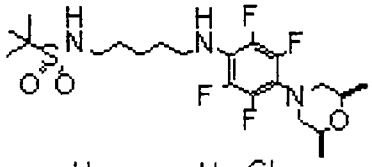
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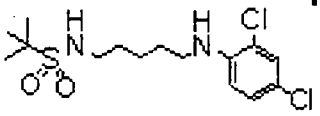
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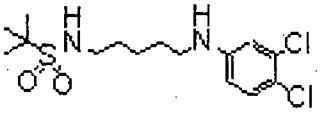
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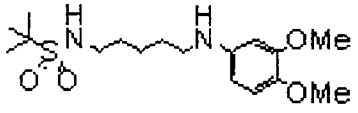
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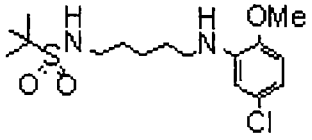
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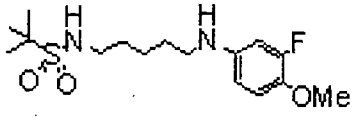
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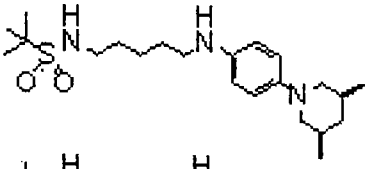
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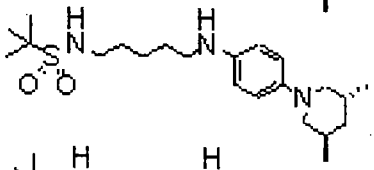
Ic-32 

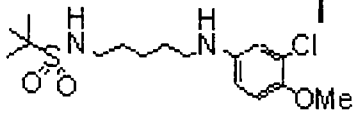
Ic-33 

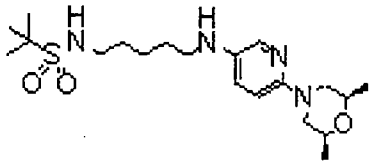
Ic-35 

Ic-36 

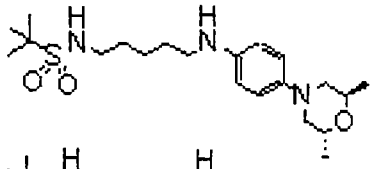
Ic-37 

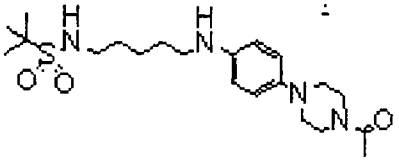
Ic-38 

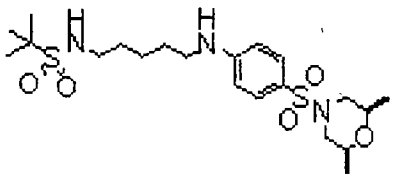
Ic-39 

Ic-40 

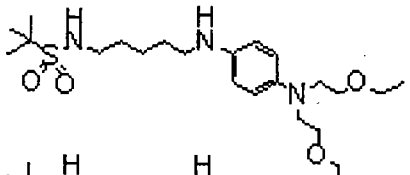
Ic-41 

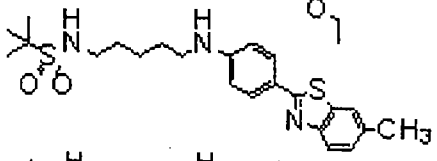
Ic-42 

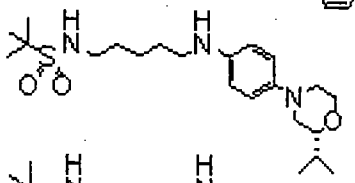
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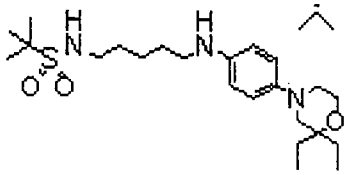
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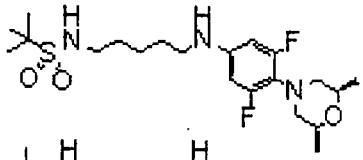
[Formula 121]

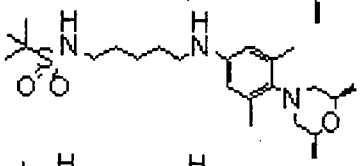
Ic-45 

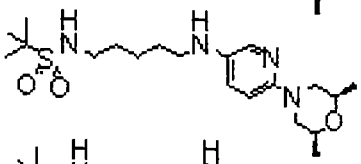
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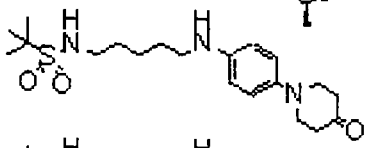
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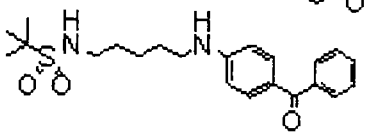
Ic-48 

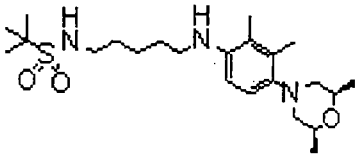
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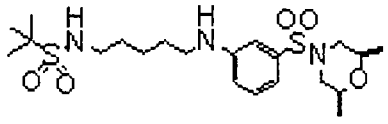
Ic-50 

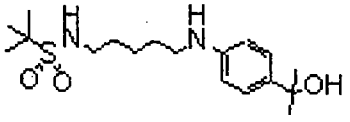
Ic-51 

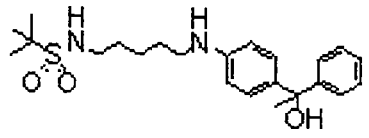
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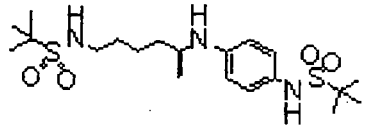
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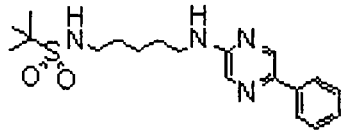
Ic-54 

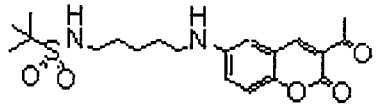
Ic-55 

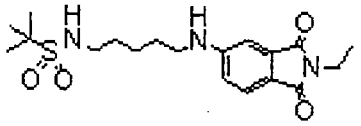
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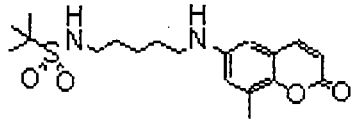
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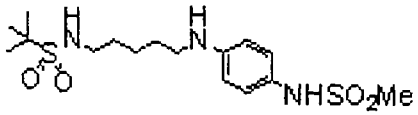
Ic-58 

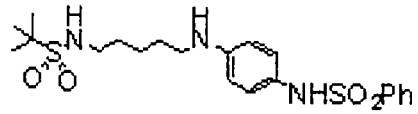
Ic-59 

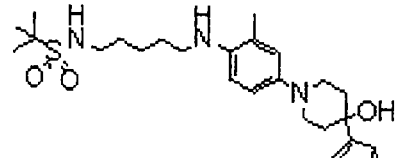
Ic-60 

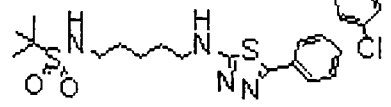
Ic-61 

Ic-62 

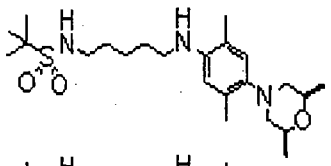
Ic-63 

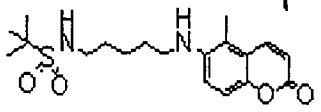
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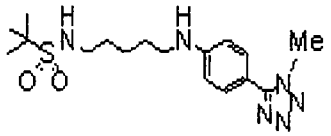
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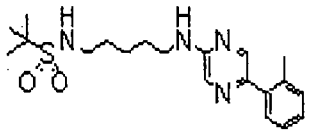
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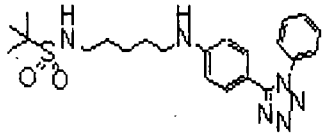
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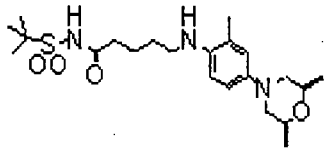
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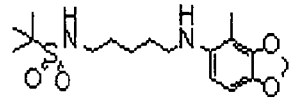
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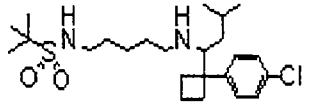
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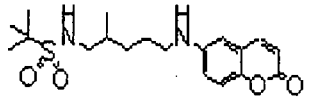
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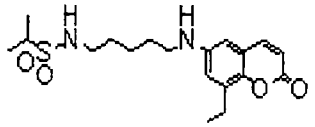
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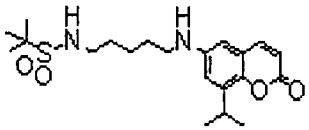
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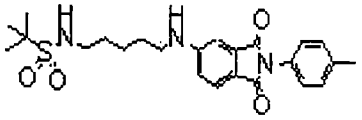
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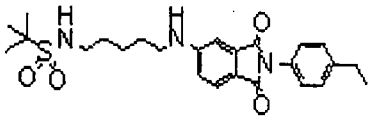
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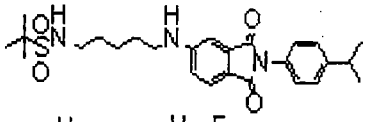
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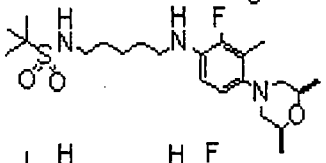
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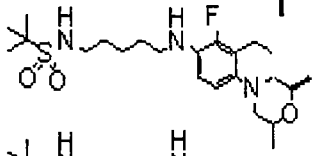
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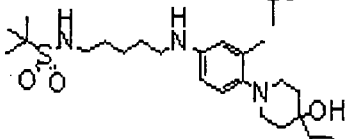
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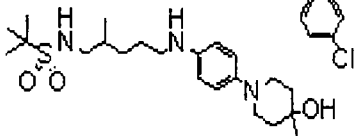
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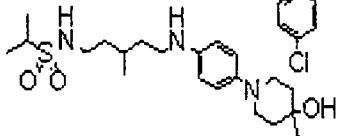
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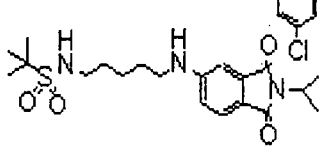
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Ic-83 

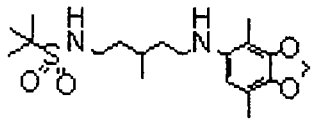
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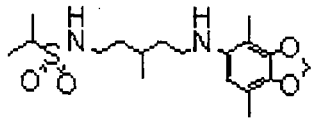
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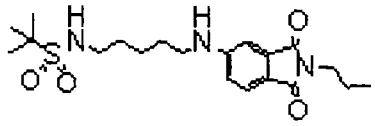
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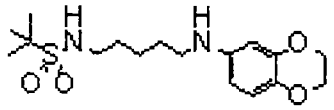
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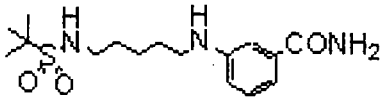
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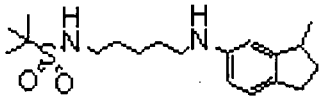
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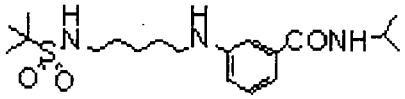
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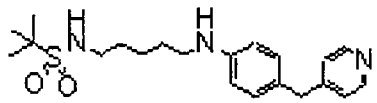
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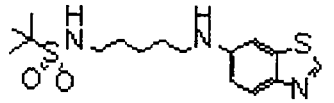
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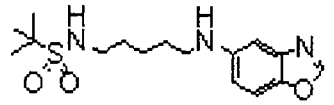
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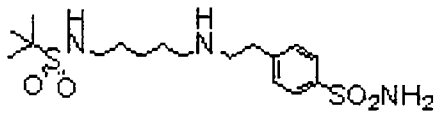
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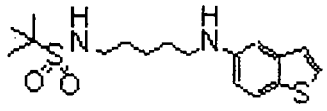
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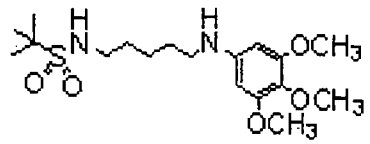
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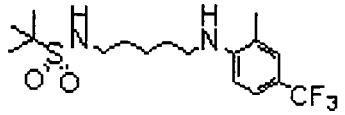
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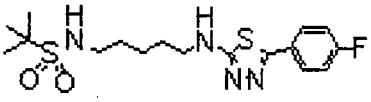
Ic-98 

Ic-99 

Ic-100 

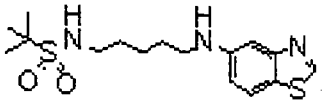
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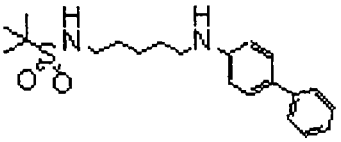
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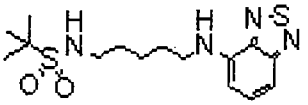
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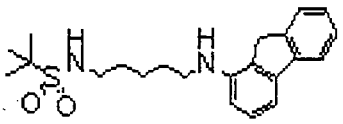
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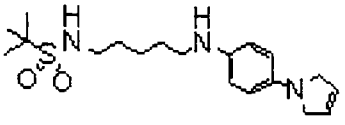
Ic-105 

Ic-106 

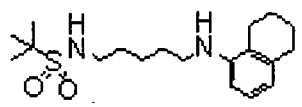
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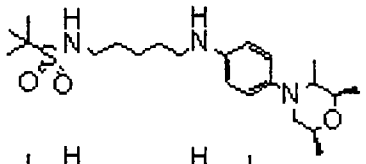
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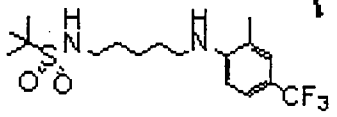
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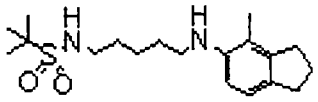
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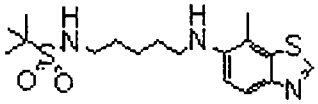
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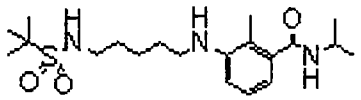
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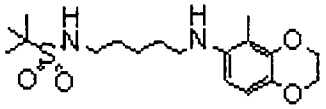
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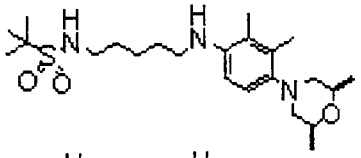
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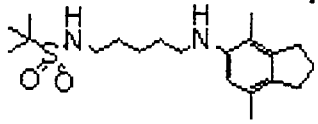
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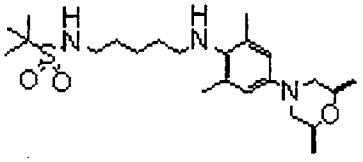
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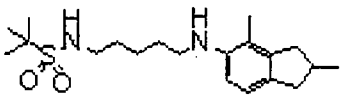
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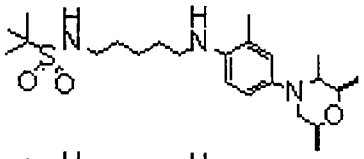
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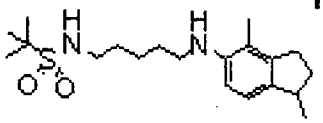
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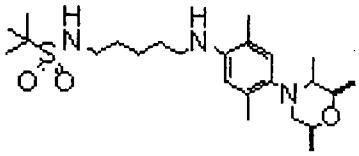
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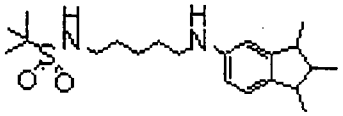
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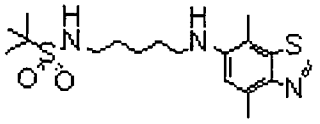
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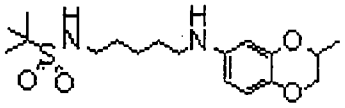
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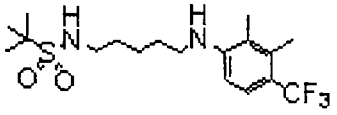
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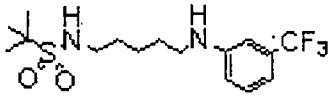
Ic-124 

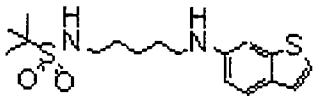
Ic-125 

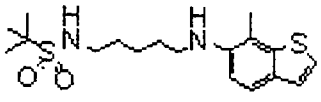
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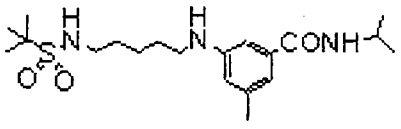
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Ic-128 

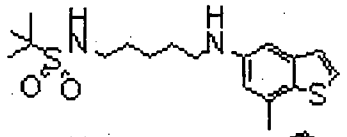
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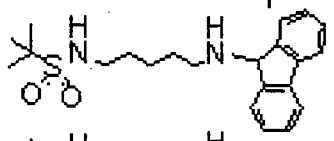
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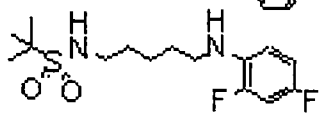
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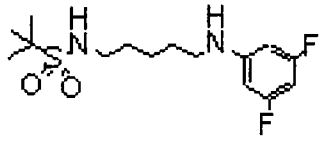
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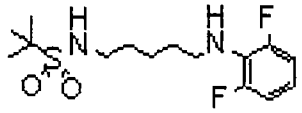
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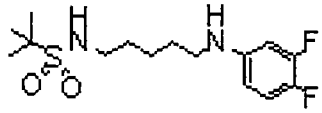
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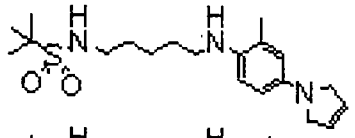
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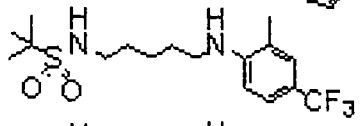
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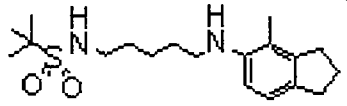
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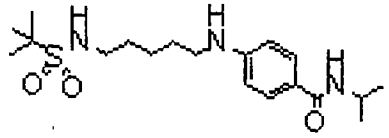
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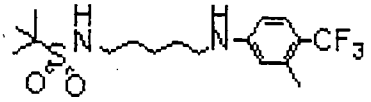
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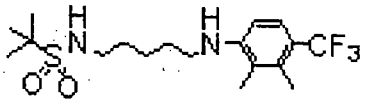
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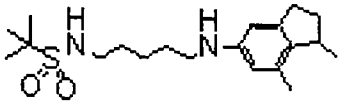
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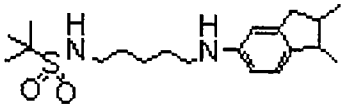
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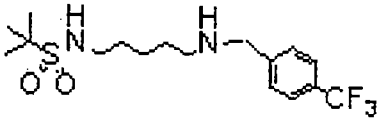
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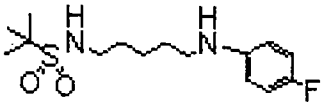
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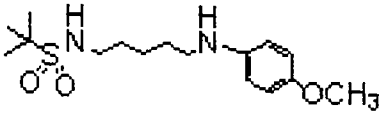
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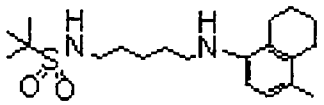
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Ic-146 

Ic-147 

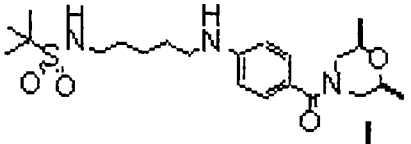
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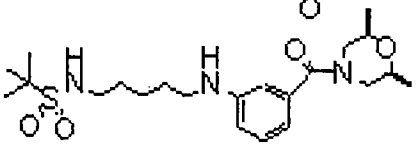
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Ic-150 

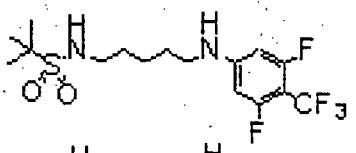
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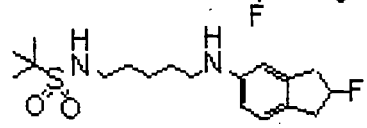
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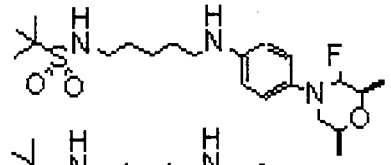
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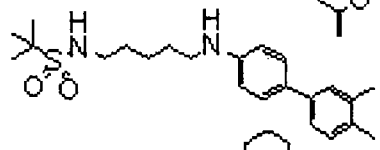
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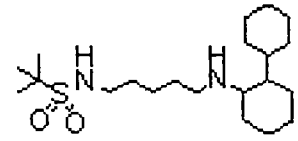
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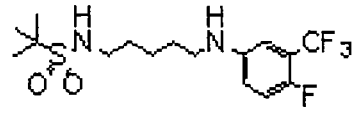
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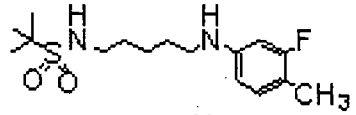
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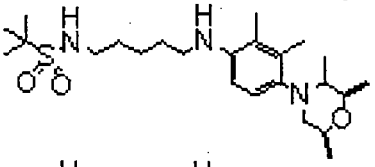
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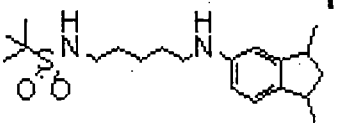
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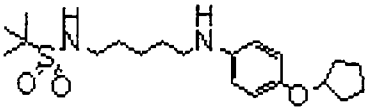
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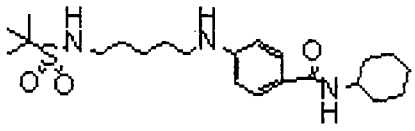
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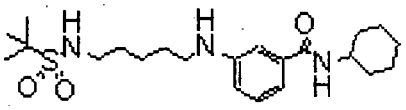
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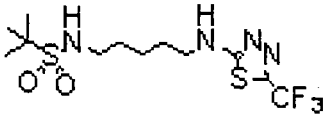
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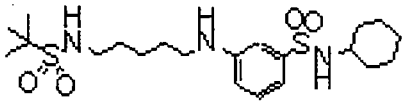
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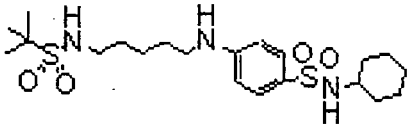
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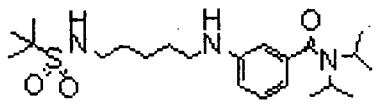
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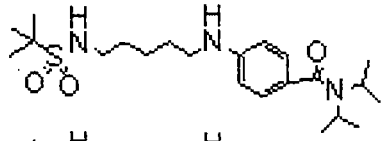
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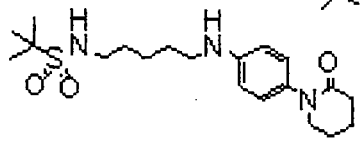
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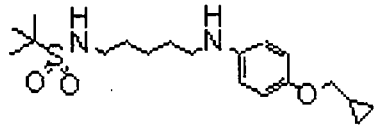
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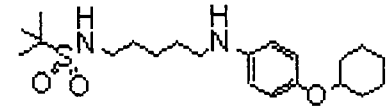
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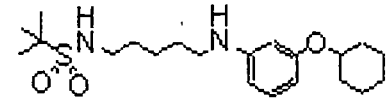
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Ic-172 

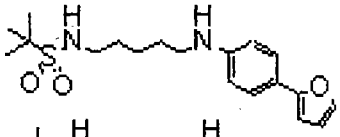
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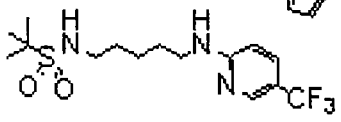
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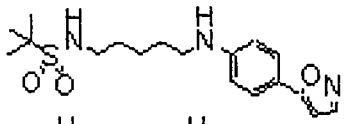
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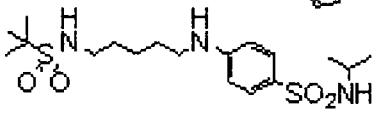
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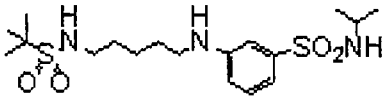
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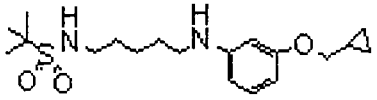
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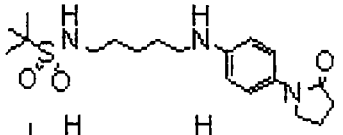
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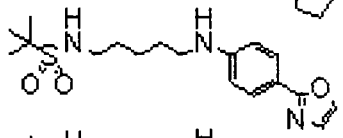
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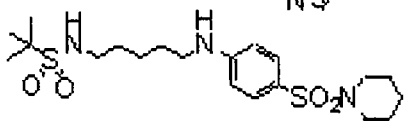
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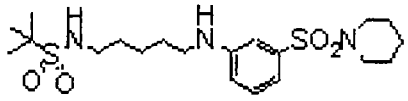
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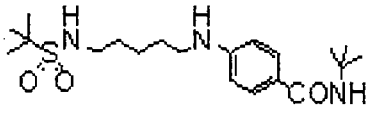
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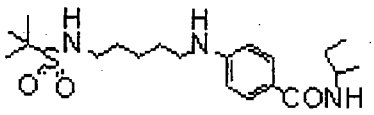
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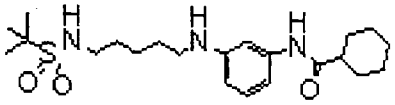
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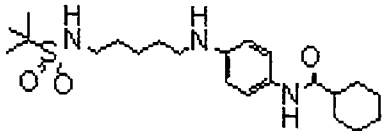
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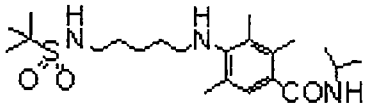
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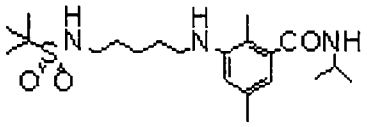
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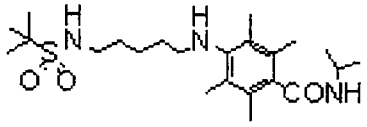
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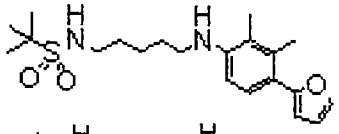
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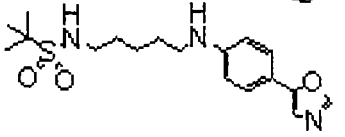
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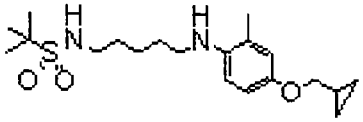
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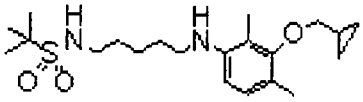
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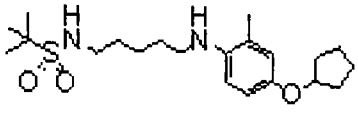
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Ic-194 

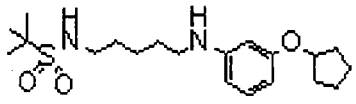
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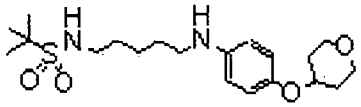
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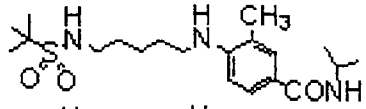
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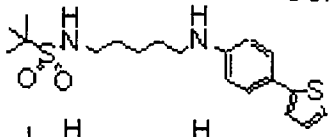
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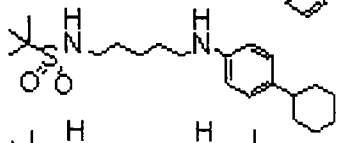
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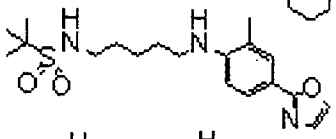
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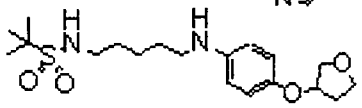
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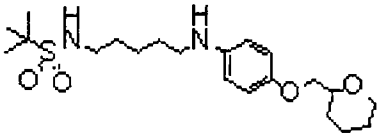
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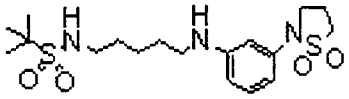
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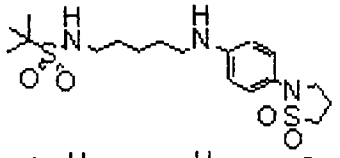
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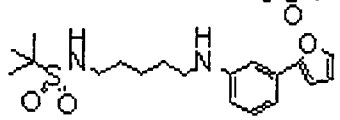
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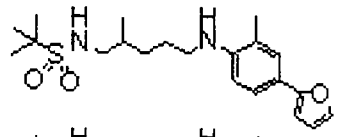
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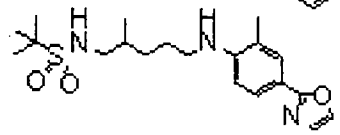
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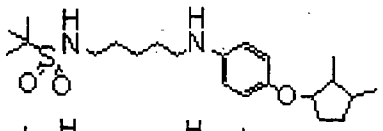
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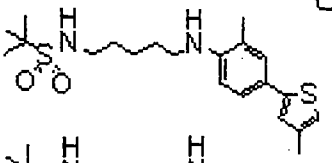
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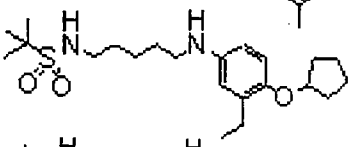
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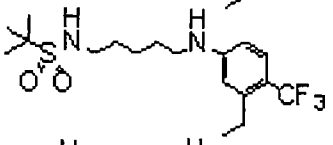
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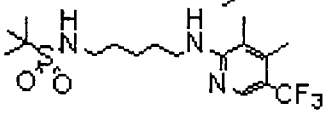
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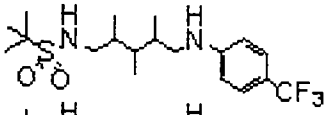
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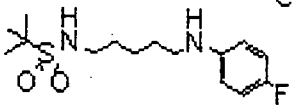
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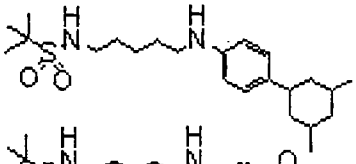
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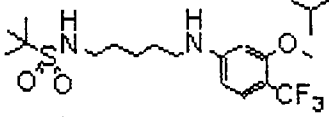
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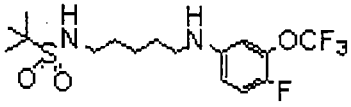
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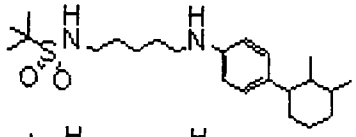
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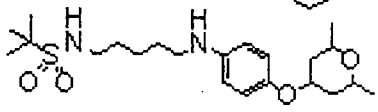
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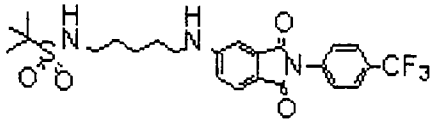
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Ic-222 

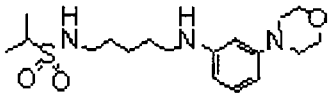
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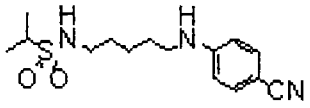
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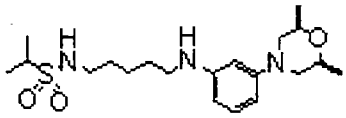
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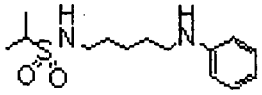
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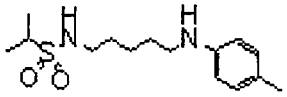
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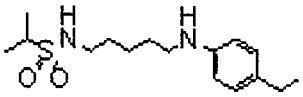
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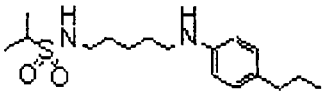
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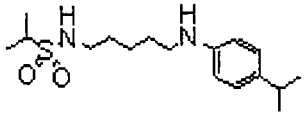
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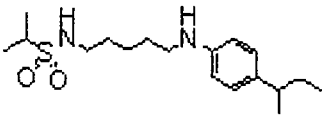
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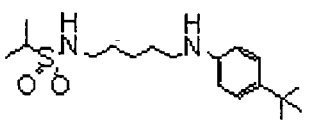
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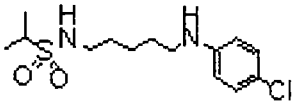
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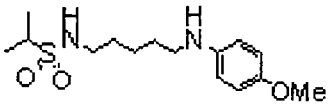
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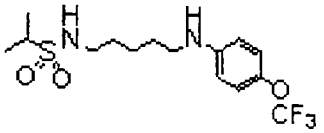
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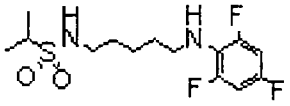
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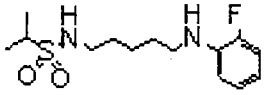
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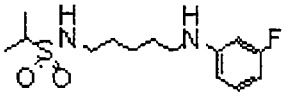
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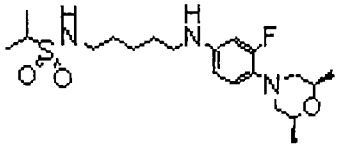
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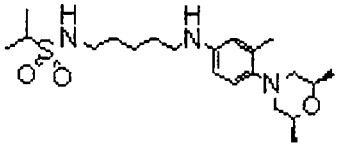
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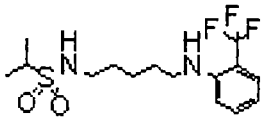
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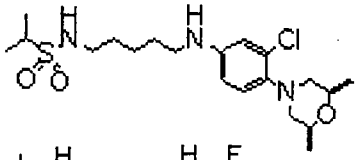
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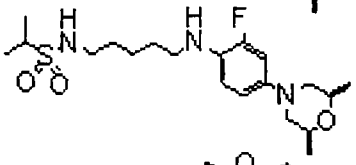
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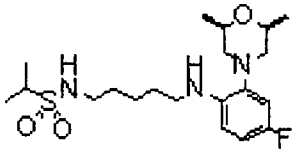
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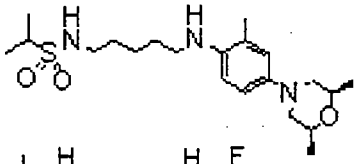
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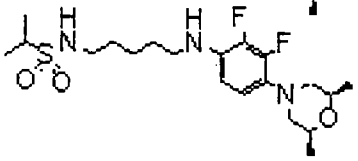
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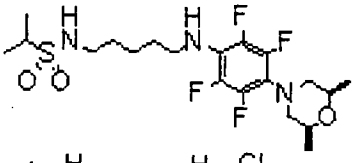
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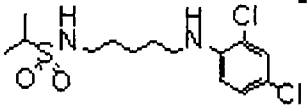
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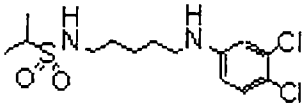
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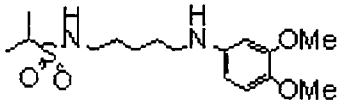
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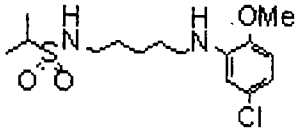
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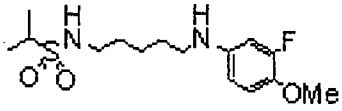
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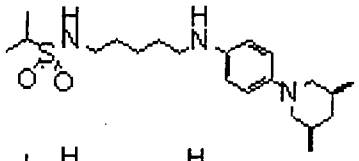
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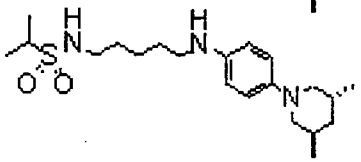
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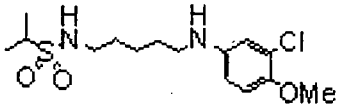
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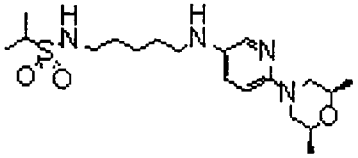
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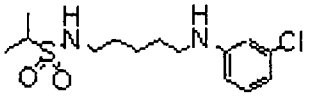
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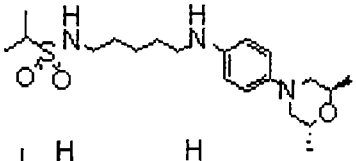
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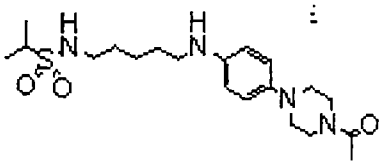
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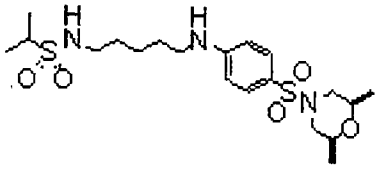
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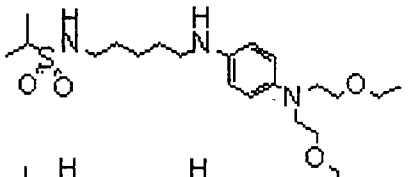
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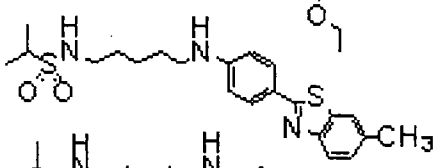
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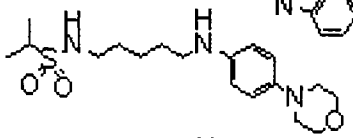
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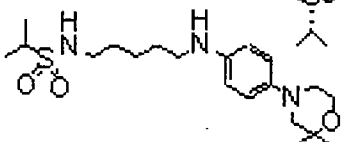
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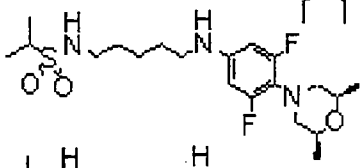
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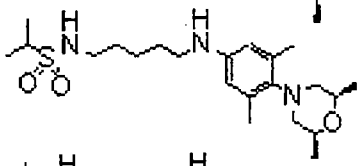
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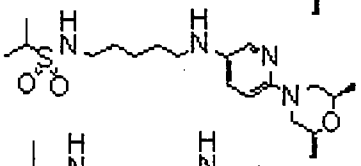
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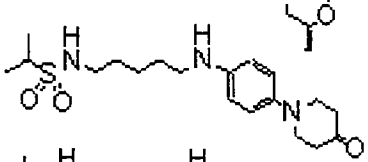
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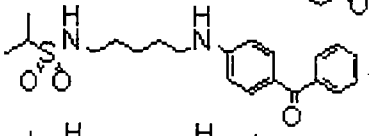
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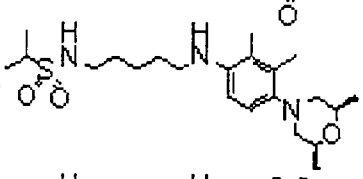
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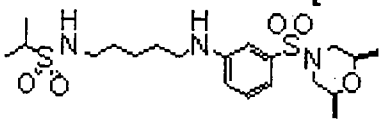
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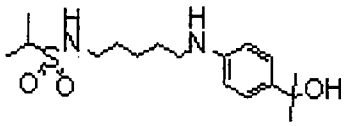
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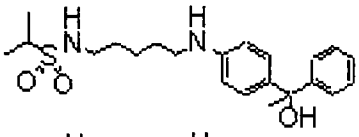
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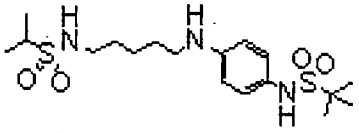
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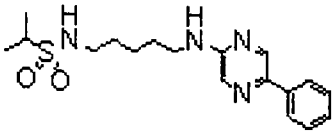
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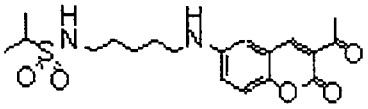
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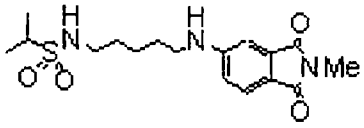
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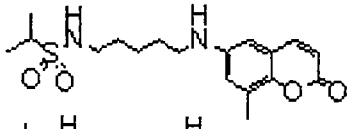
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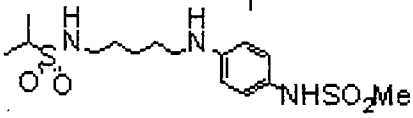
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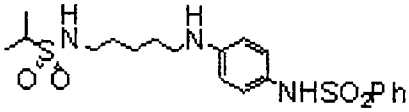
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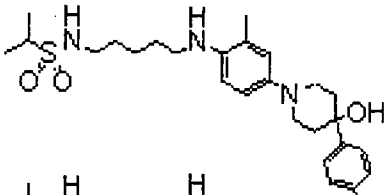
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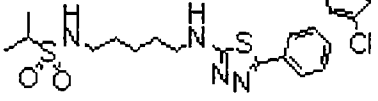
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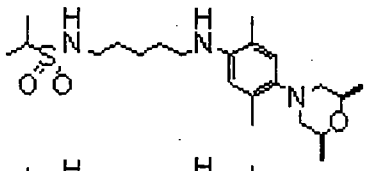
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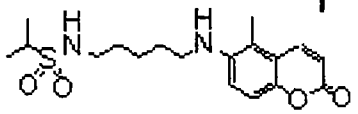
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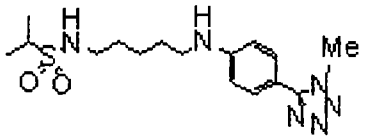
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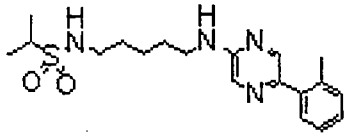
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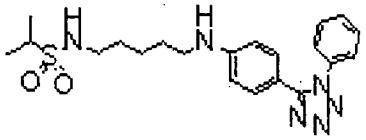
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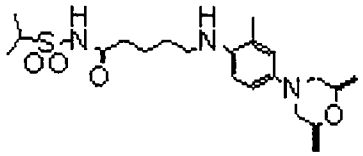
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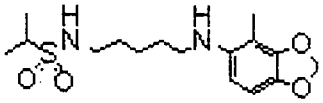
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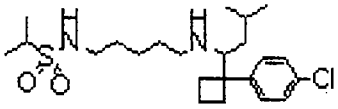
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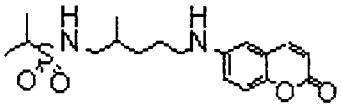
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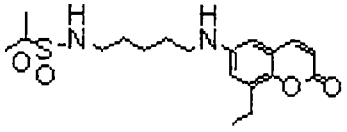
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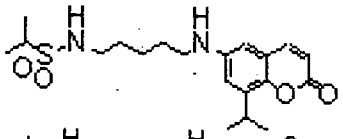
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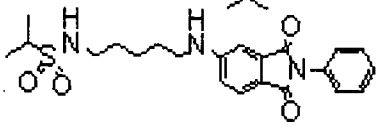
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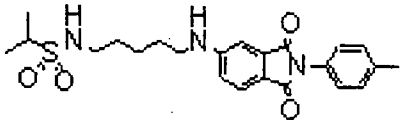
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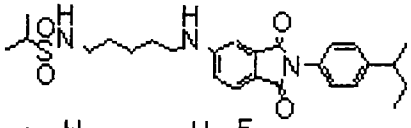
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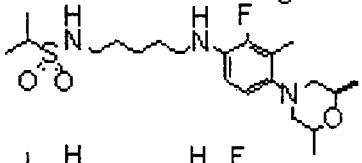
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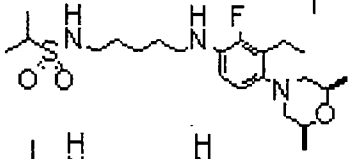
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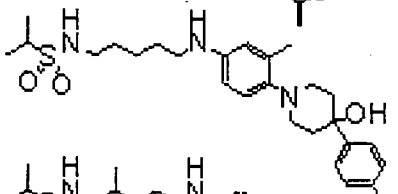
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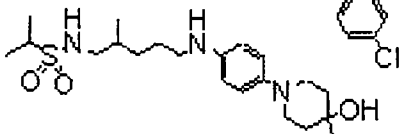
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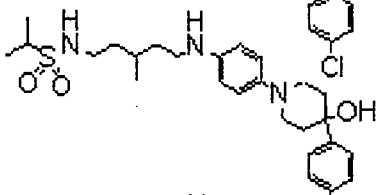
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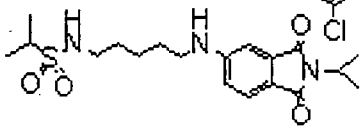
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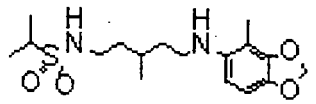
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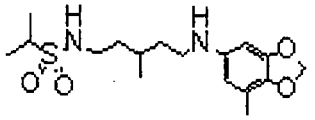
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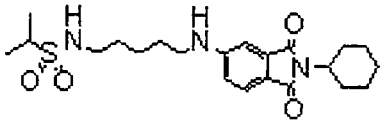
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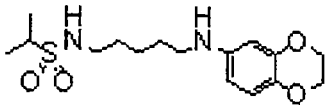
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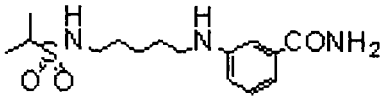
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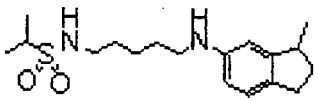
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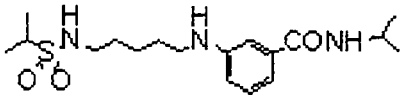
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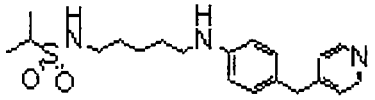
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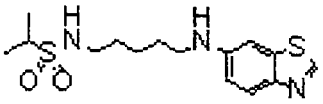
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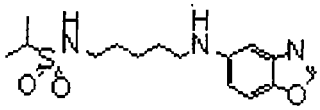
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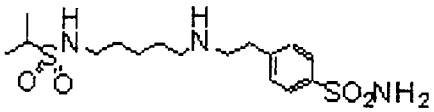
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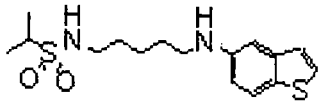
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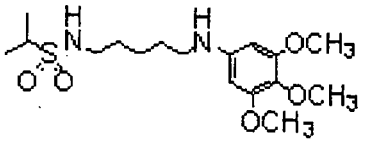
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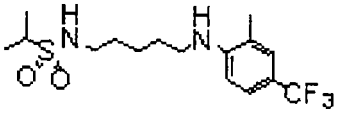
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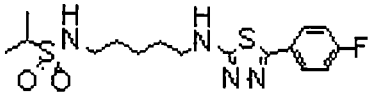
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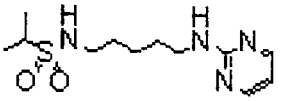
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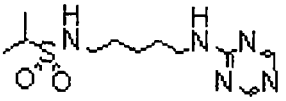
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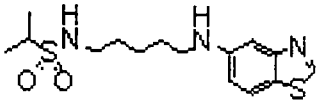
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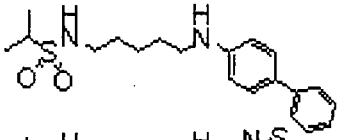
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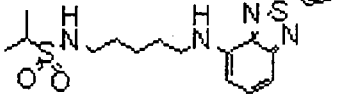
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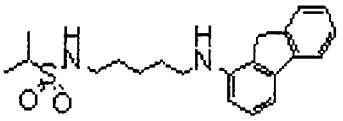
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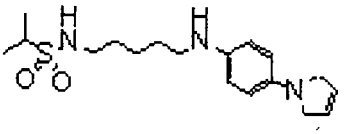
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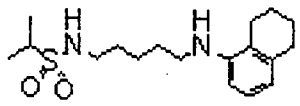
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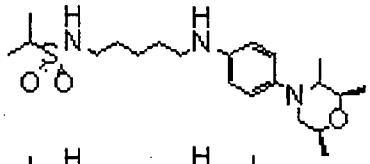
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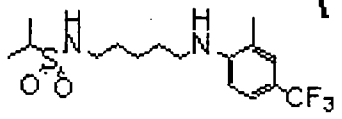
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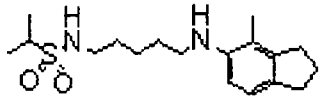
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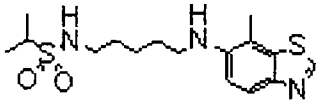
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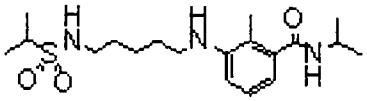
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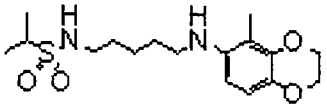
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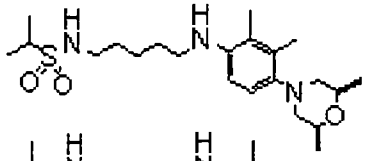
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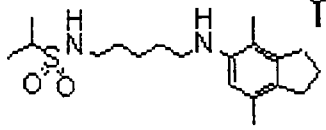
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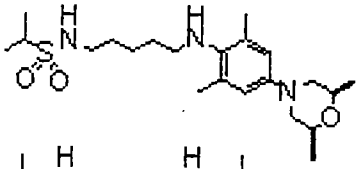
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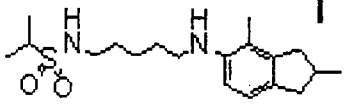
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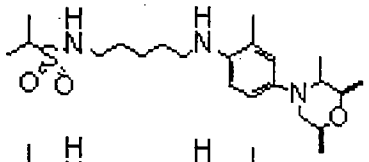
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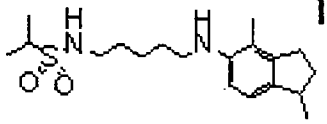
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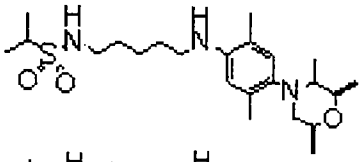
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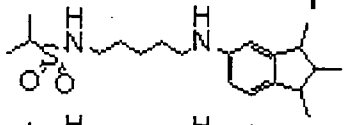
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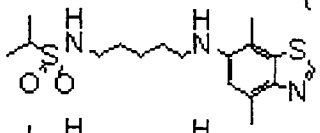
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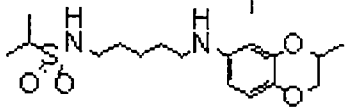
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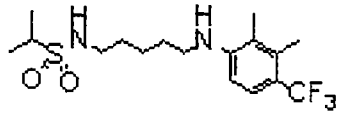
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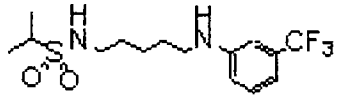
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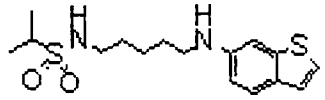
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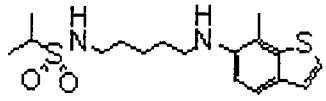
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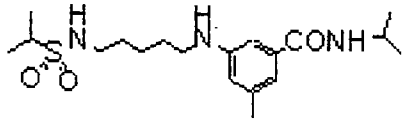
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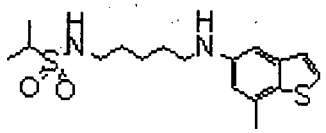
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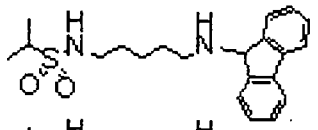
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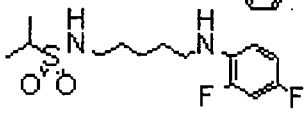
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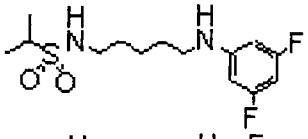
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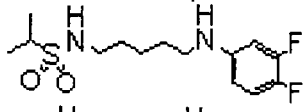
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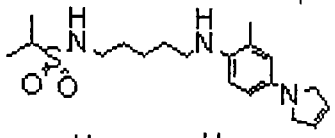
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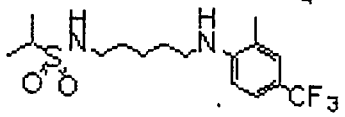
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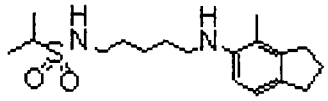
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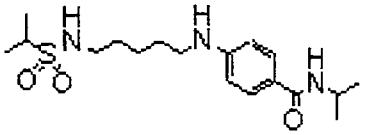
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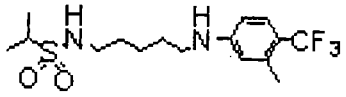
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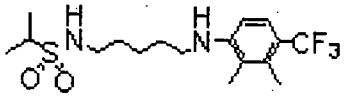
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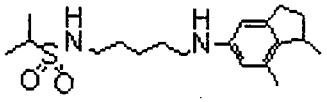
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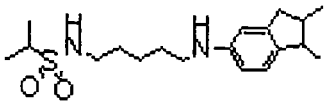
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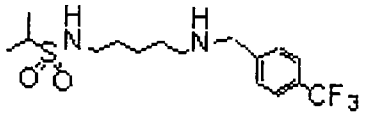
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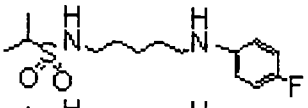
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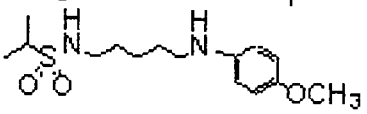
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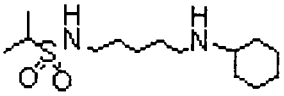
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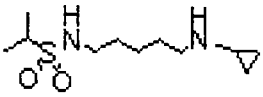
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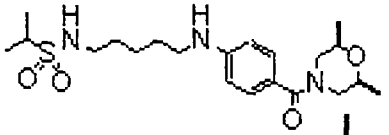
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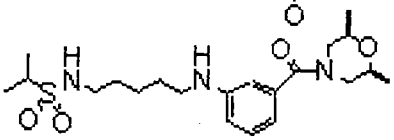
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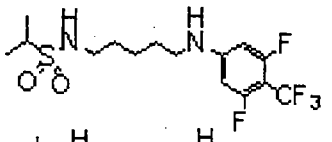
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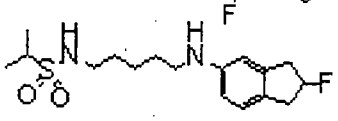
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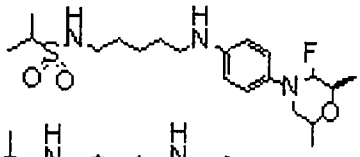
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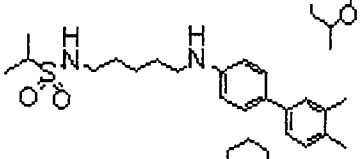
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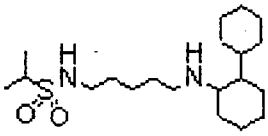
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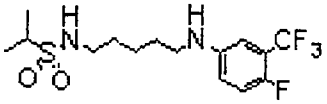
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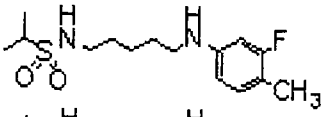
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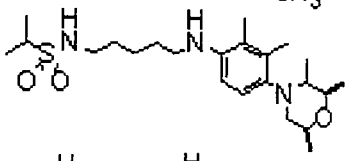
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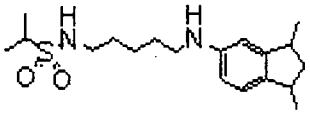
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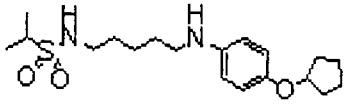
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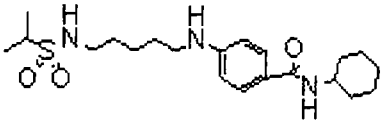
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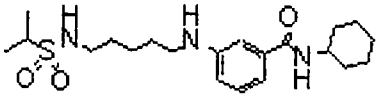
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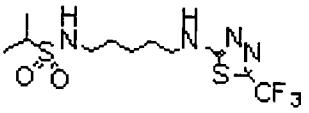
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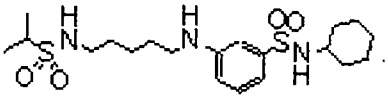
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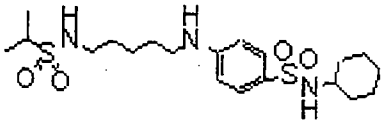
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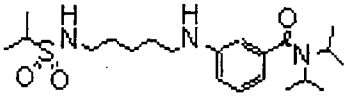
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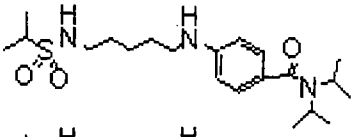
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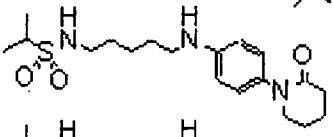
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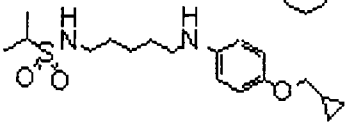
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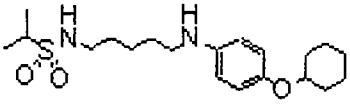
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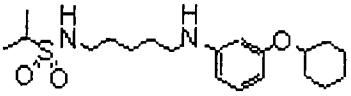
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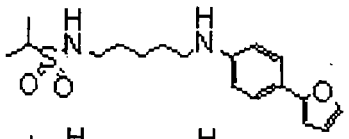
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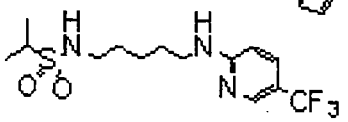
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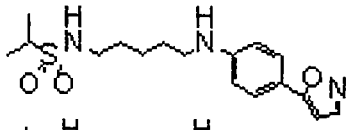
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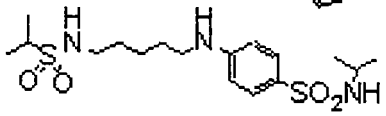
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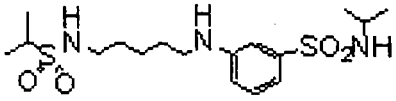
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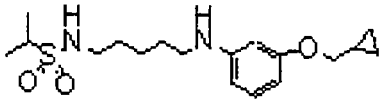
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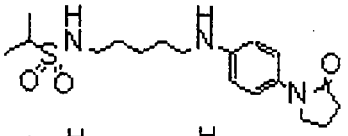
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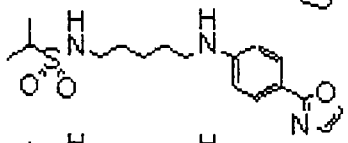
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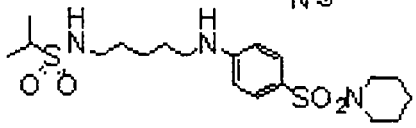
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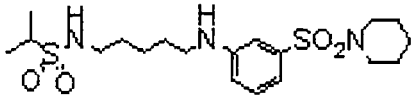
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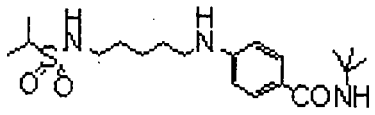
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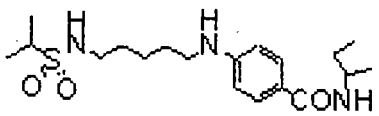
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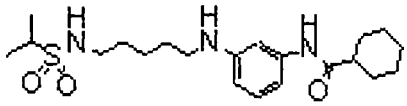
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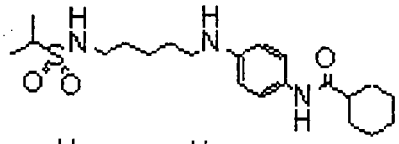
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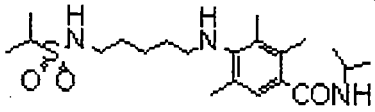
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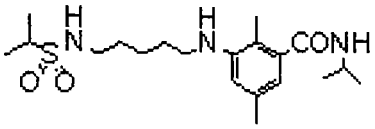
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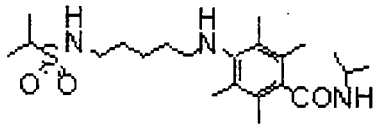
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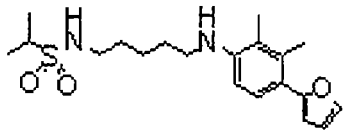
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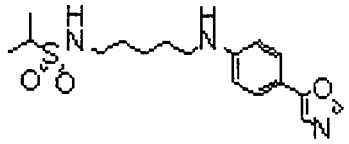
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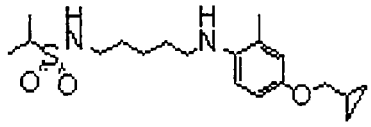
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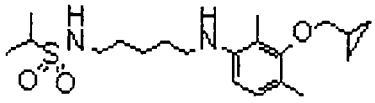
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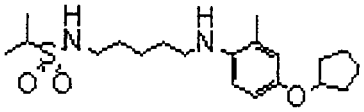
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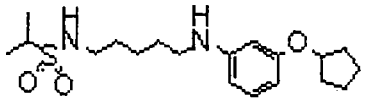
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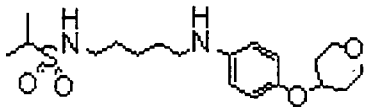
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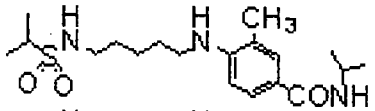
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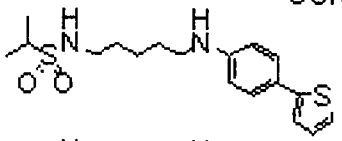
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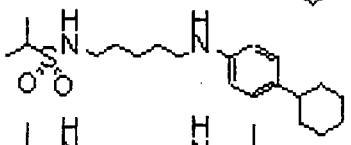
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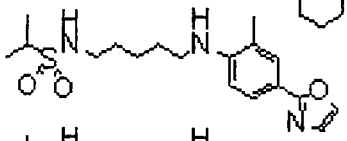
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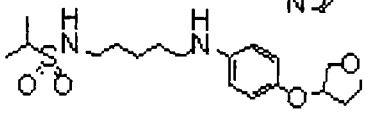
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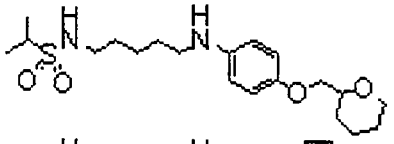
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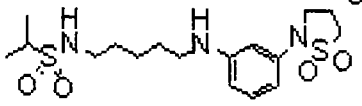
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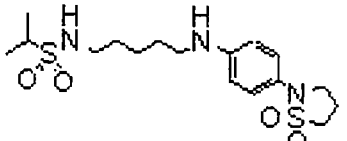
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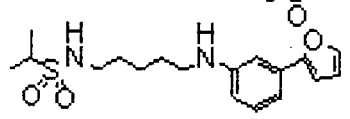
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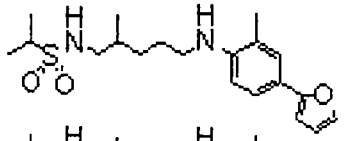
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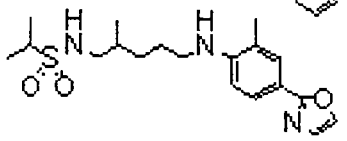
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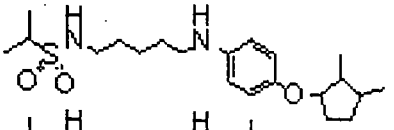
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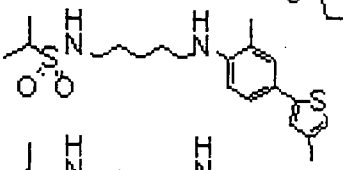
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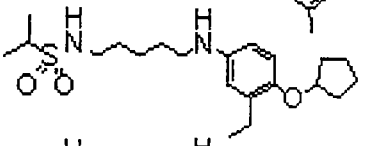
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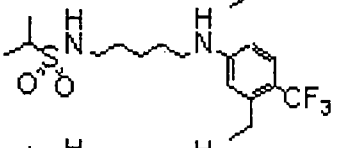
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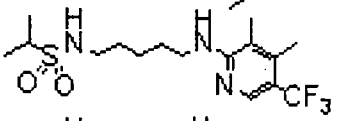
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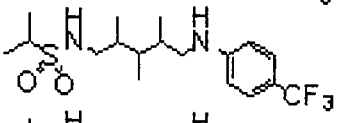
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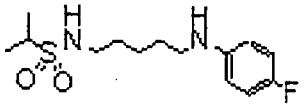
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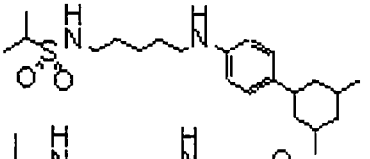
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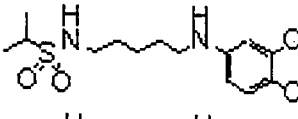
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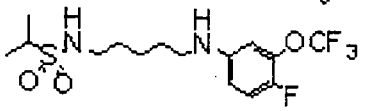
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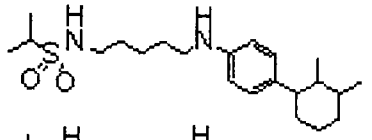
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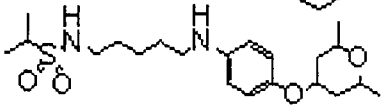
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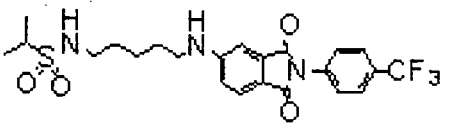
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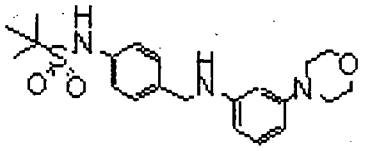
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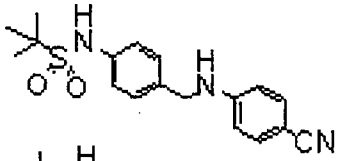
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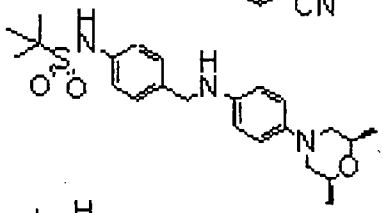
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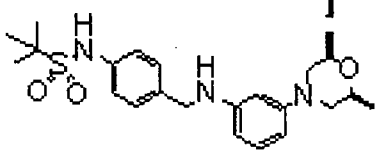
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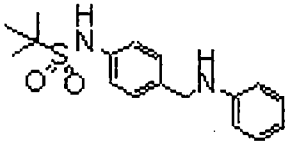
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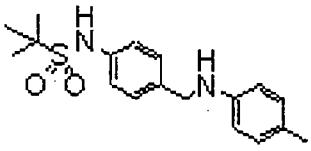
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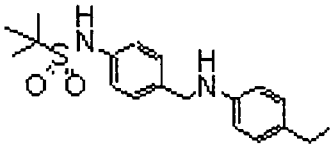
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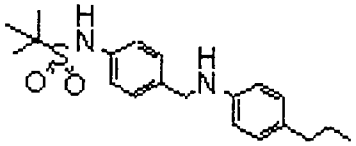
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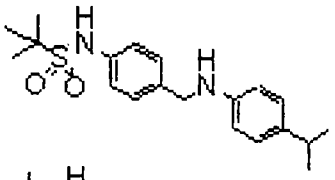
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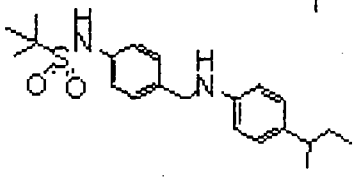
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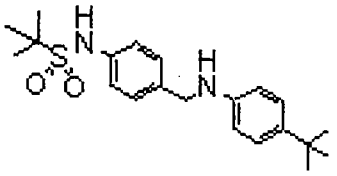
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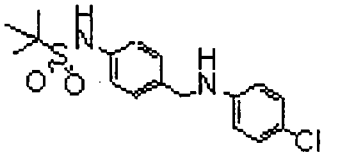
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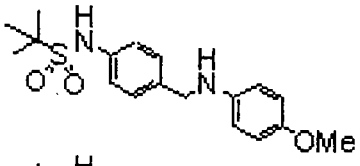
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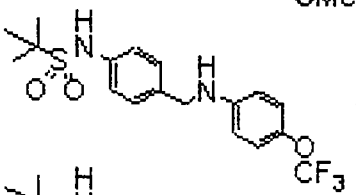
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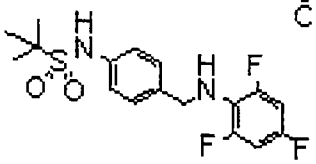
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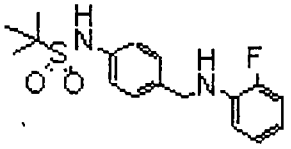
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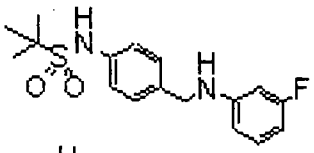
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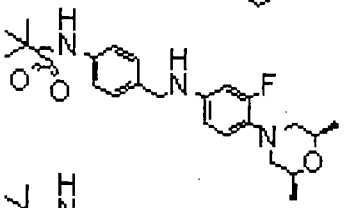
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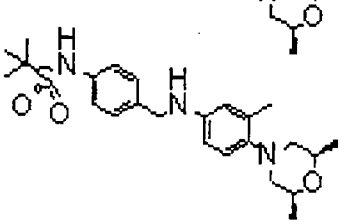
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Ig-18 

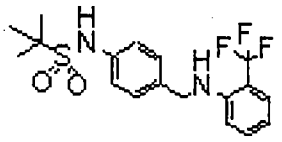
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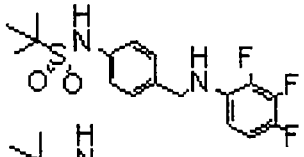
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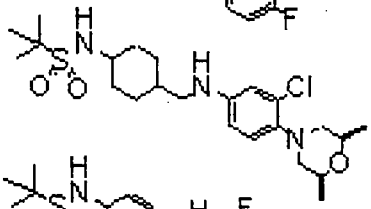
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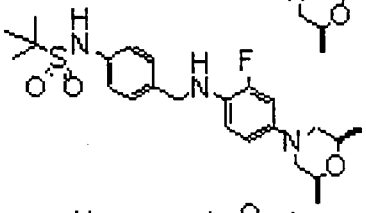
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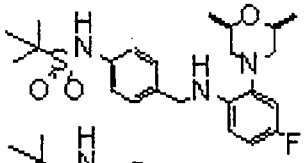
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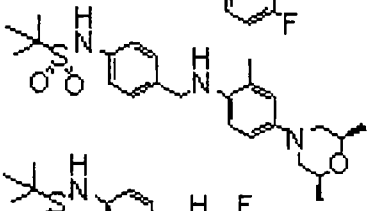
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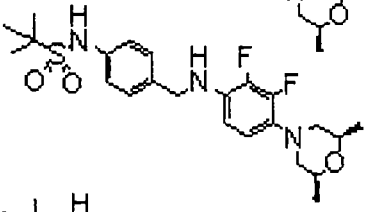
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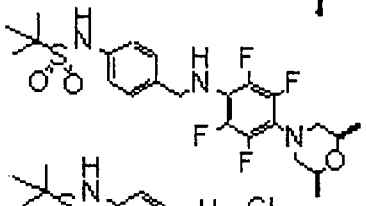
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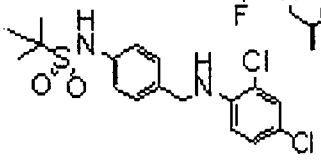
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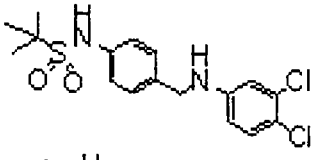
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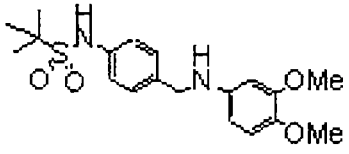
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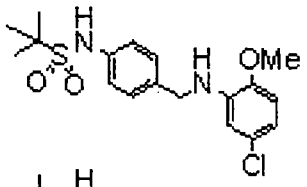
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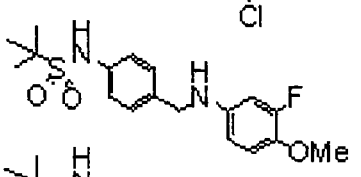
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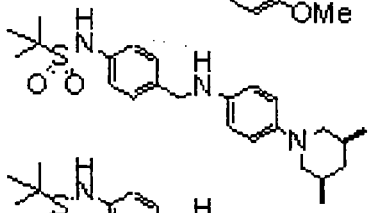
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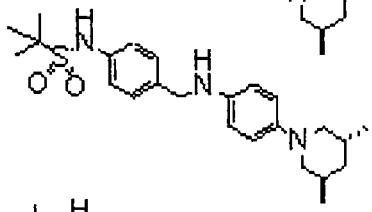
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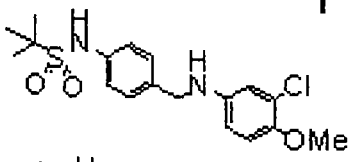
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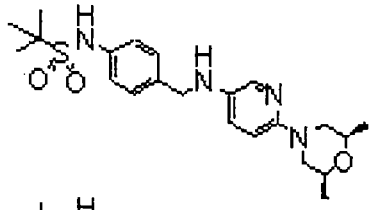
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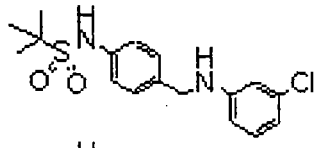
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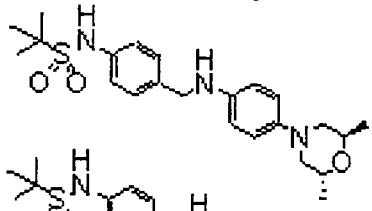
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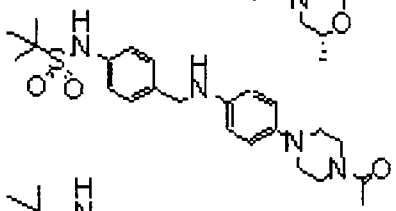
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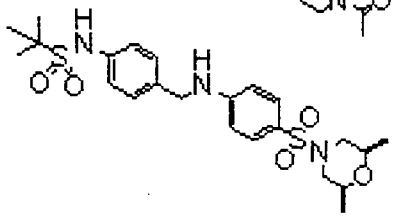
Ig-39 

Ig-40 

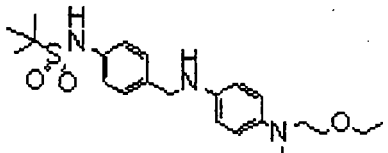
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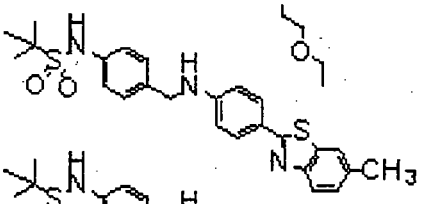
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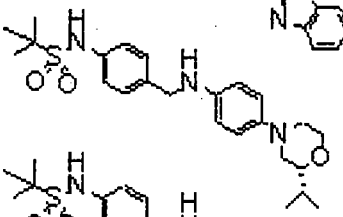
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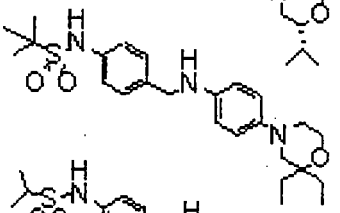
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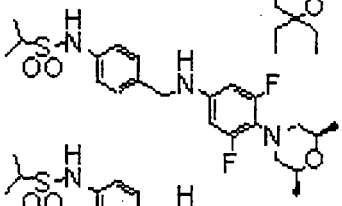
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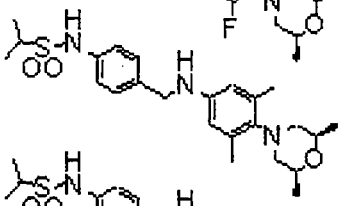
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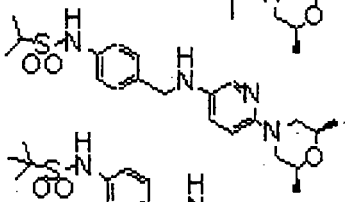
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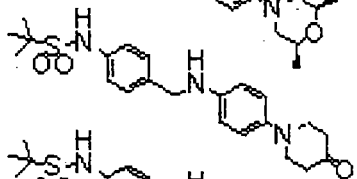
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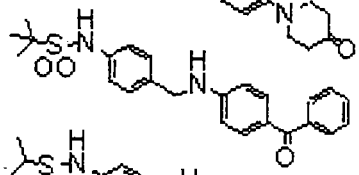
Ig-48 

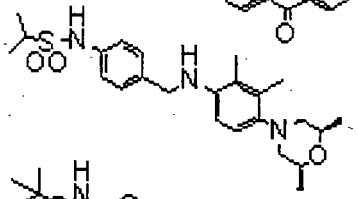
Ig-49 

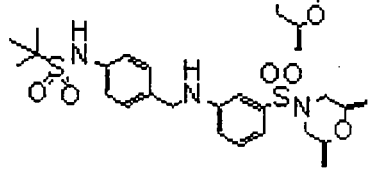
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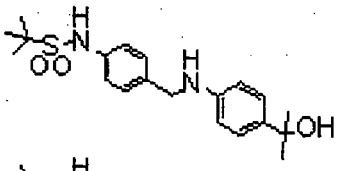
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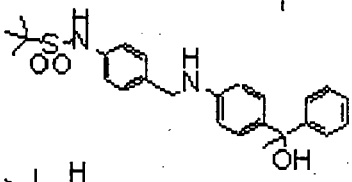
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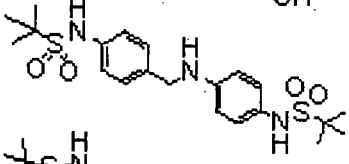
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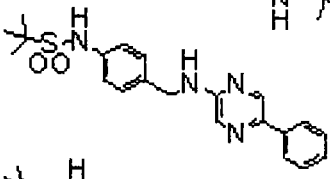
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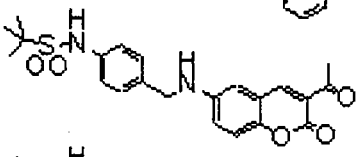
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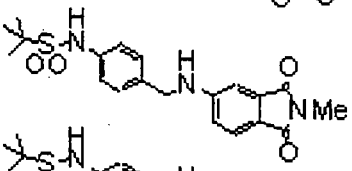
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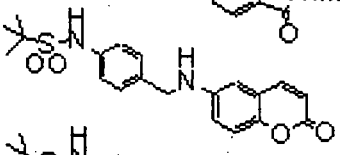
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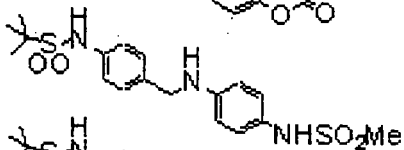
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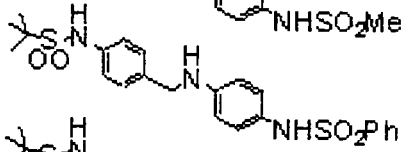
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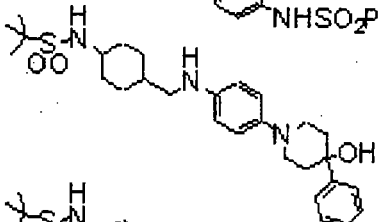
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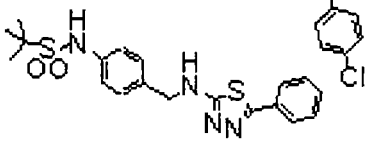
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Ig-62 

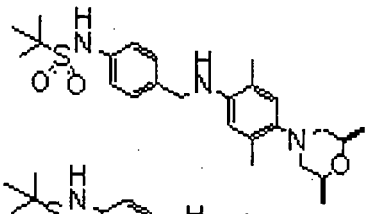
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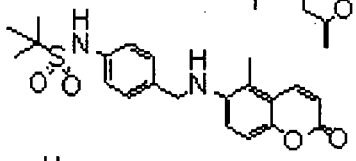
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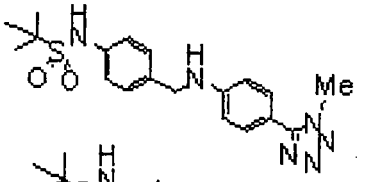
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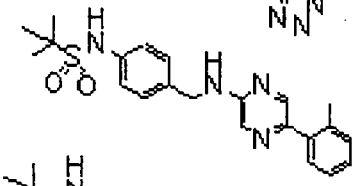
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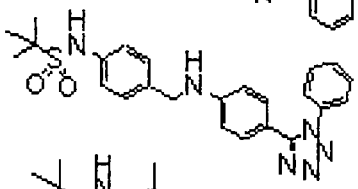
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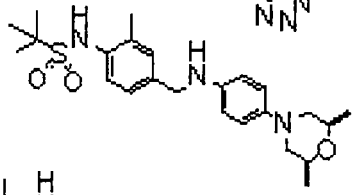
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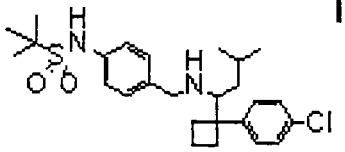
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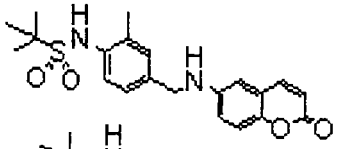
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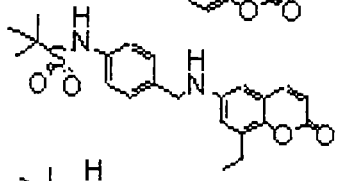
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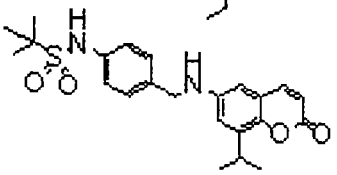
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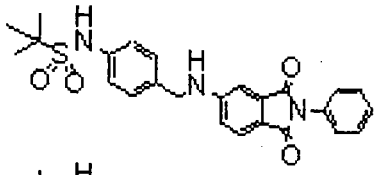
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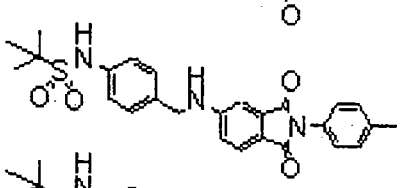
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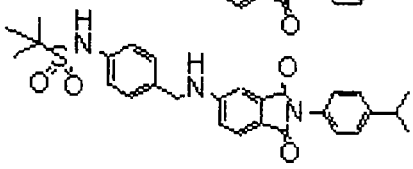
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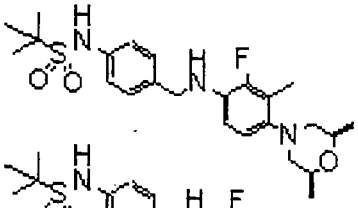
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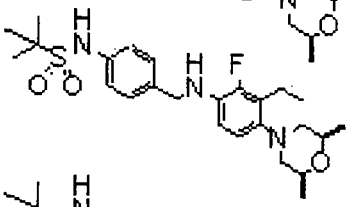
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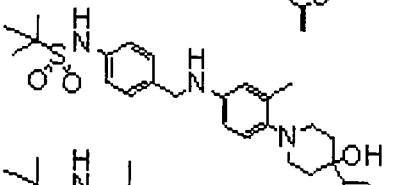
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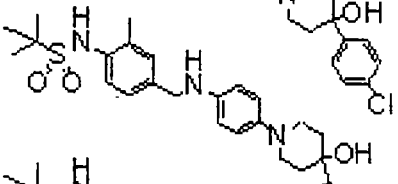
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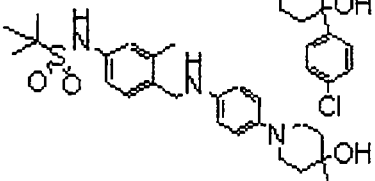
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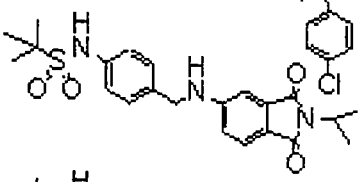
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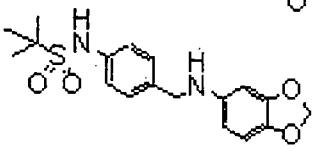
Ig-83 

Ig-84 

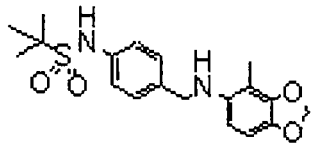
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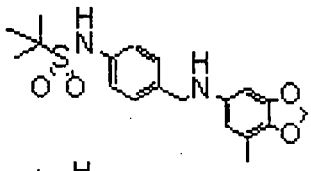
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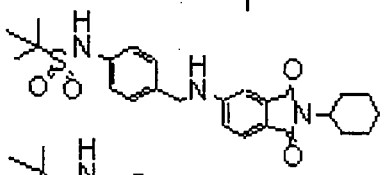
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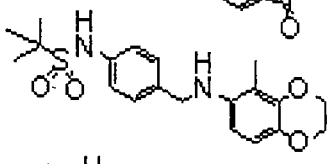
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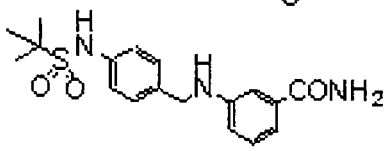
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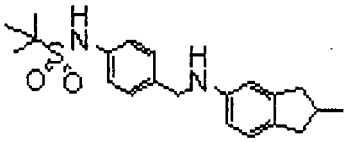
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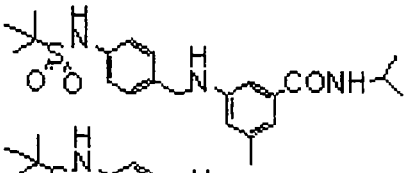
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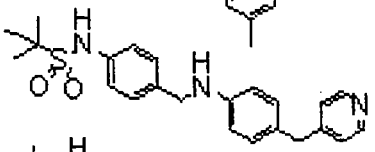
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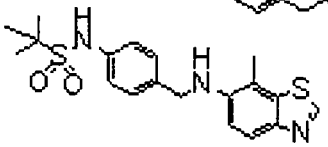
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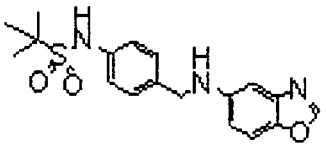
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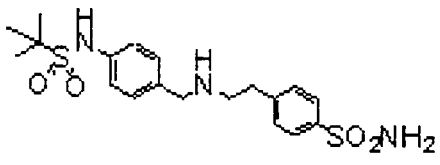
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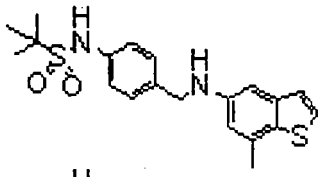
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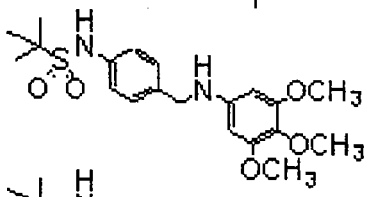
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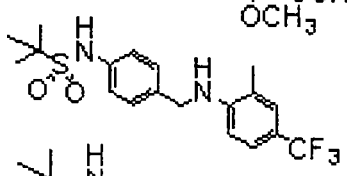
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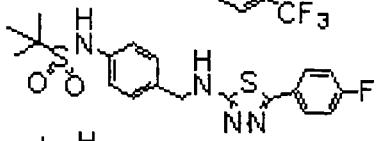
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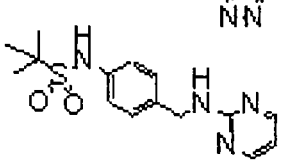
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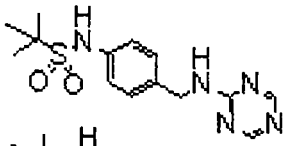
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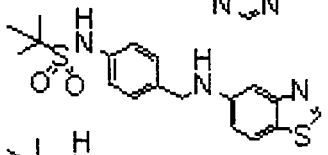
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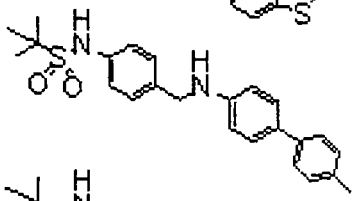
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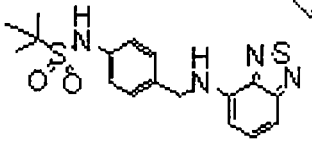
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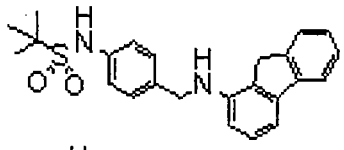
Ig-104 

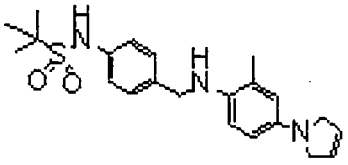
Ig-105 

Ig-106 

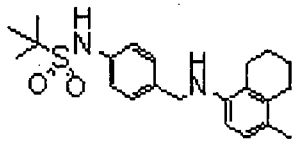
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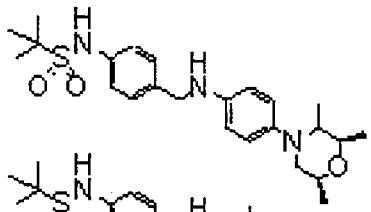
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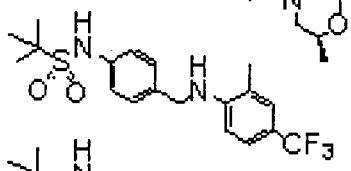
Ig-109 

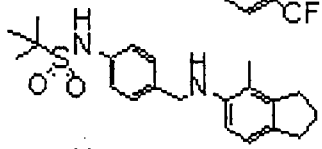
Ig-110 

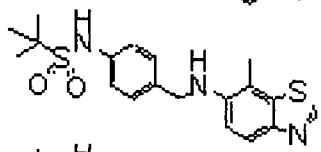
[Formula 144]

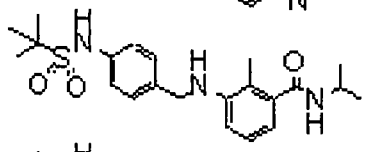
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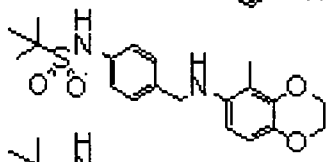
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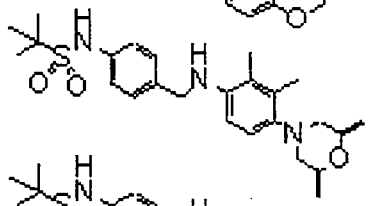
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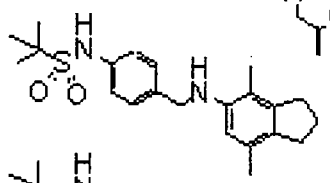
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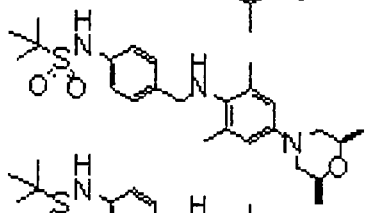
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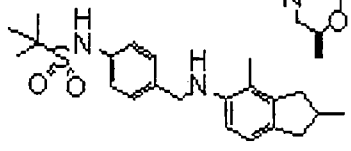
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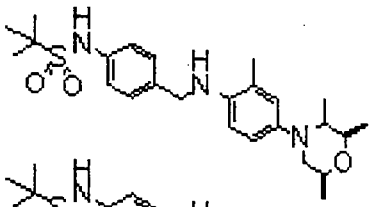
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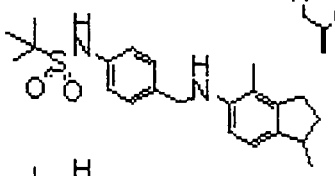
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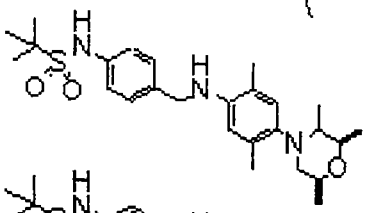
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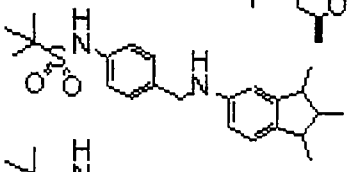
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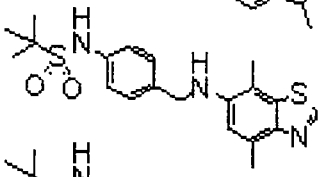
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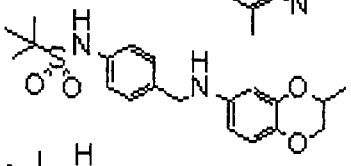
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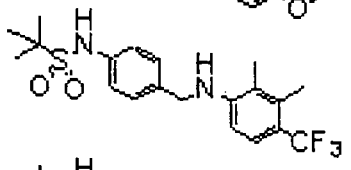
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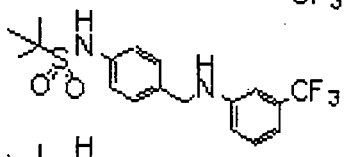
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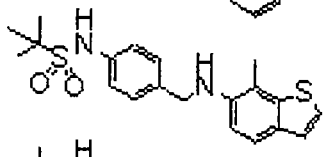
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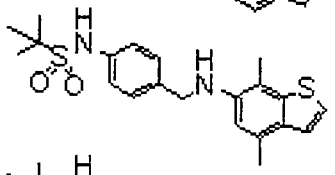
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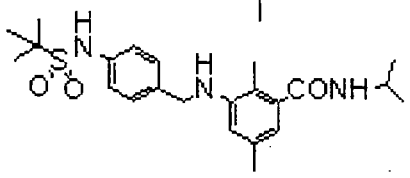
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Ig-128 

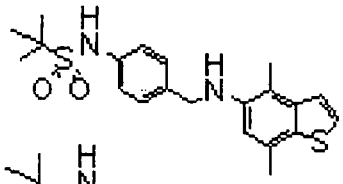
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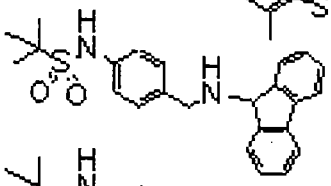
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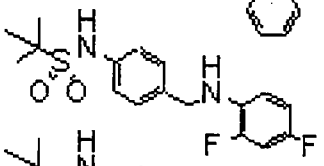
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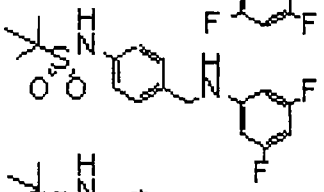
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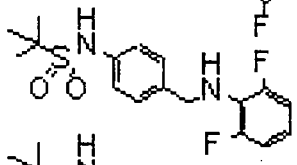
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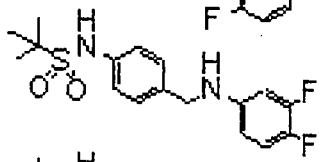
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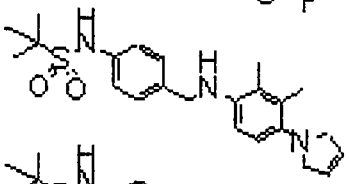
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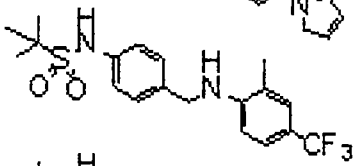
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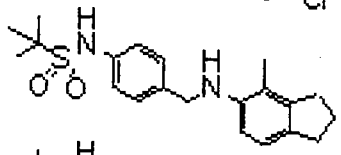
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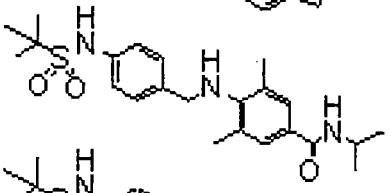
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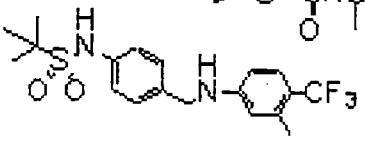
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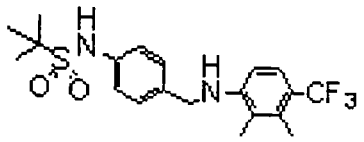
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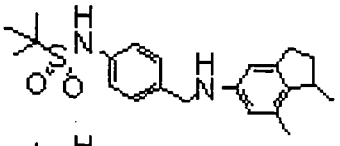
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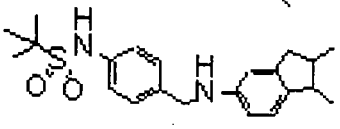
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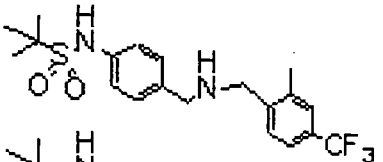
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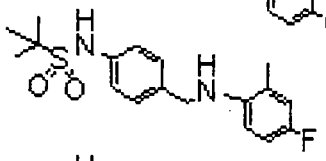
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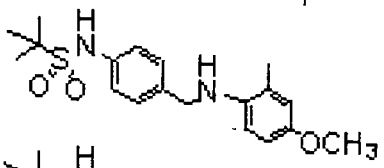
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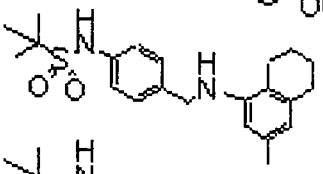
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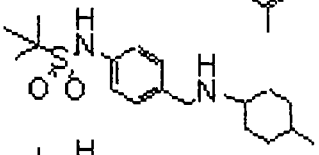
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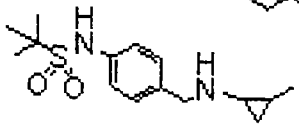
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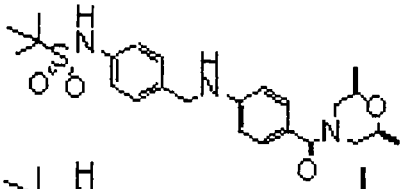
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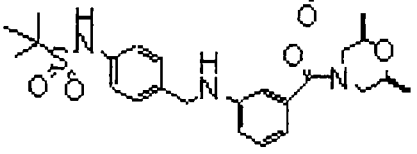
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Ig-150 

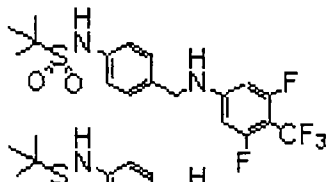
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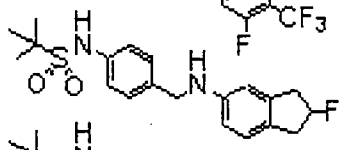
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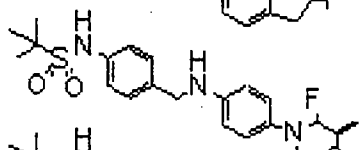
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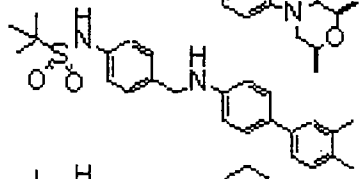
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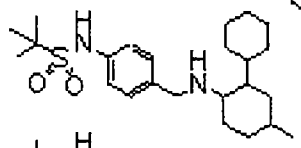
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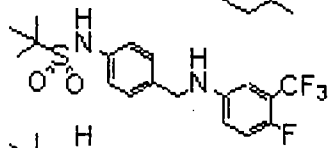
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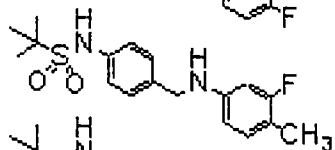
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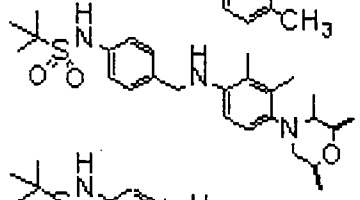
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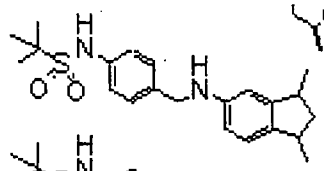
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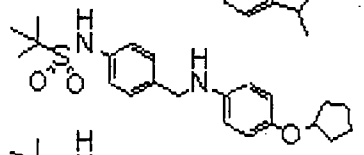
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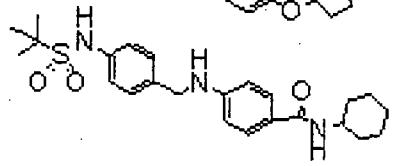
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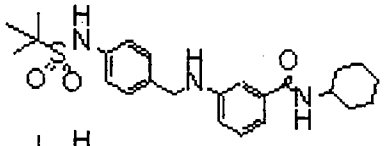
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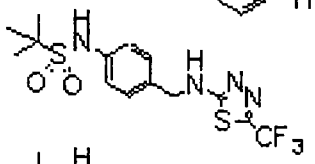
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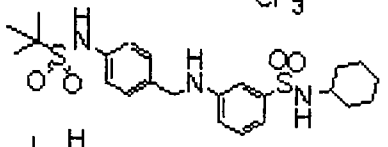
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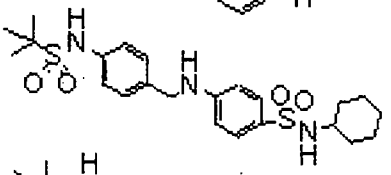
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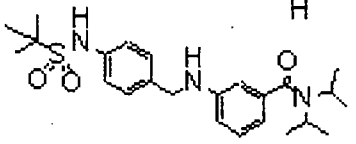
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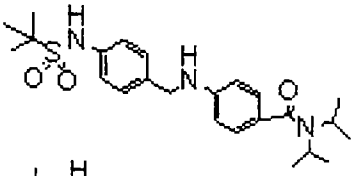
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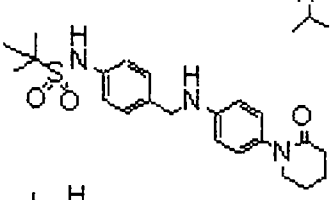
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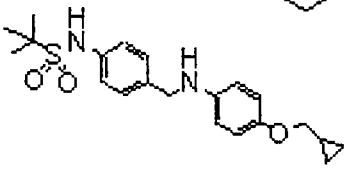
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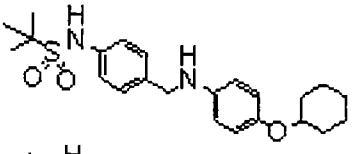
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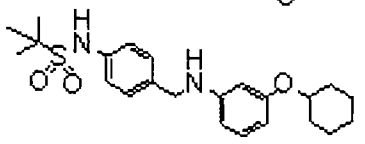
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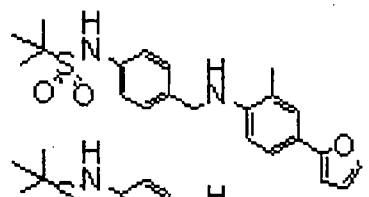
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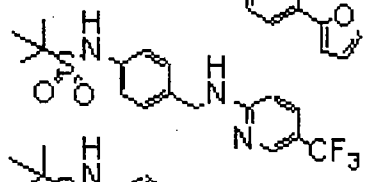
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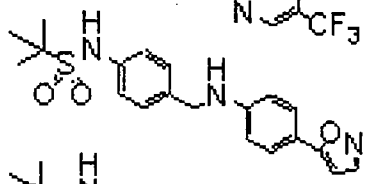
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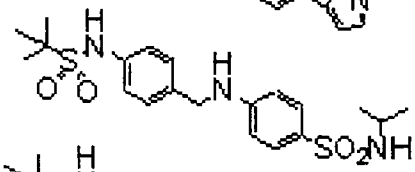
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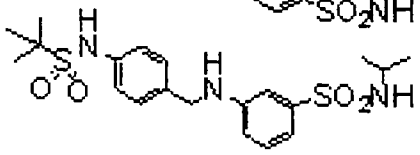
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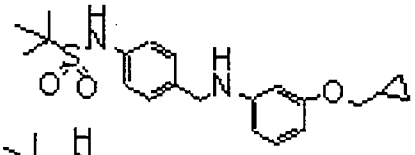
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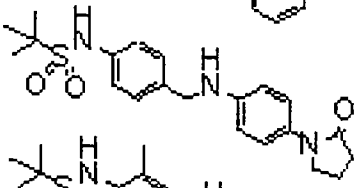
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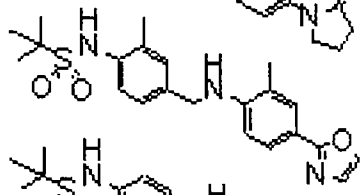
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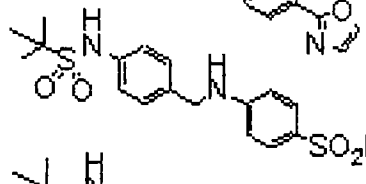
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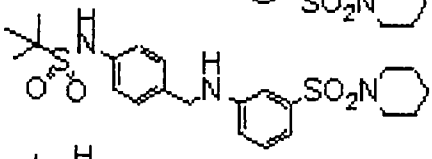
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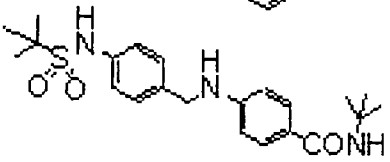
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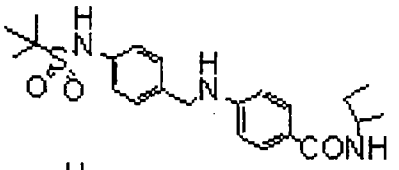
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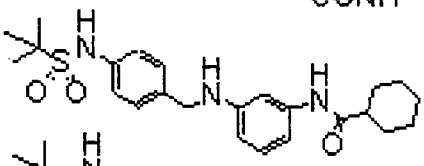
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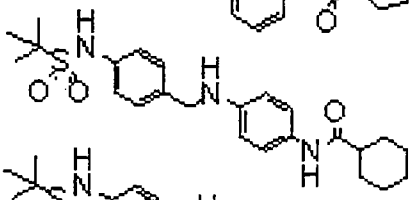
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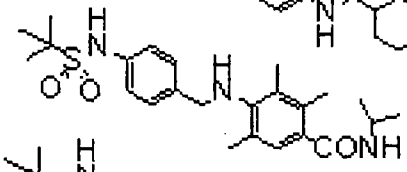
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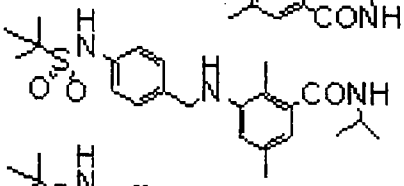
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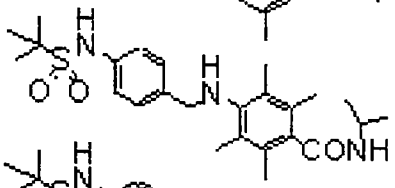
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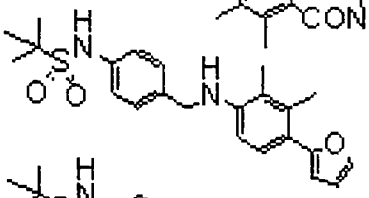
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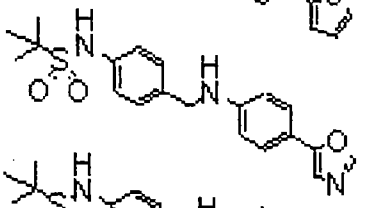
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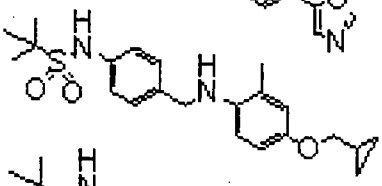
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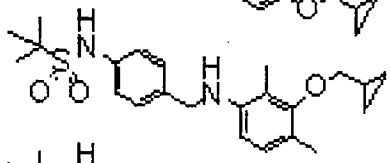
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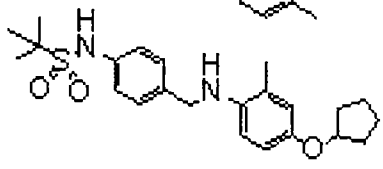
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Ig-194 

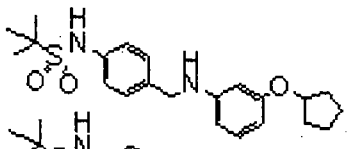
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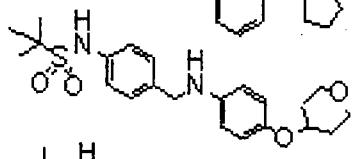
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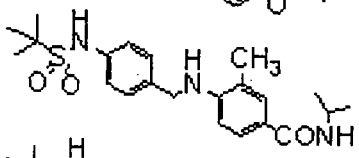
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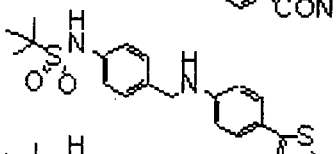
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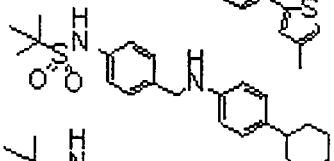
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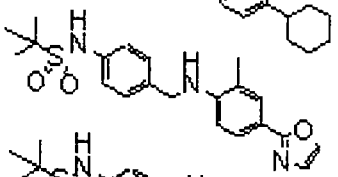
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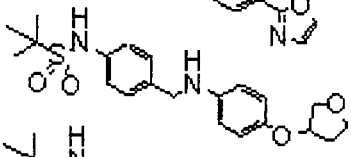
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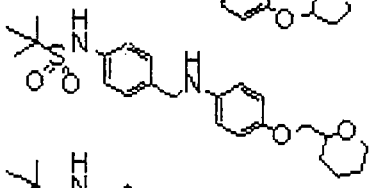
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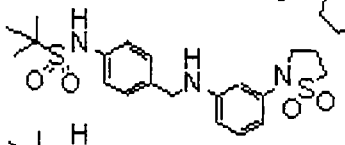
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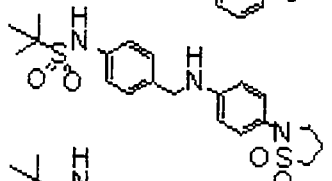
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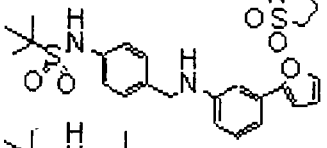
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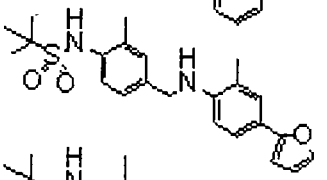
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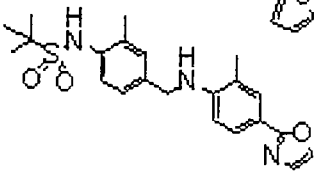
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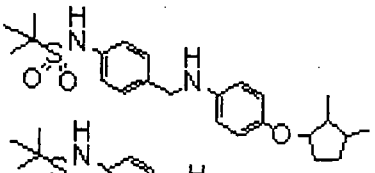
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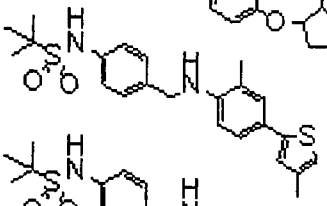
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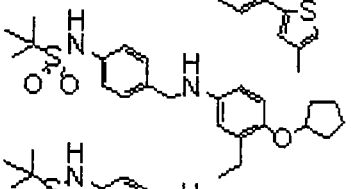
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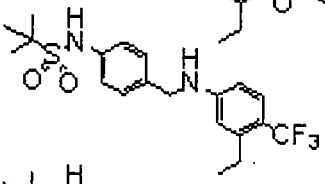
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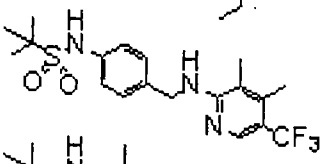
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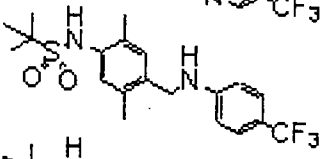
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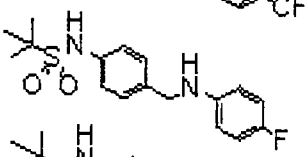
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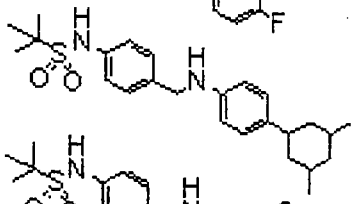
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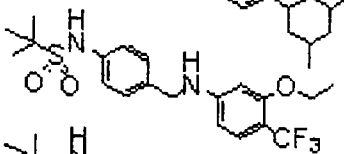
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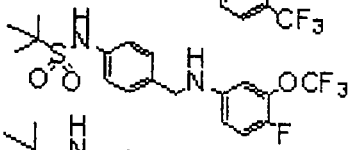
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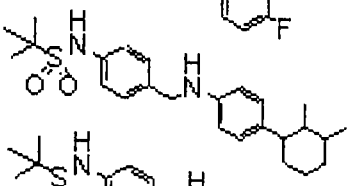
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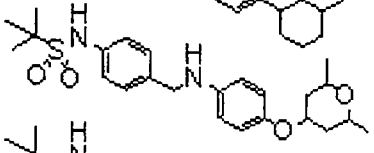
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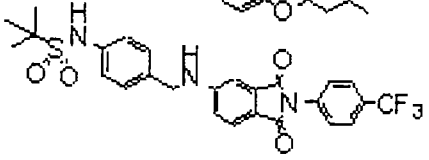
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Ig-222 

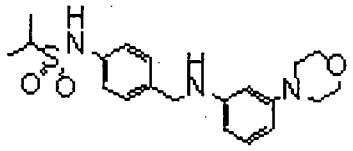
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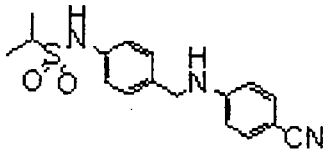
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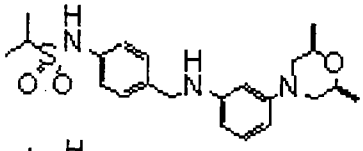
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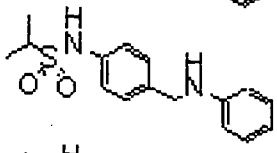
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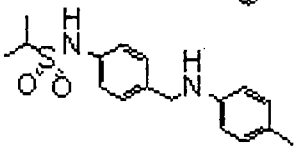
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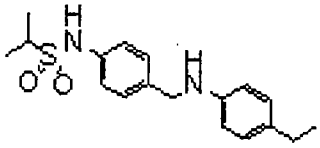
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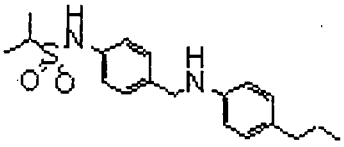
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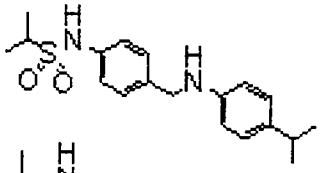
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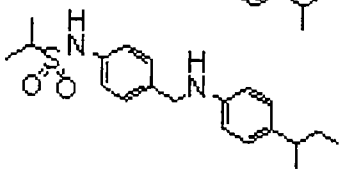
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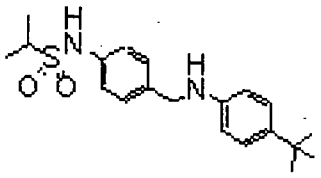
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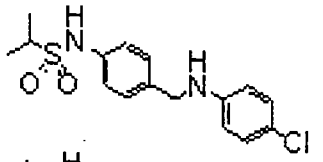
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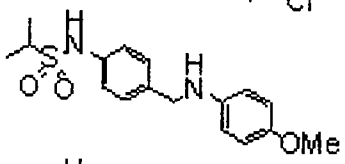
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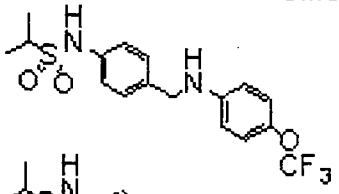
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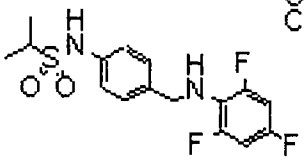
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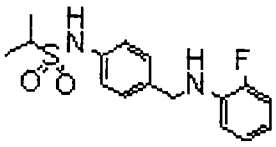
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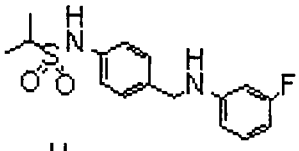
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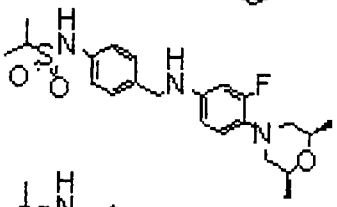
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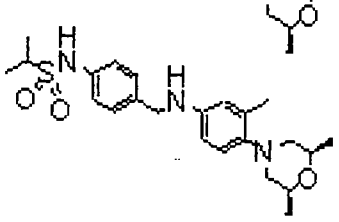
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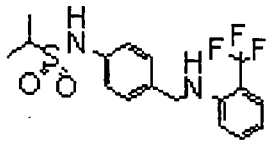
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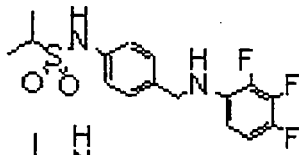
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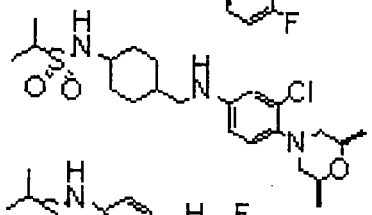
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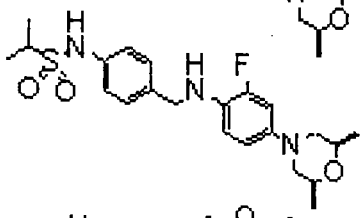
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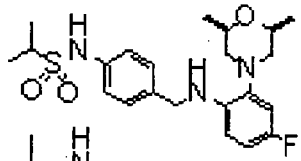
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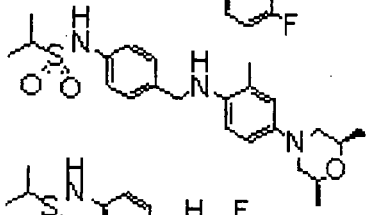
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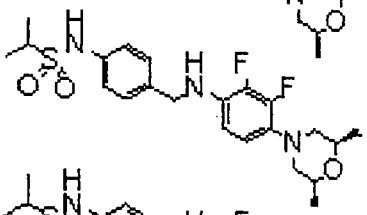
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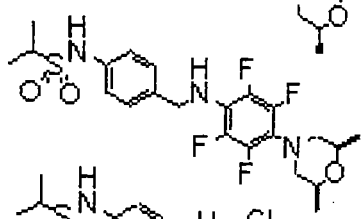
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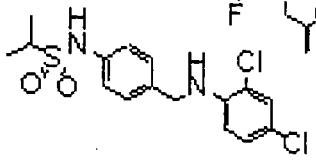
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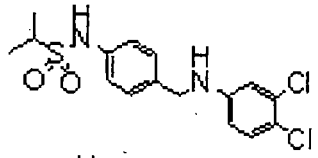
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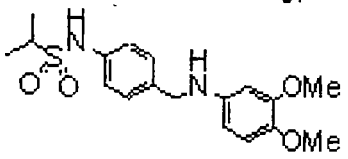
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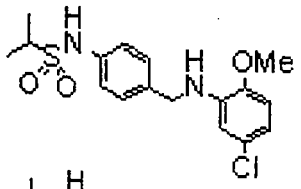
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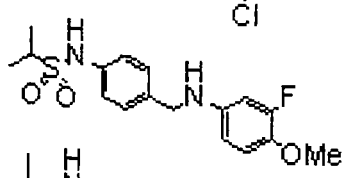
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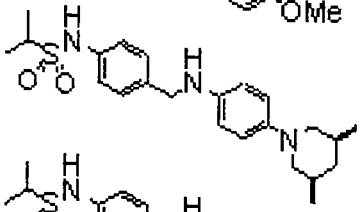
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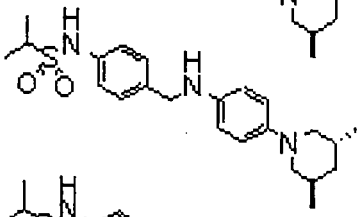
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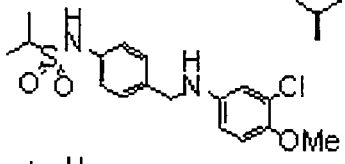
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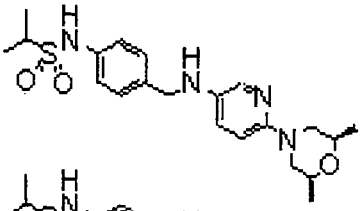
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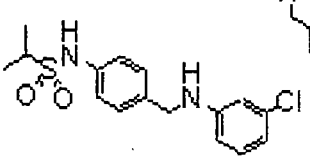
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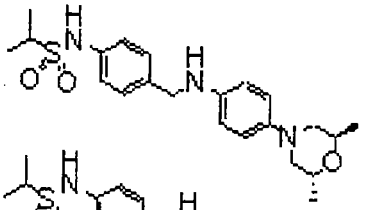
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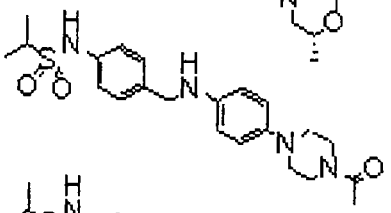
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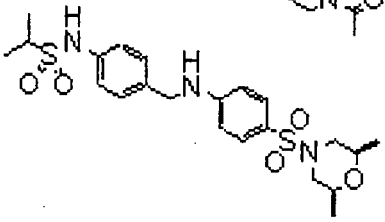
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Ih-40 

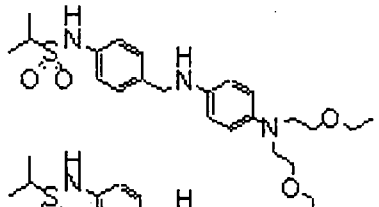
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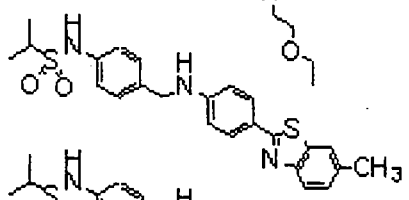
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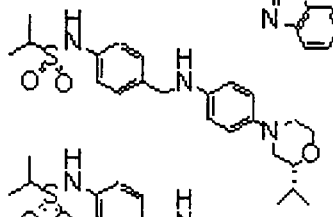
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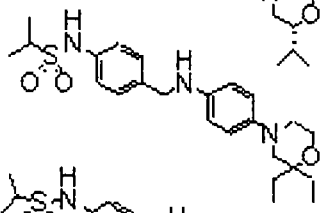
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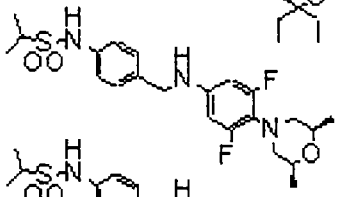
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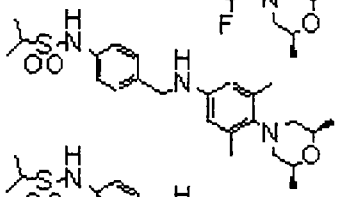
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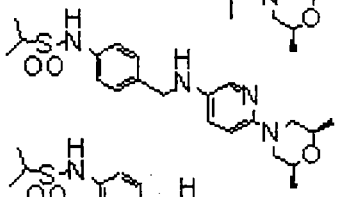
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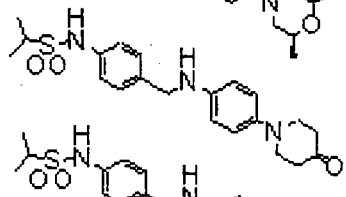
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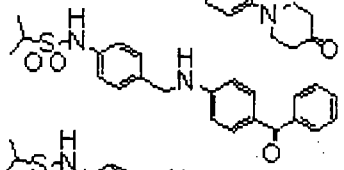
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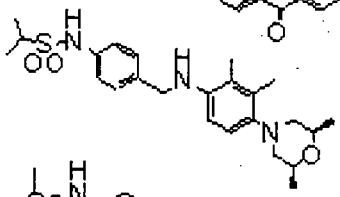
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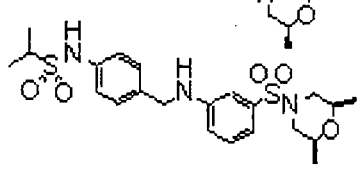
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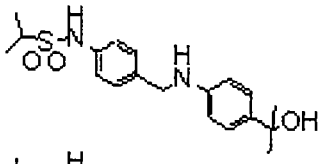
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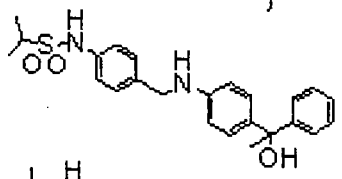
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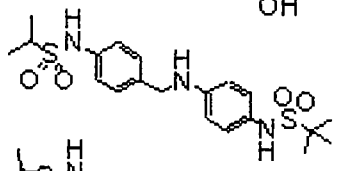
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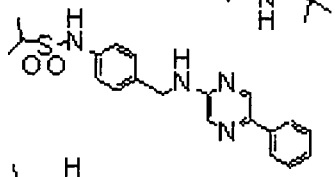
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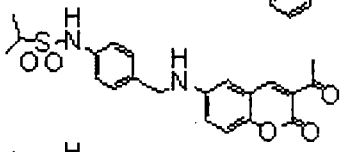
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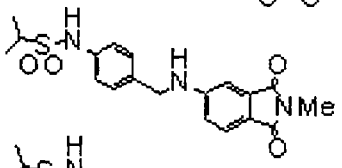
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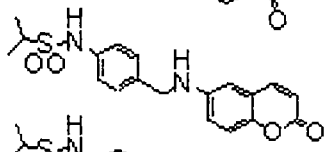
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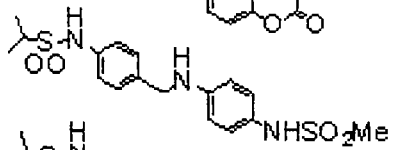
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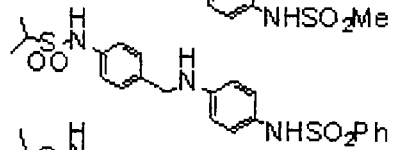
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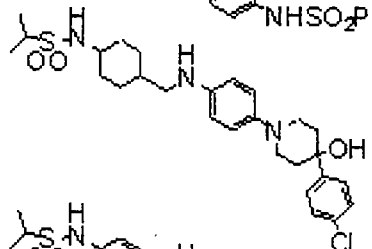
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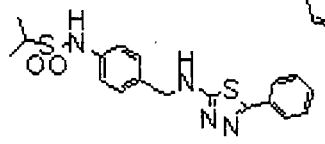
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Ih-62 

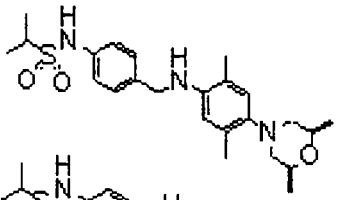
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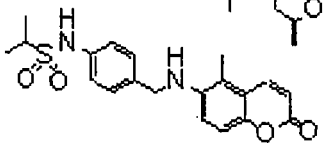
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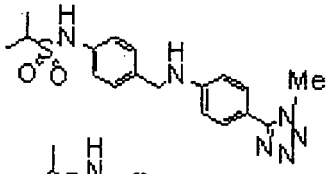
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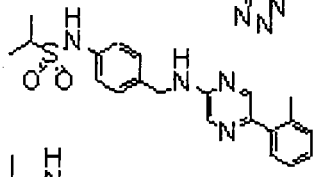
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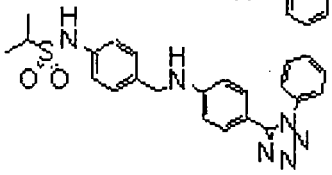
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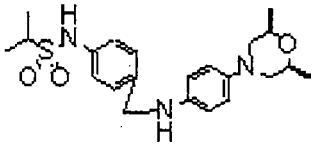
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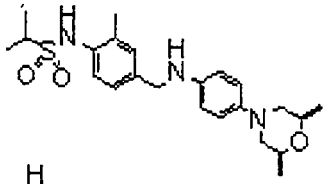
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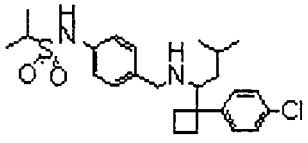
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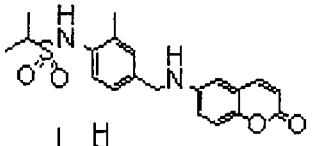
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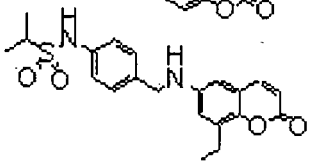
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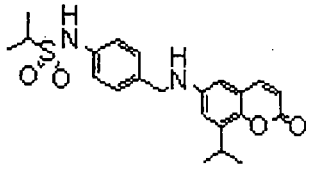
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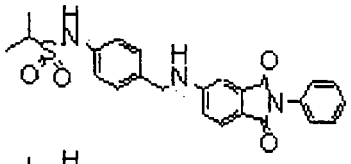
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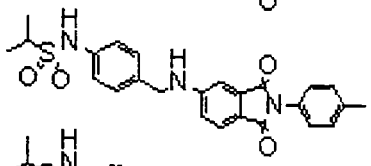
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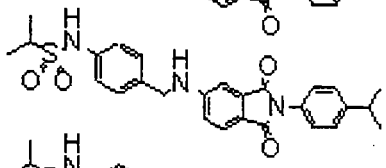
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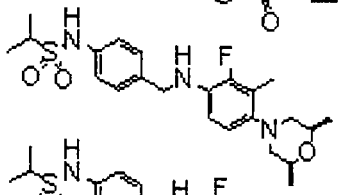
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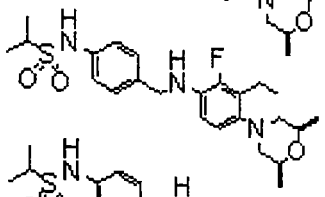
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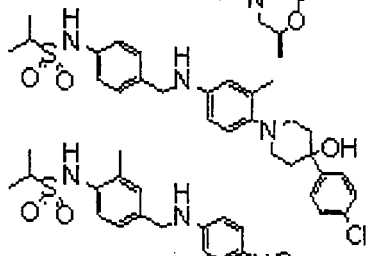
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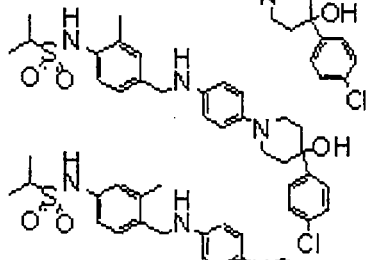
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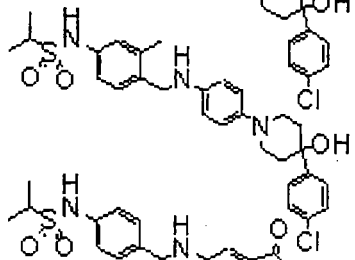
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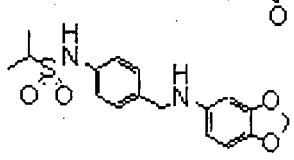
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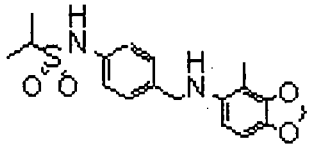
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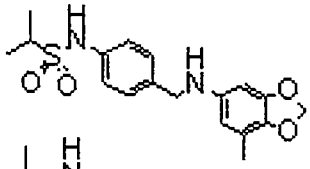
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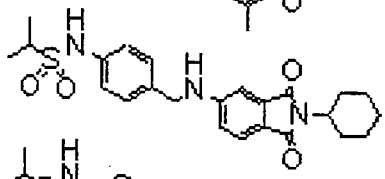
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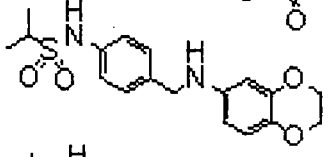
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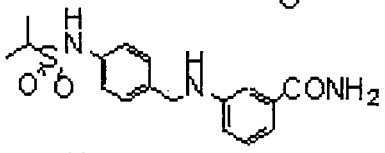
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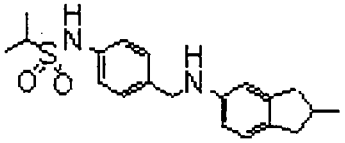
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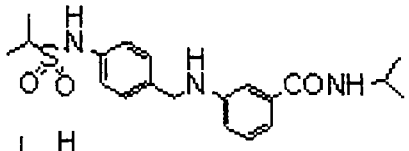
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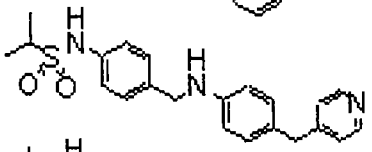
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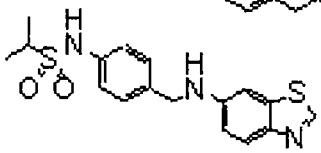
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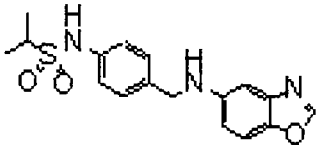
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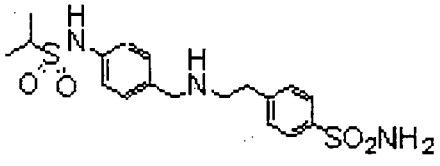
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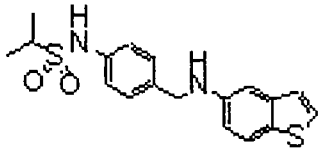
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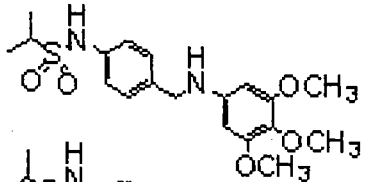
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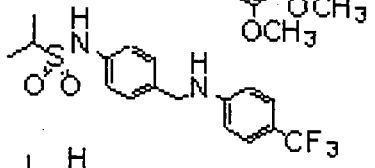
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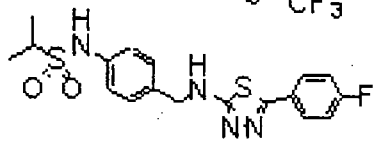
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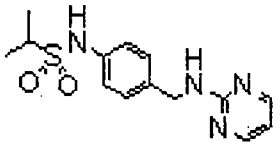
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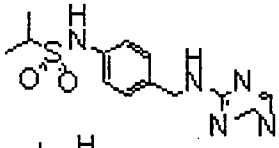
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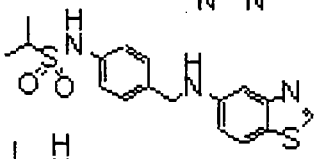
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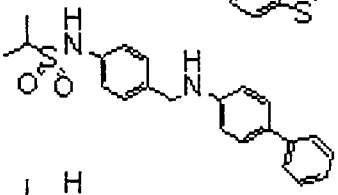
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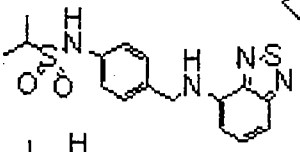
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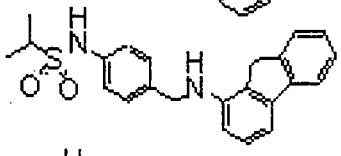
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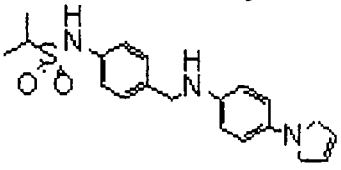
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Ih-106 

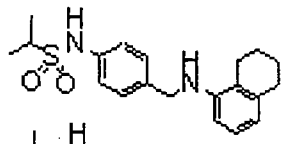
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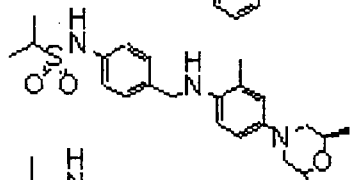
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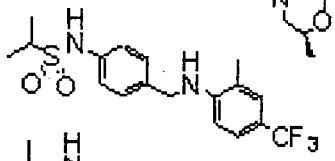
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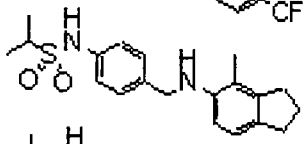
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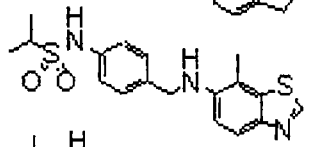
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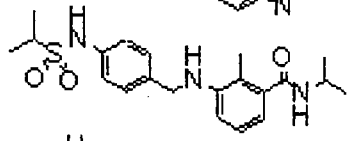
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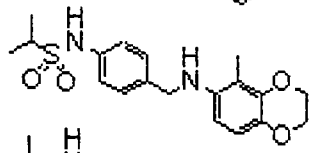
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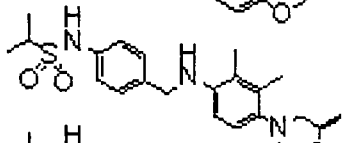
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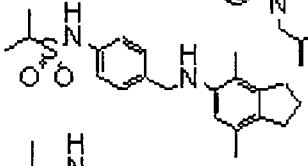
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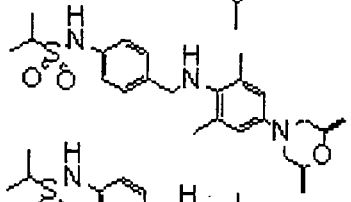
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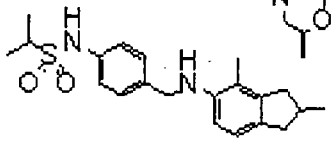
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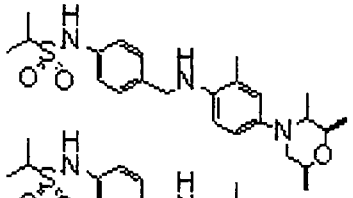
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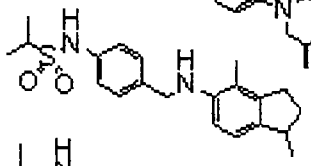
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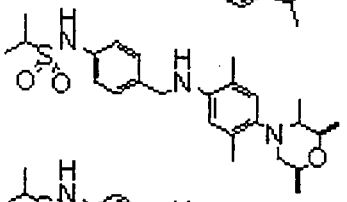
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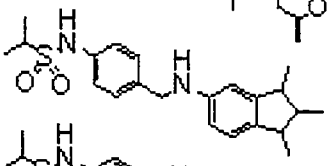
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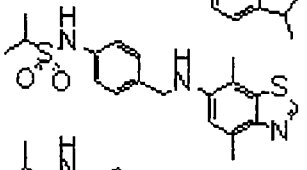
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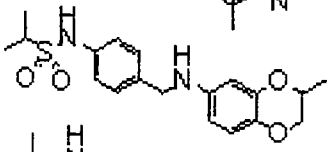
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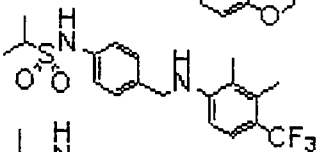
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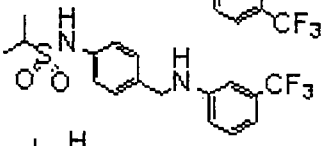
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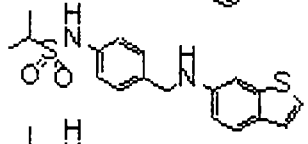
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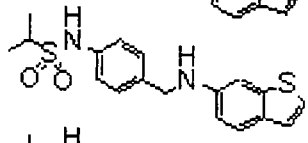
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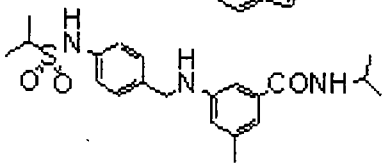
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Ih-128 

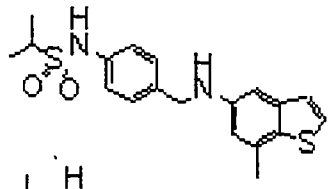
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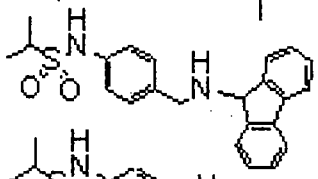
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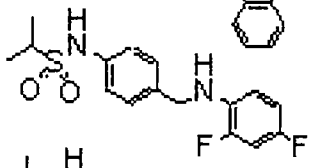
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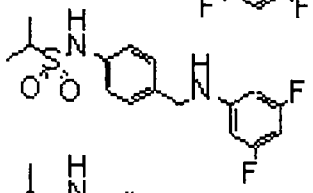
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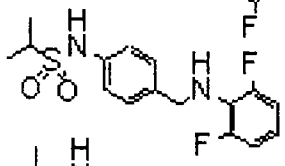
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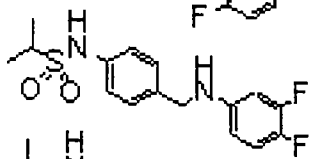
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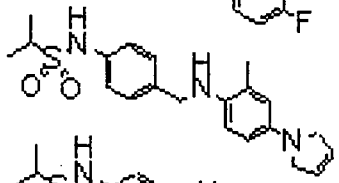
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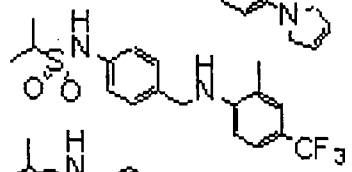
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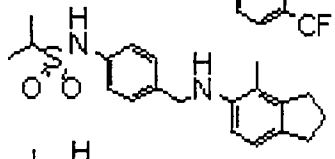
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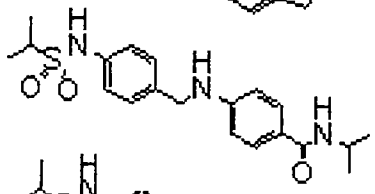
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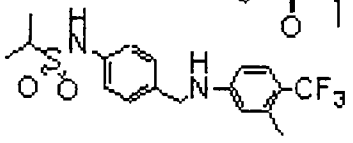
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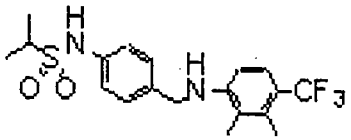
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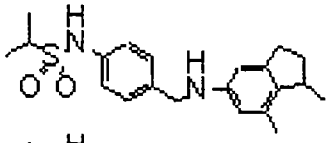
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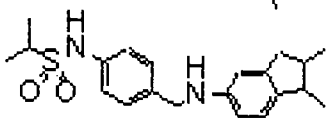
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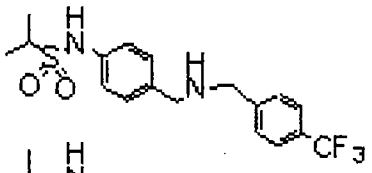
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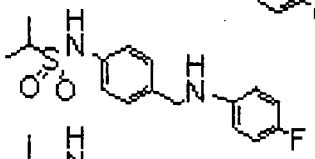
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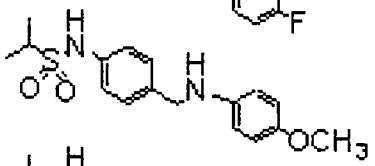
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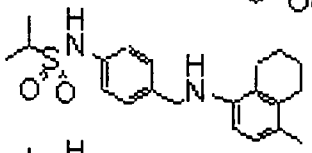
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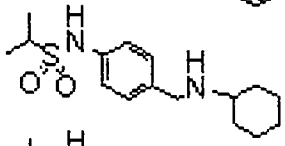
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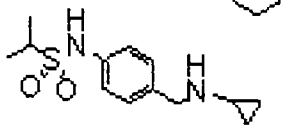
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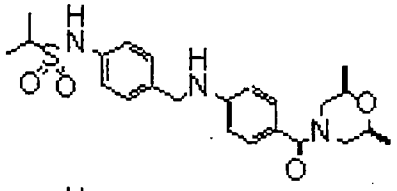
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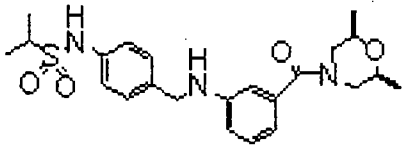
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Ih-150 

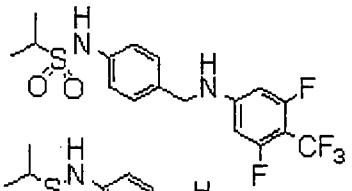
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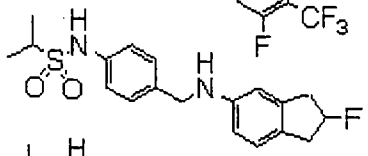
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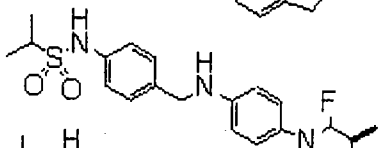
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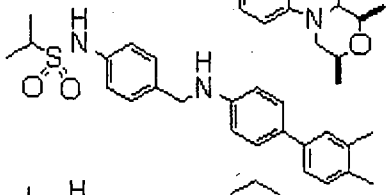
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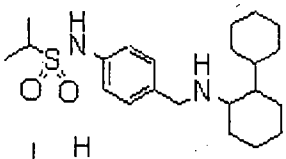
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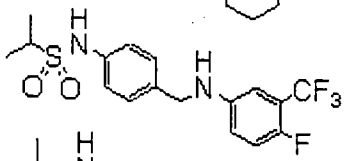
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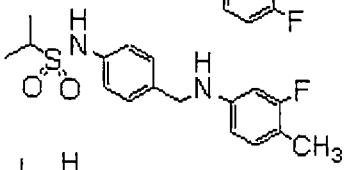
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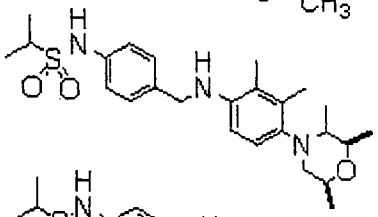
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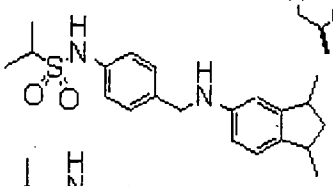
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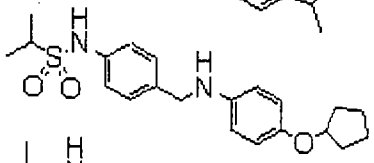
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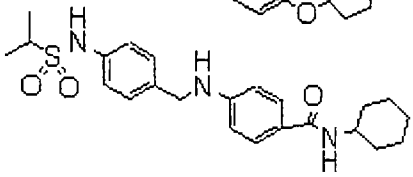
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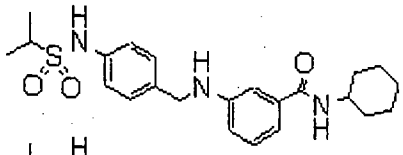
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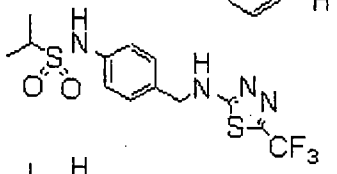
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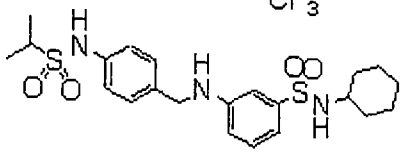
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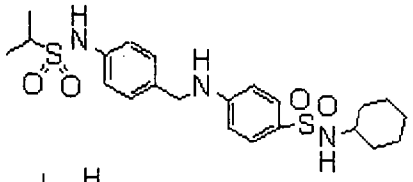
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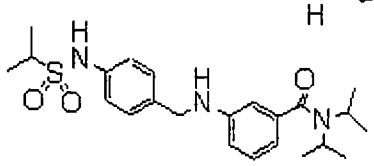
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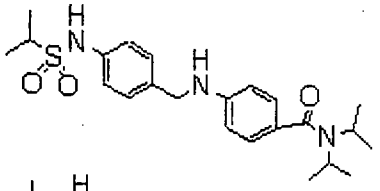
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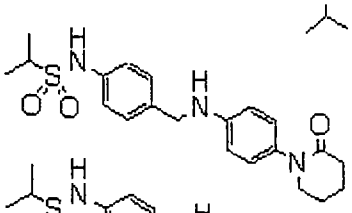
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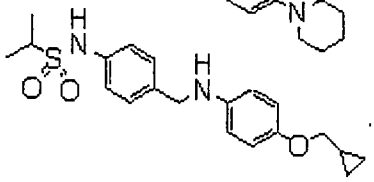
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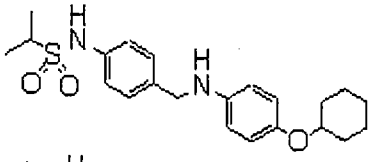
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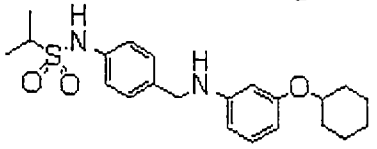
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Ih-172 

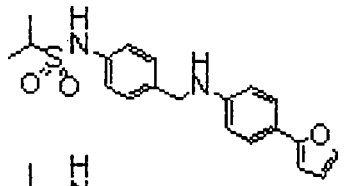
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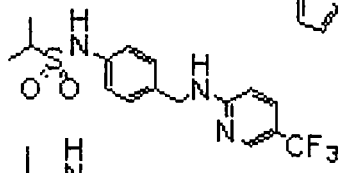
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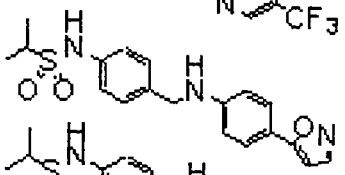
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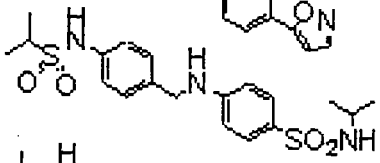
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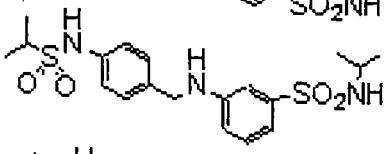
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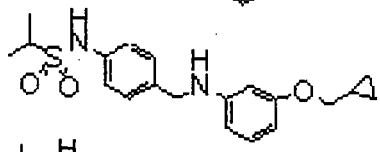
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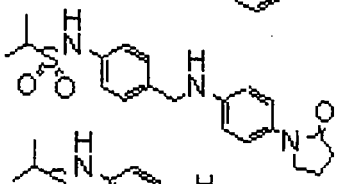
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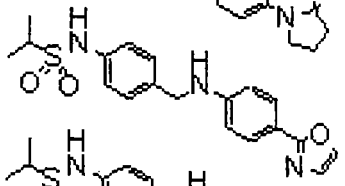
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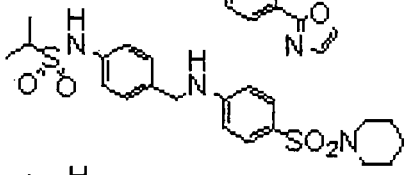
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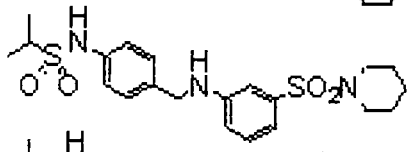
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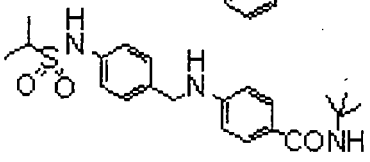
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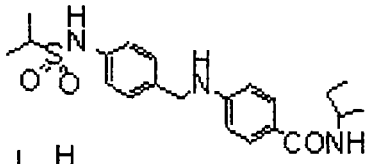
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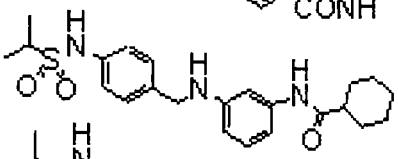
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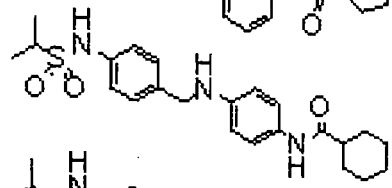
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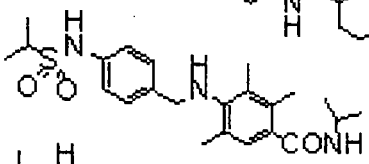
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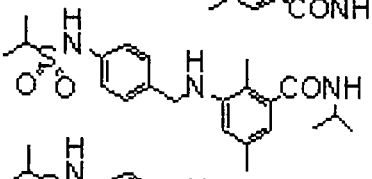
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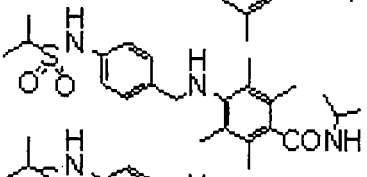
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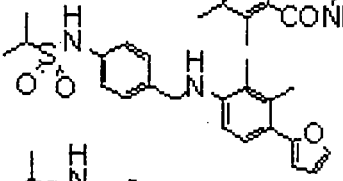
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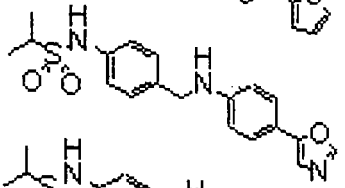
Ih-190 

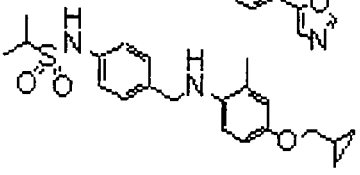
Ih-191 

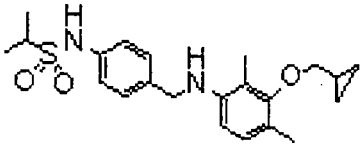
Ih-192 

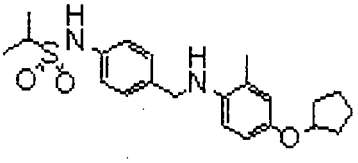
Ih-193 

Ih-194 

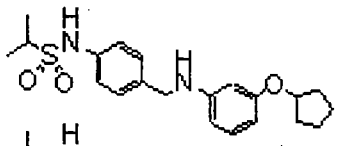
Ih-195 

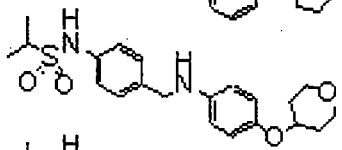
Ih-196 

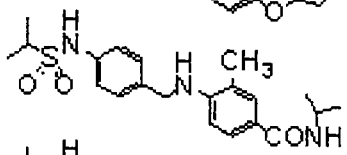
Ih-197 

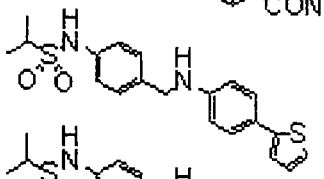
Ih-198 

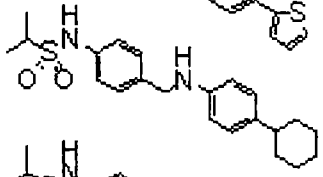
[Formula 158]

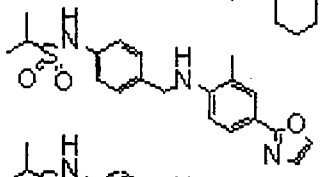
Ih-199 

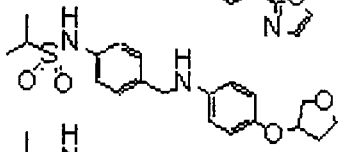
Ih-200 

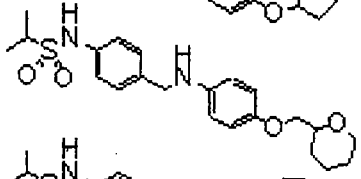
Ih-201 

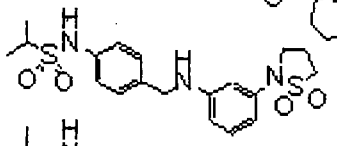
Ih-202 

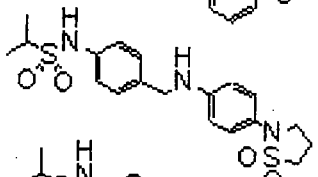
Ih-203 

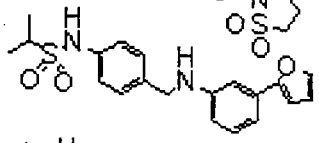
Ih-204 

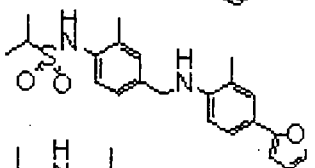
Ih-205 

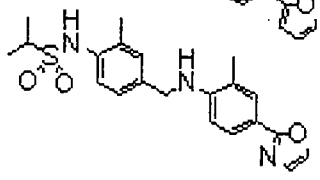
Ih-206 

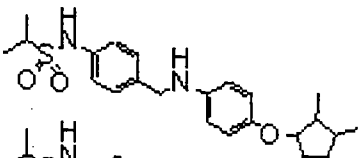
Ih-207 

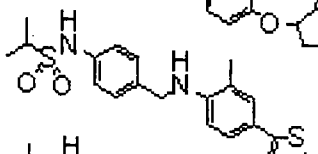
Ih-208 

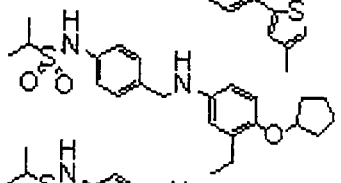
Ih-209 

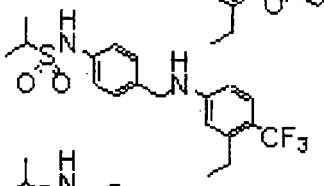
Ih-210 

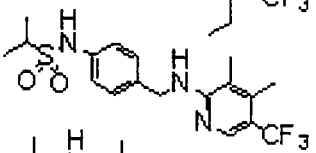
Ih-211 

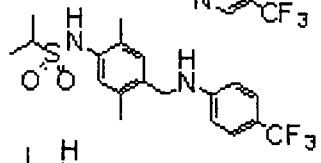
Ih-212 

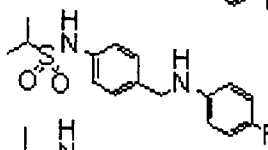
Ih-213 

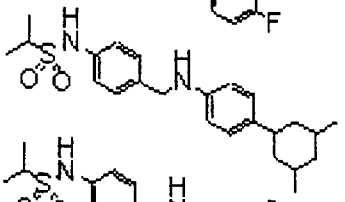
Ih-214 

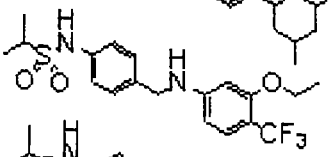
Ih-215 

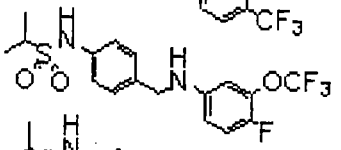
Ih-216 

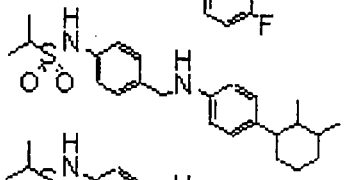
Ih-219 

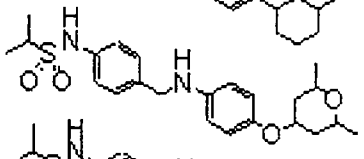
Ih-220 

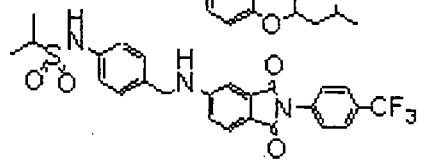
Ih-221 

Ih-222 

Ih-223 

Ih-224 

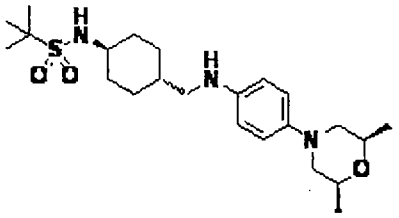
Ih-225 

Ih-226 

[0083]

Compound I-72

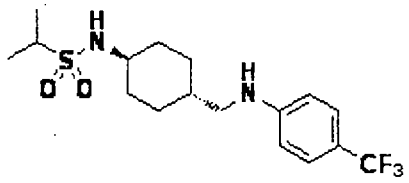
[Formula 159]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.05 (m, 2 H), 1.05-1.15 (m, 6H), 1.25 (s, 9H,), 1.15-1.32 (m, 3H), 1.41 (m, 1H), 1.75-1.98 (m, 4H), 2.11 (m, 1H), 2.58-3.38 (m, 5H), 3.58-3.76 (m, 2H), 5.17 (m, 1H), 6.25-6.92 (m, 5H) Melting point: 147 to 149 °C

Compound Ia-140

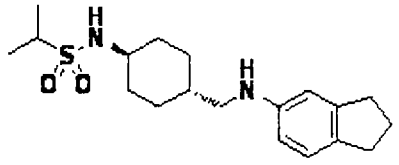
[Formula 160]



^{1}H-NMR ($CDCl_3$) δ: 1.02-1.20 (m, 2 H), 1.17-1.32 (m, 2 H), 1.37 (d, 6H, J = 6.9 Hz), 1.46-1.70 (m, 4H), 1.86-1.95 (m, 2H), 2.08-2.18 (m, 2H), 3.01 (d, 2H, J = 6.9 Hz), 3.13 (m, 1H), 3.25 (m, 1H), 3.87 (d, 1H, J = 8.4 Hz), 6.61(d, 2H, J = 8.7 Hz), 7.39 (d, 2H, J = 8.7 Hz)

Compound Ia-141

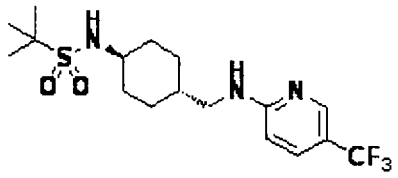
[Formula 161]



^{1}H-NMR ($CDCl_3$) δ: 1.00-1.30 (m, 4 H), 1.37 (d, 6H, J = 6.9 Hz), 1.59 (m, 1H), 1.87-1.98 (m, 2H), 1.99-2.18 (m, 5H), 2.85 (q, 3H, J = 7.5 Hz), 2.97 (d, 2H, J = 6.9 Hz), 3.12 (m, 1H), 3.23 (m, 1H), 3.88 (d, 1H, J = 8.1 Hz), 6.53 (d, 1H, J = 7.8 Hz), 6.63 (brs, 1H), 7.04 (d, 1H, J = 7.8 Hz) Mass: 351[M+H]

Compound Ia-178

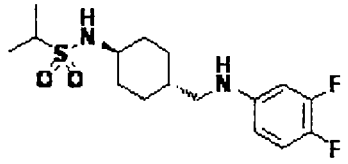
[Formula 162]



^{1}H-NMR ($CDCl_3$) δ: 1.08-1.36 (m, 4 H), 1.39 (s, 9H), 1.59 (m, 1H), 1.90-1.99 (m, 2H), 2.16-2.26 (m, 2H), 3.17-3.34 (m,3H), 3.69 (d, 1H, J = 9.3 Hz), 6.68 (d, 1H, J = 9.3 Hz), 7.77 (dd, 1H, J = 2.1 Hz and 9.3 Hz), 8.49 (brs, 1H) Mass:394[M+H]$^+$

Compound Ib-138

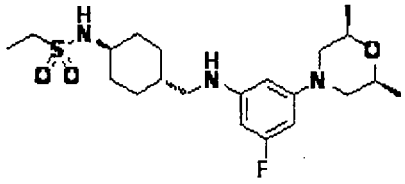
[Formula 163]



^{1}H-NMR ($CDCl_3$) δ: 1.02-1.34 (m, 4 H), 1.37 (d, 6H, J = 6.6 Hz), 1.57 (m, 1H), 1.87-1.97 (m, 2H), 2.07-2.18 (m, 2H), 2.93 (d, 2H, J = 6.6 Hz), 3.13 (m, 1H), 3.25 (m, 1H), 3.99 (d, 1H, J = 8.4 Hz), 6.38 (m, 1H), 6.49 (brs, 1H), 6.97 (q, 1H, J = 9.3 Hz) Mass:347[M+H]

Compound Ii-2

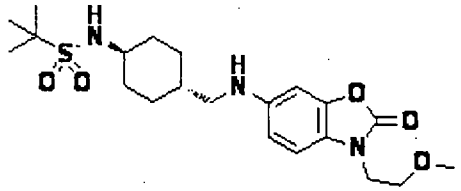
[Formula 164]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.06 (m, 2H), 1.12-1.28 (m, 11H), 1.31-1.47 (m, 1H), 1.75-1.94 (m, 4H), 2.19 (t, 2H, J = 11.3 Hz), 2.79 (t, 2H, J = 6.0 Hz), 2.93-3.08 (m, 1H), 2.97 (q, 2H, J = 7.42 Hz), 3.46 (m, 2H), 3.57-3.69 (m, 2H), 5.71 (t, 1H, J = 5.2 Hz), 5.77 (d, 1H, J = 11.5 Hz), 5.88-5.96 (m, 2H), 7.01 (d, 1H, J = 7.4 Hz).

Compound Ii-3

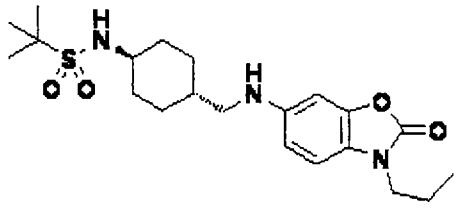
[Formula 165]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.07 (m, 2 H), 1.15-1.21 (m, 1H), 1.27 (s, 9H), 1.40-1.49 (m, 2H), 1.82 (d, 2H, J = 11.6 Hz), 1.92 (d, 2H, J = 11.6 Hz), 2.79-2.84 (m, 2H), 2.97-3.10 (m, 1H), 3.24 (s, 3H), 3.55-3.62 (m, 2H), 3.84-3.91 (m, 2H), 5.50-5.59 (m, 1H), 6.40 (d, 1H, J = 8.0 Hz), 6.56 (s, 1H), 6.72 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 8.4 Hz). Melting point: 166 to 168 °C

Compound Ii-4

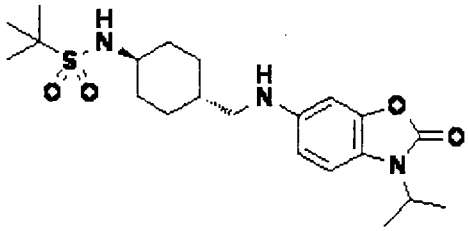
[Formula 166]



^{1}H-NMR (DMSO-d_6) δ: 0.87 (t, 3H, J = 7.2 Hz), 0.93-1.06 (m, 2H), 1.13-1.21 (m, 1H), 1.26 (s, 9H), 1.37-1.49 (m, 2H), 1.61-1.72 (m, 2H), 1.82 (d, 2H, J = 12.0 Hz), 1.91 (d, 2H, J = 12.0 Hz), 2.78-2.84 (m, 2H), 2.97-3.08 (m, 1H), 3.61-3.71 (m, 2H), 5.52-5.60 (m, 1H), 6.40 (d, 1H, J = 8.4 Hz), 6.56 (s, 1H), 6.73 (d, 1H, J = 8.8 Hz), 6.97 (d, 1H, J = 8.8 Hz). Melting point: 185 to 186 °C

Compound Ii-5

[Formula 167]

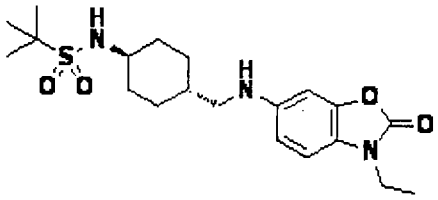


^{1}H-NMR (DMSO-d_6) δ: 0.90-1.05 (m, 2H), 1.26 (s, 9H), 1.28-1.31 (m, 1H), 1.35-1.47 (m, 8H), 1.81 (d, 2H, J = 12.4 Hz), 1.91 (d, 2H, J = 12.4 Hz), 2.77-2.84 (m,

2H), 2.96-3.07 (m, 1H), 4.30-4.42 (m, 1H), 5.51-5.64 (m, 1H), 6.39 (d, 1H, J = 8.0 Hz), 6.55 (s, 1H), 6.72 (d, 1H, J = 8.8 Hz), 7.07 (d, 1H, J = 8.8 Hz). Melting point: 156 to 157 °C

Compound Ii-6

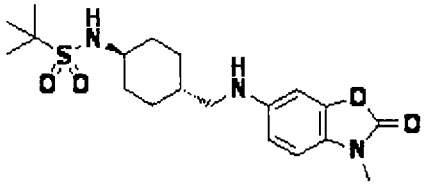
[Formula 168]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.07 (m, 2H), 1.19-1.25 (m, 4H), 1.26 (s, 9H), 1.38-1.49 (m, 2H), 1.82 (d, 2H, J = 8.8 Hz), 1.91 (d, 2H, J = 8.8 Hz), 2.79-2.84 (m, 2H), 2.97-3.07 (m, 1H), 3.69-3.80 (m, 2H), 5.51-5.63 (m, 1H), 6.41 (d, 1H, J = 8.0 Hz), 6.56 (s, 1H), 6.72 (d, 1H, J = 8.8 Hz), 6.97 (d, 1H, J = 8.8 Hz). Melting point: 178 to 179 °C

Compound Ii-7

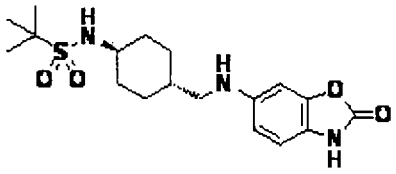
[Formula 169]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.07 (m, 2H), 1.19-1.22 (m, 1H), 1.26 (s, 9H), 1.38-1.48 (m, 2H), 1.82 (d, 2H, J = 11.6 Hz), 1.91 (d, 2H, J = 11.6 Hz), 2.79-2.84 (m, 2H), 2.95-3.09 (m, 1H), 3.25 (s, 3H), 5.52-5.60 (m, 1H), 6.41 (d, 1H, J = 8.4 Hz), 6.56 (s, 1H), 6.72 (d, 1H, J = 8.4 Hz), 6.92 (d, 1H, J = 8.4 Hz). Melting point: 206 to 207 °C

Compound Ii-8

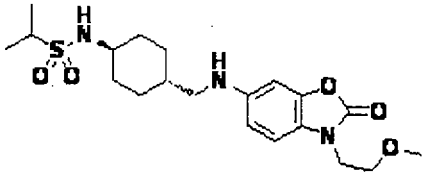
[Formula 170]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.05 (m, 2H), 1.16-1.24 (m, 1H), 1.26 (s, 9H), 1.37-1.47 (m, 2H), 1.81 (d, 2H, J = 12.8 Hz), 1.90 (d, 2H, J = 12.8 Hz), 2.75-2.81 (m, 2H), 2.96-3.08 (m, 1H), 5.45-5.52 (m, 1H), 6.33 (d, 1H, J = 8.4 Hz), 6.50 (s, 1H), 6.68-6.80 (m, 2H), 11.02 (brs, 1H). Melting point: 213 to 214 °C

Compound Ii-9

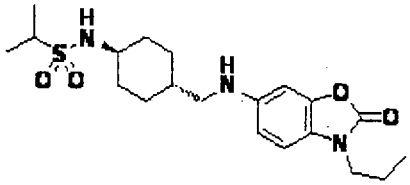
[Formula 171]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.08 (m, 2 H), 1.17-1.30 (m, 8H), 1.44 (brs, 1H), 1.82 (d, 2H, J = 12.4 Hz), 1.89 (d, 2H, J = 12.4 Hz), 2.78-2.82 (m, 2H), 2.97-3.15 (m, 2H), 3.23 (s, 3H), 3.55-3.62 (m, 2H), 3.83-3.90 (m, 2H), 5.52-5.59 (m, 1H), 6.40 (d, 1H, J = 8.0 Hz), 6.55 (s, 1H), 6.92 (d, 1H, J = 8.0 Hz), 6.97 (d, 1H, J = 8.4 Hz). Melting point: 120 to 121 °C

Compound Ii-10

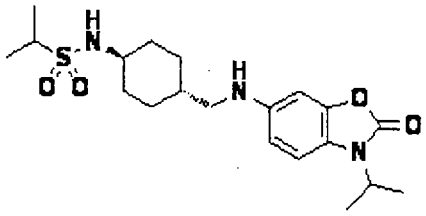
[Formula 172]



^{1}H-NMR (DMSO-d_6) δ: 0.88 (t, 3H, J = 7.2 Hz), 0.93-1.08 (m, 2H), 1.17-1.30 (m, 8H), 1.44 (brs, 1H), 1.52-1.61 (m, 2H), 1.83 (d, 2H, J = 12.0 Hz), 1.90 (d, 2H, J = 12.0 Hz), 2.78-2.84 (m, 2H), 2.98-3.15 (m, 2H), 3.62-3.71 (m, 2H), 5.52-5.60 (m, 1H), 6.41 (d, 1H, J = 8.4 Hz), 6.57 (s, 1H), 6.92 (d, 1H, J = 8.0 Hz), 6.97 (d, 1H, J = 8.4 Hz). Melting point: 144 to 145 °C

Compound Ii-11

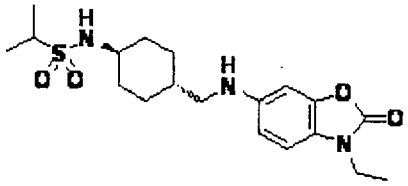
[Formula 173]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.08 (m, 2H), 1.15-1.30 (m, 8H), 1.33-1.50 (m, 7H), 1.82 (d, 2H, J = 12.0 Hz), 1.89 (d, 2H, J = 12.0 Hz), 2.78-2.86 (m, 2H), 2.96-3.14 (m, 2H), 4.30-4.45 (m, 1H), 5.50-5.61 (m, 1H), 6.40 (d, 1H, J = 7.6 Hz), 6.55 (s, 1H), 6.92 (d, 1H, J = 7.2 Hz), 7.07 (d, 1H, J = 7.6 Hz). Melting point: 137 to 138 °C

Compound Ii-12

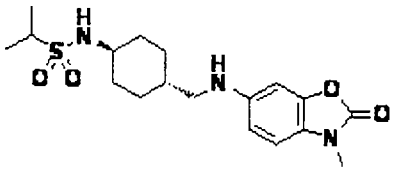
[Formula 174]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.07 (m, 2H), 1.14-1.30 (m, 11H), 1.36-1.50 (m, 1H), 1.82 (d, 2H, J = 12.0 Hz), 1.89 (d, 2H, J = 12.0 Hz), 2.78-2.85 (m, 2H), 2.97-3.15 (m, 2H), 3.69-3.79 (m, 2H), 5.52-5.60 (m, 1H), 6.41 (d, 1H, J = 8.4 Hz), 6.56 (s, 1H), 6.92 (d, 1H, J = 7.2 Hz), 6.98 (d, 1H, J = 8.4 Hz). Melting point: 158 to 159 °C

Compound Ii-13

[Formula 175]

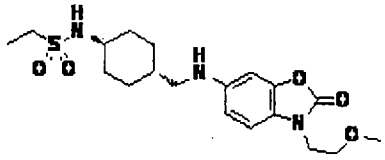


^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.12-1.30 (m, 8H), 1.34-1.51 (m, 1H), 1.82 (d, 2H, J = 12.0 Hz), 1.88 (d, 2H, J = 12.0 Hz), 2.77-2.83 (m, 2H), 2.95-3.12

(m, 2H), 3.25 (s, 3H), 5.51-5.59 (m, 1H), 6.41 (d, 1H, J = 8.8 Hz), 6.56 (s, 1H), 6.86-6.97 (m, 2H). Melting point:157 to 158 °C

Compound Ii-14

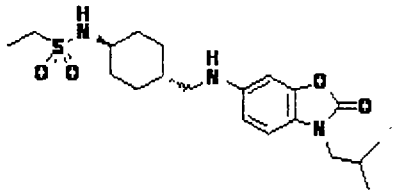
[Formula 176]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.08 (m, 2 H), 1.12-1.30 (m, 5H), 1.38-1.50 (m, 1H), 1.82 (d, 2H, J = 12.0 Hz), 1.88 (d, 2H, J = 12.0 Hz), 2.77-2.85 (m, 2H), 2.90-3.09 (m, 3H), 3.23 (s, 3H), 3.55-3.61 (m, 2H), 3.84-3.91 (m, 2H), 5.52-5.60 (m, 1H), 6.40 (d, 1H, J = 8.4 Hz), 6.55 (s, 1H), 6.89-7.00 (m, 2H). Melting point:150 to 151 °C

Compound Ii-15

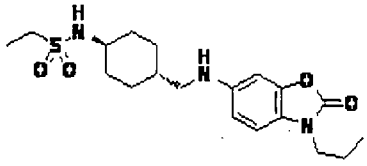
[Formula 177]



^{1}H-NMR (DMSO-d_6) δ: 0.88 (s, 3H), 0.90 (s, 3H), 0.92-1.08 (m, 2H), 1.12-1.30 (m, 5H), 1.35-1.51 (m, 1H), 1.83 (d, 2H, J = 12.4 Hz), 1.89 (d, 2H, J = 12.4 Hz), 2.00-2.16 (m, 1H), 2.77-2.84 (m, 2H), 2.90-3.10 (m, 3H), 3.42-3.55 (m, 2H), 5.50-5.65 (m, 1H), 6.40 (d, 1H, J = 8.4 Hz), 6.56 (s, 1H), 6.88-7.01 (m, 2H) Melting point: 132 to 133 °C

Compound Ii-16

[Formula 178]

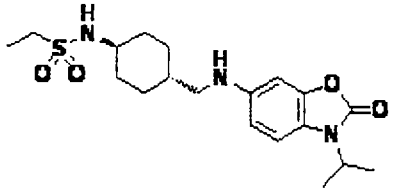


^{1}H-NMR (DMSO-d_6) δ: 0.87 (t, 3H, J = 6.8 Hz), 0.90-1.08 (m, 2H), 1.10-1.28 (m,

5H), 1.35-1.50 (m, 1H), 1.59-1.72 (m, 2H), 1.82 (d, 2H, J = 12.0 Hz), 1.89 (d, 2H, J = 12.0 Hz), 2.77-2.85 (m, 2H), 2.90-3.09 (m, 3H), 3.61-3.71 (m, 2H), 5.52-5.61 (m, 1H), 6.40 (d, 1H, J = 8.0 Hz), 6.56 (s, 1H), 6.97 (d, 2H, J = 8.0 Hz). Melting point: 136 to 137 °C

Compound Ii-17

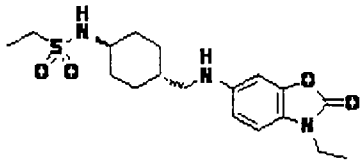
[Formula 179]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.06 (m, 2H), 1.12-1.28 (m, 5H), 1.33-1.50 (m, 7H), 1.81 (d, 2H, J = 12.0 Hz), 1.88 (d, 2H, J = 12.0 Hz), 2.78-2.84 (m, 2H), 2.90-3.08 (m, 3H), 4.28-4.44 (m, 1H), 5.49-5.79 (m, 1H), 6.39 (d, 1H, J = 8.0 Hz), 6.55 (s, 1H), 6.97 (d, 1H, J = 7.6 Hz), 7.07 (d, 1H, J = 8.0 Hz). Melting point: 124 to 125 °C

Compound Ii-18

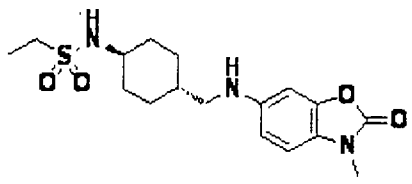
[Formula 180]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.07 (m, 2H), 1.12-1.29 (m, 8H), 1.36-1.51 (m, 1H), 1.82 (d, 2H, J = 12.0 Hz), 1.89 (d, 2H, J = 12.0 Hz), 2.78-2.86 (m, 2H), 2.90-3.09 (m, 3H), 3.68-3.80 (m, 2H), 5.51-5.61 (m, 1H), 6.41 (d, 1H, J = 8.4 Hz), 6.57 (s, 1H), 6.97 (d, 2H, J = 8.4 Hz). Melting point:163 to 164 °C

Compound Ii-19

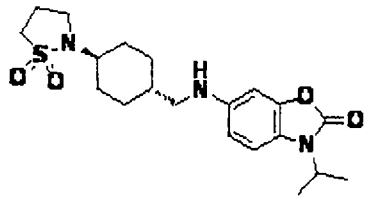
[Formula 181]



^{1}H-NMR (DMSO-d_6) δ: 0.89-1.08 (m, 2H), 1.11-1.30 (m, 5H), 1.35-1.51 (m, 1H), 1.82 (d, 2H, J = 10.8 Hz), 1.89 (d, 2H, J = 10.8 Hz), 2.75-2.88 (m, 2H), 2.89-3.10 (m, 3H), 3.25 (s, 3H), 5.48-5.60 (m, 1H), 6.42 (d, 1H, J = 7.6 Hz), 6.56 (s, 1H), 6.92 (d, 1H, J = 7.6 Hz), 6.98 (d, 1H, J = 5.6 Hz). Melting point: 189 to 190 °C

Compound Ii-20

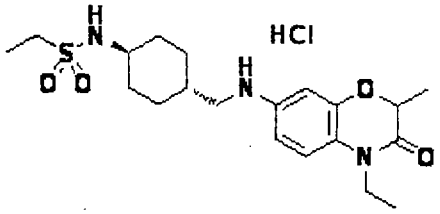
[Formula 182]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.13 (m, 2H), 1.31-1.59 (m, 10H), 1.73-1.92 (m, 4H), 2.12-2.26 (m, 2H), 2.84 (d, 2H, J = 6.0 Hz), 3.07-3.30 (m, 4H), 4.30-4.46 (m, 1H), 5.64 (brs, 1H), 6.41 (d, 1H, J = 8.4 Hz), 6.57 (s, 1H), 7.08 (d, 1H, J = 8.4 Hz). Melting point: 165 to 166 °C

Compound Ii-21

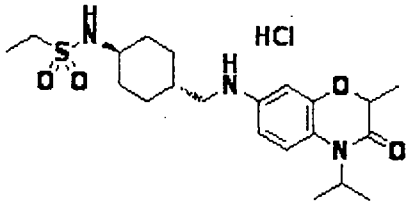
[Formula 183]



^{1}H-NMR (DMSO-d_6) δ: 0.86-1.25 (m, 10H), 1.40 (d, 3H, J = 6.9Hz), 1.52 (m, 1H), 1.82-1.93 (m, 4H), 2.95-3.00 (m, 5H), 3.63-3.91 (m, 2H), 4.61-4.68 (m, 1H), 6.73 (brs, 2H), 7.01 (d, 2H, J = 7.8Hz), 7.11 (d, 1H, J = 8.1Hz,).

Compound Ii-22

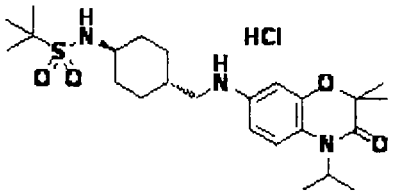
[Formula 184]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.10 (m, 2 H), 1.15-1.34 (m, 5H), 1.36-1.43 (m, 9H), 1.53 (m, 1H), 1.82.1-93 (m, 4H), 2.94-3.01 (m, 6H), 4.52 (m, 1H), 4.63 (m, 1H), 6.73 (brs, 2H), 7.02 (d, 1H, J = 7.5Hz), 7.21-7.25 (m, 1H).

Compound Ii-23

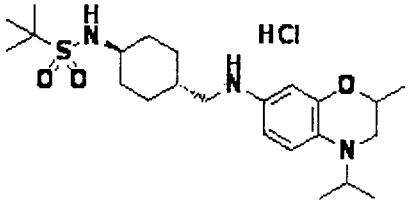
[Formula 185]



^{1}H-NMR (DMSO-d_6) δ: 0.86-1.04 (m, 4 H), 1.25 (s, 10H), 1.30 (s, 6H), 1.38 (s, 3H), 1.40 (s, 3H), 178-1.92 (m 4H), 2.76-2.80 (m, 2H), 3.03 (m, 1H), 4.54-4.63 (m, 1H), 5.57 (m, 1H), 6.16 (s, 1H), 6.22 (d, 1H, J = 8.4Hz), 6.76 (d, 1H, J = 8.4Hz), 6.98 (d, 1H, J = 8.4Hz).

Compound Ii-24

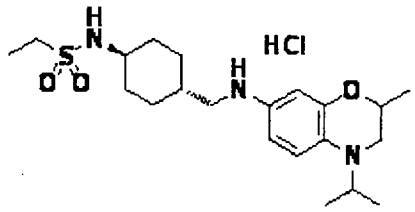
[Formula 186]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.11 (m, 5 H), 1.15-1.31 (m, 20H), 1.57 (m, 1H), 1.82.1-93 (m, 4H), 2.74-2.81 (m, 1H), 3.01-3.06 (m, 2H), 3.35 (m, 1H), 3.40 (m, 1H), 4.04-4.17 (m, 3H), 6.77 (d, 1H, J = 9.0Hz),

Compound Ii-25

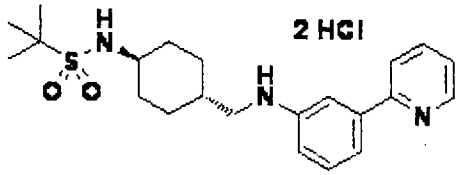
[Formula 187]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.20 (m, 13 H), 1.30 (d, 3H, J = 3H), 1.59 (m, 1H), 1.81-1.91 (m, 4H), 2.73-2.83 (m, 1H), 2.94-3.04 (m, 4H), 3.35-3.45 (m, 2H), 4.08-4.19 (m, 3H), 6.88 (brs, 3H), 7.03 (d, 1H, J = 8.4Hz).

Compound Ii-26

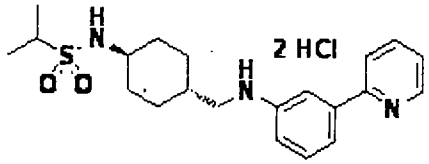
[Formula 188]



^{1}H-NMR (DMSO-d_6) δ: 1.02-1.10 (m, 2H), 1.19-1.32 (m, 2H), 1.26 (s, 9H), 1.55 (m, 1H), 1.86-1.93 (m, 4H), 3.01-3.04 (m, 3H), 6.76 (d, 1H, J = 8.7 Hz), 7.03 (m, 1H), 7.37-7.43 (m, 3H), 7.76-7.80 (m, 1H), 8.20-8.23 (m, 1H), 8.34-8.40 (m, 1H), 8.78-8.79 (m, 1H)

Compound Ii-27

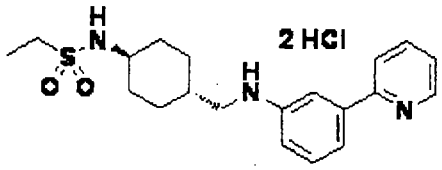
[Formula 189]



^{1}H-NMR (DMSO-d_6) δ: 1.03-1.10 (m, 2H), 1.20-1.30 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.53 (m, 1H), 1.88 (m, 4H), 2.99-3.15 (m, 3H), 7.33-7.35 (m, 3H), 7.71-7.75 (m, 1H), 8.16-8.18 (m, 1H), 829-8.32 (m, 1H), 8.76-8.78 (m, 1H)

Compound Ii-28

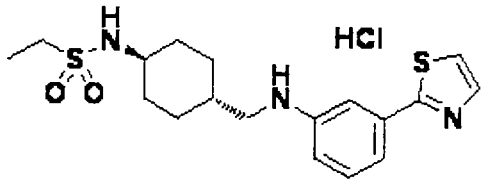
[Formula 190]



^{1}H-NMR (DMSO-d_6) δ: 1.04-1.11 (m, 2H), 1.15-1.28 (m, 2H), 1.19 (t, 3H, J =7.2 Hz), 1.59 (m, 1H), 1.87-1.91 (m, 4H), 2.93-3.08 (m, 2H), 2.97 (q, 2H, J =7.2 Hz), 3.06-3.08 (m, 2H), 7.01 (m, 1H), 7.17 (d, 1H, J =7.5Hz), 7.43 (d, 1H, J =7.5Hz), 7.50-7.57 (m, 2H), 7.80-7.84 (m, 1H), 8.25-8.27 (m, 1H), 8.39-8.44 (m, 1H), 8.80-8.82 (m, 1H)

Compound Ii-29

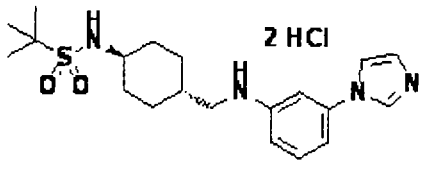
[Formula 191]



^{1}H-NMR (DMSO-d_6) δ: 0.99-1.10 (m, 2H), 1.15-1.28 (m, 2H), 1.19 (t, 3H, J =7.5 Hz), 1.52 (m, 1H), 1.84-1.91 (m, 4H), 2.94-3.01 (m, 5H), 6.88 (m, 1H), 7.00 (d, 1H, J =7.8 Hz), 7.26-7.28 (m, 2H), 7.38 (m, 1H), 7.76 (d, 1H, J = 3.3. Hz), 7.90 (d, 1H, J =3.3 Hz)

Compound Ii-30

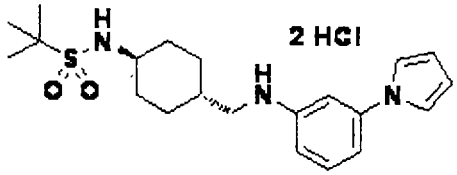
[Formula 192]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.08 (m, 2 H), 1.18-1.33 (m, 2H), 1.26 (s, 9H), 1.45 (m, 1H), 1.78-1.97 (m, 4 H), 2.86-2.94 (m, 2H), 2.95-3.10 (m, 1H), 5.91 (m, 1H), 6.55 (d, 1H, J = 7.6 Hz), 6.63-6.71 (m, 2H), 6.73 (d, 1H, J = 8.0 Hz), 7.06 (s, 1H), 7.15 (t, 1H, J = 8.0 Hz), 7.60 (s, 1H), 8.11 (s, 1H), 8.31 (s, 1H)

Compound Ii-31

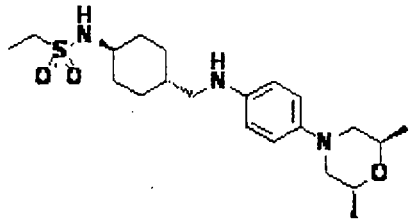
[Formula 193]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.08 (m, 2 H), 1.13-1.28 (m, 2H), 1.26 (s, 9H), 1.43 (m, 1H), 1.76-1.97 (m, 4 H), 2.83-3.18 (m, 3H), 5.79 (m, 1H), 6.21 (s, 2H), 6.44 (d, 1H, J = 6.8 Hz), 6.58-6.67 (m, 2H), 6.73 (d, 1H, J = 8.0 Hz), 7.10 (t, 1H, J = 8.0 Hz), 7.21 (s, 2H) Melting point: 205 to 206 °C

Compound Ii-32

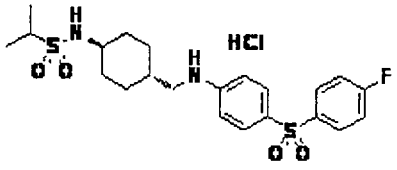
[Formula 194]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.05 (m, 2 H), 1.05-1.28 (m, 11H), 1.41 (m, 1H), 1.75-1.92 (m, 4 H), 2.11 (t, 2H, J = 10.0 Hz), 2.73-2.82 (m, 2H), 2.91-3.08 (m, 3H), 3.24 (d, 2H, J = 11.2 Hz), 3.62-3.72 (m, 2H), 5.07 (m, 1H), 6.47 (d, 2H, J = 7.2 Hz), 6.72 (d, 2H, J = 7.2 Hz), 6.97 (d, 1H, J = 7.6 Hz) Melting point: 165 to 166 °C

Compound Ii-33

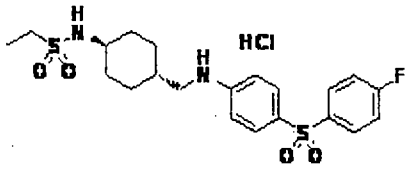
[Formula 195]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.06 (m, 2H), 1.15-1.26 (m, 8H), 1.33-1.48 (m, 1H), 1.71-1.93 (m, 4H), 2.88 (d, 2H, J = 6.5 Hz), 2.93-3.15 (m, 2H), 5.70 (brs, 2H), 6.63 (d, 2H, J = 9.1 Hz), 6.93-6.96 (m, 1H), 7.38-7.42 (m, 2H), 7.57 (d, 2H, J = 9.1 Hz), 7.88-7.93 (m, 2H)

Compound Ii-34

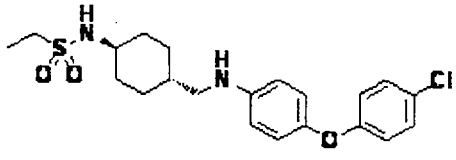
[Formula 196]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.02 (m, 2H), 1.16-1.18 (m, 5H), 1.42 (s, 1H), 1.75-1.91 (m, 4H), 2.88 (d, 2H, J = 6.6 Hz), 2.96 (q, 3H, J = 7.3 Hz), 6.63 (d, 2H, J = 8.9 Hz), 6.99-7.02 (m, 1H), 7.38-7.41 (m, 2H), 7.57 (d, 2H, J = 8.9 Hz), 7.89-7.92 (m, 2H).

Compound Ii-35

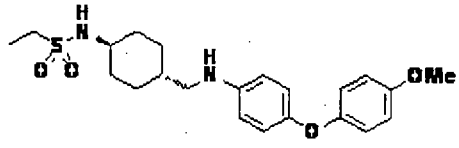
[Formula 197]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.52 (m, 5H), 1.19 (t, 3H, J = 7.2 Hz), 1.75-1.96 (m, 4H), 2.50-3.10 (m, 3H), 2.62 (q, 2H, J = 7.2 Hz), 5.55-5.70 (m, 1H), 6.57 (d, 2H, J = 8.7 Hz), 6.80-7.04 (m, 4H), 7.01 (d, 1H, J = 7.8 Hz), 7.34 (d, 2H, J = 8.7 Hz)

Compound Ii-36

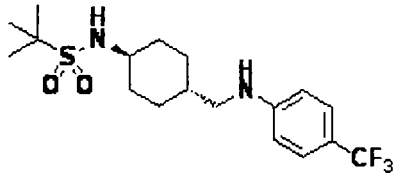
[Formula 198]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.50 (m, 5H), 1.19 (t, 3H, J = 7.2 Hz), 1.75-1.95 (m, 4H), 2.70-3.10 (m, 3H), 2.97 (q, 2H, J = 7.2 Hz), 3.70 (s, 3H), 5.40-5.50 (m, 1H), 6.53 (d, 2H, J = 8.7 Hz), 6.74 (d, 2H, J = 8.7 Hz), 6.78-6.90 (m, 4H), 6.99 (d, 1H, J = 7.8 Hz)

Compound Ii-37

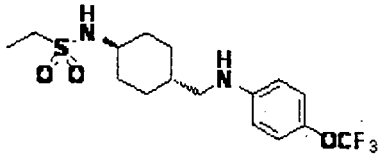
[Formula 199]



^{1}H-NMR ($CDCl_3$) δ: 1.02-1.32 (m, 4 H), 139 (s, 9H,), 1.58 (m, 1H), 1.86-1.96 (m, 2H), 2.12-2.22 (m, 2H), 3.02 (d, 2H, J = 6.6 Hz), 3.25 (m, 1H), 3.67 (d, 1H, J = 9.3 Hz), 6.67(d, 2H, J = 8.7 Hz), 7.41 (d, 2H, J = 8.7 Hz) Mass:393[M+H]

Compound Ii-38

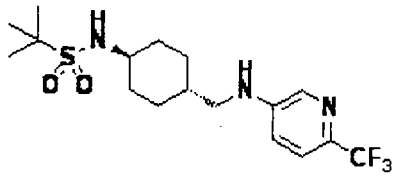
[Formula 200]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.07 (m, 2H), 1.17-1.26 (m, 2H), 1.19 (t, 3H, J = 7.1 Hz), 1.43 (s, 1H), 1.77-1.85 (m, 2H), 1.85-1.94 (m, 2H), 2.82 (t, 1H, J = 5.8 Hz), 2.98 (m, 1H), 2.97 (q, 2H, J = 7.1 Hz), 5.87 (m, 1H), 6.56 (d, 2H, J = 8.6 Hz), 6.98 (d, 1H, J = 7.6 Hz), 7.02 (d, 2H, J = 8.6 Hz).

Compound Ii-39

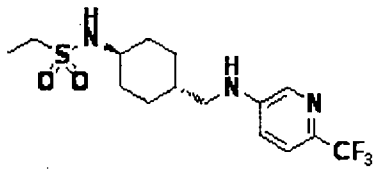
[Formula 201]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.10 (m, 2H), 1.19-1.35 (m, 2H), 1.29 (s, 9H), 1.46 (s, 1H), 1.73-1.98 (m, 4H), 2.93 (m, 1H), 3.04 (m, 1H), 6.60-6.69 (m, 2H), 6.75 (d, 1H, J = 8.8 Hz), 6.97 (d, 1H, J = 7.6 Hz), 7.49 (d, 1H, J = 8.8 Hz), 8.05 (s, 1H).

Compound Ii-40

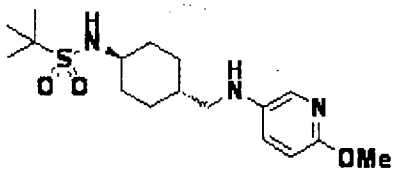
[Formula 202]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.09 (m, 2H), 1.16-1.29 (m, 2H), 1.19 (t, 3H, J = 7.3 Hz), 1.45 (s, 1H), 1.76-1.94 (m, 4H), 1.76 (s, 2H), 2.93 (t, 2H, J = 5.8 Hz), 2.97 (q, 2H, J = 7.3 Hz), 6.66 (s, 1H), 6.94-7.01 (m, 2H), 7.49 (d, 1H, J = 8.6 Hz), 8.04 (s, 1H).

Compound Ii-41

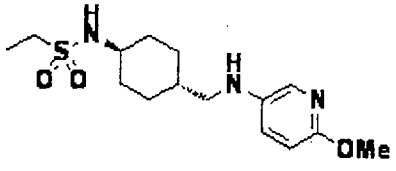
[Formula 203]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.05 (m, 2H), 1.17-1.33 (m, 2H), 1.26 (s, 9H), 1.35-1.48 (m, 1H), 1.76-1.86 (m, 2H), 1.86-1.95 (m, 2H), 2.76-2.82 (m, 1H), 2.96-3.08 (m, 1H), 3.71 (s, 3H), 5.21-5.30 (m, 1H), 6.57 (d, 1H, J = 8.6 Hz), 6.73 (d, 1H, J = 8.6 Hz), 7.02 (dd, 1H, J = 8.6, 2.3 Hz), 7.44 (d, 1H, J = 2.3 Hz).

Compound Ii-42

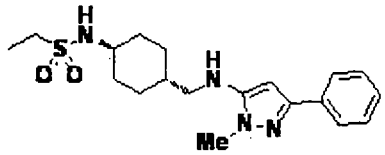
[Formula 204]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.01 (m, 2H), 1.18-1.28 (m, 2H), 1.19 (t, 3H, J = 7.1 Hz), 1.42 (s, 1H), 1.76-1.85 (m, 2H), 1.85-1.93 (m, 2H), 2.79 (t, 2H, J = 5.9 Hz), 2.97 (q, 2H, J = 7.1 Hz), 3.02 (m, 1H), 3.71 (s, 3H), 5.26 (m, 1H), 6.58 (d, 1H, J = 8.6 Hz), 6.98 (d, 2H, J = 7.8 Hz), 7.02 (d, 2H, J = 8.6 Hz), 7.44 (br s, 1H).

Compound Ii-43

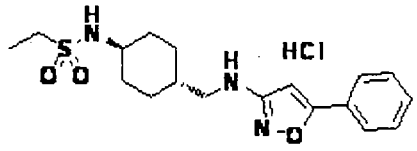
[Formula 205]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.06 (m, 2H), 1.16-1.25 (m, 2H), 1.18 (t, 3H, J =7.5 Hz), 1.51 (m, 1H), 1.83-1.91 (m, 4H), 2.85 (t, 2H, J = 6.3 Hz), 2.97 (q, 2H, J = 7.5 Hz), 3.04(m, 1H), 3.56 (s, 3H), 5.46 (t, 1H, J = 6.3 Hz), 5.76 (s, 1H), 6.49 (d, 1H, J = 7.8 Hz), 7.21 (t, 1H, J = 7.5Hz), 7.32 (t, 2H, J = 7.5 Hz), 7.68 (d, 2H, J = 7.5 Hz)

Compound Ii-44

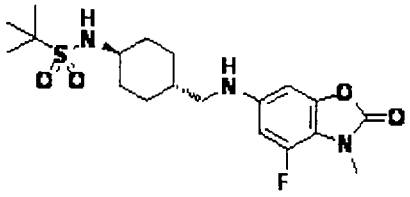
[Formula 206]



^{1}H-NMR (DMSO-d_6)δ: 0.96-1.05 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.24 (m, 2H), 1.48 (m, 1H), 1.76-1.91 (m, 4H), 2.91 (d, 2H, J = 6.6 Hz), 2.97 (q, 2H, J = 7.2 Hz), 6.35 (s, 1H), 6.99 (d, 1H, J = 7.8 Hz), 7.46-7.49 (m, 3H), 7.73-7.76 (m, 2H)

Compound Ii-45

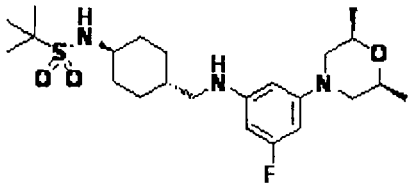
[Formula 207]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 2H), 1.15-1.22 (m, 1H), 1.26 (s, 9H), 1.37-1.51 (m, 2H), 1.81 (d, 2H, J = 11.6 Hz), 1.91 (d, 2H, J = 11.6 Hz), 2.76-2.86 (m, 2H), 2.97-3.08 (m, 1H), 3.35 (s, 3H), 5.82-5.91 (m, 1H), 6.26 (d, 1H, J = 13.6 Hz), 6.39 (s, 1H), 6.73 (brs, 1H). Melting point: 215 to 216 °C

Compound Ii-46

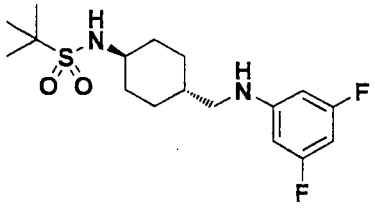
[Formula 208]



^{1}H-NMR ($CDCl_3$) δ: 1.02-1.32 (m, 4H), 1.24 (d, 6H, J = 6.0 Hz), 1.39 (s, 9H), 1.54 (m, 1H), 1.84-1.94 (m, 2H), 2.12-2.22 (m, 2H), 2.39 (t, 2H, J = 10.5 Hz), 2.94 (d, 2H, J = 6.9 Hz), 3.24 (m, 1H), 3.38 (d, 1H, J = 9.6 Hz), 3.61 (d, 1H, J = 9.6 Hz), 3.72-4.00 (m, 2H), 5.83-5.94 (m, 1H), 5.96-6.10 (m, 2H).

Compound Ii-47

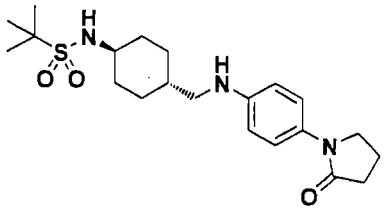
[Formula 209]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.07 (m, 2H), 1.16-1.34 (m, 11H), 1.40 (m, 1H), 1.79 (d, 2H, J = 12.5 Hz), 1.90 (d, 2H, J = 11.9 Hz), 2.82 (t, 2H, J = 5.5 Hz), 3.01 (m, 1H), 6.12-6.18 (m, 3H), 6.30 (t, 1H, J = 5.5 Hz), 6.76 (d, 1H, J = 8.7 Hz).

Compound Ii-48

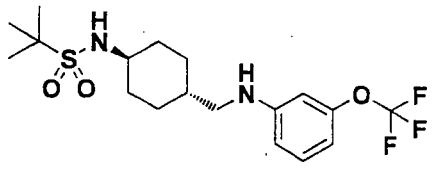
[Formula 210]



^{1}H-NMR ($CDCl_3$) δ: 1.00-1.28 (m, 4H), 1.39 (s, 9H), 1.56 (m, 1H), 1.91 (d, 2H, J = 12.4 Hz), 2.08-2.21 (m, 4H), 2.58 (t, 2H, J = 8.1 Hz), 2.97 (d, 2H, J = 6.0 Hz), 3.23 (m, 1H), 3.70 (d, 1H, J = 9.4 Hz), 3.80 (t, 2H, J = 7.1 Hz), 6.66 (d, 2H, J = 8.7 Hz), 7.36 (d, 2H, J = 8.7 Hz).

Compound Ii-49

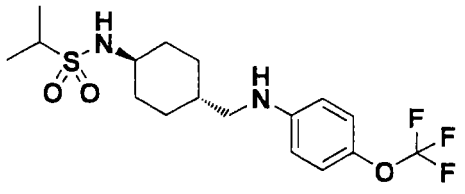
[Formula 211]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.06 (m, 2H), 1.17-1.33 (m, 11H), 1.41 (m, 1H), 1.80 (d, 2H, J = 12.9 Hz), 1.90 (d, 2H, J = 11.4 Hz), 2.82 (t, 2H, J = 6.1 Hz), 3.01 (m, 1H), 6.07 (t, 1H, J = 5.3 Hz), 6.34-6.43 (m, 2H), 6.51 (dd, 1H, J1 = 8.2 Hz, J2 = 1.8 Hz), 6.75 (d, 1H, J = 8.5 Hz), 7.11 (t, 1H, 8.2 Hz).

Compound Ii-50

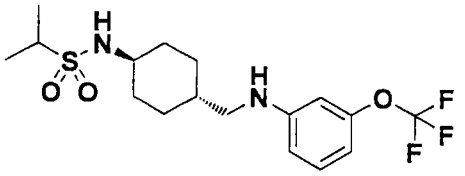
[Formula 212]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 2H), 1.14-1.31 (m, 8H), 1.43 (m, 1H), 1.76-1.94 (m, 4H), 2.82 (t, 2H, J = 6.0 Hz), 2.95-3.16 (m, 2H), 5.90 (t, 1H, J = 5.5 Hz), 6.56 (d, 2H, J = 8.7 Hz), 6.95 (d, 1H, J = 7.9 Hz), 7.03 (d, 2H, J = 8.6 Hz).

Compound Ii-51

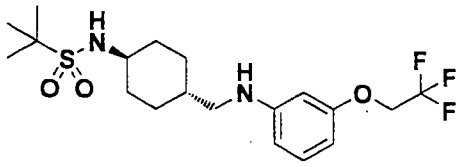
[Formula 213]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.08 (m, 2H), 1.13-1.31 (m, 8H), 1.42 (m, 1H), 1.76-1.94 (m, 4H), 2.83 (t, 2H, J = 6.0 Hz), 2.95-3.16 (m, 2H), 6.07 (t, 1H, J = 5.4 Hz), 6.36-6.46 (m, 2H), 6.53 (dd, 1H, J1 = 8.1 Hz, J2 = 1.9 Hz), 6.95 (d, 1H, J = 7.9 Hz), 7.12 (d, 1H, J = 8.1 Hz).

Compound Ii-52

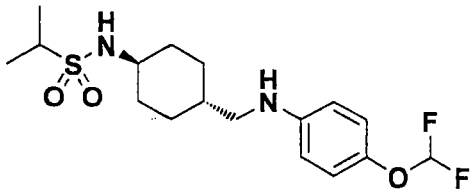
[Formula 214]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.10 (m, 2H), 1.19-1.37 (m, 11H), 1.45 (m, 1H), 1.78-1.90 (m, 4H), 2.84 (t, 2H, J = 6.0 Hz), 3.04 (m, 1H), 4.64 (q, 2H, J = 9.0 Hz), 5.73 (t, 1H, J = 5.4 Hz), 6.13-6.21 (m, 2H), 6.26 (d, 1H, J = 7.2 Hz), 6.78 (d, 1H, J = 8.4 Hz), 6.99 (t, 1H, 8.0 Hz).

Compound Ii-53

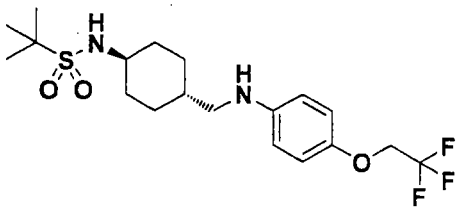
[Formula 215]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.13-1.30 (m, 8H), 1.42 (m, 1H), 1.75-1.93 (m, 4H), 2.80 (t, 2H, J = 6.2 Hz), 2.93-3.16 (m, 2H), 5.66 (t, 1H, J = 5.5 Hz), 6.53 (d, 2H, J = 9.1 Hz), 6.89 (d, 2H, J = 8.8 Hz), 6.92 (t, 1H, J_{H-F} = 75 Hz), 6.94 (d, 1H, J = 8.0 Hz).

Compound Ii-54

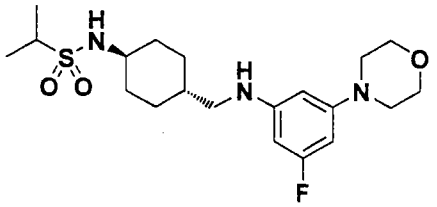
[Formula 216]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.05 (m, 2H), 1.14-1.32 (m, 11H), 1.41 (m, 1H), 1.75-1.94 (m, 4H), 2.77 (t, 2H, J = 6.0 Hz), 3.01 (m, 1H), 4.54 (q, 2H, J = 9.0 Hz), 5.33 (t, 1H, J = 5.8 Hz), 6.49 (d, 2H, J = 8.8 Hz), 6.75 (d, 1H, J = 8.8 Hz), 6.80 (d, 2H, J = 8.8 Hz).

Compound Ii-55

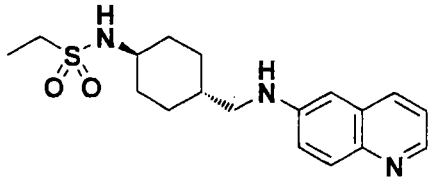
[Formula 217]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.14-1.31 (m, 8H), 1.40 (m, 1H), 1.74-1.93 (m, 4H), 2.79 (t, 2H, J = 5.9 Hz), 2.94-3.15 (m, 6H), 3.69 (t, 4H, J = 4.8 Hz), 5.70-5.94 (m, 4H), 6.94 (d, 1H, J = 8.0 Hz).

Compound Ii-56

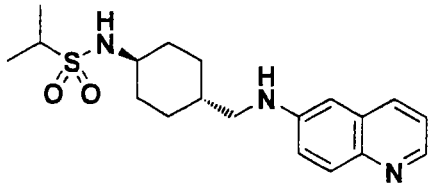
[Formula 218]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.14 (m, 2H), 1.15-1.32 (m, 5H), 1.54 (m, 1H), 1.83-1.96 (m, 4H), 2.89-3.10 (m, 5H), 6.17 (t, 1H, J = 5.2 Hz), 6.63 (d, 1H, J = 2.2 Hz), 7.02 (d, 1H, J = 7.7 Hz), 7.21 (dd, 1H, J1 = 9.1 Hz, J2 = 2.5 Hz), 7.27 (dd, 1H, J1 = 8.2 Hz, J2 = 4.4 Hz), 7.67 (d, 1H, J = 9.1 Hz), 7.97 (d, 1H, J = 8.2 Hz), 8.45 (dd, 1H, J1 = 4.3 Hz, J2 = 1.5 Hz).

Compound Ii-57

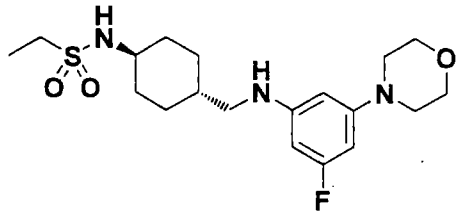
[Formula 219]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.14 (m, 2H), 1.17-1.34 (m, 8H), 1.54 (m, 1H), 1.83-1.96 (m, 4H), 2.94 (t, 2H, J = 6.0 Hz), 2.99-3.18 (m, 2H), 6.17 (t, 1H, J = 5.4 Hz), 6.63 (d, 1H, J = 2.5 Hz), 6.96 (d, 1H, J = 7.7 Hz), 7.21 (dd, 1H, J1 = 9.1 Hz, J2 = 2.5 Hz), 7.27 (dd, 1H, J1 = 8.2 Hz, J2 = 4.1 Hz), 7.67 (d, 1H, J = 9.1 Hz), 7.97 (d, 1H, J = 8.0 Hz), 8.45 (dd, 1H, J1 = 4.3 Hz, J2 = 1.5 Hz).

Compound Ii-58

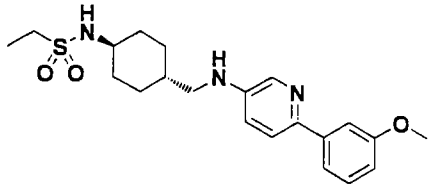
[Formula 220]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.07 (m, 2H), 1.12-1.29 (m, 5H), 1.40 (m, 1H), 1.74-1.93 (m, 4H), 2.80 (t, 2H, J = 5.9 Hz), 2.92-3.07 (m, 7H), 3.69 (t, 4H, J = 4.8 Hz), 5.69-5.95 (m, 4H), 6.99 (d, 1H, J = 7.7 Hz).

Compound Ii-59

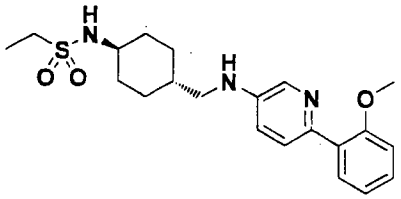
[Formula 221]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.11 (m, 2H), 1.14-1.30 (m, 5H), 1.47 (m, 1H), 1.78-1.95 (m, 4H), 2.88-3.09 (m, 5H), 3.80 (s, 3H), 6.09 (t, 1H, J = 5.6 Hz), 6.81-6.86 (m, 1H), 6.96 (dd, 1H, J1 = 8.8 Hz, J2 = 2.8 Hz), 7.01 (d, 1H, J = 7.4 Hz), 7.29 (t, 1H, J = 8.0 Hz), 7.45-7.51 (m, 2H), 7.66 (d, 1H, J = 8.5 Hz), 8.04 (d, 1H, J = 2.8 Hz).

Compound Ii-60

[Formula 222]

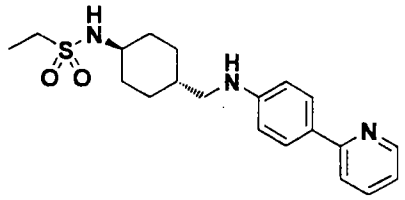


^{1}H-NMR (DMSO-d_6) δ: 1.03 (m, 2H), 1.19 (t, 2H, J = 7.8 Hz), 1.21 (m, 2H), 1.46 (m, 1H), 1.76-1.95 (m, 4H), 2.90 (t, 2H, J = 5.8 Hz), 2.97 (q, 2H, J = 7.3 Hz), 3.03 (m, 1H), 3.80 (s, 3H), 5.95 (m, 1H), 6.90 (m, 1H), 6.98 (d, 1H, J = 7.8 Hz), 6.98 (dd, 1H, J = 7.8, 7.8 Hz), 7.06 (d, 1H, J = 8.6 Hz), 7.26 (dd, 1H, J = 7.8, 7.8 Hz),

7.61 (d, 1H, J = 8.6 Hz), 7.69 (d, 1H, J = 7.8 Hz), 8.03 (s, 1H).

Compound Ii-61

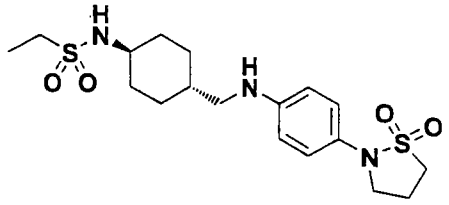
[Formula 223]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.09 (m, 2H), 1.18-1.29 (m,2H), 1.19 (t, 3H, J = 7.6 Hz), 1.47 (m, 1H), 1.87 (m, 5H), 2.90 (t, 2H, J = 6.3 Hz), 2.97 (q, 2H, J = 7.6 Hz), 3.02 (m, 1H), 5.98 (m, 1H), 6.63 (d, 2H, J = 8.3 Hz), 6.98 (d, 1H, J = 7.3 Hz), 7.14 (m, 1H), 7.73 (s, 2H), 7.83 (d, 2H, J = 8.3 Hz), 8.52 (d, 1H, J = 4.0 Hz).

Compound Ii-62

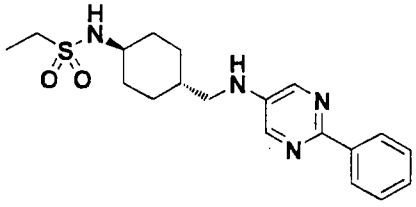
[Formula 224]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.01 (m, 2H), 1.20 (s, 9H), 1.20-1.37 (m, 2H), 1.42 (m, 1H), 1.76-1.96 (m, 4H), 2.28-2.37 (m, 2H), 2.75-2.85 (m, 2H), 3.02 (m, 1H), 3.36 (t, 2H, J = 7.8 Hz), 3.57 (t, 2H, J = 6.3 Hz), 5.66 (m, 1H), 6.54 (d, 2H, J = 8.0 Hz), 6.73 (d, 1H, J = 8.6 Hz), 7.00 (d, 1H, J = 8.0 Hz).

Compound Ii-63

[Formula 225]

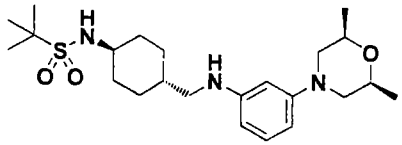


^{1}H-NMR (DMSO-d_6) δ: 0.96-1.14 (m, 2H), 1.14-1.32 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.50 (m, 1H), 1.76-1.96 (m, 4H), 2.91-3.10 (m, 3H), 2.97 (q, 2H, J = 7.2 Hz),

6.28 (m, 1H), 7.02 (d, 1H, J = 7.8 Hz), 7.32-7.46 (m, 3H), 8.20 (d, 1H, J = 6.9 Hz), 8.22 (s, 2H).

Compound Ii-64

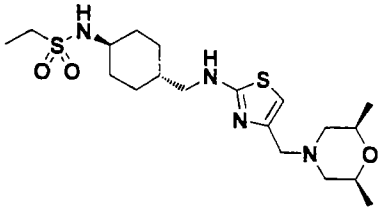
[Formula 226]



^{1}H-NMR (DMSO-d_6) δ: 1.03-1.15 (m, 2H), 1.18-1.29 (m, 2H), 1.24 (d, 6H, J = 6.3 Hz), 1.52 (m, 1H), 1.86-1.94 (m, 2H), 2.10-2.19 (m, 2H), 2.40 (t, 2H, J = 6.0 Hz), 2.95 (d, 2H, J = 6.0 Hz), 3.23 (m, 1H), 3.40 (d, 2H, J = 11.4 Hz), 3.75-3.85 (m, 2H), 3.86 (d, 1H, J = 9.3 Hz), 6.14 (d, 1H, J = 8.5 Hz), 6.15 (s, 1H), 6.29 (d, 1H, J = 8.5 Hz), 7.06 (d, 1H, J = 8.5 Hz).

Compound Ii-65

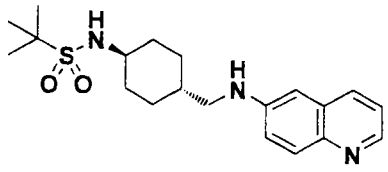
[Formula 227]



^{1}H-NMR ($CDCl_3$) δ:1.08-1.16 (m, 2H), 1.14 (d, 6H, J = 6.8 Hz), 1.21-1.30 (m, 2H), 1.29 (s, 9H), 1.78 (t, 2H, J = 10.6 Hz), 1.83-1.92 (m, 2H), 2.11-2.19 (m, 2H), 2.78 (d, 2H, J = 10.6 Hz), 3.06 (s, 2H), 3.23 (m, 1H), 3.38 (s, 2H), 3.70-3.80 (m, 2H), 4.02 (d, 1H, J = 9.9 Hz), 5.37 (s, 1H), 6.30 (s, 1H).

Compound Ii-66

[Formula 228]

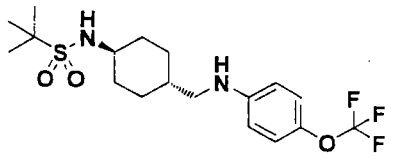


^{1}H-NMR (DMSO-d_6) δ: 1.01-1.12 (m, 2H), 1.20-1.34 (m, 2H), 1.27 (s, 9H), 1.54 (m,

1H), 1.82-1.99 (m, 4H), 2.91-2.98 (m, 2H), 3.06 (m ,1H), 6.17 (s, 1H), 6.63 (s, 1H), 6.78 (d, 1H, J = 9.0 Hz), 7.20 (m, 1H), 7.27 (m, 1H), 7.77 (d, 1H, J = 9.0 Hz), 7.98 (d, 1H, J = 9.0 Hz), 8.54 (s, 1H).

Compound Ii-67

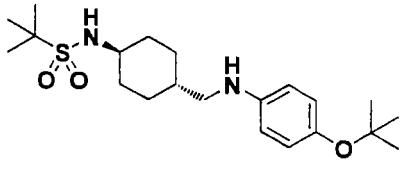
[Formula 229]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.06 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 1.88-1.96 (m, 2H), 2.78-2.86 (m, 2H), 3.02 (m ,1H), 5.89 (s, 1H), 6.56 (d, 1H, J = 8.4 Hz), 6.76 (d, 1H, J = 8.4 Hz), 7.02 (d, 1H, J = 8.4 Hz).

Compound Ii-68

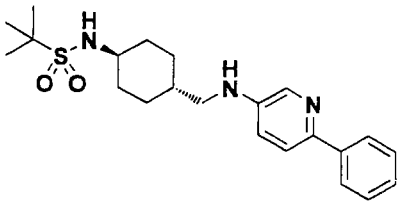
[Formula 230]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.05 (m, 2H), 1.19 (s, 9H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.42 (m, 1H), 1.80-1.96 (m, 4H), 2.77 (s, 2H), 3.04 (m, 1H), 5.29 (s, 1H), 6.44 (d, 1H, J = 7.2 Hz), 6.68 (d, 1H, J = 7.2 Hz), 6.75 (d, 1H, J = 8.4 Hz).

Compound Ii-69

[Formula 231]

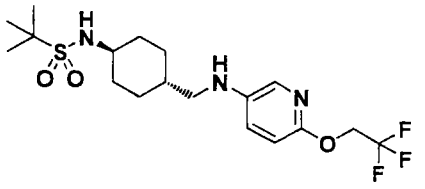


^{1}H-NMR (DMSO-d_6) δ: 0.95-1.10 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.47 (m, 1H), 1.80-1.88 (m, 2H), 1.88-1.95 (m, 2H), 2.88-2.95 (m, 2H), 3.02 (s, 1H), 6.07 (m, 1H), 6.77 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 7.6 Hz), 7.26 (t, 1H, J = 7.6 Hz),

7.35-7.42 (m, 2H), 7.46 (d, 1H, J = 8.4 Hz), 7.91 (d, 1H, J = 7.6 Hz), 8.04 (s, 1H).

Compound Ii-70

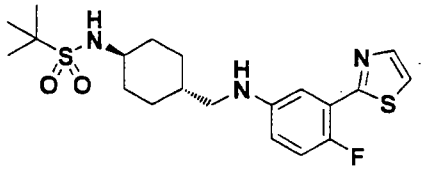
[Formula 232]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.05 (m, 2H), 1.10-1.32 (m, 2H), 1.26 (s, 9H), 1.42 (m, 1H), 1.78-1.86 (m, 2H), 1.86-1.95 (m, 2H), 2.78-2.83 (m, 2H), 3.03 (m, 1H), 4.80 (q, 2H, J = 9.2 Hz), 5.48 (t, 1H, J = 5.6 Hz), 6.69-6.76 (m, 2H), 7.08 (dd, 1H, J = 8.8, 2.4 Hz), 7.45 (d, 1H, J = 2.4 Hz).

Compound Ii-71

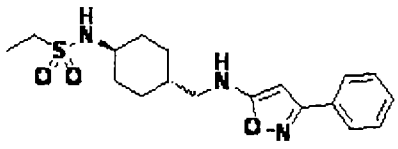
[Formula 233]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.10 (m, 2H), 1.20-1.32 (m, 2H), 1.27 (s, 9H), 1.82-1.88 (m, 2H), 1.88-1.97 (m, 2H), 2.83-2.88 (m, 2H), 3.04 (m, 1H), 5.82 (s, 1H), 6.69 (m, 1H), 6.76 (d, 1H, J = 8.8 Hz), 7.12 (dd, 1H, J = 9.2, 8.8 Hz), 7.37 (m, 1H), 7.87 (d, 1H, J = 2.8 Hz), 7.99 (s, 1H).

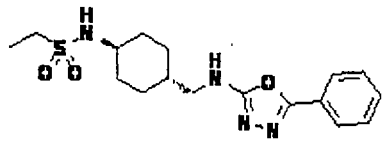
Compound Ii-72

[Formula 234]



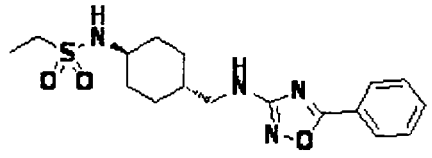
Compound Ii-73

[Formula 235]



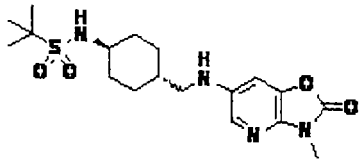
Compound Ii-74

[Formula 236]



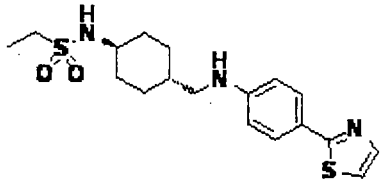
Compound Ii-75

[Formula 237]



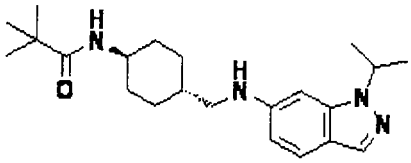
Compound Ii-76

[Formula 238]



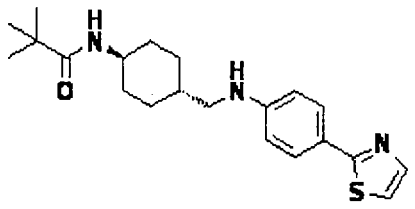
Compound Ii-77

[Formula 239]



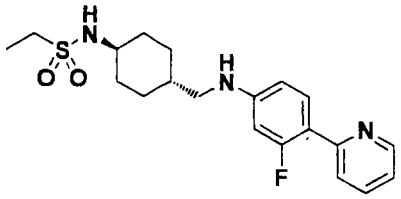
Compound Ii-78

[Formula 240]



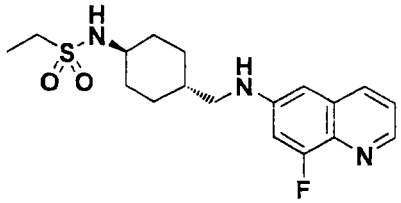
Compound Ii-79

[Formula 241]



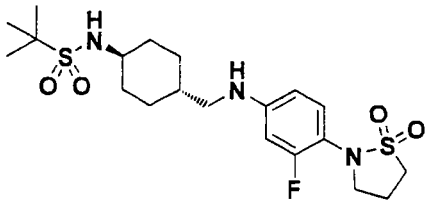
Compound Ii-80

[Formula 242]



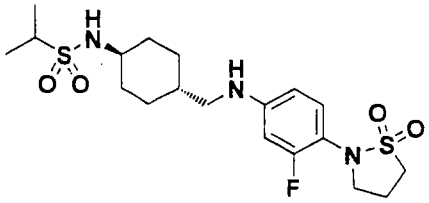
Compound Ii-81

[Formula 243]



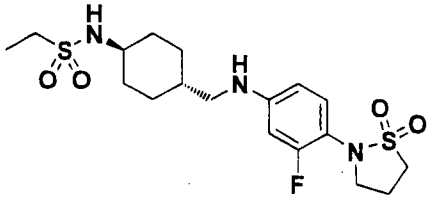
Compound Ii-82

[Formula 244]



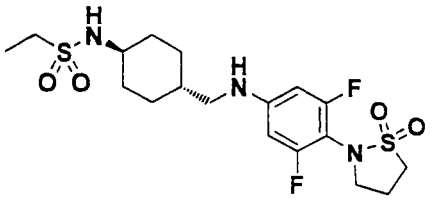
Compound Ii-83

[Formula 245]



Compound Ii-84

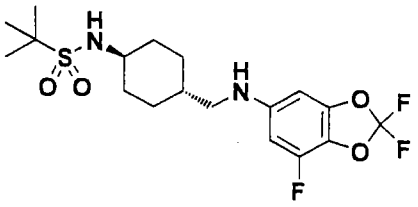
[Formula 246]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.08 (m, 2H), 1.14-1.30 (t, 3H, J = 7.5 Hz), 1.41 (m, 1H), 1.73-1.94 (m, 4H), 2.34-2.46 (m, 2H), 2.85 (t, 2H, J = 6.6 Hz), 2.97 (q, 2H, J = 7.5 Hz), 3.00 (m, 1H), 3.25 (t, 2H, J = 7.5 Hz), 3.53 (t, 2H, J = 6.6 Hz), 6.27 (d, 2H, J = 11.7 Hz), 6.52 (t, 1H, J = 5.1 Hz), 7.00 (d, 1H, J = 7.2 Hz).

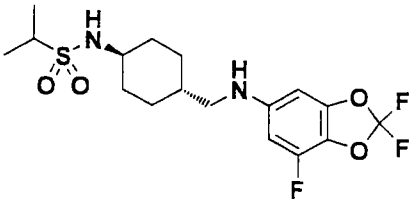
Compound Ii-85

[Formula 247]



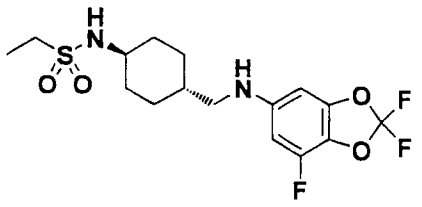
Compound Ii-86

[Formula 248]



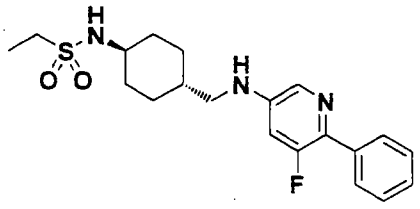
Compound Ii-87

[Formula 249]



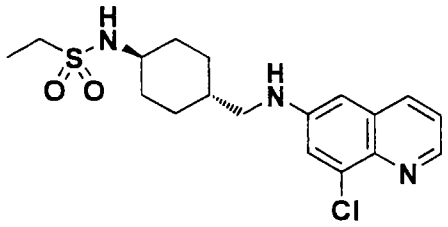
Compound Ii-88

[Formula 250]



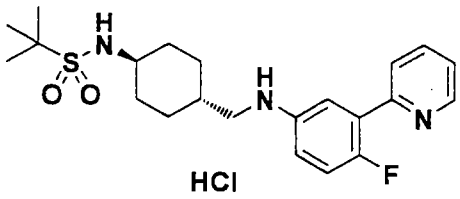
Compound Ii-89

[Formula 251]



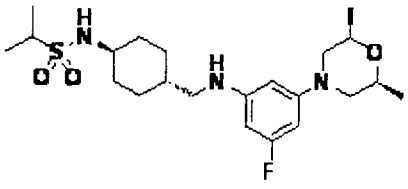
Compound Ii-90

[Formula 252]



Compound Ii-91

[Formula 253]

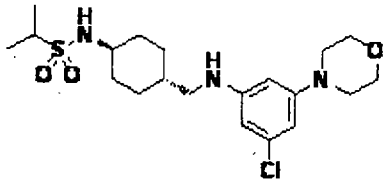


^{1}H-NMR (DMSO-d_6) δ: 0.92-1.05 (m, 2H), 1.13 (d, 6H, J = 6.0 Hz), 1.18-1.30 (m,

2H), 1.21 (d, 6H, J = 6.4 Hz), 1.40 (m, 1H), 1.76-1.83 (m, 2H), 1.83-1.93 (m, 2H), 2.19 (dd, 1H, J = 11.2, 11.2 Hz), 2.76-2.82 (m, 2H), 3.01 (m, 1H), 3.09 (m, 1H), 3.45 (d, 2H, J = 11.2 Hz), 3.58-3.69 (m, 2H), 5.67 (m, 1H), 5.77 (d, 1H, J = 12.0 Hz), 5.90 (s, 1H), 5.91 (m, 1H), 6.91 (d, 1H, J = 7.6 Hz).

Compound Ii-92

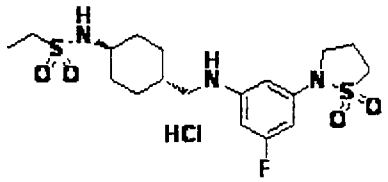
[Formula 254]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.07 (m, 2H), 1.14-1.30 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.32-1.46 (m, 1H), 1.75-1.92 (m, 4H), 2.78-2.83 (m, 2H), 2.95-3.18 (m, 6H), 3.66-3.72 (m, 4H), 5.75 (brs, 1H), 6.00 (s, 1H), 6.04 (s, 1H), 6.11 (s, 1H), 6.95 (d, 1H, J = 9.0 Hz).

Compound Ii-93

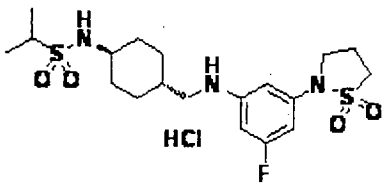
[Formula 255]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.08 (m, 2H), 1.13-1.27 (m, 5H), 1.42 (m, 1H), 1.74-1.93 (m, 4H), 2.30-2.40 (m, 2H), 2.81 (d, 2H, J = 6.6 Hz), 2.97 (q, 2H, J = 7.5 Hz), 3.00 (m, 1H), 3.49 (t, 2H, J = 7.5 Hz), 3.66 (t, 2H, J = 6.6 Hz), 5.00-5.50 (brs, 2H), 6.07-6.15 (m, 2H), 6.25(s, 1H), 7.00 (d, 1H, J = 6.6Hz).

Compound Ii-94

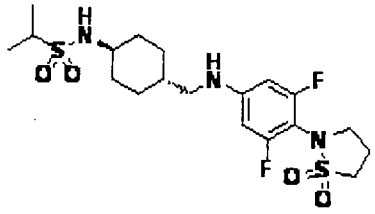
[Formula 256]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.07 (m, 2H), 1.15-1.32 (m, 5H), 1.21 (d, 6H, J = 6.9 Hz), 1.42 (m, 1H), 1.74-1.93 (m, 4H), 2.30-2.42 (m, 2H), 2.81 (d, 2H, J = 6.6 Hz), 2.92-3.18 (m, 2H), 3.49 (t, 2H, J = 7.5 Hz), 3.66 (t, 2H, J = 6.6 Hz), 4.70-5.30 (brs, 2H), 6.05-6.16 (m, 2H), 6.25 (s, 1H), 6.95 (d, 1H, J = 8.1Hz).

Compound Ii-95

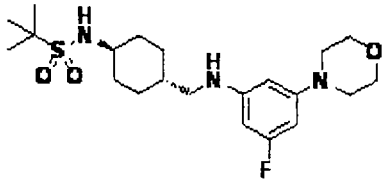
[Formula 257]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.16-1.31 (d, 6H, J = 6.9 Hz), 1.40 (m, 1H), 1.73-1.94 (m, 4H), 2.34-2.46 (m, 2H), 2.84 (t, 2H, J = 6.0 Hz), 2.94-3.16 (m, 2H), 3.28 (t, 2H, J = 7.5 Hz), 3.53 (t, 2H, J = 6.6 Hz), 6.27 (d, 2H, J = 11.7 Hz), 6.52 (t, 1H, J = 5.4 Hz), 6.94 (d, 1H, J = 7.8 Hz).

Compound Ii-96

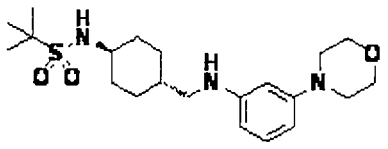
[Formula 258]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.04 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.40 (m, 1H), 1.76-1.95 (m, 4H), 2.77-2.83 (m, 2H), 2.99-3.04 (m, 5H), 3.67-3.72 (m, 4H), 5.71 (m, 1H), 5.79 (d, 1H, J = 11.7 Hz), 5.89 (s, 1H), 5.90 (m, 1H), 6.72 (d, 1H, J = 8.4 Hz).

Compound Ii-97

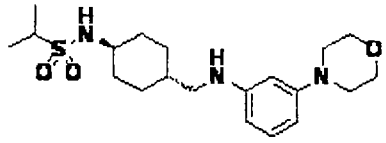
[Formula 259]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.03 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.41 (m, 1H), 1.77-1.93 (m, 4H), 2.78-2.83 (m, 2H), 2.97-3.05 (m, 5H), 3.68-3.72 (m, 4H), 5.36 (m, 1H), 6.04 (d, 1H, J = 8.0 Hz), 6.10 (s, 1H), 6.11 (d, 1H, J = 8.0 Hz), 6.72 (d, 1H, J = 8.0 Hz), 6.89 (dd, 1H, J = 8.0, 8.0 Hz).

Compound Ii-98

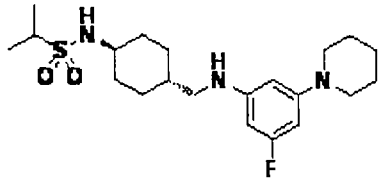
[Formula 260]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.04 (m, 2H), 1.17-1.29 (m, 2H), 1.21 (d, 6H, J = 6.4 Hz), 1.41 (m, 1H), 1.75-1.92 (m, 4H), 2.77-2.83 (m, 2H), 2.95-3.05 (m, 5H), 3.09 (m, 1H), 3.67-3.72 (m, 4H), 5.36 (m, 1H), 6.04 (d, 1H, J = 8.0 Hz), 6.10 (s, 1H), 6.11 (d, 1H, J = 8.0 Hz), 6.89 (dd, 1H, J = 8.0, 8.0 Hz), 6.92 (d, 1H, J = 8.0 Hz).

Compound Ii-99

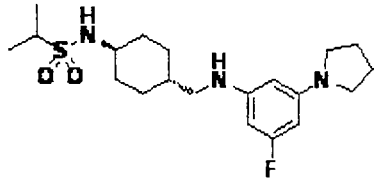
[Formula 261]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.15-1.31 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.39 (m, 1H), 1.47-1.62 (m, 6H), 1.74-1.94 (m, 4H), 2.78 (t, 2H, J = 6.0 Hz), 2.93-3.16 (m, 6H), 5.64-5.76 (m, 2H), 5.83-5.92 (m, 2H), 6.94 (d, 1H, J = 7.8 Hz).

Compound Ii-100

[Formula 262]

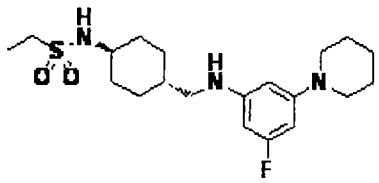


^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.15-1.30 (m, 2H), 1.21 (d, 6H, J = 6.9

Hz), 1.40 (m, 1H), 1.74-1.96 (m, 8H), 2.79 (t, 2H, J = 6.0 Hz), 2.93-3.18 (m, 6H), 5.48-5.67 (m, 4H), 6.94 (d, 1H, J = 8.1 Hz).

Compound Ii-101

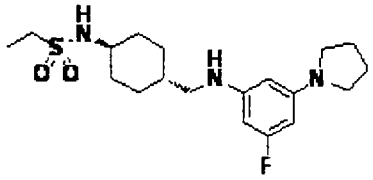
[Formula 263]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 2H), 1.13-1.29 (m, 2H), 1.18 (t, 3H, J = 7.5 Hz), 1.39 (m, 1H), 1.47-1.62 (m, 6H), 1.75-1.94 (m, 4H), 2.79 (t, 2H, J = 6.0 Hz), 2.97 (q, 2H, J = 7.5 Hz), 3.03-3.10 (m, 4H), 5.64-5.75 (m, 2H), 5.83-5.91 (m, 2H), 7.00 (d, 1H, J = 7.8 Hz).

Compound Ii-102

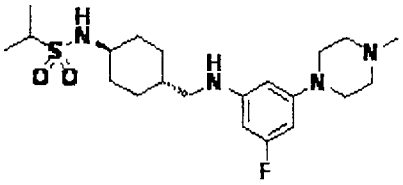
[Formula 264]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.07 (m, 2H), 1.13-1.29 (m, 2H), 1.18 (t, 3H, J = 7.5 Hz), 1.41 (m, 1H), 1.74-1.96 (m, 8H), 2.79 (t, 2H, J = 6.0 Hz), 2.97 (q, 2H, J = 7.5 Hz), 3.00 (m, 1H), 3.09-3.19 (m, 4H), 5.46-5.66 (m, 4H), 6.99 (d, 1H, J = 7.2 Hz).

Compound Ii-103

[Formula 265]

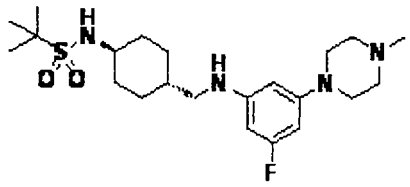


^{1}H-NMR (DMSO-d_6) δ: 0.91-1.03 (m, 2H), 1.16-1.29 (m, 2H), 1.21 (d, 6H, J = 6.8 Hz), 1.40 (m, 1H), 1.75-1.92 (m, 4H), 2.20 (s, 3H), 2.35-2.43 (m, 4H), 2.75-2.82 (m, 2H), 2.88-3.13 (m, 6H), 5.67 (m, 1H), 5.76 (d, 1H, J = 11.2 Hz), 5.82-5.92 (m, 2H),

6.91 (d, 1H, J = 8.0 Hz).

Compound Ii-104

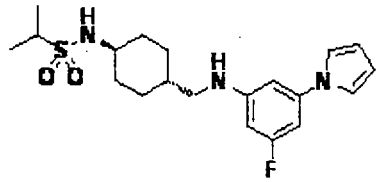
[Formula 266]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.02 (m, 2H), 1.19-1.32 (m, 2H), 1.26 (s, 9H), 1.39 (m, 1H), 1.75-1.95 (m, 4H), 2.19 (s, 3H), 2.38-2.42 (m, 4H), 2.77-2.83 (m, 5H), 2.98-3.09 (m, 5H), 5.67 (m, 1H), 5.76 (d, 1H, J = 11.2 Hz), 5.88 (m, 1H), 5.88 (s, 1H), 6.72 (d, 1H, J = 8.8 Hz).

Compound Ii-105

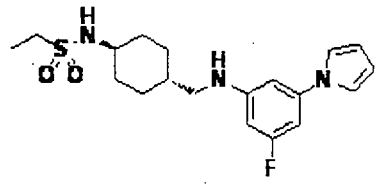
[Formula 267]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.09 (m, 2H), 1.18-1.31 (m, 2H), 1.22 (d, 6H, J = 6.8 Hz), 1.44 (m, 1H), 1.78-1.93 (m, 4H), 2.87-2.92 (m, 2H), 3.03 (m, 1H), 3.10 (m, 1H), 6.13 (m, 1H), 6.21 (m, 1H), 6.22 (s, 2H), 6.51 (s, 1H), 6.52 (d, 1H, J = 8.0 Hz), 6.92 (d, 1H, J = 8.0 Hz), 7.26 (s, 2H).

Compound Ii-106

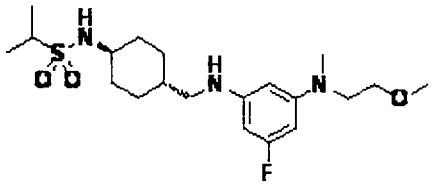
[Formula 268]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.08 (m, 2H), 1.17-1.29 (m, 5H), 1.40-1.68 (m, 3H), 1.80-1.92 (m, 2H), 2.90 (t, 2H, J = 6.0 Hz), 2.94-3.06 (m, 3H), 6.12-6.22 (m, 4H), 6.50-6.54 (m, 2H), 6.94-7.00 (m, 1H), 7.26-7.27 (m, 2H).

Compound Ii-107

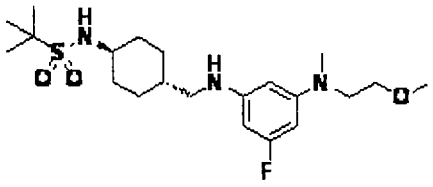
[Formula 269]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.03 (m, 2H), 1.16-1.29 (m, 2H), 1.21 (d, 6H, J = 6.4 Hz), 1.40 (m, 1H), 1.74-1.92 (m, 4H), 2.75-2.81 (m, 2H), 2.84 (s, 3H), 3.00 (m, 1H), 3.09 (m, 1H), 3.25 (s, 3H), 3.35-3.47 (m, 4H), 5.59-5.67 (m, 4H), 6.91 (d, 1H, J = 8.0 Hz).

Compound Ii-108

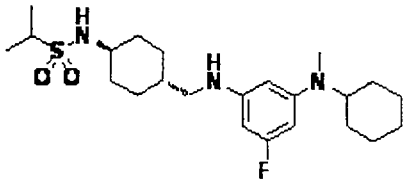
[Formula 270]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.03 (m, 2H), 1.18-1.32 (m, 2H), 1.26 (s, 9H), 1.40 (m, 1H), 1.75-1.94 (m, 4H), 2.75-2.81 (m, 2H), 2.83 (s, 3H), 3.01 (m, 1H), 3.25 (s, 3H), 3.34-3.47 (m, 4H), 5.58-5.70 (m, 4H), 6.72 (d, 1H, J = 8.4 Hz).

Compound Ii-109

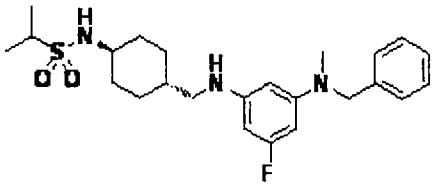
[Formula 271]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.51 (m, 10H), 1.21 (d, 6H, J = 6.9 Hz), 1.56-1.67 (m, 3H), 1.71-1.93 (m, 6H), 2.64 (s, 3H), 2.78 (t, 2H, J = 6.0 Hz), 2.93-3.17 (m, 2H), 3.44 (m, 1H), 5.56-5.77 (m, 4H), 6.94 (d, 1H, J = 7.8 Hz).

Compound Ii-110

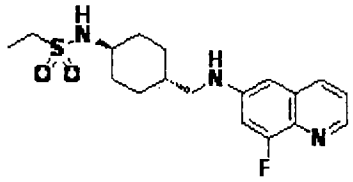
[Formula 272]



^{1}H-NMR (DMSO-d_6) δ: 0.83-1.01 (m, 2H), 1.00-1.40 (m, 3H), 1.21 (d, 6H, J = 6.9 Hz), 1.68-1.91 (m, 4H), 2.73 (t, 2H, J = 6.0 Hz), 2.90-3.15 (m, 2H), 2.95 (s, 3H), 4,48 (s, 2H), 5.60-5.72 (m, 4H), 6.94 (d, 1H, J = 7.8 Hz), 7.15-7.35 (m, 5H).

Compound Ii-111

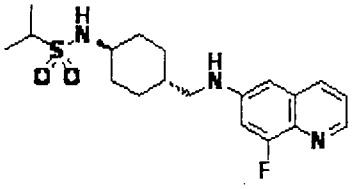
[Formula 273]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.14 (m, 2H), 1.14-1.33 (m, 5H), 1.45-1.61 (m, 1H), 1.81-1.96 (m, 4H), 2.90-3.10 (m, 5H), 6.34 (t, 1H, J = 5.2 Hz), 6.51 (d, 1H, J = 2.2 Hz), 6.99-7.07 (m, 2H), 7.36 (dd, 1H, J = 8.2, 4.1 Hz), 8.02 (d, 1H, J = 8.5 Hz), 8.48 (dd, 1H, J = 4.1, 1.4 Hz).

Compound Ii-112

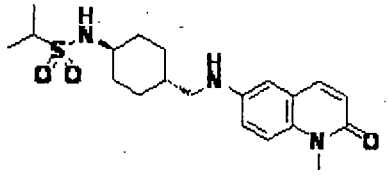
[Formula 274]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.13 (m, 2H), 1.17-1.34 (m, 8H), 1.45-1.59 (m, 1H), 1.81-1.99 (m, 4H), 2.94 (t, 2H, J = 5.9 Hz), 2.99-3.21 (m, 2H), 6.33 (t, 1H, J = 5.4 Hz), 6.51 (d, 1H, J = 2.2 Hz), 6.96 (d, 1H, J = 7.7 Hz), 7.02 (dd, 1H, J = 13.5, 2.2 Hz), 7.36 (dd, 1H, J = 8.2, 4.1 Hz), 8.02 (d, 1H, J = 8.5 Hz), 8.48 (dd, 1H, J = 4.1, 1.4 Hz).

Compound Ii-113

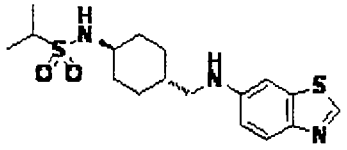
[Formula 275]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.13 (m, 2H), 1.15-1.34 (m, 8H), 1.39-1.57 (m, 1H), 1.79-1.95 (m, 4H), 2.87 (t, 2H, J = 6.2 Hz), 2.94-3.16 (m, 2H), 3.54 (s, 3H), 5.66 (t, 1H, J = 5.5 Hz), 6.49 (d, 1H, J = 9.6 Hz), 6.73 (d, 1H, J = 2.8 Hz), 6.91-7.02 (m, 2H), 7.29 (d, 1H, J = 9.3 Hz), 7.72 (d, 1H, J = 9.3 Hz).

Compound Ii-114

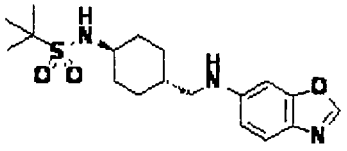
[Formula 276]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.10 (m, 2H), 1.14-1.33 (m, 8H), 1.41-1.56 (m, 1H), 1.79-1.94 (m, 4H), 2.89 (t, 2H, J = 6.0 Hz), 2.95-3.16 (m, 2H), 6.00 (t, 1H, J = 5.4 Hz), 6.84 (dd, 1H, J = 8.8, 2.2 Hz), 6.95 (d, 1H, J = 8.0 Hz), 7.07 (d, 1H, J = 2.2 Hz), 7.72 (d, 1H, J = 8.8 Hz), 8.86 (s, 1H).

Compound Ii-115

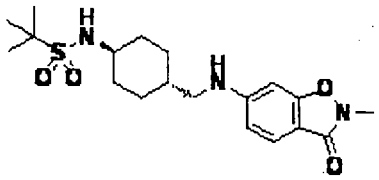
[Formula 277]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.06 (m, 4H), 1.26 (s, 9H), 1.40-1.51 (m, 1H), 1.84 (d, 2H, J = 12.4 Hz), 1.91 (d, 2H, J = 12.4 Hz), 2.85-2.90 (m, 2H), 2.97-3.06 (m, 1H), 5.93-5.99 (m, 1H), 6.63-6.79 (m, 3H), 7.40 (d, 1H, J = 8.8 Hz), 8.32 (s, 1H).

Compound Ii-116

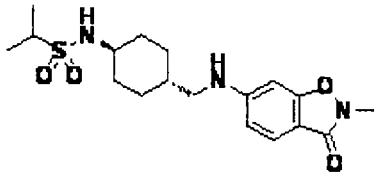
[Formula 278]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.07 (m, 4H), 1.26 (s, 9H), 1.39-1.47 (m, 1H), 1.80 (d, 2H, J = 12.4 Hz), 1.91 (d, 2H, J = 12.4 Hz), 2.87-2.93 (m, 2H), 2.98-3.06 (m, 1H), 3.37 (s, 3H), 6.27 (s, 1H), 6.55 (d, 1H, J = 8.8 Hz), 6.73 (d, 1H, J = 8.8 Hz), 6.80 (t, 1H, J = 5.2 Hz), 7.32 (d, 1H, J = 8.8 Hz).

Compound Ii-117

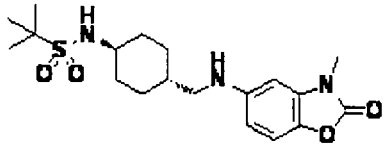
[Formula 279]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.08 (m, 4H), 1.20 (s, 3H), 1.22 (s, 3H), 1.39-1.51 (m, 1H), 1.80 (d, 2H, J = 12.4 Hz), 1.88 (d, 2H, J = 12.4 Hz), 2.87-2.94 (m, 2H), 2.97-3.07 (m, 1H), 3.08-3.14 (m, 1H), 3.37 (s, 3H), 6.27 (s, 1H), 6.55 (d, 1H, J = 8.4 Hz), 6.82 (t, 1H, J = 5.6 Hz), 6.94 (d, 1H, J = 8.0 Hz), 7.32 (d, 1H, J = 8.4 Hz).

Compound Ii-118

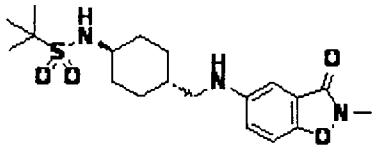
[Formula 280]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.06 (m, 4H), 1.26 (s, 9H), 1.38-1.50 (m, 1H), 1.83 (d, 2H, J = 12.4 Hz), 1.90 (d, 2H, J = 12.4 Hz), 2.80-2.86 (m, 2H), 2.96-3.06 (m, 1H), 3.26 (s, 3H), 5.58-5.65 (m, 1H), 6.27 (d, 1H, J = 8.4 Hz), 6.38 (s, 1H), 6.75 (d, 1H, J = 8.4 Hz), 6.99 (d, 1H, J = 8.4 Hz).

Compound Ii-119

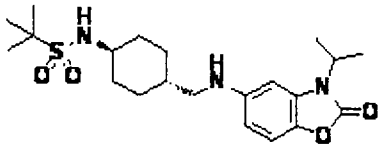
[Formula 281]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.06 (m, 4H), 1.26 (s, 9H), 1.39-1.50 (m, 1H), 1.84 (d, 2H, J = 12.4 Hz), 1.90 (d, 2H, J = 12.4 Hz), 2.81-2.89 (m, 2H), 2.96-3.07 (m, 1H), 3.51 (s, 3H), 5.79-5.84 (m, 1H), 6.60 (s, 1H), 6.75 (d, 1H, J = 8.8 Hz), 7.03 (d, 1H, J = 8.8 Hz), 7.19 (d, 1H, J = 8.8 Hz).

Compound Ii-120

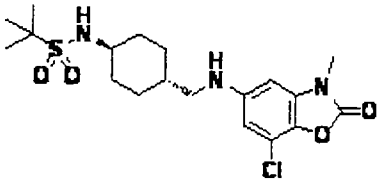
[Formula 282]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.10 (m, 4H), 1.26 (s, 9H), 1.37-1.40 (m, 1H), 1.42 (s, 3H), 1.44 (s, 3H), 1.83 (d, 2H, J = 12.4 Hz), 1.91 (d, 2H, J = 12.4 Hz), 2.79-2.96 (m, 2H), 2.97-3.07 (m, 1H), 4.33-4.46 (m, 1H), 5.50-5.59 (m, 1H), 6.25 (d, 1H, J = 8.8 Hz), 6.57 (s, 1H), 6.75 (d, 1H, J = 8.4 Hz), 7.00 (d, 1H, J = 8.4 Hz).

Compound Ii-121

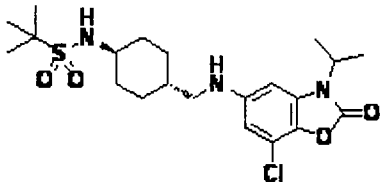
[Formula 283]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 4H), 1.26 (s, 9H), 1.36-1.49 (m, 1H), 1.82 (d, 2H, J = 12.4 Hz), 1.90 (d, 2H, J = 12.4 Hz), 2.80-2.87 (m, 2H), 2.95-3.97 (m, 1H), 3.27 (s, 3H), 5.85-5.92 (m, 1H), 6.33 (s, 1H), 6.36 (s, 1H), 6.75 (d, 1H, J = 8.8 Hz).

Compound Ii-122

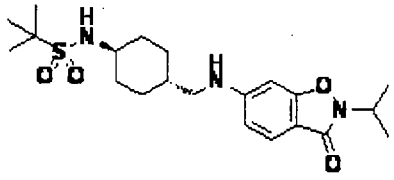
[Formula 284]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 4H), 1.26 (s, 9H), 1.38-1.41 (m, 1H), 1.42 (s, 3H), 1.43 (s, 3H), 1.82 (d, 2H, J = 11.8 Hz), 1.90 (d, 2H, J = 11.8 Hz), 2.83-2.88 (m, 2H), 2.98-3.06 (m, 1H), 4.33-4.47 (m, 1H), 6.35 (s, 1H), 6.54 (s, 1H), 6.76 (d, 1H, J = 8.4 Hz), 8.32 (s, 1H).

Compound Ii-123

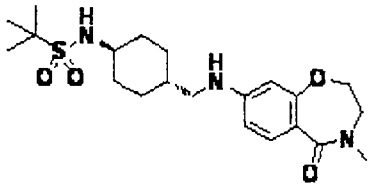
[Formula 285]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.06 (m, 4H), 1.22 (s, 3H), 1.24 (s, 3H), 1.26 (s, 9H), 1.39-1.50 (m, 1H), 1.81 (d, 2H, J = 12.4 Hz), 1.90 (d, 2H, J = 12.4 Hz), 2.87-2.93 (m, 2H), 2.96-3.07 (m, 1H), 4.39-4.47 (m, 1H), 6.30 (s, 1H), 6.54 (d, 1H, J = 8.8 Hz), 6.77 (d, 1H, J = 8.8 Hz), 6.86 (t, 1H, J = 5.2 Hz), 7.32 (d, 1H, J = 8.4 Hz).

Compound Ii-124

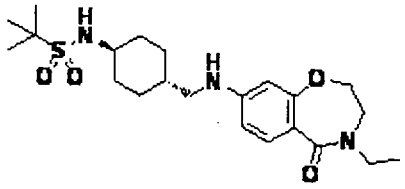
[Formula 286]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.05 (m, 4H), 1.26 (s, 9H), 1.36-1.51 (m, 1H), 1.79 (d, 2H, J = 12.4 Hz), 1.90 (d, 2H, J = 12.4 Hz), 2.80-2.86 (m, 2H), 3.01 (s, 3H), 3.02-3.05 (m, 1H), 3.49 (t, 2H, J = 4.8 Hz), 4.26 (t, 2H, J = 4.8 Hz), 6.02 (s, 1H), 6.20 (t, 1H, J = 5.6 Hz), 6.31 (d, 1H, J = 8.8 Hz), 6.74 (d, 1H, J = 8.8 Hz), 7.43 (d, 1H, J = 8.4 Hz).

Compound Ii-125

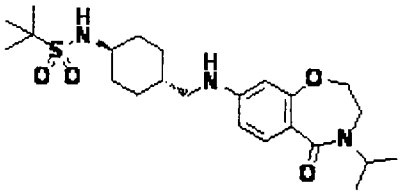
[Formula 287]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.02 (m, 4H), 1.08 (t, 3H, J = 7.2 Hz), 1.25 (s, 9H), 1.35-1.42 (m, 1H), 1.79 (d, 2H, J = 12.0 Hz), 1.90 (d, 2H, J = 12.0 Hz), 2.80-2.86 (m, 2H), 2.96-3.05 (m, 1H), 3.42-3.51 (m, 4H), 4.20-4.26 (m, 2H), 6.03 (s, 1H), 6.20 (s, 1H), 6.31 (d, 1H, J = 8.8 Hz), 6.75 (d, 1H, J = 8.8 Hz), 7.42 (d, 1H, J = 8.8 Hz).

Compound Ii-126

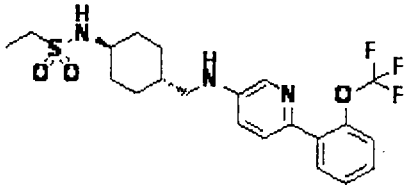
[Formula 288]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.02 (m, 4H), 1.09 (s, 3H), 1.11 (s, 3H), 1.25 (s, 9H), 1.43-1.55 (m, 1H), 1.80 (d, 2H, J = 12.4 Hz), 1.91 (d, 2H, J = 12.0 Hz), 2.84 (m, 2H), 2.97-3.08 (m, 1H), 3.37 (t, 2H, J = 5.2 Hz), 4.18 (t, 2H, J = 5.2 Hz), 4.71-4.80 (m, 1H), 6.05 (s, 1H), 6.19 (t, 1H, J = 5.2 Hz), 6.32 (d, 1H, J = 8.8 Hz), 6.74 (d, 1H, J = 8.4 Hz), 7.18 (d, 1H, J = 8.4 Hz).

Compound Ii-127

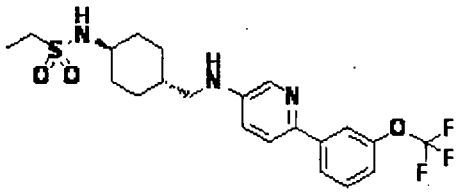
[Formula 289]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.12 (m, 2H), 1.14-1.39 (m, 5H), 1.34-1.56 (m, 1H), 1.70-1.97 (m, 4H), 2.87-3.10 (m, 5H), 6.17 (t, 1H, J = 5.2 Hz), 6.94-7.06 (m, 2H), 7.35-7.47 (m, 4H), 7.75-7.80 (m, 1H), 8.07 (d, 1H, J = 3.0 Hz).

Compound Ii-128

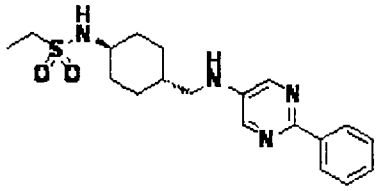
[Formula 290]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.12 (m, 2H), 1.14-1.31 (m, 5H), 1.31-1.55 (m, 1H), 1.70-1.96 (m, 4H), 2.89-3.09 (m, 5H), 6.24 (t, 1H, J = 5.4 Hz), 6.94-7.05 (m, 2H), 7.24 (d, 1H, J = 6.9 Hz), 7.52 (t, 1H, J = 8.0 Hz), 7.75 (d, 1H, J = 8.8 Hz), 7.88-7.97 (m, 2H), 8.07 (d, 1H, J = 2.5 Hz).

Compound Ii-129

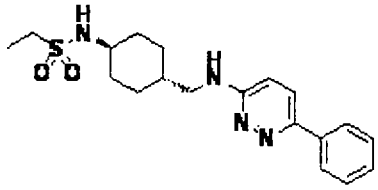
[Formula 291]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.12 (m, 2H), 1.18-1.30 (m, 2H), 1.19 (t, 3H, J = 6.8 Hz), 1.48 (m, 1H), 1.79-1.95 (m, 4H), 2.92-3.09 (m, 3H), 2.97 (q, 2H, J = 6.8 Hz), 6.27 (m, 1H), 7.01 (d, 1H, J = 8.0 Hz), 7.39-7.47 (m, 2H), 7.56 (m, 1H), 8.18-8.25 (m, 2H), 8.23 (s, 2H).

Compound Ii-130

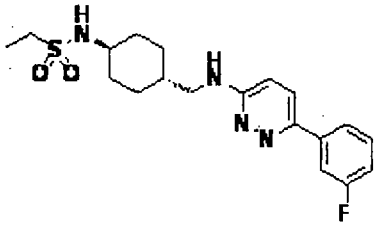
[Formula 292]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.12 (m, 2H), 1.15-1.30 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.45-1.64 (m, 1H), 1.78-1.96 (m, 4H), 2.97 (q, 2H, J = 7.2 Hz), 2.95-3.15 (m, 1H), 3.22-3.28 (m, 2H), 6.89 (d, 1H, J = 9.0 Hz), 6.94-7.02 (m, 2H), 7.38 (t, 1H, J = 6.0 Hz), 7.46 (t, 2H, J = 7.5 Hz), 7.78 (d, 1H, J = 9.0 Hz), 7.96 (d, 2H, J = 9.0 Hz).

Compound Ii-131

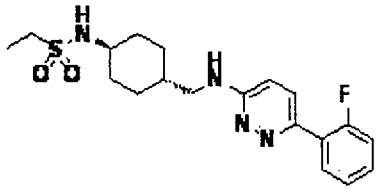
[Formula 293]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.12 (m, 2H), 1.15-1.30 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.48-1.62 (m, 1H), 1.78-1.96 (m, 4H), 2.98 (q, 2H, J = 7.2 Hz), 2.94-3.10 (m, 1H), 3.22-3.28 (m, 2H), 6.89 (d, 1H, J = 9.0 Hz), 7.02 (d, 1H, J = 9.0 Hz), 7.10 (t, 1H, J = 5.4 Hz), 7.22 (td, 1H, J = 9.0, 3.0 Hz), 7.47-7.56 (m, 1H), 7.77-7.88 (m, 3H).

Compound Ii-132

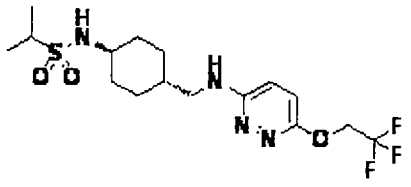
[Formula 294]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.13 (m, 2H), 1.15-1.32 (m, 2H), 1.19 (t, 3H, J = 7.5 Hz), 1.48-1.65 (m, 1H), 1.78-1.96 (m, 4H), 2.98 (q, 2H, J = 7.2 Hz), 2.94-3.12 (m, 1H), 3.22-3.28 (m, 2H), 6.89 (d, 1H, J = 9.0 Hz), 7.01 (d, 1H, J = 6.0 Hz), 7.09 (t, 1H, J = 5.4 Hz), 7.27-7.35 (m, 2H), 7.42-7.50 (m, 1H), 7.57 (dd, 1H, J = 9.0, 3.0 Hz), 7.86 (td, 1H, J = 7.5, 3.0 Hz).

Compound Ii-133

[Formula 295]

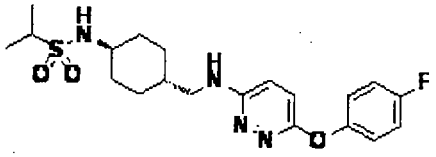


^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 2H), 1.15-1.30 (m, 2H), 1.21 (d, 6H, J = 6.6

Hz), 1.42-1.58 (m, 1H), 1.72-1.94 (m, 4H), 2.95-3.20 (m, 4H), 4.89-4.98 (m, 2H), 6.65 (brs, 1H), 6.92 (d, 1H, J = 9.0 Hz), 6.91-6.98 (m, 1H), 7.03 (d, 1H, J = 9.0 Hz).

Compound Ii-134

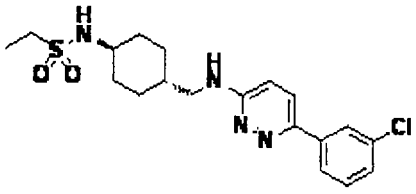
[Formula 296]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.08 (m, 2H), 1.15-1.30 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.42-1.58 (m, 1H), 1.72-1.94 (m, 4H), 2.92-3.20 (m, 4H), 6.74 (t, 1H, J = 6.0 Hz), 6.94 (t, 1H, J = 6.0 Hz), 6.97 (s, 1H), 7.08-7.24 (m, 5H).

Compound Ii-135

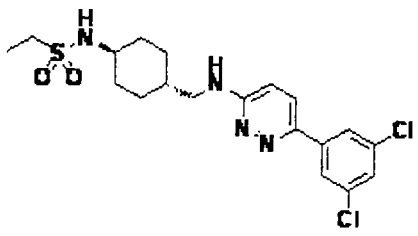
[Formula 297]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.10 (m, 2H), 1.12-1.30 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.48-1.60 (m, 1H), 1.76-1.94 (m, 4H), 2.92-3.10 (m, 1H), 2.97 (q, 2H, J = 7.2 Hz), 3.18-3.30 (m, 2H), 6.89 (d, 1H, J = 9.6 Hz), 7.02 (brs, 1H), 7.11 (t, 1H, J = 5.4 Hz), 7.42-7.56 (m, 2H), 7.85 (d, 1H, J = 9.6 Hz), 7.93 (d, 1H, J = 7.5 Hz), 8.03 (s, 1H).

Compound Ii-136

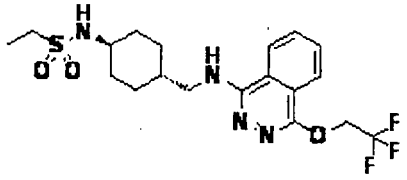
[Formula 298]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.12 (m, 2H), 1.13-1.30 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.48-1.62 (m, 1H), 1.78-1.96 (m, 4H), 2.92-3.12.(m, 1H), 2.97 (q, 2H, J = 7.2 Hz), 3.22-3.32 (m, 2H), 6.89 (d, 1H, J = 9.0 Hz), 7.01 (d, 1H, J = 7.5 Hz), 7.20 (t, 1H, J = 6.0 Hz), 7.62 (s, 1H), 7.91 (d, 1H, J = 9.0 Hz), 8.02 (s, 2H).

Compound Ii-137

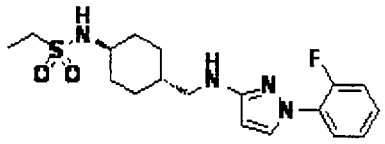
[Formula 299]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.12 (m, 2H), 1.13-1.30 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.65-1.95 (m, 5H), 2.93-3.12 (m, 1H), 2.97 (q, 2H, J = 7.2 Hz), 3.25-3.40 (m, 2H), 5.07-5.16 (m, 2H), 7.01 (d, 1H, J = 7.5 Hz), 7.25 (t, 1H, J = 6.0 Hz), 7.92-8.03 (m, 3H), 8.33 (d, 1H, J = 6.0 Hz).

Compound Ii-138

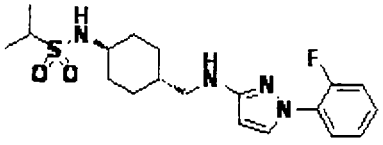
[Formula 300]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.26 (m, 4H), 1.19 (t, 3H, J = 7.5 Hz), 1.36-1.43 (m, 1H), 1.78-1.90 (m, 4H), 2.90-3.07 (m, 3H), 2.96 (q, 2H, J = 7.5 Hz), 5.69 (t, 1H, J = 5.7 Hz), 5.81 (d, 1H, J = 2.4 Hz), 7.00 (d, 1H, J = 7.8 Hz), 7.16-7.39 (m, 3H), 7.73-7.79 (m, 1H), 7.86-7.88 (m, 1H).

Compound Ii-139

[Formula 301]

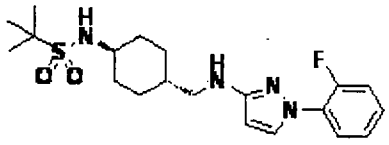


^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 4H), 1.20 (s, 3H), 1.22 (s, 3H), 1.40-1.52 (m,

1H), 1.81 (d, 2H, J = 12.4 Hz), 1.88 (d, 2H, J = 12.4 Hz), 2.90-2.98 (m, 2H), 2.99-3.13 (m, 2H), 5.68 (t, 1H, J = 5.6 Hz), 5.81 (s, 1H), 6.93 (d, 1H, J = 8.8 Hz), 7.16-7.40 (m, 3H), 7.76 (t, 1H, J = 8.0 Hz), 7.87 (s, 1H).

Compound Ii-140

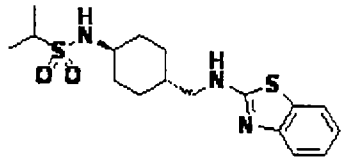
[Formula 302]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.06 (m, 4H), 1.26 (s, 9H), 1.40-1.49 (m, 1H), 1.82 (d, 2H, J = 12.4 Hz), 1.91 (d, 2H, J = 12.4 Hz), 2.90-2.99 (m, 2H), 3.01-3.06 (m, 1H), 5.67 (t, 1H, J = 6.0 Hz), 5.81 (s, 1H), 6.74 (d, 1H, J = 8.4 Hz), 7.14-7.40 (m, 3H), 7.76 (t, 1H, J = 8.4 Hz), 7.87 (s, 1H).

Compound Ii-141

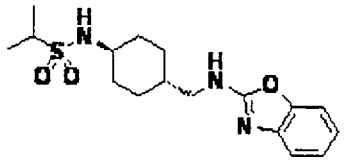
[Formula 303]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.06 (m, 2H), 1.18-1.27 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.45-1.59 (m, 1H), 1.76-1.81 (m, 2H), 1.87-1.91 (m, 2H), 2.97-3.09 (m, 1H), 3.10-3.13 (m, 1H), 3.17-3.22 (m, 2H), 6.94-7.02 (m, 2H), 6.98 (td, 1H, J = 7.8, 1.2 Hz), 7.36 (dd, 1H, J = 7.8, 0.6 Hz), 7.65 (dd, 1H, J = 7.8, 0.6 Hz), 8.00-8.05 (m, 1H).

Compound Ii-142

[Formula 304]

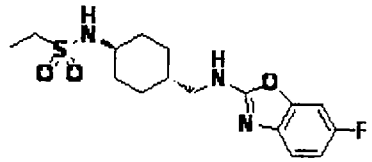


^{1}H-NMR (DMSO-d_6) δ: 0.96-1.04 (m, 2H), 1.18-1.28 (m, 2H), 1.20 (d, 6H, J = 6.9

Hz), 1.43-1.59 (m, 1H), 1.74-1.79 (m, 2H), 1.85-1.90 (m, 2H), 2.92-3.07 (m, 1H), 3.09-3.18 (m, 3H), 6.92-6.99 (m, 2H), 7.10 (td, 1H, J = 7.8, 1.2 Hz), 7.21 (dd, 1H, J = 7.8, 0.6 Hz), 7.31 (dd, 1H, J = 7.8, 0.6 Hz), 7.89-7.97 (m, 1H).

Compound Ii-143

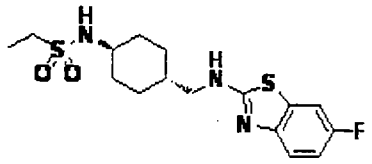
[Formula 305]



^{1}H-NMR (DMSO-d_6)δ: 0.97-1.07 (m, 2H), 1.17-1.23 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.42-1.57 (m, 1H), 1.73-1.78 (m, 2H), 1.86-1.90 (m, 2H), 2.93-3.02 (m, 1H), 2.97 (q, 2H, J = 7.2 Hz), 3.11 (t, 2H, J = 6.3 Hz), 6.91-7.02 (m, 2H), 7.19 (dd, 1H, J = 8.4, 4.8 Hz), 7.34 (dd, 1H, J = 9.3, 2.4 Hz), 8.00 (t, 1H, J = 6.0 Hz).

Compound Ii-144

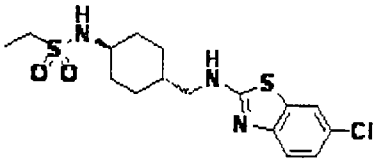
[Formula 306]



^{1}H-NMR (DMSO-d_6)δ: 0.97-1.08 (m, 2H), 1.16-1.24 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.42-1.59 (m, 1H), 1.74-1.80 (m, 2H), 1.85-1.90 (m, 2H), 2.92-3.03 (m, 1H), 2.97 (q, 2H, J = 7.5 Hz), 3.18 (t, 2H, J = 6.3 Hz), 6.99-7.07 (m, 2H), 7.33 (dd, 1H, J = 9.0, 4.8 Hz), 7.58 (dd, 1H, J = 8.7, 2.7 Hz), 8.00 (t, 1H, J = 5.4 Hz).

Compound Ii-145

[Formula 307]

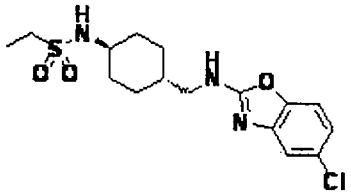


^{1}H-NMR (DMSO-d_6) δ: 0.97-1.09 (m, 2H), 1.17-1.23 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.43-1.59 (m, 1H), 1.72-1.81 (m, 2H), 1.85-1.92 (m, 2H), 2.95-3.06 (m, 1H),

2.97 (q, 2H, J = 7.5 Hz), 3.19 (t, 2H, J = 6.0 Hz), 7.01 (d, 1H, J = 8.1 Hz), 7.20-7.23 (m, 1H), 7.33 (dd, 1H, J = 8.7, 0.6 Hz), 7.58 (dd, 1H, J = 2.1, 0.9 Hz), 8.11-8.18 (m, 1H).

Compound Ii-146

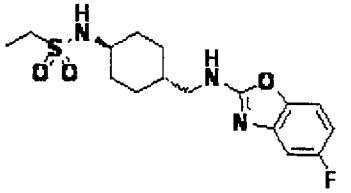
[Formula 308]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.06 (m, 2H), 1.15-1.21 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.42-1.58 (m, 1H), 1.70-1.81 (m, 2H), 1.82-1.96 (m, 2H), 2.93-3.00 (m, 3H), 3.13-3.19 (m, 2H), 6.98-7.02 (m, 2H), 7.26-7.27 (m, 1H), 7.32-7.35 (m, 1H), 8.18-8.21 (m, 1H).

Compound Ii-147

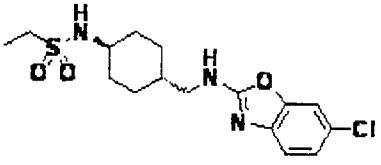
[Formula 309]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.04 (m, 2H), 1.16-1.23 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.43-1.59 (m, 1H), 1.73-1.78 (m, 2H), 1.86-1.89 (m, 2H), 2.93-3.00 (m, 3H), 3.11-3.15 (m, 2H), 6.72-6.79 (m, 1H), 7.00-7.08 (m, 2H), 7.29-7.34 (m, 1H), 8.13-8.16 (m, 1H).

Compound Ii-148

[Formula 310]

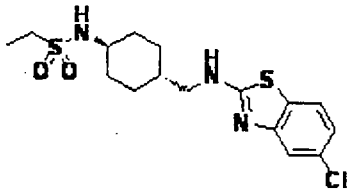


^{1}H-NMR (DMSO-d_6) δ: 0.94-1.06 (m, 2H), 1.15-1.26 (m, 2H), 1.18 (t, 3H, J = 7.2

Hz), 1.45-1.58 (m, 1H), 1.72-1.80 (m, 2H), 1.84-1.92 (m, 2H), 2.96 (q, 2H, J = 7.2 Hz), 2.96-3.05 (m, 1H), 3.09-3.16 (m, 2H), 6.99 (d, 1H, J = 8.0 Hz), 7.13 (dd, 1H, J = 8.0, 2.0 Hz), 7.20 (d, 1H, J = 8.4 Hz), 7.49 (d, 1H, J = 2.0 Hz), 8.11 (t, 1H, J = 6.0 Hz).

Compound Ii-149

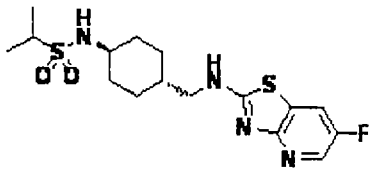
[Formula 311]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.08 (m, 2H), 1.12-1.24 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.43-1.59 (m, 1H), 1.74-1.80 (m, 2H), 1.86-1.91 (m, 2H), 2.93-3.01 (m, 3H), 3.17-3.22 (m, 2H), 7.00-7.05 (m, 2H), 7.37-7.39 (m, 1H), 7.65-7.68 (m, 1H), 8.22-8.26 (m, 1H).

Compound Ii-150

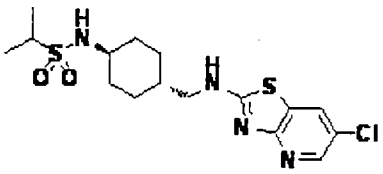
[Formula 312]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.08 (m, 2H), 1.15-1.29 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.44-1.60 (m, 1H), 1.74-1.80 (m, 2H), 1.86-1.91 (m, 2H), 2.95-3.17 (m, 2H), 3.21-3.27 (m, 2H), 6.95-6.98 (m, 1H), 8.10 (dd, 1H, J = 8.4, 2.7 Hz), 8.19 (dd, 1H, J = 3.0, 1.5 Hz), 8.44-8.47 (m, 1H).

Compound Ii-151

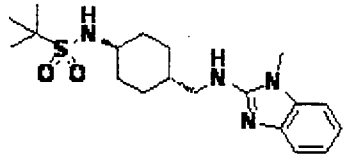
[Formula 313]



^{1}H-NMR (DMSO-d_6) δ: 0.99-1.04 (m, 2H), 1.15-1.23 (m, 2H), 1.21 (d, 6H, J = 6.3 Hz), 1.43-1.59 (m, 1H), 1.73-1.81 (m, 2H), 1.85-1.91 (m, 2H), 2.97-3.18 (m, 2H), 3.21-3.29 (m, 2H), 6.95-6.98 (m, 1H), 8.20-8.23 (m, 2H), 8.58-8.61 (m, 1H).

Compound Ii-152

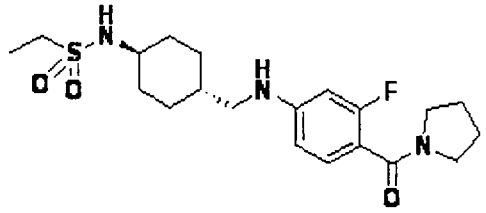
[Formula 314]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.04 (m, 2H), 1.15-1.26 (m, 2H), 1.25 (s, 9H), 1.56-1.62 (m, 1H), 1.78-1.83 (m, 2H), 1.87-1.93 (m, 2H), 2.98-3.08 (m, 1H), 3.17 (t, 2H, J = 6.3 Hz), 3.48 (s, 3H), 6.47 (d, 2H, J = 8.7 Hz), 6.89-6.96 (m, 2H), 7.11-7.19 (m, 2H).

Compound Ii-153

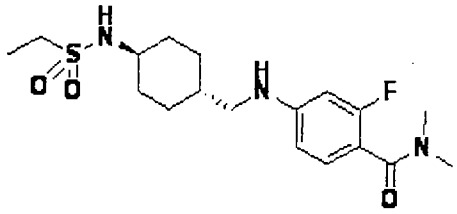
[Formula 315]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.04 (m, 2H), 1.13-1.30 (m, 2H), 1.18 (t, 3H, J = 7.5 Hz), 1.41 (m, 1H), 1.71-1.94 (m, 4H), 2.80-2.89 (m, 2H), 2.92-3.10 (m, 2H), 2.97 (q, 2H, J = 7.5 Hz), 3.21-3.30 (m, 2H), 6.25-6.35 (m, 2H), 6.39 (dd, 1H, J = 8.4, 2.1 Hz), 7.01 (d, 1H, J = 7.5 Hz), 7.01 (dd, 1H, J = 8.4, 8.4 Hz).

Compound Ii-154

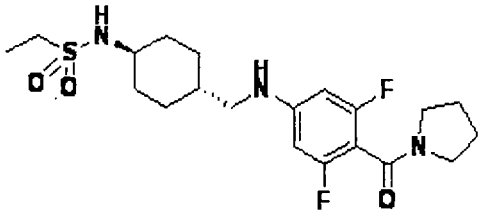
[Formula 316]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.09 (m, 2H), 1.16-1.28 (m, 2H), 1.18 (t, 3H, J = 7.5 Hz), 1.42 (m, 1H), 1.74-1.95 (m, 4H), 2.80-3.16 (m, 9H), 2.97 (q, 2H, J = 7.5 Hz), 6.24-6.36 (m, 2H), 6.30 (dd, 1H, J = 8.4, 2.1 Hz), 7.10 (dd, 1H, J = 8.4, 2.1 Hz), 7.05 (d, 1H, J = 8.4 Hz).

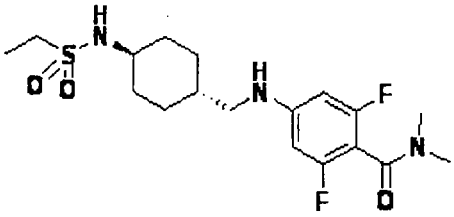
Compound Ii-155

[Formula 317]



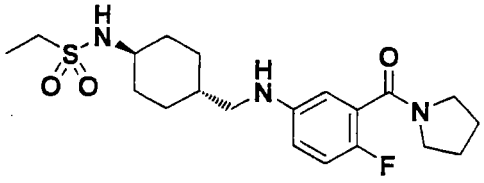
Compound Ii-156

[Formula 318]



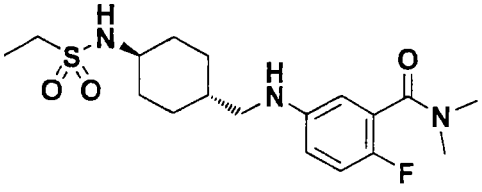
Compound Ii-157

[Formula 319]



Compound Ii-158

[Formula 320]

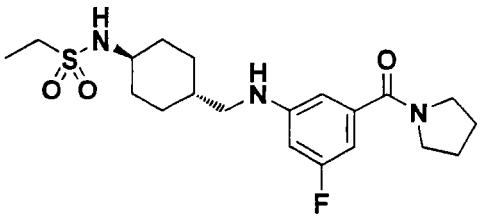


^{1}H-NMR (DMSO-d_6) δ: 0.91-1.07 (m, 2H), 1.10-1.30 (m, 5H), 1.41 (m, 1H), 1.76-

1.94 (m, 4H), 2.74-2.83 (m, 2H), 2.83 (s, 3H), 2.90-3.08 (m, 3H), 2.96 (s, 3H), 5.68 (m, 1H), 6.39 (m, 1H), 6.58 (m, 1H), 6.95 (dd, 1H, J = 8.4, 8.4 Hz), 7.00 (d, 1H, J = 7.8 Hz).

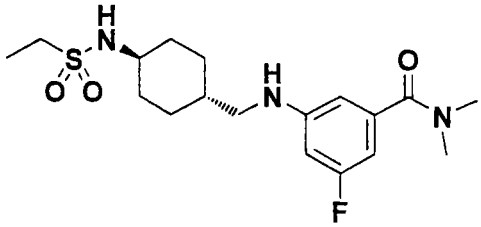
Compound Ii-159

[Formula 321]



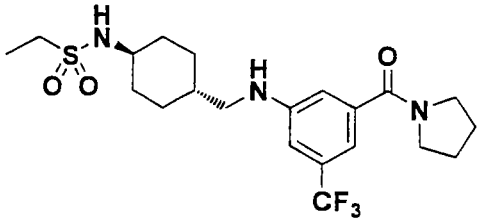
Compound Ii-160

[Formula 322]



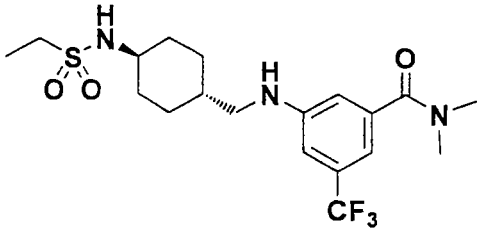
Compound Ii-161

[Formula 323]



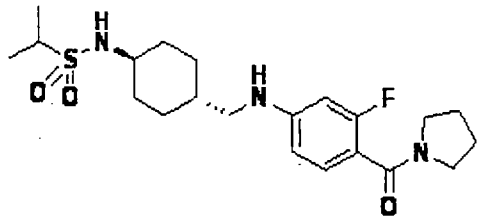
Compound Ii-162

[Formula 324]



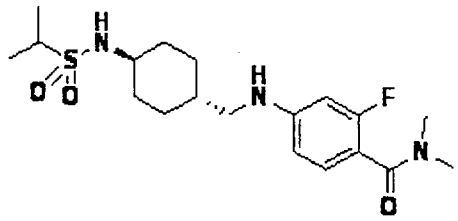
Compound Ii-163

[Formula 325]



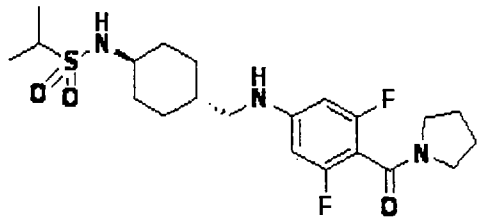
Compound Ii-164

[Formula 326]



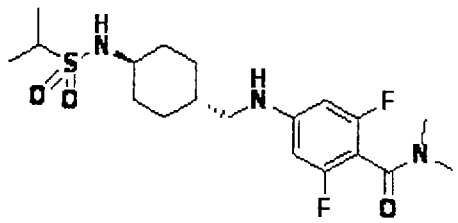
Compound Ii-165

[Formula 327]



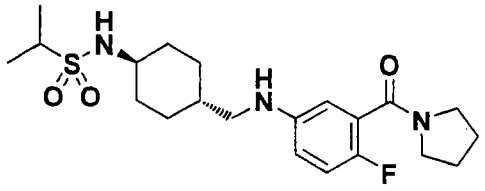
Compound Ii-166

[Formula 328]



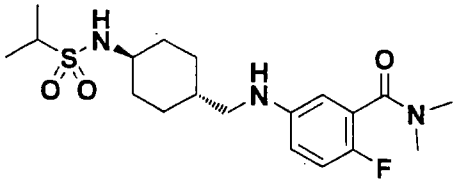
Compound Ii-167

[Formula 329]



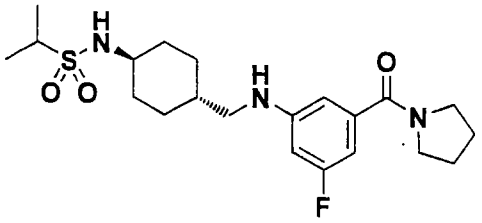
Compound Ii-168

[Formula 330]



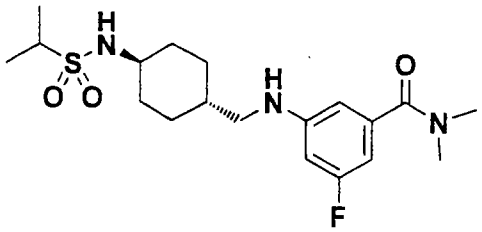
Compound Ii-169

[Formula 331]



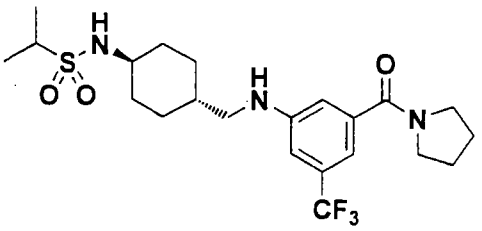
Compound Ii-170

[Formula 332]



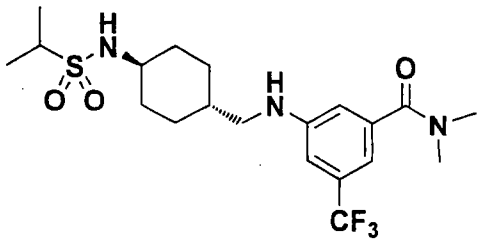
Compound Ii-171

[Formula 333]



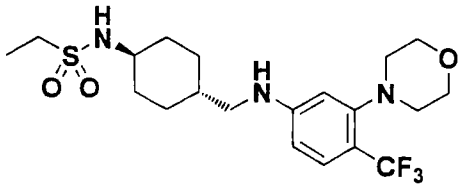
Compound Ii-172

[Formula 334]



Compound Ii-173

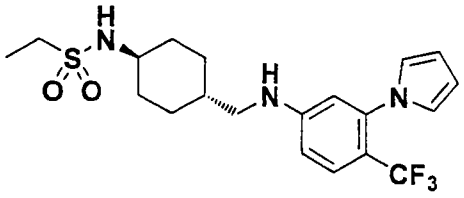
[Formula 335]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.08 (m, 2H), 1.15-1.28 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.43 (m, 1H), 1.76-1.85 (m, 2H), 1.85-1.93 (m, 2H), 2.76-2.82 (m, 2H), 2.88 (t, 2H, J = 6.0 Hz), 2.97 (t, 2H, J = 7.2 Hz), 3.00 (m, 1H), 3.64-3.70 (m, 4H), 6.33 (m, 1H), 6.37 (d, 1H, J = 8.4 Hz), 6.56 (s, 1H), 7.00 (d, 1H, J = 7.8 Hz), 7.28 (d, 1H, J = 8.4 Hz).

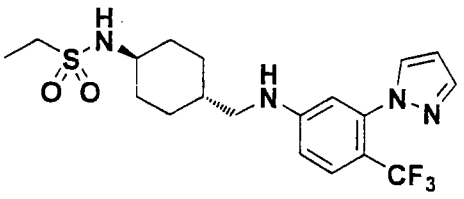
Compound Ii-174

[Formula 336]



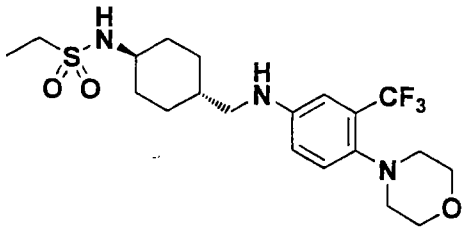
Compound Ii-175

[Formula 337]



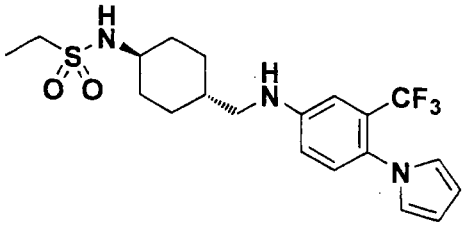
Compound Ii-176

[Formula 338]



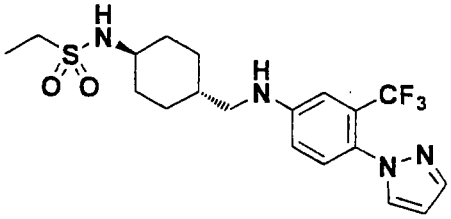
Compound Ii-177

[Formula 339]



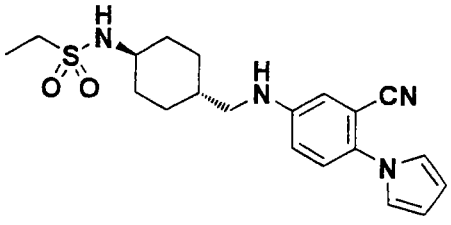
Compound Ii-178

[Formula 340]



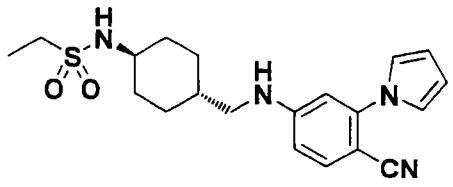
Compound Ii-179

[Formula 341]



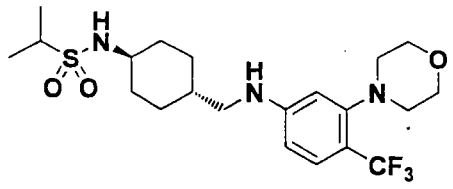
Compound Ii-180

[Formula 342]



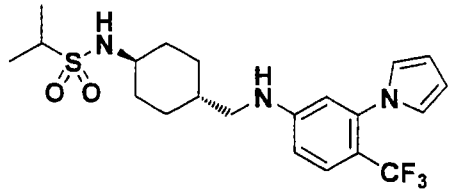
Compound Ii-181

[Formula 343]



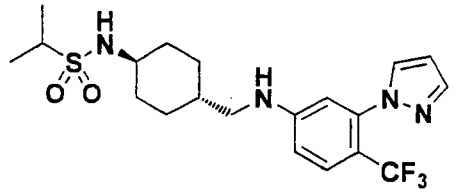
Compound Ii-182

[Formula 344]



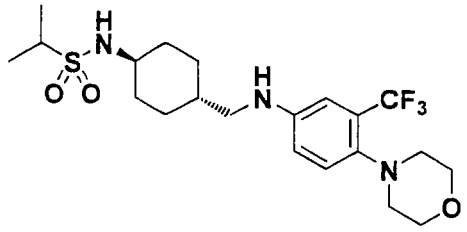
Compound Ii-183

[Formula 345]



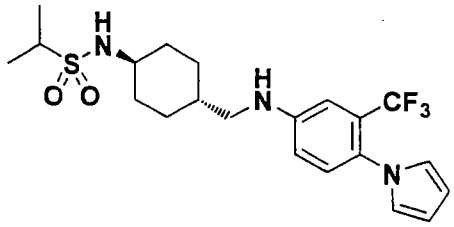
Compound Ii-184

[Formula 346]



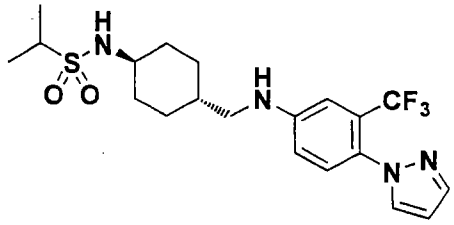
Compound Ii-185

[Formula 347]



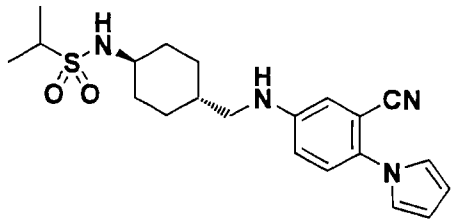
Compound Ii-186

[Formula 348]



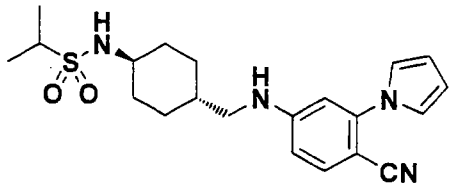
Compound Ii-187

[Formula 349]



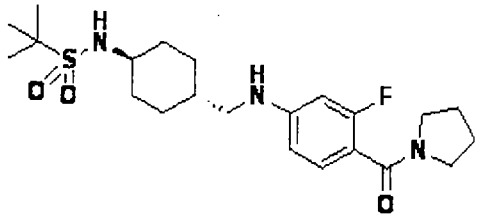
Compound Ii-188

[Formula 350]



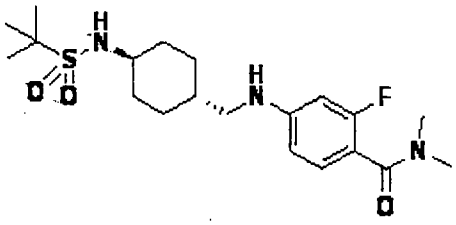
Compound Ii-189

[Formula 351]



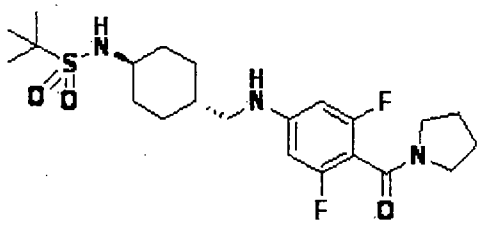
Compound Ii-190

[Formula 352]



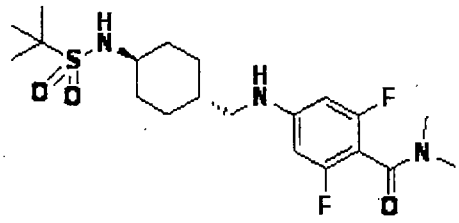
Compound Ii-191

[Formula 353]



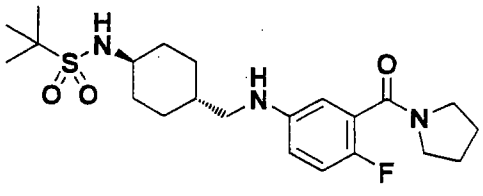
Compound Ii-192

[Formula 354]



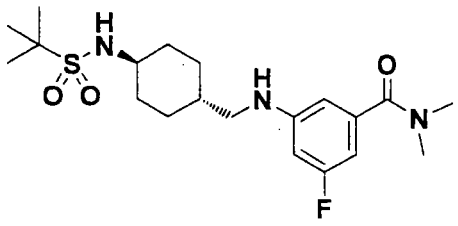
Compound Ii-193

[Formula 355]



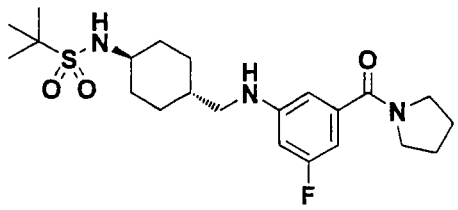
Compound Ii-194

[Formula 356]



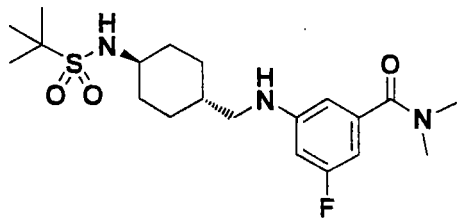
Compound Ii-195

[Formula 357]



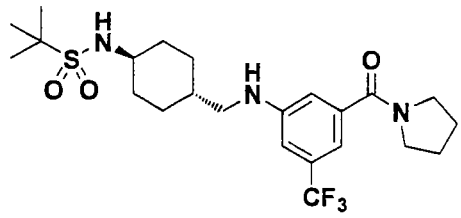
Compound Ii-196

[Formula 358]



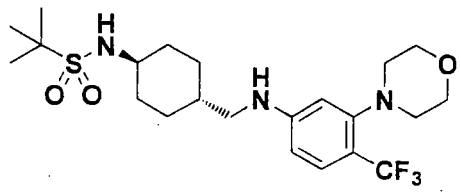
Compound Ii-197

[Formula 359]



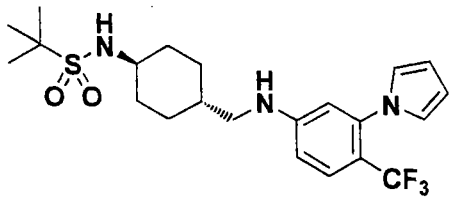
Compound Ii-198

[Formula 360]



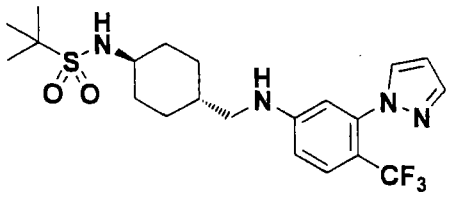
Compound Ii-199

[Formula 361]



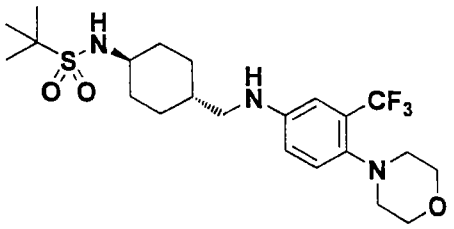
Compound Ii-200

[Formula 362]



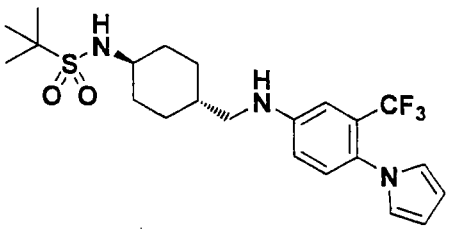
Compound Ii-201

[Formula 363]



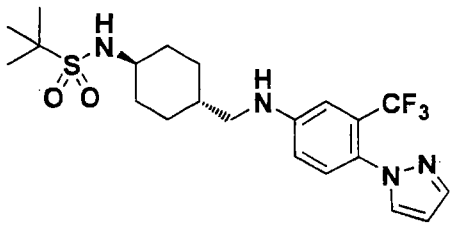
Compound Ii-202

[Formula 364]



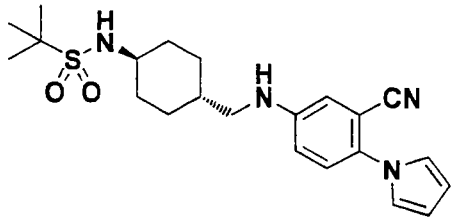
Compound Ii-203

[Formula 365]



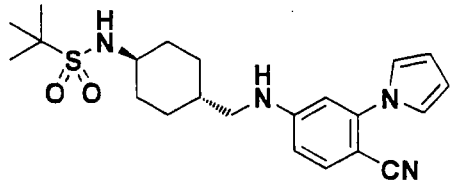
Compound Ii-204

[Formula 366]



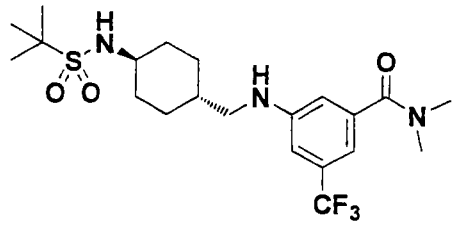
Compound Ii-205

[Formula 367]



Compound Ii-206

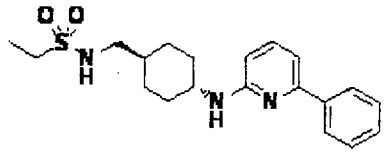
[Formula 368]



[0084]

Compound Ij-2

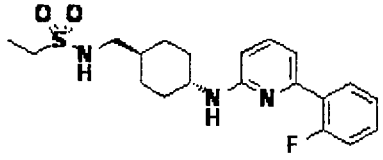
[Formula 369]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.24 (m, 4H), 1.19 (t, 3H, J = 7.5 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.02-2.14 (m, 2H), 2.80 (t, 2H, J = 6.0 Hz), 2.86 (q, 2H, J = 7.2 Hz), 3.64-3.82 (m, 1H), 6.40 (d, 2H, J = 8.1 Hz), 7.01 (d, 2H, J = 7.2 Hz), 7.32-7.50 (m, 4H), 7.99 (d, 2H, J = 6.9 Hz)

Compound Ij-3

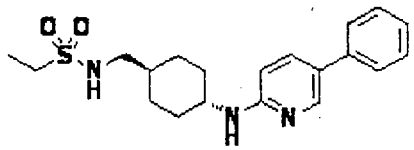
[Formula 370]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.26 (m, 4H), 1.18 (t, 3H, J = 7.5 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.02-2.14 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.5 Hz), 3.60-3.78 (m, 1H), 6.40-6.50 (m,2H), 6.85-6.92 (m, 1H), 6.97-7.03 (m, 1H), 7.22-7.35 (m, 2H), 7.36-7.46 (m, 2H), 7.88-7.96 (m, 1H)

Compound Ij-4

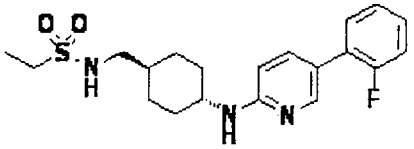
[Formula 371]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.5 Hz), 3.60-3.78 (m, 1H), 6.50 (t, 1H, J = 3.9 Hz), 6.53 (s, 1H), 7.00 (t, 1H, J = 5.7 Hz), 7.25 (t, 1H, J = 7.2 Hz), 7.34-7.45 (m, 2H), 7.55 (d, 2H, J = 7.2 Hz), 7.67 (dd, 1H, J = 8.7, 2.7 Hz), 8.29 (d, 1H, J = 2.7 Hz)

Compound Ij-5

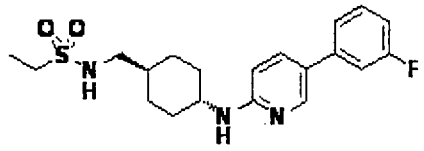
[Formula 372]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.5 Hz), 3.60-3.78 (m, 1H), 6.52 (d, 1H, J = 8.4 Hz), 6.60 (d, 1H, J = 7.8 Hz), 7.01 (t, 1H, J = 5.7 Hz), 7.20-7.36 (m, 3H), 7.46 (t, 1H, J = 8.1 Hz), 7.55 (d, 1H, J = 8.7 Hz), 8.15 (s, 1H)

Compound Ij-6

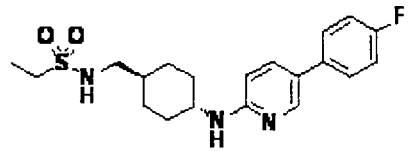
[Formula 373]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.5 Hz), 3.60-3.78 (m, 1H), 6.51 (d, 1H, J = 8.7 Hz), 6.60 (d, 1H, J = 7.5 Hz), 7.01 (t, 1H, J = 5.7 Hz), 7.02-7.12 (m, 1H), 7.36-7.48 (m, 3H), 7.71 (dd, 1H, J = 8.7, 2.1 Hz), 8.33 (d, 1H, J = 2.1 Hz)

Compound Ij-7

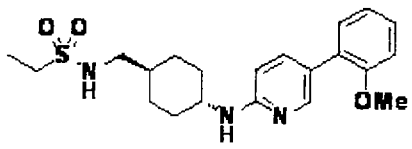
[Formula 374]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.5 Hz), 3.60-3.78 (m, 1H), 6.50 (d, 2H, J = 8.7 Hz), 6.99 (t, 1H, J = 6.0 Hz), 7.16-7.26 (m, 2H), 7.52-7.68 (m, 3H), 8.25 (s, 1H)

Compound Ij-8

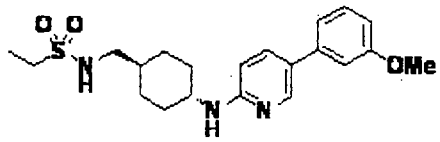
[Formula 375]



^{1}H-NMR ($CDCl_3$) δ: 1.15-1.26 (m, 4H), 1.40 (t, 3H, J = 7.5 Hz), 1.55-1.58 (m, 1H), 1.93 (d, 2H, J = 9.7 Hz), 2.23 (d, 2H, J = 9.7 Hz), 3.01-3.11 (m, 4H), 3.56-3.61 (m, 1H), 3.84 (s, 3H), 4.34 (t, 1H, J = 6.1 Hz), 4.83-4.86 (m, 1H), 6.46 (d, 1H, J = 8.6 Hz), 6.99 (d, 1H, J = 8.5 Hz), 7.05 (d, 1H, J = 8.5 Hz), 7.29 (s, 1H), 7.30-7.34 (m, 1H), 7.69 (dd, 1H, J = 8.7, 2.4 Hz), 8.25 (s, 1H).

Compound Ij-9

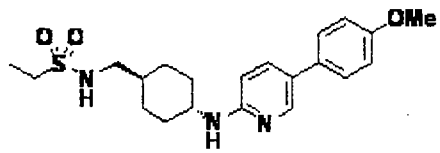
[Formula 376]



^{1}H-NMR ($CDCl_3$) δ: 1.16-1.24 (m, 4H), 1.40 (t, 3H, J = 6.2 Hz), 1.55-1.59 (m, 1H), 1.94 (d, 2H, J = 11.8 Hz), 2.23 (d, 2H, J = 11.8 Hz), 3.03-3.09 (m, 4H), 3.58-3.62 (m, 1H), 3.88 (s, 3H), 4.29 (t, 1H, J = 6.4 Hz), 4.85-4.89 (m, 1H), 6.49 (d, 1H, J = 8.7 Hz), 6.88 (dd, 1H, J = 8.7, 2.2 Hz), 7.04-7.06 (m, 1H), 7.10 (d, 1H, J = 8.7 Hz), 7.36 (t, 1H, J = 7.9 Hz), 7.70 (dd, 1H, J = 8.7, 2.2 Hz), 8.32 (s, 1H).

Compound Ij-10

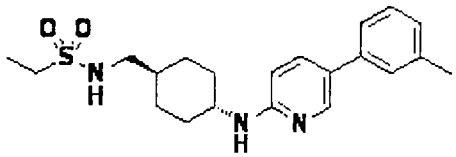
[Formula 377]



^{1}H-NMR ($CDCl_3$) δ: 1.19-1.30 (m, 4H), 1.41 (t, 3H, J = 6.3 Hz), 1.56-1.59 (m, 1H), 1.94 (d, 2H, J = 11.1 Hz), 2.23 (d, 2H, J = 11.1 Hz), 3.01-3.11 (m, 4H), 3.57-3.61 (m, 1H), 3.87 (s, 3H), 4.27 (t, 1H, J = 6.4 Hz), 4.98 (s, 1H), 6.50 (dd, 1H, J = 8.7, 2.2 Hz), 6.99 (d, 2H, J = 8.9 Hz), 7.43 (d, 2H, J = 8.7 Hz), 7.68 (dd, 1H, J = 8.7, 2.2 Hz), 8.25 (s, 1H).

Compound Ij-11

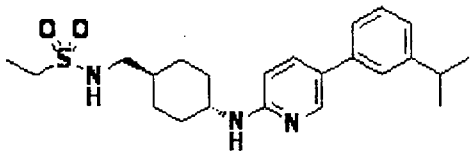
[Formula 378]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.08 (m, 2H), 1.09-1.25 (m, 5H), 1.39 (m, 1H), 1.75-1.86 (m, 2H), 1.95-2.07 (m, 2H), 2.34 (s, 3H), 2.78 (t, 2H, J = 6.2 Hz), 2.98 (q, 2H, J = 7.3 Hz), 3.65 (m, 1H), 6.45-6.53 (m, 2H), 7.01 (t, 1H, J = 5.6 Hz), 7.07 (d, 1H, J = 7.1 Hz), 7.23-7.38 (m, 3H), 7.64 (dd, 1H, J1 = 8.8 Hz, J2 = 2.5 Hz), 8.26 (d, 1H, J = 2.5 Hz).

Compound Ij-12

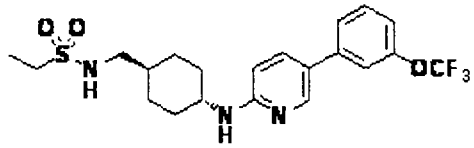
[Formula 379]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.08 (m, 2H), 1.09-1.27 (m, 11H), 1.39 (m, 1H), 1.76-1.87 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J = 6.2 Hz), 2.84-3.03 (m, 3H), 3.66 (m, 1H), 6.45-6.54 (m, 2H), 7.01 (t, 1H, J = 5.8 Hz), 7.13 (d, 1H, J = 6.9 Hz), 7.27-7.41 (m, 3H), 7.66 (dd, 1H, J1 = 8.8 Hz, J2 = 2.5 Hz), 8.27 (d, 1H, J = 2.2 Hz).

Compound Ij-13

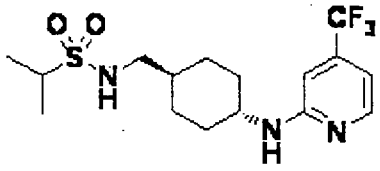
[Formula 380]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.09 (m, 2H), 1.09-1.25 (m, 5H), 1.39 (m, 1H), 1.76-1.85 (m, 2H), 1.95-2.06 (m, 2H), 2.78 (t, 2H, J = 6.2 Hz), 2.98 (q, 2H, J = 7.3 Hz), 3.68 (m, 1H), 6.52 (d, 1H, J = 8.8 Hz), 6.66 (d, 1H, J = 8.0 Hz), 7.02 (t, 1H, J = 5.5 Hz), 7.23 (d, 1H, J = 8.1 Hz), 7.49-7.55 (m, 2H), 7.62 (d, 1H, J1 = 8.5 Hz), 7.72 (dd, 1H, J1 = 8.8 Hz, J2 = 2.5 Hz), 8.35 (d, 1H, J = 2.5 Hz).

Compound Ij-14

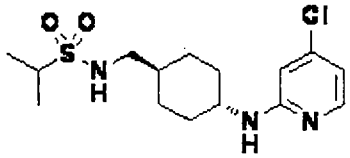
[Formula 381]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.22 (m, 4H), 1.22 (d, 6H, J = 6.4 Hz), 1.39 (m, 1H), 1.76-1.86 (m, 2H), 1.95-2.03 (m, 2H), 2.81 (t, 2H, J = 6.4 Hz), 3.10-3.20 (m, 1H), 3.60-3.75 (m, 1H), 6.65 (d, 1H, J = 4.8 Hz), 6.70 (s, 1H), 6.88-6.98 (m, 2H), 8.16 (d, 1H, J = 5.2 Hz).

Compound Ij-15

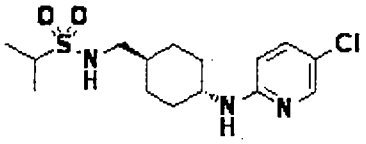
[Formula 382]



^{1}H-NMR ($CDCl_3$) δ: 1.02-1.28 (m, 4H), 1.38 (d, 6H, J = 6.9 Hz), 1.52 (m, 1H), 1.85-1.94 (m, 2H), 2.11-2.21 (m, 2H), 3.01 (t, 2H, J = 6.6 Hz), 3.10-3.25 (m, 1H), 3.38-3.54 (m, 1H), 4.22 (t, 1H, J = 6.3 Hz), 4.58 (d, 1H, J = 7.8 Hz), 6.34 (d, 1H, J = 1.8 Hz), 6.53 (dd, 1H, J = 5.4, 1.8 Hz), 7.93 (d, 1H, J = 5.4 Hz).

Compound Ij-16

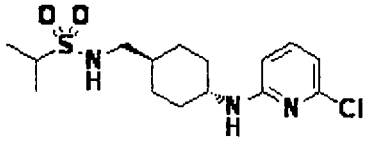
[Formula 383]



^{1}H-NMR ($CDCl_3$) δ: 1.03-1.28 (m, 4H), 1.37 (d, 6H, J = 6.9 Hz), 1.52 (m, 1H), 1.84-1.93 (m, 2H), 2.11-2.21 (m, 2H), 3.01 (t, 2H, J = 6.6 Hz), 3.09-3.24 (m, 1H), 3.40-3.54 (m, 1H), 4.26 (t, 1H, J = 6.6 Hz), 4.44 (d, 1H, J = 8.1 Hz), 6.29 (d, 1H, J = 8.7 Hz), 7.33 (dd, 1H, J = 8.7, 2.7 Hz), 7.99 (d, 1H, J = 2.7 Hz).

Compound Ij-17

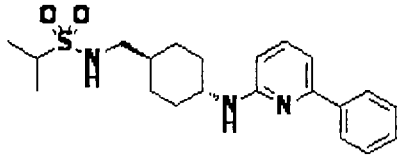
[Formula 384]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.22 (m, 4H), 1.21 (d, 6H, J = 6.8 Hz), 1.36 (m, 1H), 1.76-1.84 (m, 2H), 1.92-2.00 (m, 2H), 2.80 (t, 2H, J = 6.4 Hz), 3.08-3.18 (m, 1H), 3.45-3.56 (m, 1H), 6.36 (d, 1H, J = 8.4 Hz), 6.43 (d, 1H, J = 7.2 Hz), 6.75 (d, 1H, J = 7.6 Hz), 6.94 (t, 1H, J = 6.0 Hz), 7.33 (t, 1H, J = 7.6 Hz).

Compound Ij-18

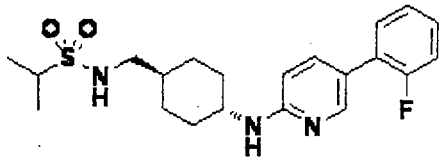
[Formula 385]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.24 (m, 4H), 1.22 (d, 6H, J = 6.9 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.83 (t, 2H, J = 6.0 Hz), 3.10-3.22 (m, 1H), 3.64-3.82 (m, 1H), 6.40 (d, 2H, J = 8.4 Hz), 6.95-7.05 (m, 2H), 7.35-7.50 (m, 4H), 7.99 (d, 2H, J = 7.2 Hz)

Compound Ij-19

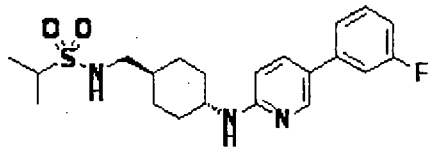
[Formula 386]



^{1}H-NMR ($CDCl_3$) δ: 1.22-1.38 (m, 4H), 1.38 (d, 6H, J = 8.0 Hz), 1.54 (m, 1H), 1.86-1.95 (m, 2H), 2.18-2.26 (m, 2H), 3.03 (t, 2H, J = 6.0 Hz), 3.12-3.22 (m, 1H), 3.52-3.64 (m, 1H), 4.16 (t, 1H, J = 6.4 Hz), 4.82-4.92 (m, 1H), 6.46 (d, 1H, J = 8.0 Hz), 7.10-7.20 (m, 2H), 7.23-7.33 (m, 1H), 7.37 (t, 1H, J = 8.0 Hz), 7.65 (d, 1H, J = 8.7 Hz), 8.24 (s, 1H).

Compound Ij-20

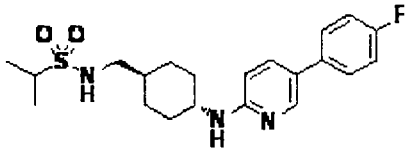
[Formula 387]



^{1}H-NMR ($CDCl_3$) δ: 1.22-1.38 (m, 4H), 1.39 (d, 6H, J = 8.0 Hz), 1.54 (m, 1H), 1.86-1.95 (m, 2H), 2.18-2.26 (m, 2H), 3.03 (t, 2H, J = 6.0 Hz), 3.12-3.22 (m, 1H), 3.52-3.64 (m, 1H), 4.16 (t, 1H, J = 6.4 Hz), 4.78-4.88 (m, 1H), 6.46 (d, 1H, J = 8.0 Hz), 6.98(t, 1H, J = 5.7 Hz), 7.18 (d, 1H, J = 8.0 Hz), 7.23-7.29 (m, 1H), 7.33-7.40 (m, 1H), 7.65 (d, 1H, J = 8.7 Hz), 8.29 (s, 1H).

Compound Ij-21

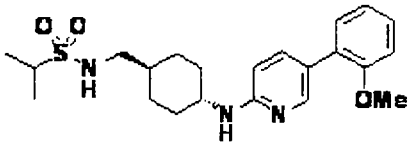
[Formula 388]



^{1}H-NMR ($CDCl_3$) δ: 1.10-1.30 (m, 4H), 1.38 (d, 6H, J = 8.0 Hz), 1.54 (m, 1H), 1.86-1.95 (m, 2H), 2.18-2.26 (m, 2H), 3.03 (t, 2H, J = 6.0 Hz), 3.13-3.22 (m, 1H), 3.52-3.64 (m, 1H), 4.15 (t, 1H, J = 6.4 Hz), 4.78-4.88 (m, 1H), 6.46 (d, 1H, J = 8.0 Hz), 7.07-7.14 (m, 2H), 7.40-7.46 (m, 2H), 7.62 (d, 1H, J = 8.7 Hz), 8.23 (s, 1H).

Compound Ij-22

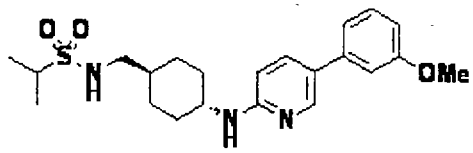
[Formula 389]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.25 (m, 4H), 1.22 (d, 6H, J = 6.6 Hz), 1.25-1.50 (br, 1H), 1.81 (d, 2H, J = 11.4 Hz), 2.00 (d, 2H, J = 10.5 Hz), 2.81 (t, 2H, J = 6.6 Hz), 3.05-3.22 (m, 1H), 3.58-3.80 (m, 1H), 3.76 (s, 3H), 6.49 (d, 2H, J = 8.7 Hz), 6.50-6.70 (br, 1H), 6.95-7.10 (m, 3H), 7.20-7.32 (m, 2H), 7.51 (d, 1H, J = 7.2Hz), 8.05 (br, 1H). ESI(positive) 418.3 [M+H]+

Compound Ij-23

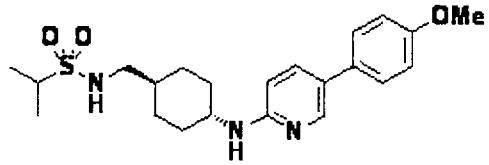
[Formula 390]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.32 (m, 4H), 1.22 (d, 6H, J = 6.6 Hz), 1.25-1.55 (br, 1H), 1.82 (d, 2H, J = 11.4 Hz), 2.01 (d, 2H, J = 10.2 Hz), 2.81 (t, 2H, J = 6.6 Hz), 3.05-3.22 (m, 1H), 3.58-3.78 (m, 1H), 3.80 (s, 3H), 6.59 (d, 2H, J = 9.6 Hz), 6.85 (dd, 1H, J = 8.4 Hz, 2.4 Hz), 6.99 (t, 3H, J = 5.7Hz), 7.05-7.18 (m, 2H), 7.32 (d, 1H, J = 7.8Hz), 7.76 (d, 1H, J = 8.4Hz), 8.27 (d, 1H, J = 2.1 Hz). ESI(positive) 418.3 [M+H]+

Compound Ij-24

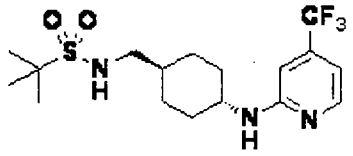
[Formula 391]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.25 (m, 4H), 1.22 (d, 6H, J = 6.6 Hz), 1.28-1.48 (m, 1H), 1.81 (d, 2H, J = 10.8 Hz), 2.00 (d, 2H, J = 9.6 Hz), 2.81 (t, 2H, J = 6.6 Hz), 3.08-3.22 (m, 1H), 3.58-3.74 (m, 1H), 3.77 (s, 3H), 6.51 (d, 2H, J = 8.7 Hz), 6.97 (d, 2H, J = 8.7 Hz), 6.98 (brs, 1H), 7.48 (d, 2H, J = 8.7 Hz), 7.63 (dd, 1H, J = 11.4Hz, 2.4Hz), 8.21 (d, 1H, J = 2.4 Hz). ESI(positive) 418.3[M+H]÷

Compound Ij-25

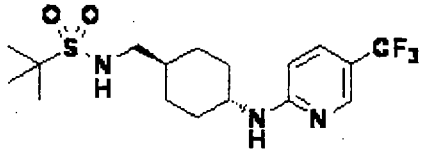
[Formula 392]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.22 (m, 4H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.95-2.05 (m, 2H), 2.88 (t, 2H, J = 6.0 Hz), 3.60-3.80 (m, 1H), 6.65 (d, 1H, J = 5.4 Hz), 6.70 (s, 1H), 6.87 (t, 1H, J = 6.0 Hz), 6.94 (d, 1H, J = 7.8 Hz), 8.16 (d, 1H, J = 5.4 Hz)

Compound Ij-26

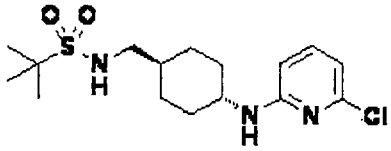
[Formula 393]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.22 (m, 4H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.94-2.04 (m, 2H), 2.88 (t, 2H, J = 6.0 Hz), 3.60-3.80 (m, 1H), 6.53 (d, 1H, J = 8.7 Hz), 6.87 (t, 1H, J = 5.7 Hz), 7.19 (d, 1H, J = 7.5 Hz), 7.59 (dd, 1H, J = 9.0, 2.4 Hz), 8.26 (d, 1H, J = 2.4 Hz)

Compound Ij-27

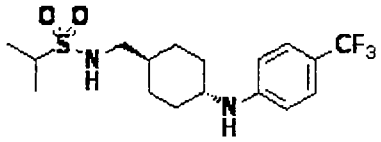
[Formula 394]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.22 (m, 4H), 1.26 (s, 9H), 1.38 (m, 1H), 1.76-1.86 (m, 2H), 1.92-2.02 (m, 2H), 2.88 (t, 2H, J = 6.0 Hz), 3.40-3.60 (m, 1H), 6.36 (d, 1H, J = 8.1 Hz), 6.43 (d, 1H, J = 6.9 Hz), 6.80 (d, 1H, J = 7.5 Hz), 6.86 (t, 1H, J = 5.4 Hz), 7.34 (t, 1H, J = 8.4 Hz)

Compound Ij-28

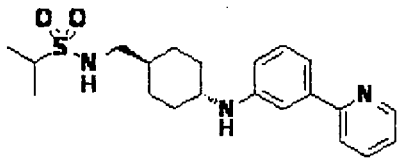
[Formula 395]



^{1}H-NMR ((DMSO-d_6) δ: 0.93-1.18 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.39 (m, 1H), 1.75-1.86 (m, 2H), 1.94-2.05 (m, 2H), 2.80 (t, 2H, J = 6.0 Hz), 3.09-3.27 (m, 2H), 6.19 (d, 1H, J = 8.1 Hz), 6.64 (d, 2H, J = 8.7 Hz), 6.98 (t, 1H, J = 6.0 Hz), 7.33 (d, 2H, J = 8.7 Hz) Mass:379[M+H]$^+$

Compound Ij-29

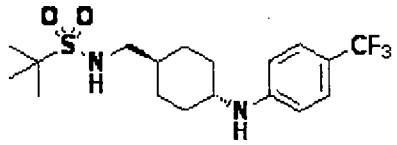
[Formula 396]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.18 (m, 4H), 1.22 (s, 3H), 1.24 (s, 3H), 1.32-1.49 (m, 2H), 1.82 (d, 2H, J = 11.2 Hz), 2.04 (d, 2H, J = 11.2 Hz), 2.75-2.87 (m, 2H), 3.07-3.28 (m, 2H), 6.64 (s, 1H), 6.96 (s, 1H), 7.10-7.22 (m, 2H), 7.25-7.39 (m, 2H), 7.77-7.90 (m, 2H), 8.63 (s, 1H). Melting point:161-162℃

Compound Ij-30

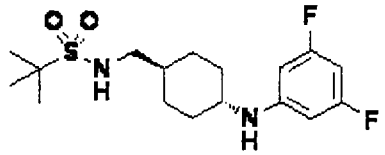
[Formula 397]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.22 (m, 4H), 1.27 (s, 9H), 1.37 (m, 1H), 1.76-1.86 (m, 2H), 1.94-2.05 (m, 2H), 2.88 (t, 2H, J = 6.3 Hz), 3.19 (m, 1H), 6.19 (d, 1H, J = 7.5 Hz), 6.64 (d, 2H, J = 8.7 Hz), 6.88 (d, 1H, J = 6.0Hz), 7.33 (d, 2H, J = 8.7 Hz)
Mass:392M+

Compound Ij-31

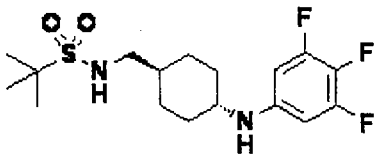
[Formula 398]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.16 (m, 4H), 1.26 (s, 9H), 1,36 (m, 1H), 1.72-1.83 (m, 2H), 1.92-2.02 (m, 2H), 2.87 (t, 2H, J = 6.3 Hz), 3.12 (m, 1H), 6.09-6.23 (m, 4H), 6.87 (t, 1H, J = 6.0 Hz) Mass:361[M+H]$^+$

Compound Ij-32

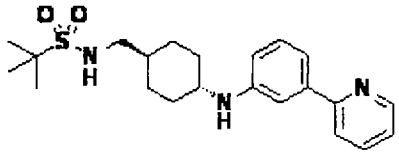
[Formula 399]



^{1}H-NMR ($CDCl_3$) δ: 1.00-1.20 (m, 4H), 1.40 (s, 9H), 1.42-1.64 (m, 2H), 1.84-1.95 (m, 2H), 2.09-2.20 (m, 2H), 3.07 (m, 1H), 3.07 (t, 2H, J = 6.3 Hz), 3.90 (m, 1H), 6.10 (dd, 2H, J = 9.6, 5.4 Hz).

Compound Ij-33

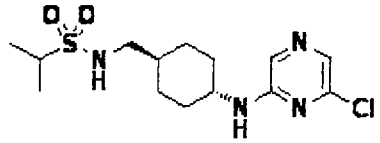
[Formula 400]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.21 (m, 5H), 1.28 (s, 9H), 1.33-1.46 (m, 1H), 1.82 (d, 2H, J = 11.6 Hz), 2.04 (d, 2H, J = 11.6 Hz), 2.86-2.95 (m, 2H), 3.03-3.29 (m, 1H), 6.59-6.71 (m, 1H), 6.80-6.92 (m, 1H), 7.09-7.21 (m, 2H), 7.27-7.37 (m, 2H), 7.77-7.88 (m, 2H), 8.58-8.67 (s, 1H). Melting point:172-173 °C

Compound Ij-34

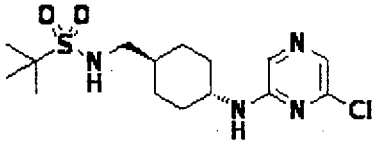
[Formula 401]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.08 (m, 2H), 1.12-1.24(m, 2H), 1.21 (d, 6H, J = 6.4 Hz), 1.38 (m, 1H), 1.76-1.86 (m, 2H), 1.92-2.00 (m, 2H), 2.80 (t, 2H, J = 6.4 Hz), 3.10-3.20 (m, 1H), 3.48-3.60 (m, 1H), 6.95 (t, 1H, J = 5.6 Hz), 7.41 (d, 1H, J = 7.6 Hz), 7.63 (s, 1H), 7.82 (s, 1H).

Compound Ij-35

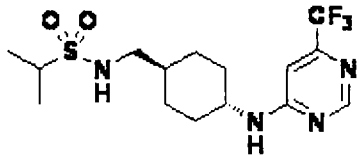
[Formula 402]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.26 (m, 4H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.92-2.02 (m, 2H), 2.88 (t, 2H, J = 6.0 Hz), 3.48-3.62 (m, 1H), 6.87 (t, 1H, J = 6.0 Hz), 7.45 (d, 1H, J = 7.5 Hz), 7.63 (s, 1H), 7.82 (s, 1H)

Compound Ij-36

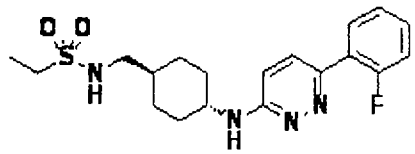
[Formula 403]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.06 (m, 2H), 1.12-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.39 (m, 1H), 1.78-1.84 (m, 2H), 1.95-1.99 (m, 2H), 2.81 (t, 2H, J = 6.0 Hz), 3.10-3.20 (m, 1H), 3.74-3.88 (m, 1H), 6.80 (s, 1H), 6.98 (t, 1H, J = 6.0 Hz), 7.93 (d, 2H, J = 7.2 Hz), 8.53 (s, 1H).

Compound Ij-37

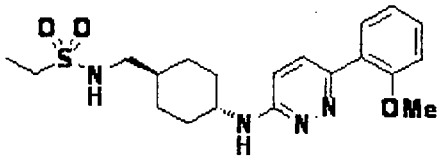
[Formula 404]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.30 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J = 6.0 Hz), 2.99 (q, 2H, J = 7.5 Hz), 3.72-3.90 (m, 1H), 6.85 (d, 1H, J = 9.6 Hz), 6.93 (d, 1H, J = 7.5 Hz), 7.04 (t, 1H, J = 5.7 Hz), 7.26-7.38 (m, 2H), 7.40-7.52 (m, 1H), 7.57 (d, 1H, J = 9.0 Hz), 7.85 (t, 1H, J =7.8 Hz)

Compound Ij-38

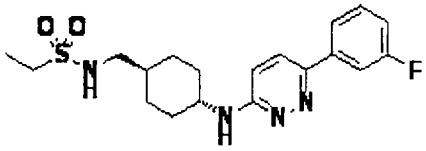
[Formula 405]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.30 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J = 6.0 Hz), 2.99 (q, 2H, J = 7.5 Hz), 3.72-3.90 (m, 1H), 3.80 (s, 3H), 6.72 (d, 1H, J = 7.8 Hz), 6.77 (d, 1H, J = 9.0 Hz), 6.98-7.10 (m, 2H), 7.12 (d, 1H, J = 8.4 Hz), 7.38 (t, 1H, J = 8.1 Hz), 7.56 (d, 1H, J = 9.3 Hz), 7.61 (d, 1H, J = 7.8 Hz)

Compound Ij-39

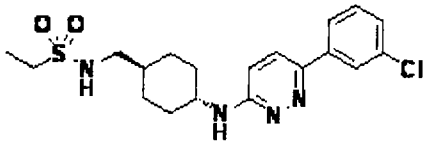
[Formula 406]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.30 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 2.99 (q, 2H, J = 7.5 Hz), 3.72-3.90 (m, 1H), 6.85 (d, 1H, J = 9.6 Hz), 6.92 (d, 1H, J = 7.5 Hz), 7.04 (t, 1H, J = 5.7 Hz), 7.21 (t, 1H, J = 8.7 Hz), 7.46-7.56 (m, 1H), 7.75-7.88 (m, 3H)

Compound Ij-40

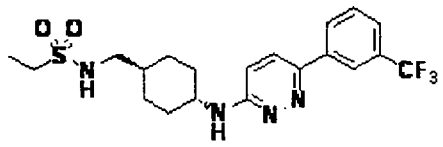
[Formula 407]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.10 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.15-1.26 (m, 2H), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 2.99 (q, 2H, J = 7.5 Hz), 3.76-3.87 (m, 1H), 6.85 (d, 1H, J = 9.6 Hz), 6.91 (d, 1H, J = 7.5 Hz), 7.01 (t, 1H, J = 5.7 Hz), 7.42-7.52 (m, 2H), 7.83 (d, 1H, J = 8.0 Hz), 7.93 (d, 1H, J = 8.0 Hz), 8.02 (s, 1H).

Compound Ij-41

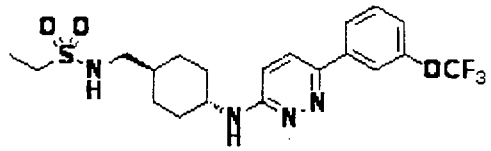
[Formula 408]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.30 (m, 4H), 1.20 (t, 3H, J = 7.5 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 2.99 (q, 2H, J = 7.5 Hz), 3.76-3.90 (m, 1H), 6.88 (d, 1H, J = 9.3 Hz), 6.97 (d, 1H, J = 7.5 Hz), 7.03 (t, 1H, J = 5.7 Hz), 7.67-7.77 (m, 2H), 7.92 (d, 1H, J = 9.6 Hz), 8.26 (d, 1H, J = 6.9 Hz), 8.33(s, 1H)

Compound Ij-42

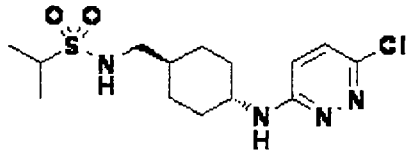
[Formula 409]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.10 (m, 2H), 1.20 (t, 3H, J= 7.2 Hz), 1.22-1.28 (m, 1H), 1.35-1.50 (m, 2H), 1.84 (d, 2H, J = 12.0 Hz), 2.08 (d, 2H, J = 12.0 Hz), 2.63-2.76 (m, 2H), 2.91-3.03 (m, 2H), 3.75-3.90 (m, 1H), 6.86 (d, 1H, J = 9.2 Hz), 6.93 (d, 1H, J = 7.2 Hz), 6.98-7.07 (m, 1H), 7.36 (d, 1H, J = 7.2 Hz), 7.59 (t, 1H, J = 8.0 Hz), 7.85 (d, 1H, J = 9.2 Hz), 7.91-8.02 (m, 2H). Melting point:144-145 °C

Compound Ij-43

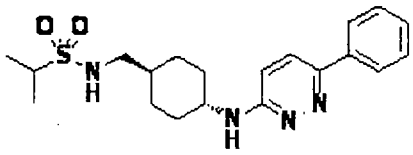
[Formula 410]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.06 (m, 2H), 1.10-1.24 (m, 2H), 1.21 (d, 6H, J = 6.8 Hz), 1.39 (m, 1H), 1.76-1.86 (m, 2H), 1.98-2.06 (m, 2H), 2.81 (t, 2H, J = 6.4 Hz), 3.10-3.20 (m, 1H), 3.62-3.74 (m, 1H), 6.84 (d, 1H, J =9.2 Hz), 6.88-6.98 (m, 2H), 7.31 (d, 1H, J = 9.6 Hz).

Compound Ij-44

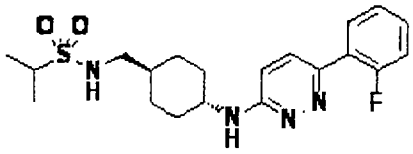
[Formula 411]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.26 (m, 4H), 1.20 (d, 6H, J = 6.6 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.06-3.20 (m, 1H), 3.72-3.90 (m, 1H), 6.75-6.88 (m, 2H), 6.97 (t, 1H, J = 6.0 Hz), 7.30-7.48 (m, 3H), 7.76 (d, 1H, J = 9.3 Hz), 7.94 (d, 2H, J =8.4 Hz)

Compound Ij-45

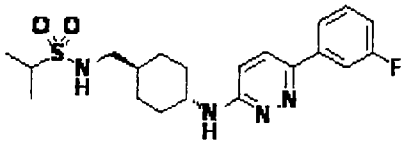
[Formula 412]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J = 6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J = 6.3 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 6.85 (d, 1H, J = 9.0 Hz), 6.91 (d, 1H, J = 7.5 Hz), 6.98 (t, 1H, J = 6.0 Hz), 7.25-7.36 (m, 2H), 7.40-7.50 (m, 1H), 7.57 (d, 1H, J = 6.9 Hz), 7.85 (t, 1H, J =8.1 Hz)

Compound Ij-46

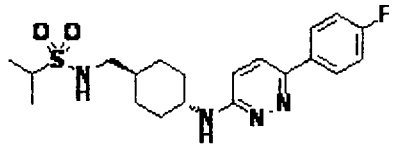
[Formula 413]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J = 6.6 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J = 6.3 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 6.85 (d, 1H, J = 9.3 Hz), 6.90 (d, 1H, J = 7.5 Hz), 6.98 (t, 1H, J = 6.0 Hz), 7.21 (t, 1H, J = 7.8 Hz), 7.46-7.56 (m, 1H), 7.75-7.86 (m, 3H)

Compound Ij-47

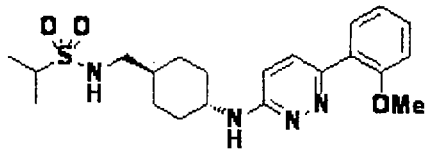
[Formula 414]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J = 6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J = 6.0 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 6.81 (d, 1H, J = 7.5 Hz), 6.84 (d, 1H, J = 9.3 Hz), 6.98 (t, 1H, J = 6.3 Hz), 7.25-7.35 (m, 2H), 7.77 (d, 1H, J = 9.3 Hz), 7.96-8.06 (m, 2H)

Compound Ij-48

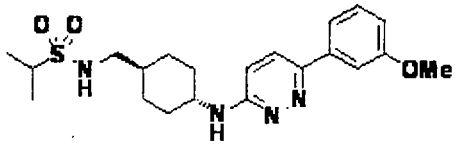
[Formula 415]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J = 6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J = 6.3 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 3.80 (s, 3H), 6.71 (d, 1H, J = 7.8 Hz), 6.76 (d, 1H, J = 9.3 Hz), 6.98 (t, 1H, J = 5.7 Hz), 7.05 (d, 1H, J = 7.2 Hz), 7.12 (d, 1H, J = 7.8 Hz), 7.38 (t, 1H, J = 8.4 Hz), 7.56 (d, 1H, J = 9.3 Hz), 7.62 (d, 1H, J = 6.9 Hz)

Compound Ij-49

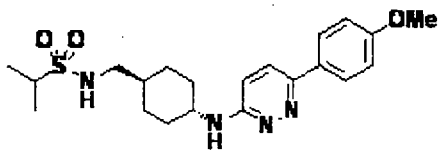
[Formula 416]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J = 6.6 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J = 6.0 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 3.82 (s, 3H), 6.78-6.88 (m, 2H), 6.92-7.04 (m, 2H), 7.37 (t, 1H, J = 7.5 Hz), 7.46-7.58 (m, 2H), 7.79 (d, 1H, J = 9.3 Hz)

Compound Ij-50

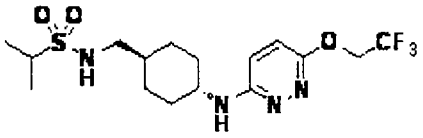
[Formula 417]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J = 6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J = 6.0 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 3.80 (s, 3H), 6.70 (d, 1H, J = 7.8 Hz), 6.82 (d, 1H, J = 9.3 Hz), 6.95-7.05 (m, 3H), 7.72 (d, 1H, J = 9.3 Hz), 7.90 (d, 2H, J = 9.0 Hz).

Compound Ij-51

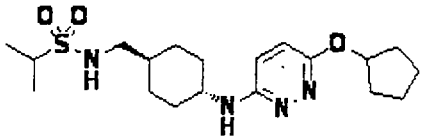
[Formula 418]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.05 (m, 2H), 1.07-1.20 (m, 2H), 1.22 (d, 6H, J = 6.9 Hz), 1.39 (m, 1H), 1.76-1.85 (m, 2H), 2.02-2.10 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.09-3.20 (m, 1H), 3.57-3.68 (m, 1H), 4.89-4.98 (m, 2H), 6.47 (d, 1H, J = 8.0 Hz), 6.88 (d, 1H, J = 7.5 Hz), 6.96 (t, 1H, J = 6.0 Hz), 7.02 (d, 1H, J = 7.5 Hz).

Compound Ij-52

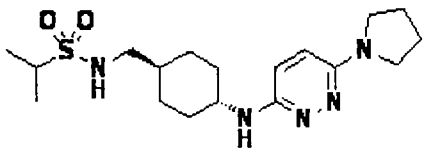
[Formula 419]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.05 (m, 2H), 1.07-1.20 (m, 2H), 1.22 (d, 6H, J = 6.9 Hz), 1.39 (m, 1H), 1.52-1.74 (m, 6H), 1.77-1.85 (m, 2H), 1.87-1.97 (m, 2H), 2.02-2.09 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.09-3.20 (m, 1H), 3.55-3.65 (m, 1H), 5.25-5.32 (m, 1H), 6.19 (d, 1H, J = 8.0 Hz), 6.77 (s, 2H), 6.95 (t, 1H, J = 6.0 Hz).

Compound Ij-53

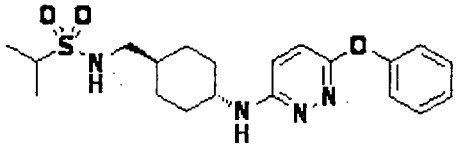
[Formula 420]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.15 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 1.88-1.95 (m, 4H), 2.02-2.09 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 3.09-3.20 (m, 1H), 3.25-3.35 (m, 4H), 3.55-3.65 (m, 1H), 5.80-5.85 (m, 1H), 6.72 (d, 1H, J = 8.0 Hz), 6.80 (d, 1H, J = 8.0 Hz), 6.96 (t, 1H, J = 6.0 Hz).

Compound Ij-54

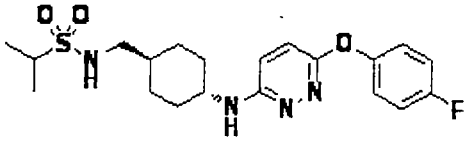
[Formula 421]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.20 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 2.02-2.09 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 3.09-3.20 (m, 1H), 3.58-3.65 (m, 1H), 6.56 (d, 1H, J = 8.0 Hz), 6.90-6.98 (m, 2H), 7.03-7.10 (m, 3H), 7.15 (t, 1H, J = 8.0 Hz), 6.38 (t, 2H, J = 8.0 Hz).

Compound Ij-55

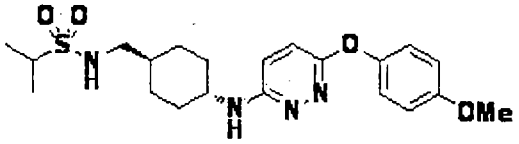
[Formula 422]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.20 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 2.02-2.09 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 3.09-3.20 (m, 1H), 3.58-3.65 (m, 1H), 6.55 (d, 1H, J = 8.0 Hz), 6.90-6.98 (m, 2H), 7.05-7.15 (m, 3H), 7.21 (t, 2H, J = 8.0 Hz).

Compound Ij-56

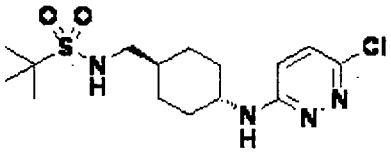
[Formula 423]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.20 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 2.02-2.09 (m, 2H), 2.80 (t, 2H, J = 6.3 Hz), 3.09-3.20 (m, 1H), 3.58-3.65 (m, 1H), 3.75 (s, 3H), 6.49 (d, 1H, J = 8.0 Hz), 6.87-6.98 (m, 4H), 7.00-7.07 (m, 3H).

Compound Ij-57

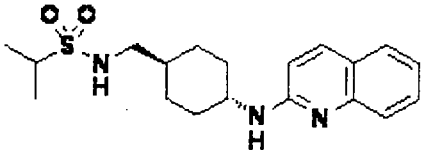
[Formula 424]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.28 (m, 4H), 1.27 (s, 9H), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.00-2.10 (m, 2H), 2.88 (t, 2H, J = 6.0 Hz), 3.60-3.76 (m, 1H), 6.82-6.92 (m, 2H), 6.96 (d, 1H, J = 7.8 Hz), 7.32 (d, 1H, J = 9.6 Hz).

Compound Ij-58

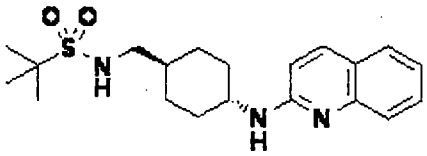
[Formula 425]



^{1}H-NMR (DMSO-d_6) δ: 0.99-1.28 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.39 (m, 1H), 1.78-1.86 (m, 2H), 2.04-2.10 (m, 2H), 2.82 (t, 2H, J = 6.1 Hz), 3.06-3.20 (m, 1H), 3.80-3.96 (m, 1H), 6.71 (d, 1H, J = 9.0 Hz), 6.76-6.86 (m, 1H), 6.90-6.98 (m, 1H), 7.10 (t, 1H, J = 8.1 Hz), 7.39-7.50 (m, 2H), 7.56 (d, 1H, J = 7.5 Hz), 7.78 (d, 1H, J = 7.5 Hz).

Compound Ij-59

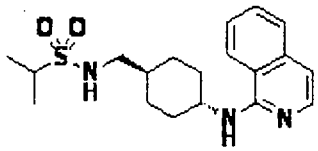
[Formula 426]



^{1}H-NMR (DMSO-d_6) δ: 0.99-1.28 (m, 4H), 1.27 (s, 9H), 1.40 (m, 1H), 1.80-1.85 (m, 2H), 2.04-2.09 (m, 2H), 2.91 (t, 2H, J = 6.1 Hz), 3.80-3.96 (m, 1H), 6.70 (d, 1H, J = 9.0 Hz), 6.81-6.87 (m, 2H), 7.10 (t, 1H, J = 8.1 Hz), 7.39-7.44 (m, 2H), 7.56 (d, 1H, J = 7.5 Hz), 7.79 (d, 1H, J = 7.5 Hz).

Compound Ij-60

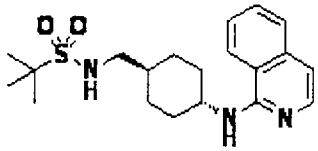
[Formula 427]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.09 (m, 2H), 1.23 (d, 6H, J = 6.9 Hz), 1.31-1.50 (m, 2H), 1.82-1.87 (m, 2H), 2.01-2.05 (m, 2H), 2.83 (t, 2H, J = 6.0 Hz), 3.11-3.20 (m, 1H), 4.00-4.18 (m, 1H), 6.83 (d, 1H, J = 5.7 Hz), 6.90-7.06 (m, 2H), 7.45 (t, 1H, J = 6.9 Hz), 7.59 (t, 1H, J = 8.1 Hz), 7.67 (d, 1H, J = 8.4 Hz), 7.83 (d, 1H, J = 5.7 Hz), 8.27 (d, 1H, J = 7.5 Hz).

Compound Ij-61

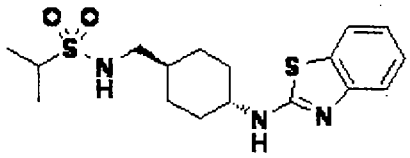
[Formula 428]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.09 (m, 2H), 1.28 (s, 9H), 1.29-1.50 (m, 2H), 1.82-1.87 (m, 2H), 2.01-2.05 (m, 2H), 2.91 (t, 2H, J = 7.8 Hz), 4.00-4.18 (m, 1H), 6.82-6.89 (m, 2H), 6.97 (d, 1H, J = 7.5 Hz), 7.45 (t, 1H, J = 7.2 Hz), 7.59 (t, 1H, J = 8.1 Hz), 7.67 (d, 1H, J = 7.8 Hz), 7.84 (d, 1H, J = 6.0 Hz), 8.27 (d, 1H, J = 8.4 Hz).

Compound Ij-62

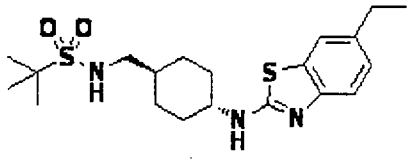
[Formula 429]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.14 (m, 2H), 1.18-1.30 (m, 2H), 1.22 (d, 6H, J = 6.6 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.10-3.20 (m, 1H), 3.58-3.70 (m, 1H), 6.95-7.03 (m, 2H), 7.20 (t, 1H, J = 7.5 Hz), 7.37 (d, 1H, J = 8.1 Hz), 7.64 (d, 1H, J = 7.5 Hz), 7.92 (d, 1H, J = 7.8 Hz).

Compound Ij-63

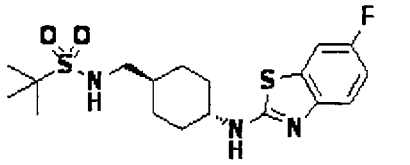
[Formula 430]



^{1}H-NMR (DMSO-d_6) δ: 1.00 (dd, 2H, J = 24.8, 10.6 Hz), 1.15-1.22 (m, 2H), 1.18 (t, 3H, J = 7.6 Hz), 1.27 (s, 9H), 1.34-1.40 (m, 1H), 1.81 (d, 2H, J = 11.6 Hz), 2.07 (d, 2H, J = 11.6 Hz), 2.60 (q, 2H, J = 7.6 Hz), 2.89 (t, 2H, J = 6.3 Hz), 3.52-3.63 (m, 1H), 6.87 (t, 1H, J = 5.8 Hz), 7.04 (d, 1H, J = 7.9 Hz), 7.27 (d, 1H, J = 8.2 Hz), 7.47 (s, 1H), 7.80 (d, 1H, J = 7.6 Hz).

Compound Ij-64

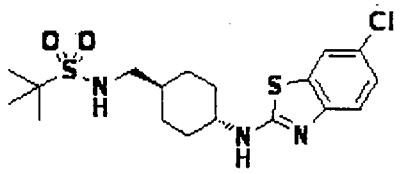
[Formula 431]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.10 (m, 2H), 1.12-1.25 (m, 2H), 1.27 (s, 9H), 1.37 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.89 (t, 2H, J = 6.0 Hz), 3.50-3.66 (m, 1H), 6.87 (t, 1H, J = 5.7 Hz), 7.03 (dd, 1H, J = 8.7, 2.7 Hz), 7.32-7.37 (m, 1H), 7.58 (dd, 1H, J = 8.7, 2.7 Hz), 7.92 (d, 1H, J = 7.2 Hz).

Compound Ij-65

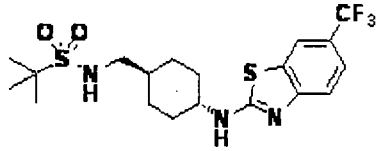
[Formula 432]



^{1}H-NMR (DMSO-d_6) δ: 1.01 (dd, 2H, J = 24.6, 10.2 Hz), 1.21 (dd, 2H, J = 24.6, 10.2 Hz), 1.27 (s, 9H), 1.34-1.40 (m, 1H), 1.82 (d, 2H, J = 11.2 Hz), 2.08 (d, 2H, J = 11.2 Hz), 2.89 (t, 2H, J = 6.2 Hz), 3.59-3.65 (m, 1H), 6.87 (t, 1H, J = 5.8 Hz), 7.21 (dd, 1H, J = 8.6, 2.4 Hz), 7.34 (d, 1H, J = 8.6 Hz), 7.77 (d, 1H, J = 1.8 Hz), 8.06 (d, 1H, J = 7.6 Hz).

Compound Ij-66

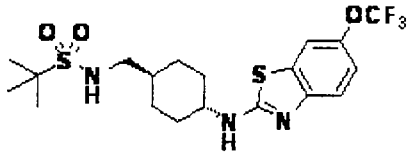
[Formula 433]



^{1}H-NMR ($CDCl_3$) δ: 1.09-1.46 (m, 4H), 1.41 (s, 9H), 1.54 (m, 1H), 1.90-2.00 (m, 2H), 2.24-2.34 (m, 2H), 3.09 (t, 2H, J = 6.6 Hz), 3.46-3.60 (m, 1H), 3.99 (t, 1H, J = 6.6 Hz), 6.58 (brs, 1H), 7.58(s, 2H), 7.85 (s, 1H).

Compound Ij-67

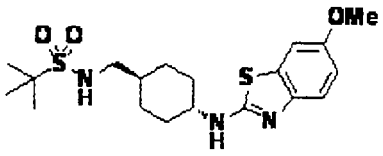
[Formula 434]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.30 (m, 4H), 1.27 (s, 9H), 1.30-1.48 (m, 1H), 1.82 (d, 2H, J = 11.1 Hz), 2.08 (d, 2H, J = 9.6 Hz), 2.89 (t, 2H, J = 6.3 Hz), 3.55-3.70 (m, 1H), 6.87 (t, 1H, J = 5.7 Hz), 7.17 (m, 1H), 7.41 (d, 1H, J = 8.7 Hz), 7.77 (d, 1H, J = 1.5 Hz), 8.10 (d, 1H, J = 7.5 Hz). ESI(positive)m/z 466.2 [M+H]+

Compound Ij-68

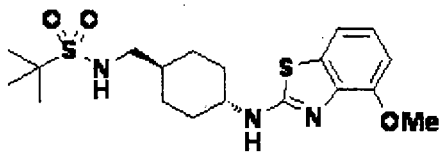
[Formula 435]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.28 (m, 4H), 1.25 (s, 9H), 1.32 (m, 1H), 1.76-1.82 (m, 2H), 2.00-2.10 (m, 2H), 2.87 (t, 2H, J = 6.6 Hz), 3.50-3.62 (m, 1H), 3.71 (s, 3H), 6.77 (dd, 1H, J = 8.7, 2.7 Hz), 6.84 (t, 1H, J = 5.7 Hz), 7.22-7.28 (m, 2H), 7.66 (d, 1H, J = 7.2 Hz).

Compound Ij-69

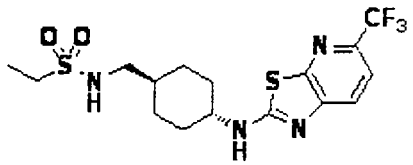
[Formula 436]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.10 (m, 2H), 1.12-1.25 (m, 2H), 1.27 (s, 9H), 1.37 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.90 (t, 2H, J = 6.0 Hz), 3.52-3.68 (m, 1H), 3.84 (s, 3H), 6.82 (d, 1H, J = 8.1 Hz), 6.88 (t, 1H, J = 5.4 Hz), 6.95 (t, 1H, J = 7.8 Hz), 7.23 (d, 1H, J = 7.8 Hz), 7.83 (d, 1H, J = 7.8 Hz).

Compound Ij-70

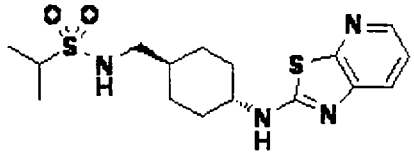
[Formula 437]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.10 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.17-1.32 (m, 2H), 1.40 (m, 1H), 1.76-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.79 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.2 Hz), 3.60-3.78 (m, 1H), 7.03 (t, 1H, J = 6.3 Hz), 7.45-7.54 (m, 2H), 8.10 (s, 1H), 8.34 (d, 1H, J = 7.2 Hz).

Compound Ij-71

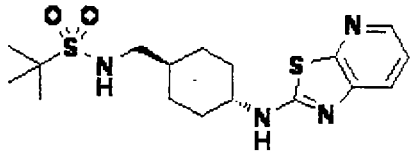
[Formula 438]



^{1}H-NMR (DMSO-d_6) δ: 1.01 (dd, 2H, J = 26.1, 12.3 Hz), 1.16-1.22 (m, 2H), 1.22 (d, 6H, J = 6.6 Hz), 1.35-1.41 (m, 1H), 1.70-1.77 (m, 1H), 1.82 (d, 2H, J = 11.6 Hz), 2.08 (d, 2H, J = 11.6 Hz), 2.81 (t, 2H, J = 6.3 Hz), 3.66-3.72 (m, 1H), 6.99 (t, 1H, J = 6.3 Hz), 7.23 (dd, 1H, J = 8.1, 4.7 Hz), 7.66 (d, 1H, J = 8.1 Hz), 8.07 (d, 1H, J = 4.7 Hz), 8.26 (d, 1H, J = 6.3 Hz).

Compound Ij-72

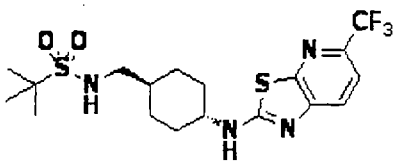
[Formula 439]



^{1}H-NMR (DMSO-d_6) δ: 1.01 (dd, 2H, J = 24.8, 11.3 Hz), 1.18-1.23 (m, 2H), 1.27 (s, 9H), 1.36-1.39 (m, 1H), 1.82 (d, 2H, J = 11.5 Hz), 2.08 (d, 2H, J = 11.5 Hz), 2.89 (t, 2H, J = 6.1 Hz), 3.65-3.73 (m, 1H), 6.87 (t, 1H, J = 5.7 Hz), 7.23 (dd, 1H, J = 8.1, 4.8 Hz), 7.66 (d, 1H, J = 7.9 Hz), 8.07 (d, 1H, J = 4.7 Hz), 8.26 (d, 1H, J = 7.6 Hz).

Compound Ij-73

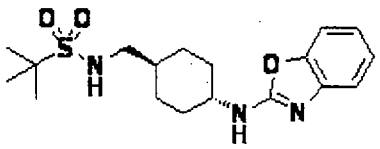
[Formula 440]



^{1}H-NMR ($CDCl_3$)δ: 1.09-1.46 (m, 4H), 1.41 (s, 9H), 1.55 (m, 1H), 1.92-2.02 (m, 2H), 2.24-2.34 (m, 2H), 3.09 (t, 2H, J = 6.3 Hz), 3.58-3.72 (m, 1H), 3.98 (t, 1H, J = 6.0 Hz), 6.30 (brs, 1H), 7.62(d, 1H, J = 8.1 Hz), 7.77 (d, 1H, J = 8.4 Hz).

Compound Ij-74

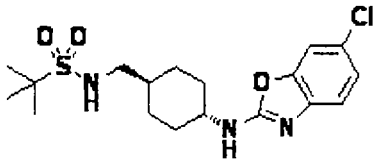
[Formula 441]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.08 (m, 2H), 1.12-1.40 (m, 3H), 1.25 (s, 9H), 1.76-1.86 (m, 2H), 1.98-2.10 (m, 2H), 2.87 (d, 2H, J = 6.3 Hz), 3.40-3.56 (m, 1H), 6.85 (brs, 1H), 6.93 (t, 1H, J = 7.5 Hz), 7.07 (t, 1H, J = 7.5 Hz), 7.20 (d, 1H, J = 7.5 Hz), 7.29 (d, 1H, J = 7.8 Hz), 7.79 (brs, 1H).

Compound Ij-75

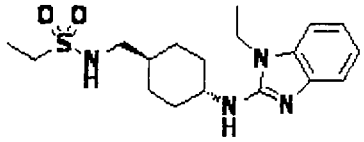
[Formula 442]



^{1}H-NMR ($CDCl_3$) δ: 1.08-1.26 (m, 2H), 1.36-1.60 (m, 3H), 1.40 (s, 9H), 1.92-2.02 (m, 2H), 2.22-2.32 (m, 2H), 3.08 (t, 2H, J = 6.6 Hz), 3.68-3.80 (m, 1H), 4.03 (t, 1H, J = 6.0 Hz), 7.06 (brs, 1H), 7.20-7.36(m, 3H).

Compound Ij-76

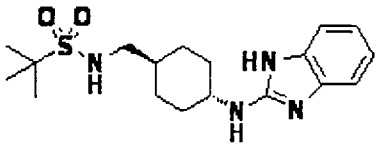
[Formula 443]



^{1}H-NMR (DMSO-d_6) δ: 1.02 (dd, 2H, J = 25.2, 12.4 Hz), 1.17 (t, 3H, J = 7.1 Hz), 1.20 (t, 3H, J = 7.3 Hz), 1.26-1.35 (m, 2H), 1.37-1.42 (m, 1H), 1.83 (d, 2H, J = 11.6 Hz), 2.05 (d, 2H, J = 11.6 Hz), 2.80 (t, 2H, J = 6.4 Hz), 2.99 (q, 2H, J = 7.3 Hz), 3.65-3.72 (m, 1H), 4.01 (q, 2H, J = 7.1 Hz), 6.32 (d, 1H, J = 7.9 Hz), 6.86-6.94 (m, 2H), 7.01 (t, 1H, J = 6.0 Hz), 7.12 (d, 1H, J = 6.9 Hz), 7.17 (d, 1H, J = 6.8 Hz).

Compound Ij-77

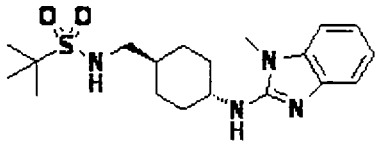
[Formula 444]



^{1}H-NMR (DMSO-d_6) δ: 1.02 (dd, 2H, J = 24.8, 10.8 Hz), 1.19-1.21 (m, 2H), 1.30 (s, 9H), 1.37-1.41 (m, 1H), 1.84 (d, 2H, J = 10.6 Hz), 2.06 (d, 2H, J = 10.6 Hz), 2.92 (t, 2H, J = 6.3 Hz), 3.50-3.52 (m, 1H), 6.42 (d, 1H, J = 8.1 Hz), 6.83 (d, 1H, J = 7.9 Hz), 6.88-6.92 (m, 2H), 7.11-7.14 (m, 2H), 10.58 (s, 1H).

Compound Ij-78

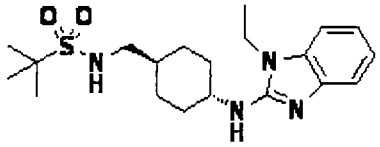
[Formula 445]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.05 (m, 2H), 1.20-1.26 (m, 2H), 1.28 (s, 9H), 1.34-1.38 (m, 1H), 1.84 (d, 2H, J = 11.5 Hz), 2.07 (d, 2H, J = 11.5 Hz), 2.90 (t, 2H, J = 6.1 Hz), 3.47 (s, 3H), 3.63-3.69 (m, 1H), 6.34 (d, 1H, J = 7.6 Hz), 6.87-6.93 (m, 3H), 7.11 (d, 1H, J = 8.4 Hz), 7.17 (d, 1H, J = 8.4 Hz).

Compound Ij-79

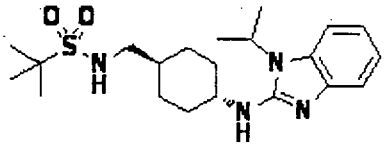
[Formula 446]



^{1}H-NMR (DMSO-d_6) δ: 1.03 (dd, 2H, J = 23.6, 10.8 Hz), 1.18 (t, 3H, J = 7.5 Hz), 1.25-1.34 (m, 2H), 1.29 (s, 9H), 1.37-1.40 (m, 1H), 1.86 (d, 2H, J = 11.7 Hz), 2.07 (d, 2H, J = 11.7 Hz), 2.92 (t, 2H, J = 6.2 Hz), 3.67-3.73 (m, 1H), 4.03 (q, 2H, J = 7.1 Hz), 6.34 (d, 1H, J = 7.9 Hz), 6.87-6.96 (m, 3H), 7.14 (dd, 1H, J = 8.1, 1.2 Hz), 7.19 (dd, 1H, J = 8.1, 1.2 Hz).

Compound Ij-80

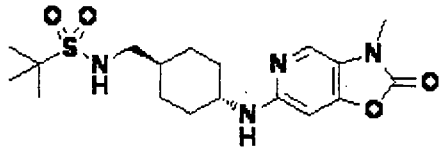
[Formula 447]



^{1}H-NMR (DMSO-d_6) δ: 1.00 (dd, 2H, J = 23.2, 11.9 Hz), 1.19-1.25 (m, 2H), 1.28 (s, 9H), 1.33-1.38 (m, 1H), 1.45 (s, 3H), 1.47 (s, 3H), 1.83 (d, 2H, J = 11.1 Hz), 2.07 (d, 2H, J = 11.1 Hz), 2.90 (t, 2H, J = 6.1 Hz), 3.62-3.70 (m, 1H), 4.57-4.66 (m, 1H), 6.21 (d, 1H, J = 7.9 Hz), 6.82-6.94 (m, 3H), 7.18 (d, 1H, J = 7.6 Hz), 7.31 (d, 1H, J = 7.6 Hz).

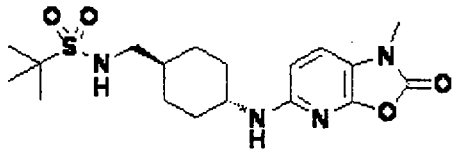
Compound Ij-81

[Formula 448]



Compound Ij-82

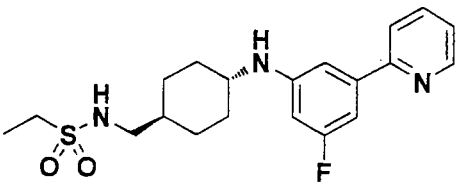
[Formula 449]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.19 (m, 4H), 1.28 (s, 9H), 1.32-1.45 (m, 1H), 1.80 (d, 2H, J = 11.2 Hz), 1.98 (d, 2H, J = 11.2 Hz), 2.84-2.93 (m, 2H), 3.26 (s, 3H), 3.40-3.53 (m, 1H), 6.29 (d, 1H, J = 8.0 Hz), 6.38 (d, 1H, J = 7.2 Hz), 6.86 (s, 1H), 7.33 (d, 1H, J = 8.4 Hz).

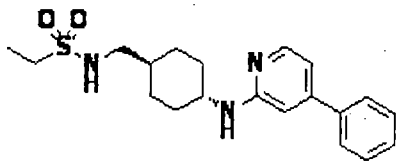
Compound Ij-83

[Formula 450]



Compound Ij-84

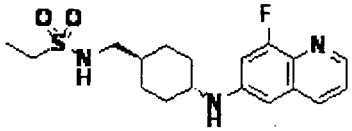
[Formula 451]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.20 (m, 4H), 1.18 (t, 3H, J = 7.2 Hz), 1.40 (m, 1H), 1.75-1.85 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.2 Hz), 3.60-3.78 (m, 1H), 6.38 (d, 1H, J = 8.1 Hz), 6.67 (s, 1H), 6.72 (d, 1H, J = 5.4 Hz), 7.00 (t, 1H, J = 6.0 Hz), 7.36-7.54 (m, 3H), 7.62 (d, 2H, J = 6.9 Hz), 8.00 (d, 1H, J = 5.4 Hz)

Compound Ij-85

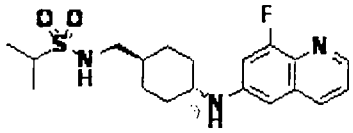
[Formula 452]



^{1}H-NMR (DMSO-d_6) δ: 1.00-1.20 (m, 4H), 1.20 (t, 3H, J = 7.2 Hz), 1.43 (m, 1H), 1.80-1.88 (m, 2H), 2.03-2.13 (m, 2H), 2.81 (t, 3H, J = 6.0 Hz), 3.00 (q, 2H, J = 7.2 Hz), 3.26 (m, 1H), 6.17 (d, 1H, J = 7.6 Hz), 6.57 (s, 1H), 6.96-7.07 (m, 2H), 7.35 (dd, 1H, J = 8.4, 4.0 Hz), 8.02 (d, 1H, J = 8.4 Hz), 8.47 (d, 1H, J = 4.0 Hz).

Compound Ij-86

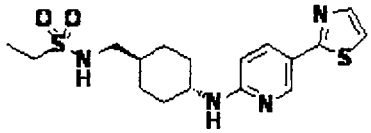
[Formula 453]



^{1}H-NMR (DMSO-d_6) δ: 1.00-1.24 (m, 4H), 1.23 (d, 6H, J = 6.4 Hz), 1.42 (m, 1H), 1.80-1.88 (m, 2H), 2.03-2.12 (m, 2H), 2.79-2.87 (m, 2H), 3.16 (m, 1H), 3.27 (m, 1H), 6.17 (d, 1H, J = 8.0 Hz), 6.57 (s, 1H), 6.99 (d, 1H, J = 8.0 Hz), 7.01 (s, 1H), 7.35 (dd, 1H, J = 8.0, 4.0 Hz), 8.02 (d, 1H, J = 8.0 Hz), 8.47 (d, 1H, J = 2.8 Hz).

Compound Ij-87

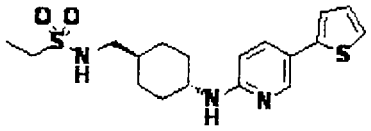
[Formula 454]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.08 (m, 2H), 1.11-1.25 (m, 2H), 1.20 (t, 3H, J = 7.2 Hz), 1.40 (m, 1H), 1.76-1.86 (m, 2H), 1.97-2.04 (m, 2H), 2.73-2.82 (m, 2H), 2.99 (q, 2H, J = 7.2 Hz), 3.70 (m, 1H), 6.53 (d, 1H, J = 8.8 Hz), 6.53 (d, 1H, J = 8.8 Hz), 7.01 (t, 1H, J = 6.0 Hz), 7.58 (d, 1H, J = 3.2 Hz), 7.79 (d, 1H, J = 3.2 Hz), 7.86 (d, 1H, J = 8.8 Hz), 8.55 (s, 1H).

Compound Ij-88

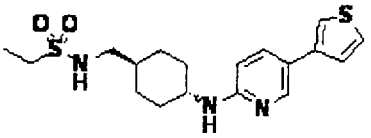
[Formula 455]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.07 (m, 2H), 1.09-1.20 (m, 2H), 1.19 (t, 6H, J = 7.2 Hz), 1.39 (m, 1H), 1.75-1.83 (m, 2H), 1.95-2.03 (m, 2H), 2.74-2.81 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.66 (m, 1H), 6.48 (d, 1H, J = 8.4 Hz), 6.60 (d, 1H, J = 7.6 Hz), 7.00 (t, 1H, J = 5.6 Hz), 7.06 (dd, 1H, J = 4.8, 2.4 Hz), 7.25 (d, 1H, J = 2.4 Hz), 7.37 (d, 1H, J = 4.8 Hz), 7.60 (dd, 1H, J = 8.4, 2.0 Hz), 8.26 (s, 1H).

Compound Ij-89

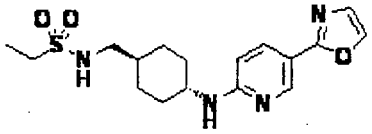
[Formula 456]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.07 (m, 2H), 1.10-1.20 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.39 (m, 1H), 1.76-1.84 (m, 2H), 1.96-2.04 (m, 2H), 2.73-2.81 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.65 (m, 1H), 6.41-6.50 (m, 2H), 7.01 (t, 1H, J = 6.0 Hz), 7.44 (d, 1H, J = 4.0 Hz), 7.58 (m, 1H), 7.59 (s, 1H), 7.68 (d, 1H, J = 8.0 Hz), 8.34 (s, 1H).

Compound Ij-90

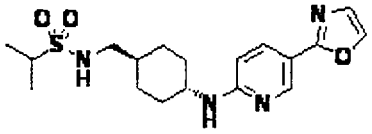
[Formula 457]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.08 (m, 2H), 1.12-1.25 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.39 (m, 1H), 1.76-1.86 (m, 2H), 1.94-2.03 (m, 2H), 2.75-2.82 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.71 (m, 1H), 6.54 (d, 1H, J = 8.8 Hz), 6.98-7.07 (m, 2H), 7.25 (s, 1H), 7.85 (dd, 1H, J = 8.8, 2.0 Hz), 8.07 (s, 1H), 8.56 (d, 1H, J = 2.0 Hz).

Compound Ij-91

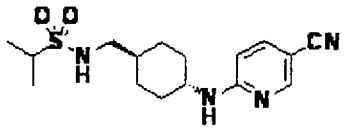
[Formula 458]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.07 (m, 2H), 1.11-1.22 (m, 2H), 1.21 (d, 6H, J = 6.8 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 1.95-2.03 (m, 2H), 2.77-2.83 (m, 2H), 3.14 (m, 1H), 3.72 (m, 1H), 6.53 (d, 1H, J = 8.8 Hz), 6.97 (t, 1H, J = 6.0 Hz), 7.02 (d, 1H, J = 7.6 Hz), 7.25 (s, 1H), 7.84 (dd, 1H, J = 8.8, 2.0 Hz), 8.06 (s, 1H), 8.56 (d, 1H, J = 2.0 Hz).

Compound Ij-92

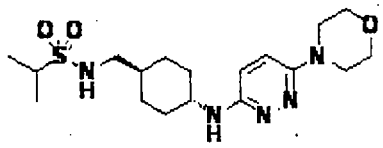
[Formula 459]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.03 (m, 2H), 1.11-1.23 (m, 2H), 1.21 (d, 6H, J = 6.8 Hz), 1.37 (m, 1H), 1.75-1.83 (m, 2H), 1.91-1.99 (m, 2H), 2.36-2.42 (m, 2H), 3.12 (m, 1H), 3.70 (m, 1H), 6.49 (d, 1H, J = 9.2 Hz), 6.97 (t, 1H, J = 6.0 Hz), 7.47 (d, 1H, J = 8.0 Hz), 7.62 (d, 1H, J = 8.0 Hz), 8.36 (s, 1H).

Compound Ij-93

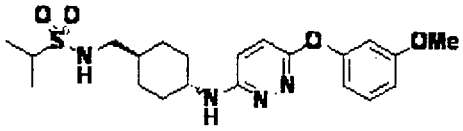
[Formula 460]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.13 (m, 4H), 1.23 (d, 6H, J = 6.9 Hz), 1.31-1.44 (m, 1H), 1.78-1.82 (m, 2H), 2.03-2.06 (m, 2H), 2.76-2.82 (m, 2H), 3.10-3.19 (m, 1H), 3.20-3.25 (m, 4H), 3.58-3.65 (m, 1H), 3.69-3.74 (m, 4H), 6.04 (d, 1H, J = 7.5 Hz), 6.72 (d, 1H, J = 9.6 Hz), 6.95-6.99 (m, 1H), 7.10 (d, 1H, J = 9.6 Hz).

Compound Ij-94

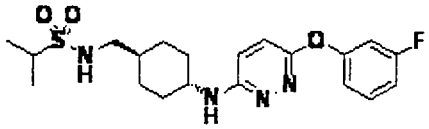
[Formula 461]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.42 (m, 5H), 1.22 (d, 6H, J = 6.9 Hz), 1.79-1.83 (m, 2H), 2.03-2.07 (m, 2H), 2.80 (d, 2H, J = 6.3 Hz), 3.10-3.19 (m, 1H), 3.54-3.70 (m, 1H), 3.74 (s, 3H), 6.57-6.64 (m, 3H), 6.72-6.75 (m, 1H), 6.90-7.09 (m, 3H), 7.24-7.30 (m, 1H).

Compound Ij-95

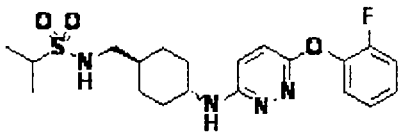
[Formula 462]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.04 (m, 2H), 1.10-1.18 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.34-1.44 (m, 1H), 1.78-1.87 (m, 2H), 2.02-2.12 (m, 2H), 2.77-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.52-3.70 (m, 1H), 6.64 (d, 1H, J = 8.0 Hz), 6.88-7.06 (m, 5H), 7.12 (d, 1H, J = 8.0 Hz), 7.37-7.46 (m, 1H).

Compound Ij-96

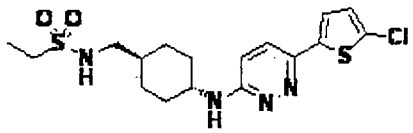
[Formula 463]



^{1}H-NMR (DMSO-d_6) δ: 0.90-1.04 (m, 2H), 1.05-1.18 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.84 (m, 2H), 1.98-2.08 (m, 2H), 2.76-2.84 (m, 2H), 3.08-3.18 (m, 1H), 3.52-3.64 (m, 1H), 6.55 (d, 1H, J = 8.0 Hz), 6.91-7.00 (m, 2H), 7.15-7.38 (m, 5H).

Compound Ij-97

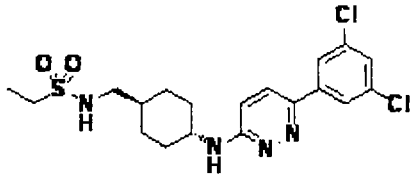
[Formula 464]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.08 (m, 2H), 1.12-1.25 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.35-1.47 (m, 1H), 1.78-1.87 (m, 2H), 2.02-2.10 (m, 2H), 2.78-2.83 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.70-3.82 (m, 1H), 6.82 (d, 1H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.0 Hz), 7.01 (t, 1H, J = 4.5 Hz), 7.13 (d, 1H, J = 4.0 Hz), 7.43 (d, 1H, J = 4.0 Hz), 7.76 (d, 1H, J = 8.0 Hz).

Compound Ij-98

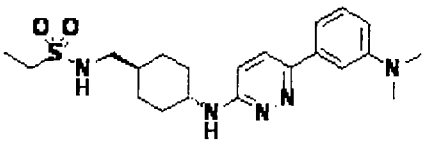
[Formula 465]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.10 (m, 2H), 1.17-1.28 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.37-1.49 (m, 1H), 1.80-1.88 (m, 2H), 2.04-2.12 (m, 2H), 2.77-2.83 (m, 2H), 2.99 (q, 2H, J = 7.2 Hz), 3.76-3.88 (m, 1H), 6.85 (d, 1H, J = 8.0 Hz), 6.99-7.05 (m, 2H), 7.61 (s, 1H), 7.90 (d, 1H, J = 8.0 Hz), 8.02 (s, 2H).

Compound Ij-99

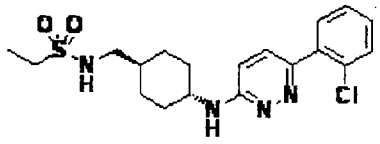
[Formula 466]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.10 (m, 2H), 1.14-1.26 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.37-1.48 (m, 1H), 1.80-1.88 (m, 2H), 2.04-2.13 (m, 2H), 2.77-2.83 (m, 2H), 2.96 (s, 6H), 2.99 (q, 2H, J = 7.2 Hz), 3.76-3.86 (m, 1H), 6.72-6.78 (m, 2H), 6.82 (d, 1H, J = 8.0 Hz), 7.02 (t, 1H, J = 4.5 Hz), 7.18 (d, 1H, J = 8.0 Hz), 7.26 (t, 1H, J = 8.0 Hz), 7.34 (s, 1H), 7.74 (d, 1H, J = 8.0 Hz).

Compound Ij-100

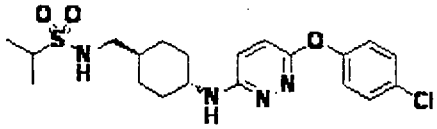
[Formula 467]



^{1}H-NMR (DMSO-d_6)δ: 0.98-1.10 (m, 2H), 1.16-1.27 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.37-1.48 (m, 1H), 1.80-1.88 (m, 2H), 2.04-2.13 (m, 2H), 2.77-2.83 (m, 2H), 2.99 (q, 2H, J = 7.2 Hz), 3.76-3.86 (m, 1H), 6.83 (d, 1H, J = 8.0 Hz), 6.89 (d, 1H, J = 8.0 Hz), 7.02 (t, 1H, J = 4.5 Hz), 7.42-7.50 (m, 3H), 7.53-7.59 (m, 2H).

Compound Ij-101

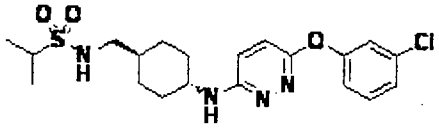
[Formula 468]



^{1}H-NMR (DMSO-d_6)δ: 0.92-1.05 (m, 2H), 1.08-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.36-1.43 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.09 (m, 2H), 2.77-2.83 (m, 2H), 3.10-3.20 (m, 1H), 3.56-3.68 (m, 1H), 6.62 (d, 1H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.0 Hz), 6.98 (t, 1H, J = 4.5 Hz), 7.10-7.15 (m, 3H), 7.43 (d, 2H, J = 8.0 Hz).

Compound Ij-102

[Formula 469]

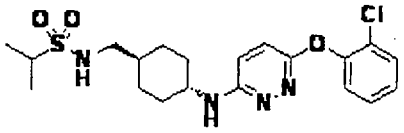


^{1}H-NMR (DMSO-d_6) δ: 0.92-1.05 (m, 2H), 1.08-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.36-1.43 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.09 (m, 2H), 2.77-2.83 (m, 2H),

3.10-3.20 (m, 1H), 3.57-3.68 (m, 1H), 6.65 (d, 1H, J = 8.0 Hz), 6.94 (d, 1H, J = 8.0 Hz), 6.97 (t, 1H, J = 4.5 Hz), 7.06 (d, 1H, J = 8.0 Hz), 7.13 (d, 1H, J = 8.0 Hz), 7.18-7.26 (m, 2H), 7.41 (t, 1H, J = 8.0 Hz).

Compound Ij-103

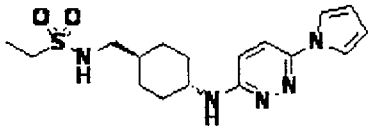
[Formula 470]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.04 (m, 2H), 1.05-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.33-1.43 (m, 1H), 1.77-1.82 (m, 2H), 2.00-2.07 (m, 2H), 2.76-2.82 (m, 2H), 3.08-3.20 (m, 1H), 3.52-3.64 (m, 1H), 6.57 (d, 1H, J = 8.0 Hz), 6.92-7.00 (m, 2H), 7.17 (d, 1H, J = 8.0 Hz), 7.23-7.28 (m, 2H), 7.38 (t, 1H, J = 8.0 Hz), 7.56 (d, 1H, J = 8.0 Hz).

Compound Ij-104

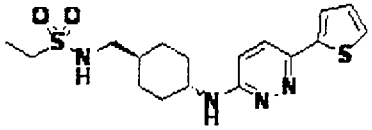
[Formula 471]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.08 (m, 2H), 1.12-1.24 (m, 2H), 1.19 (t, 3H, J = 7.6 Hz), 1.35-1.46 (m, 1H), 1.78-1.86 (m, 2H), 2.04-2.12 (m, 2H), 2.76-2.82 (m, 2H), 2.98 (q, 2H, J = 7.6 Hz), 3.67-3.78 (m, 1H), 6.27 (s, 2H), 6.71 (d, 1H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.0 Hz), 7.02 (brs, 1H), 7.52 (s, 2H), 7.67 (d, 1H, J = 8.0 Hz).

Compound Ij-105

[Formula 472]

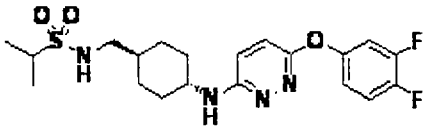


^{1}H-NMR (DMSO-d_6) δ: 0.96-1.08 (m, 2H), 1.13-1.25 (m, 2H), 1.19 (t, 3H, J = 7.6 Hz), 1.35-1.46 (m, 1H), 1.78-1.87 (m, 2H), 2.04-2.12 (m, 2H), 2.76-2.83 (m, 2H), 2.99 (q, 2H, J = 7.6 Hz), 3.72-3.82 (m, 1H), 6.82 (d, 1H, J = 8.0 Hz), 6.85 (d, 1H, J

= 8.0 Hz), 7.03 (t, 1H, J = 4.5 Hz), 7.12 (t, 1H, J = 4.0 Hz), 7.51 (d, 1H, J = 4.0 Hz), 7.56 (d, 1H, J = 4.0 Hz), 7.76 (d, 1H, J = 8.0 Hz).

Compound Ij-106

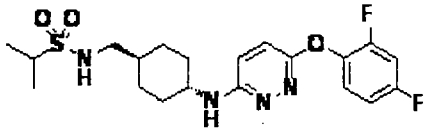
[Formula 473]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.33-1.45 (m, 1H), 1.76-1.85 (m, 2H), 2.02-2.08 (m, 2H), 2.76-2.83 (m, 2H), 3.10-3.20 (m, 1H), 3.57-3.67 (m, 1H), 6.63 (d, 1H, J = 8.0 Hz), 6.92-7.00 (m, 3H), 7.13 (d, 1H, J = 8.0 Hz), 7.29-7.36 (m, 1H), 7.42-7.50 (m, 1H).

Compound Ij-107

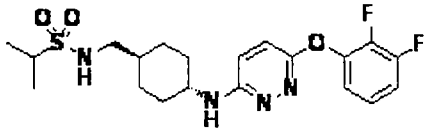
[Formula 474]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.83 (m, 2H), 1.98-2.06 (m, 2H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.52-3.63 (m, 1H), 6.57 (d, 1H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.0 Hz), 6.97 (t, 1H, J = 4.5 Hz), 7.12 (t, 1H, J = 4.0 Hz), 7.19 (d, 1H, J = 8.0 Hz), 7.33-7.47 (m, 2H).

Compound Ij-108

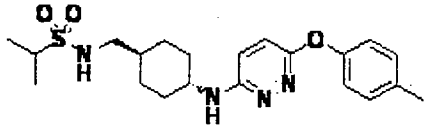
[Formula 475]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.83 (m, 2H), 1.98-2.07 (m, 2H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.54-3.63 (m, 1H), 6.63 (d, 1H, J = 8.0 Hz), 6.93-7.00 (m, 2H), 7.14 (t, 1H, J = 8.0 Hz), 7.20-7.37 (m, 3H).

Compound Ij-109

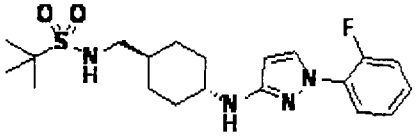
[Formula 476]



^{1}H-NMR (DMSO-d_6) δ: 0.82-1.05 (m, 2H), 1.05-1.20 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.32-1.43 (m, 1H), 1.76-1.83 (m, 2H), 2.00-2.08 (m, 2H), 2.29 (s, 3H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.56-3.66 (m, 1H), 6.55 (d, 1H, J = 8.0 Hz), 6.90 (d, 1H, J = 8.0 Hz), 6.93-7.00 (m, 3H), 7.05 (d, 1H, J = 8.0 Hz), 7.17 (d, 2H, J = 8.0 Hz).

Compound Ij-110

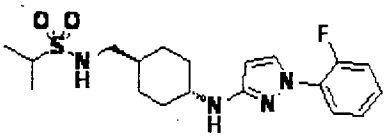
[Formula 477]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.19 (m, 4H), 1.28 (s, 9H), 1.32-1.43 (m, 1H), 1.80 (d, 2H, J = 12.0 Hz), 2.07 (d, 2H, J = 12.0 Hz), 2.88 (t, 2H, J = 6.4 Hz), 3.16-3.27 (m, 1H), 5.47 (d, 1H, J = 7.6 Hz), 5.80 (s, 1H), 6.83 (d, 1H, J = 6.0 Hz), 7.15-7.40 (m, 3H), 7.75 (t, 1H, J = 8.4 Hz), 7.86 (s, 1H).

Compound Ij-111

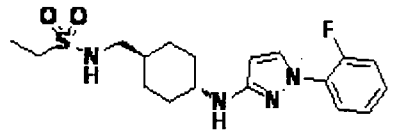
[Formula 478]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.19 (m, 4H), 1.21 (d, 6H, J = 6.9 Hz), 1.32-1.43 (m, 1H), 1.76-1.82 (m, 2H), 2.02-2.12 (m, 2H), 2.77-2.83 (m, 2H), 3.08-3.27 (m, 2H), 5.48 (d, 1H, J = 8.1 Hz), 5.80 (d, 1H, J = 2.7 Hz), 6.95 (t, 1H, J = 6.0 Hz), 7.15-7.39 (m, 3H), 7.75 (td, 1H, J = 8.4, 1.8 Hz), 7.86 (t, 1H, J = 2.7 Hz).

Compound Ij-112

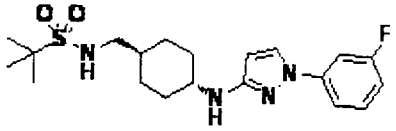
[Formula 479]



^{1}H-NMR (DMSO-d_6) δ: 0.91-1.19 (m, 4H), 1.18 (t, 3H, J = 7.2 Hz), 1.30-1.45 (m, 1H), 1.76-1.82 (m, 2H), 2.02-2.12 (m, 2H), 2.77-2.83 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz) 3.10-3.30 (m, 1H), 5.48 (d, 1H, J = 7.8 Hz), 5.80 (d, 1H, J = 2.7 Hz), 6.99 (t, 1H, J = 6.0 Hz), 7.15-7.40 (m, 3H), 7.75 (td, 1H, J = 8.4, 1.8 Hz), 7.86 (t, 1H, J = 2.7 Hz).

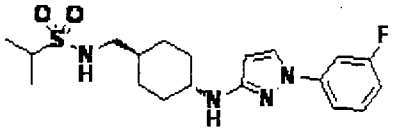
Compound Ij-113

[Formula 480]



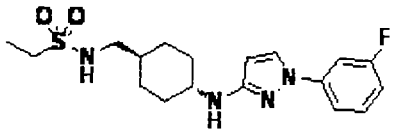
Compound Ij-114

[Formula 481]



Compound Ij-115

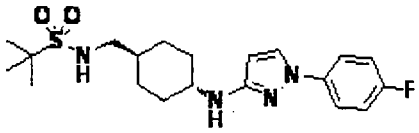
[Formula 482]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.30-1.45 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.74-2.82 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz) 3.15-3.30 (m, 1H), 5.53 (d, 1H, J = 8.1 Hz), 5.80 (d, 1H, J = 2.4 Hz), 6.92 (t, 1H, J = 8.4 Hz), 7.01 (t, 1H, J = 6.0 Hz), 7.37-7.43 (m, 3H), 8.21 (d, 1H, J = 2.4 Hz).

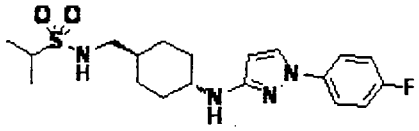
Compound Ij-116

[Formula 483]



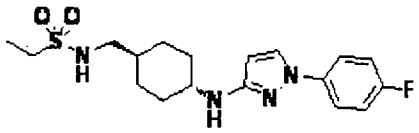
Compound Ij-117

[Formula 484]



Compound Ij-118

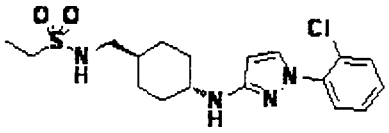
[Formula 485]



^{1}H-NMR (DMSO-d_6)δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J = 7.5 Hz), 1.30-1.45 (m, 1H), 1.75-1.86 (m, 2H), 2.02-2.12 (m, 2H), 2.74-2.83 (m, 2H), 2.97 (q, 2H, J = 7.5 Hz) 3.13-3.30 (m, 1H), 5.38 (d, 1H, J = 8.4 Hz), 5.75 (d, 1H, J = 2.7 Hz), 6.99 (t, 1H, J = 6.3 Hz), 7.18-7.28 (m, 2H), 7.63-7.70 (m, 2H), 8.11 (d, 1H, J = 2.7 Hz).

Compound Ij-119

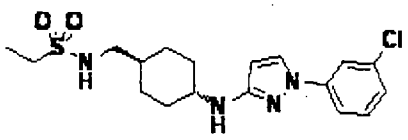
[Formula 486]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.19 (m, 4H), 1.18 (t, 3H, J = 7.5 Hz), 1.28-1.45 (m, 1H), 1.73-1.83 (m, 2H), 2.02-2.13 (m, 2H), 2.73-2.81 (m, 2H), 2.95 (q, 2H, J = 7.5 Hz) 3.12-3.30 (m, 1H), 5.36 (d, 1H, J = 7.5 Hz), 5.76 (d, 1H, J = 2.4 Hz), 6.98 (t, 1H, J = 6.0 Hz), 7.30 (td, 1H, J = 7.5, 1.8 Hz), 7.42 (td, 1H, J = 7.8, 1.5 Hz), 7.53-7.60 (m, 2H), 7.84 (d, 1H, J = 2.7 Hz).

Compound Ij-120

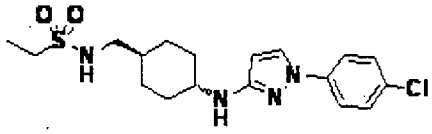
[Formula 487]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J = 7.5 Hz), 1.30-1.45 (m, 1H), 1.74-1.84 (m, 2H), 2.02-2.10 (m, 2H), 2.75-2.82 (m, 2H), 2.97 (q, 2H, J = 7.5 Hz) 3.20-3.30 (m, 1H), 5.52 (d, 1H, J = 7.8 Hz), 5.80 (d, 1H, J = 2.4 Hz), 6.99 (t, 1H, J = 6.0 Hz), 7.13 (d, 1H, J = 8.1 Hz), 7.40 (t, 1H, J = 8.1 Hz), 7.62 (d, 1H, J = 8.4 Hz), 7.72 (s, 1H), 8.22 (d, 1H, J = 2.4 Hz).

Compound Ij-121

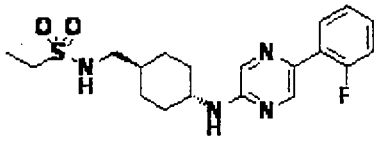
[Formula 488]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J = 7.5 Hz), 1.30-1.45 (m, 1H), 1.74-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.75-2.82 (m, 2H), 2.98 (q, 2H, J = 7.5 Hz) 3.15-3.30 (m, 1H), 5.47 (d, 1H, J = 8.1 Hz), 5.78 (d, 1H, J = 2.4 Hz), 7.00 (t, 1H, J = 6.0 Hz), 7.43 (d, 2H, J = 7.8 Hz), 7.67 (d, 2H, J = 9.0 Hz), 8.17 (d, 1H, J = 2.4 Hz).

Compound Ij-122

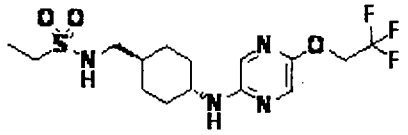
[Formula 489]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.07 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.32-1.50 (m, 1H), 1.81-1.84 (m, 2H), 1.99-2.07 (m, 2H), 2.77-2.81 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.60-3.77 (m, 1H), 7.01-7.05 (m, 1H), 7.22-7.40 (m, 4H), 7.81-7.87 (m, 1H), 8.02 (s, 1H), 8.36 (s, 1H).

Compound Ij-123

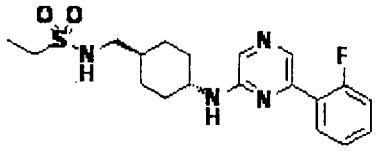
[Formula 490]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.12 (m, 4H), 1.18 (t, 3H, J = 7.2 Hz), 1.32-1.50 (m, 1H), 1.77-1.81 (m, 2H), 1.96-1.99 (m, 2H), 2.74-2.78 (m, 2H), 2.97 (q, 2H, J = 7.2 Hz), 3.54-3.70 (m, 1H), 4.81 (q, 2H, J = 9.0 Hz), 6.50-6.53 (m, 1H), 6.99-7.03 (m, 1H), 7.50 (d, 1H, J =0.9 Hz) 7.83 (d, 1H, J = 0.9 Hz).

Compound Ij-124

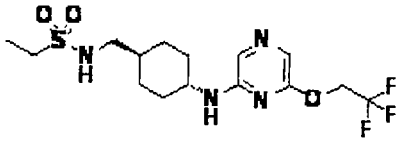
[Formula 491]



^{1}H-NMR (DMSO-d_6) δ: 0.95-1.23 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.32-1.50 (m, 1H), 1.77-1.81 (m, 2H), 2.03-2.07 (m, 2H), 2.74-2.80 (m, 2H), 2.97 (q, 2H, J = 7.2 Hz), 3.61-3.73 (m, 1H), 7.00-7.04 (m, 1H), 7.09-7.12 (m, 1H), 7.29-7.37 (m, 2H), 7.45-7.52 (m, 1H), 7.88-7.94 (m, 2H), 8.04-8.05 (m, 1H).

Compound Ij-125

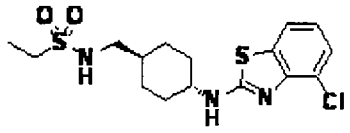
[Formula 492]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.14 (m, 4H), 1.19 (t, 3H, J = 7.2 Hz), 1.32-1.50 (m, 1H), 1.79-1.83 (m, 2H), 1.97-2.03 (m, 2H), 2.76-2.81 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.50-3.63 (m, 1H), 4.43 (q, 2H, J = 9.0 Hz), 7.00-7.04 (m, 1H), 7.13-7.15 (m, 1H), 7.35 (s, 1H) 7.55 (s, 1H).

Compound Ij-126

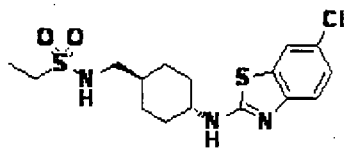
[Formula 493]



^{1}H-NMR (DMSO-d_6) δ: 1.02-1.08 (m, 2H), 1.17-1.29 (m, 2H), 1.19 (t, 3H, J = 7.5 Hz), 1.36-1.43 (m, 1H), 1.79-1.85 (m, 2H), 2.05-2.11 (m, 2H), 2.79 (t, 2H, J = 6.0 Hz), 2.99 (q, 2H, J = 7.5 Hz), 3.53-3.62 (m, 1H), 6.98 (t, 1H, J = 7.8 Hz), 7.03 (t, 1H, J = 6.3 Hz), 7.28 (dd, 1H, J = 7.5, 1.2 Hz), 7.63 (dd, 1H, J = 7.5, 1.2 Hz), 8.28 (d, 1H, J = 7.5 Hz).

Compound Ij-127

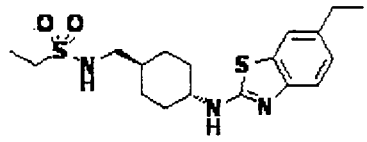
[Formula 494]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.05 (m, 2H), 1.18-1.24 (m, 2H), 1.16 (t, 3H, J = 7.5 Hz), 1.34-1.41 (m, 1H), 1.77-1.81 (m, 2H), 2.02-2.08 (m, 2H), 2.76 (t, 2H, J = 6.0 Hz), 2.96 (q, 2H, J = 7.5 Hz), 3.55-3.64 (m, 1H), 7.00 (t, 1H, J = 7.8 Hz), 7.18 (dd, 1H, J = 8.4, 1.8 Hz), 7.32 (dd, 1H, J = 8.4, 0.6 Hz), 7.74 (d, 1H, J = 1.8 Hz), 8.04 (d, 1H, J = 7.8 Hz).

Compound Ij-128

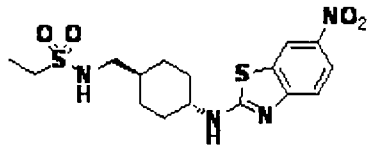
[Formula 495]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.07 (m, 2H), 1.15-1.26 (m, 8H), 1.32-1.43 (m, 1H), 1.78-1.84 (m, 2H), 1.98-2.09 (m, 2H), 2.60 (q, 2H, J = 7.5 Hz), 2.78 (t, 2H, J = 6.3 Hz), 2.96 (q, 2H, J = 7.5 Hz), 3.55-3.64 (m, 1H), 6.98-7.05 (m, 2H), 7.27 (dd, 1H, J = 7.8, 1.8 Hz), 7.47 (m, 1H), 7.84 (d, 1H, J =7.5 Hz).

Compound Ij-129

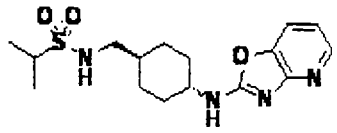
[Formula 496]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.15 (m, 2H), 1.15-1.35 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.33-1.48 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.78-2.84 (m, 2H), 2.97 (q, 2H, J = 7.2 Hz), 3.62-3.80 (m, 1H), 7.02 (t, 1H, J = 6.0 Hz), 7.45 (d, 1H, J = 9.0 Hz), 8.09 (dd, 1H, J = 9.0, 2.4 Hz), 8.68 (d, 1H, J = 2.4 Hz), 8.70 (brs, 1H).

Compound Ij-130

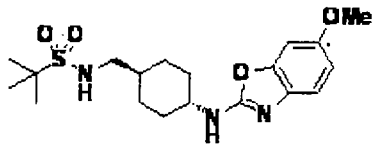
[Formula 497]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.10 (m, 2H), 1.15-1.46 (m, 3H), 1.21 (d, 6H, J = 6.6 Hz), 1.78-1.88 (m, 2H), 1.98-2.08 (m, 2H), 2.76-2.86 (m, 2H), 3.10-3.20 (m, 1H), 3.46-3.62 (m, 1H), 6.91-6.96 (m, 1H), 7.01 (brs, 1H), 7.64 (d, 1H, J = 7.8 Hz), 8.07 (d, 1H, J = 5.1 Hz), 8.35 (d, 1H, J = 7.8 Hz).

Compound Ij-131

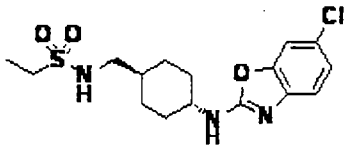
[Formula 498]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.05 (m, 2H), 1.15-1.30 (m, 2H), 1.27 (s, 9H), 1.30-1.43 (m, 1H), 1.77-1.86 (m, 2H), 1.98-2.08 (m, 2H), 2.86-2.92 (m, 2H), 3.35-3.50 (m, 1H), 3.73 (s, 3H), 6.69 (dd, 1H, J = 8.4, 2.0 Hz), 6.86 (t, 1H, J = 6.0 Hz), 7.01 (d, 1H, J = 2.0 Hz), 7.10 (d, 1H, J = 8.4 Hz), 7.62 (d, 1H, J = 7.6 Hz).

Compound Ij-132

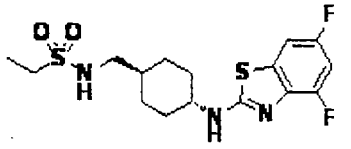
[Formula 499]



^{1}H-NMR (DMSO-d_6)δ: 0.92-1.08 (m, 2H), 1.15-1.33 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.33-1.42 (m, 1H), 1.76-1.86 (m, 2H), 1.98-2.08 (m, 2H), 2.76-2.82 (m, 2H), 2.97 (q, 2H, J = 7.2 Hz), 3.40-3.58 (m, 1H), 7.01 (t, 1H, J = 6.0 Hz), 7.13 (d, 1H, J = 8.4 Hz), 7.20 (d, 1H, J = 8.4 Hz), 7.49 (s, 1H), 8.01 (d, 1H, J = 7.6 Hz).

Compound Ij-133

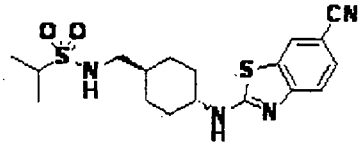
[Formula 500]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.10 (m, 2H), 1.16-1.28 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.33-1.46 (m, 1H), 1.78-1.85 (m, 2H), 2.04-2.12 (m, 2H), 2.76-2.82 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.55-3.70 (m, 1H), 7.01 (t, 1H, J = 6.0 Hz), 7.12 (t, 1H, J = 9.6 Hz), 7.48 (d, 1H, J = 7.6 Hz), 8.13 (d, 1H, J = 7.6 Hz).

Compound Ij-134

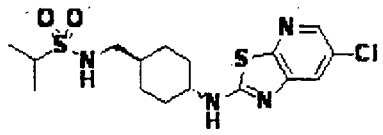
[Formula 501]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.08 (m, 2H), 1.15-1.26 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.33-1.42 (m, 1H), 1.39-1.84 (m, 2H), 2.05-2.09 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.10-3.20 (m, 1H), 3.61-3.75 (m, 1H), 6.98 (t, 1H, J = 6.0 Hz), 7.45 (dd, 1H, J = 7.5, 0.6 Hz), 7.60 (dd, 1H, J = 8.4, 1.5 Hz), 8.17 (d, 1H, J = 1.5 Hz), 8.50 (d, 1H, J = 7.5 Hz).

Compound Ij-135

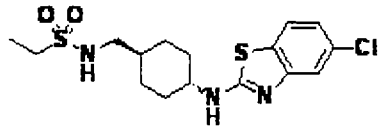
[Formula 502]



^{1}H-NMR (DMSO-d_6) δ: 0.98-1.08 (m, 2H), 1.15-1.25 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.35-1.44 (m, 1H), 1.80-1.84 (m, 2H), 2.05-2.08 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.10-3.19 (m, 1H), 3.62-3.78 (m, 1H), 6.98 (t, 1H, J = 6.0 Hz), 7.79 (d, 1H, J = 2.1 Hz), 8.10 (d, 1H, J = 2.1, 1.5 Hz), 8.52 (d, 1H, J = 6.9 Hz).

Compound Ij-136

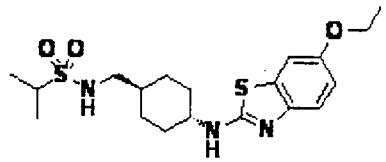
[Formula 503]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.08 (m, 2H), 1.17-1.24 (m, 2H), 1.19 (t, 3H, J = 7.5 Hz), 1.33-1.41 (m, 1H), 1.78-1.83 (m, 2H), 2.04-2.08 (m, 2H), 2.78 (t, 2H, J = 6.3 Hz), 2.98 (q, 2H, J = 7.2 Hz), 3.56-3.67 (m, 1H), 7.00-7.04 (m, 2H), 7.39 (d, 1H, J = 2.1 Hz), 7.66 (dd, 1H, J = 8.4, 1.8 Hz), 8.14 (d, 1H, J = 7.5 Hz).

Compound Ij-137

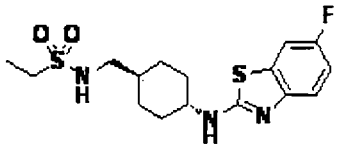
[Formula 504]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.10 (m, 2H), 1.12-1.28 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.31 (t, 3H, J = 6.9 Hz), 1.33-1.46 (m, 1H), 1.76-1.85 (m, 2H), 2.02-2.16 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.22 (m, 1H), 3.50-3.64 (m, 1H), 3.98 (q, 2H, J = 6.9 Hz), 6.78 (dd, 1H, J = 8.7, 2.7 Hz), 6.98 (t, 1H, J = 6.0 Hz), 7.23-7.27 (m, 2H), 7.68 (d, 1H, J = 7.2 Hz).

Compound Ij-138

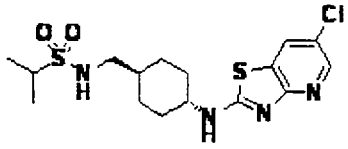
[Formula 505]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.08 (m, 2H), 1.14-1.26 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.33-1.45 (m, 1H), 1.77-1.86 (m, 2H), 2.03-2.12 (m, 2H), 2.76-2.82 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.52-3.68 (m, 1H), 6.97-7.06 (m, 2H), 7.34 (dd, 1H, J = 8.4, 4.8 Hz), 7.56 (dd, 1H, J = 8.4, 2.4 Hz), 7.91 (d, 1H, J = 7.6 Hz).

Compound Ij-139

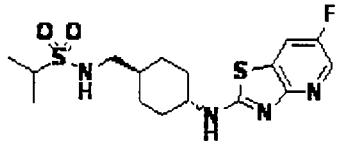
[Formula 506]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.12 (m, 2H), 1.16-1.32 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.32-1.46 (m, 1H), 1.78-1.86 (m, 2H), 2.02-2.16 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.21 (m, 1H), 3.58-3.76 (m, 1H), 7.00 (t, 1H, J = 6.0 Hz), 8.19-8.23 (m, 2H), 8.52 (d, 1H, J = 6.9 Hz).

Compound Ij-140

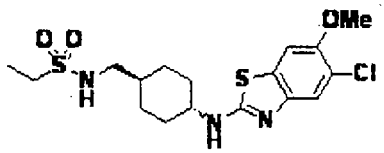
[Formula 507]



^{1}H-NMR (DMSO-d_6) δ: 0.96-1.12 (m, 2H), 1.12-1.30 (m, 2H), 1.21 (d, 6H, J = 6.6 Hz), 1.32-1.46 (m, 1H), 1.78-1.86 (m, 2H), 2.02-2.16 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.58-3.78 (m, 1H), 7.01 (t, 1H, J = 6.0 Hz), 8.08 (dd, 1H, J = 8.4, 2.7 Hz), 8.19 (d, 1H, J = 2.7 Hz), 8.38 (d, 1H, J = 7.2 Hz).

Compound Ij-141

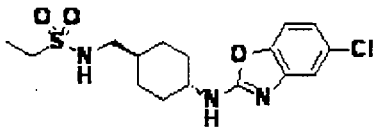
[Formula 508]



^{1}H-NMR (DMSO-d_6) δ: 0.97-1.08 (m, 2H), 1.15-1.22 (m, 5H), 1.34-1.42 (m, 1H), 1.78-1.83 (m, 2H), 2.04-2.08 (m, 2H), 2.78 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.2 Hz), 3.53-3.62 (m, 1H), 3.81 (s, 1H), 7.02 (t, 1H, J = 6.3 Hz), 7.41 (s, 1H), 7.53 (s, 1H), 7.88 (d, 1H, J = 7.5 Hz).

Compound Ij-142

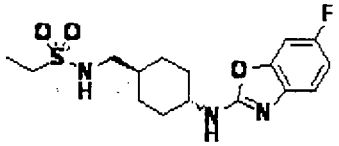
[Formula 509]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.06 (m, 2H), 1.17-1.30 (m, 2H), 1.18 (t, 3H, J = 7.5 Hz), 1.32-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 7.2 Hz), 3.41-3.58 (m, 1H), 6.97 (dd, 1H, J = 8.4, 2.4 Hz), 6.99-7.03 (m, 1H), 7.27 (d, 1H, J = 2.4 Hz), 7.34 (dd, 1H, J = 8.4, 0.3 Hz), 8.07-8.14 (m, 1H).

Compound Ij-143

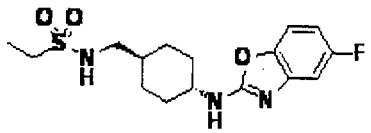
[Formula 510]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.08 (m, 2H), 1.16-1.33 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.33-1.45 (m, 1H), 1.77-1.86 (m, 2H), 2.00-2.08 (m, 2H), 2.74-2.82 (m, 2H), 2.98 (q, 2H, J = 7.2 Hz), 3.38-3.54 (m, 1H), 6.90-7.00 (m, 1H), 7.02 (t, 1H, J = 4.5 Hz), 7.19 (dd, 1H, J = 8.4, 5.1 Hz), 7.33 (dd, 1H, J = 8.4, 2.7 Hz), 7.88 (d, 1H, J = 7.8 Hz).

Compound Ij-144

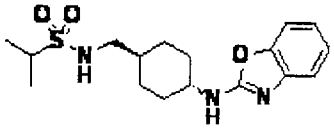
[Formula 511]



^{1}H-NMR (DMSO-d$_6$) δ: 0.94-1.06 (m, 2H), 1.19-1.29 (m, 2H), 1.18 (t, 3H, J = 7.2 Hz), 1.31-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J = 6.0 Hz), 2.98 (q, 2H, J = 6.9 Hz), 3.41-3.57 (m, 1H), 6.71-6.79 (m, 1H), 7.06-7.08 (m, 2H), 7.31 (dd, 1H, J = 8.7, 4.8 Hz), 8.03 (d, 1H, J = 7.8 Hz).

Compound Ij-145

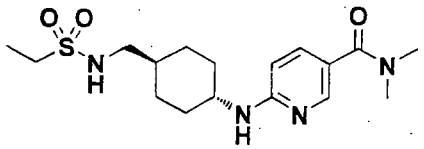
[Formula 512]



^{1}H-NMR (DMSO-d$_6$) δ: 0.95-1.16 (m, 2H), 1.18-1.44 (m, 3H), 1.21 (d, 6H, J = 6.6 Hz), 1.78-1.86 (m, 2H), 2.02-2.12 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.40-3.58 (m, 1H), 6.95 (t, 1H, J = 7.8 Hz), 7.01 (brs, 1H), 7.09 (t, 1H, J = 6.9 Hz), 7.22 (d, 1H, J = 6.6 Hz), 7.31 (d, 1H, J = 7.8 Hz), 7.83 (d, 1H, J = 7.8 Hz).

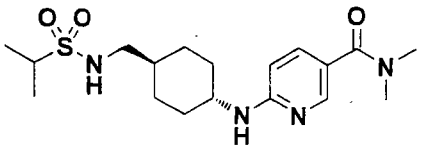
Compound Ij-146

[Formula 513]



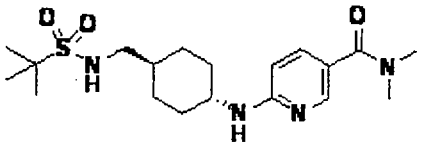
Compound Ij-147

[Formula 514]



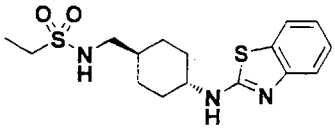
Compound Ij-148

[Formula 515]



Compound Ij-149

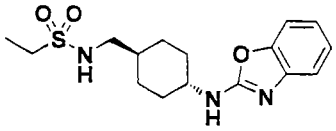
[Formula 516]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.10 (m, 2H), 1.13-1.30 (m, 2H), 1.19 (t, 3H, J = 7.5 Hz), 1.39 (m, 1H), 1.76-1.87 (m, 2H), 2.02-2.14 (m, 2H), 2.79 (t, 2H, J = 6.3 Hz), 2.98 (q, 2H, J = 7.5 Hz), 3.56-3.70 (m, 1H), 6.95-7.05 (m, 2H), 7.20 (t, 1H, J = 7.8 Hz), 7.37 (d, 1H, J = 7.8 Hz), 7.64 (d, 1H, J = 7.5 Hz), 7.92 (d, 1H, J = 7.5 Hz). Melting point: 168-169°C Anal. Calcd for C16H23N3O2S2: C,54.36; H,6.56; N,11.89; S,18.14. Found: C,54.33; H,6.55; N,11.89; S,18.05.

Compound Ij-150

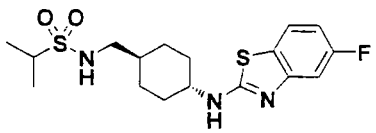
[Formula 517]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.10 (m, 2H), 1.12-1.30 (m, 2H), 1.19 (t, 3H, J = 7.2 Hz), 1.39 (m, 1H), 1.77-1.87 (m, 2H), 1.99-2.12 (m, 2H), 2.78 (t, 2H, J = 6.6 Hz), 2.98 (q, 2H, J = 7.2 Hz), 3.40-3.58 (m, 1H), 6.95 (t, 1H, J = 7.8 Hz), 7.02 (t, 1H, J = 6.0 Hz), 7.09 (t, 1H, J = 7.8 Hz), 7.22 (d, 1H, J = 7.5 Hz), 7.31 (d, 1H, J = 8.1 Hz), 7.83 (d, 1H, J = 7.8 Hz). Melting point: 170-171°C Anal. Calcd for $C16H23N_3O_3S$: C,56.95; H,6.87; N,12.45; S,9.50. Found: C,56.91; H,6.91; N,12.43; S,9.51.

Compound Ij-151

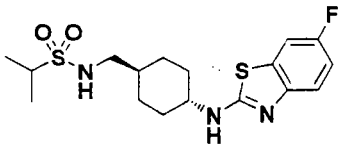
[Formula 518]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.10 (m, 2H), 1.12-1.30 (m, 2H), 1.21 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.76-1.87 (m, 2H), 2.02-2.14 (m, 2H), 2.81 (t, 2H, J = 6.0 Hz), 3.08-3.22 (m, 1H), 3.54-3.70 (m, 1H), 6.83 (t, 1H, J = 10.5 Hz), 6.99 (t, 1H, J = 5.4 Hz), 7.17 (dd, 1H, J = 10.5, 2.1 Hz), 7.63 (dd, 1H, J = 8.4, 5.7 Hz), 8.10 (d, 1H, J = 7.5 Hz). Melting point : 165-166°C Anal. Calcd for C17H24FN3O2S2: C,52.96; H,6.27; F,4.93; N,10.90; S,16.63. Found: C,52.99; H,6.31; F,5.00; N,10.91; S,16.84.

Compound Ij-152

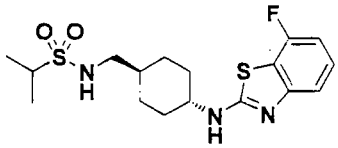
[Formula 519]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.09 (m, 2H), 1.11-1.28 (m, 2H), 1.22 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.75-1.82 (m, 2H), 2.02-2.12 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.10-3.20 (m, 1H), 3.52-3.67 (m, 1H), 6.98 (t, 1H, J = 6.0 Hz), 7.03 (td, 1H, J = 9.6, 2.7 Hz), 7.34 (dd, 1H, J = 9.0, 5.1 Hz), 7.57 (dd, 1H, J = 9.0, 2.7 Hz), 7.91 (d, 1H, J = 7.2 Hz). Melting point:151-152°C Anal. Calcd for $C_{17}H_{24}FN_3O_2S_2$: C,52.96; H,6.27; F,4.93; N,10.90; S,16.63. Found: C,52.97; H,6.28; F,4.90; N,10.87; S,16.71.

Compound Ij-153

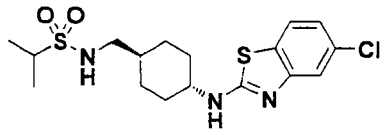
[Formula 520]



^{1}H-NMR (DMSO-d_6) δ: 0.94-1.12 (m, 2H), 1.14-1.31 (m, 2H), 1.22 (d, 6H, J = 6.6 Hz), 1.39 (m, 1H), 1.76-1.87 (m, 2H), 2.02-2.15 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.10-3.22 (m, 1H), 3.55-3.70 (m, 1H), 6.84-6.94 (m, 1H), 6.99 (t, 1H, J = 6.0 Hz), 7.18-7.28 (m, 2H), 8.21 (d, 1H, J = 7.2 Hz).

Compound Ij-154

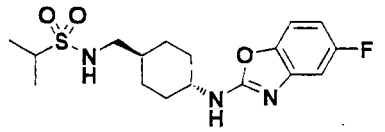
[Formula 521]



^{1}H-NMR (DMSO-d_6) δ: 0.93-1.10 (m, 2H), 1.13-1.30 (m, 2H), 1.22 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.76-1.87 (m, 2H), 2.02-2.14 (m, 2H), 2.81 (t, 2H, J = 6.0 Hz), 3.08-3.22 (m, 1H), 3.54-3.70 (m, 1H), 6.98 (t, 1H, J = 6.0 Hz), 7.02 (dd, 1H, J = 8.1, 2.1 Hz), 7.39 (d, 1H, J = 2.1 Hz), 7.66 (d, 1H, J = 8.1 Hz), 8.15 (d, 1H, J = 7.5 Hz). Melting point:166-167°C Anal. Calcd for $C_{17}H_{24}ClN_3O_2S_2$: C,50.79; H,6.02; Cl,8.82; N,10.45; S,15.95. Found: C,50.84; H,6.04; Cl,8.80; N,10.44; S,16.00.

Compound Ij-155

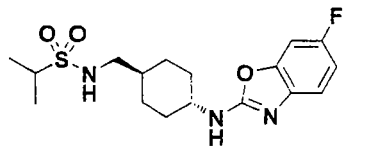
[Formula 522]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 2H), 1.20-1.34 (m, 2H), 1.22 (d, 6H, J = 6.8 Hz), 1.38 (m, 1H), 1.78-1.86 (m, 2H), 1.99-2.14 (m, 2H), 2.80 (t, 2H, J = 6.4 Hz), 3.10-3.20 (m, 1H), 3.42-3.54 (m, 1H), 6.74 (td, 1H, J = 8.8, 2.8 Hz), 6.98 (t, 1H, J = 5.6 Hz), 7.06 (dd, 1H, J = 9.6, 2.8 Hz), 7.30 (dd, 1H, J = 8.0, 4.4 Hz), 8.02 (d, 1H, J = 8.0 Hz). Anal. Calcd for $C_{17}H_{24}FN_3O_3S$: C,55.27; H,6.55; F,5.14; N,11.37; S,8.68. Found: C,55.16; H,6.50; F,5.16; N,11.30; S,8.42.

Compound Ij-156

[Formula 523]

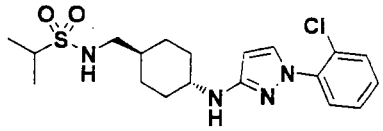


^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 2H), 1.20-1.34 (m, 2H), 1.22 (d, 6H, J = 6.9 Hz), 1.38 (m, 1H), 1.78-1.86 (m, 2H), 2.00-2.14 (m, 2H), 2.81 (t, 2H, J = 6.3 Hz), 3.10-3.21 (m, 1H), 3.38-3.54 (m, 1H), 6.90-7.00 (m, 2H), 7.19 (dd, 1H, J = 8.4, 4.8 Hz), 7.33 (dd, 1H, J = 8.4, 2.4 Hz), 7.86 (d, 1H, J = 7.8 Hz). Melting point: 170-171°C Anal. Calcd for $C_{17}H_{24}FN_3O_3S$: C,55.27; H,6.55; F,5.14; N,11.37; S,8.68.

Found: C,55.31; H,6.59; F,5.13; N,11.46; S,8.59.

Compound Ij-157

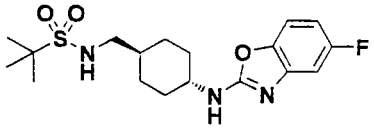
[Formula 524]



^{1}H-NMR (DMSO-d_6) δ: 0.88-1.20 (m, 4H), 1.20 (d, 6H, J = 6.9 Hz), 1.36 (m, 1H), 1.75-1.83 (m, 2H), 2.02-2.13 (m, 2H), 2.79 (t, 2H, J = 6.0 Hz), 3.05-3.25 (m, 2H), 5.36 (d, 1H, J = 7.8 Hz), 5.76 (d, 1H, J = 2.4 Hz), 6.95(t, 1H, J = 6.9 Hz), 7.30 (td, 1H, J = 7.5, 1.8 Hz), 7.42 (td, 1H, J = 7.8, 1.5 Hz), 7.53-7.60 (m, 2H), 7.84 (d, 1H, J = 2.7 Hz). Melting point: 142-143°C

Compound Ij-158

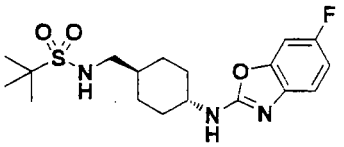
[Formula 525]



^{1}H-NMR (DMSO-d_6) δ: 0.92-1.08 (m, 2H), 1.19-1.34 (m, 2H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.86 (m, 2H), 1.99-2.14 (m, 2H), 2.88 (t, 2H, J = 6.3 Hz), 3.40-3.56 (m, 1H), 6.75 (td, 1H, J = 8.7, 2.7 Hz), 6.87 (t, 1H, J = 6.0 Hz), 7.06 (dd, 1H, J = 9.3, 2.7 Hz), 7.31 (dd, 1H, J = 8.7, 4.5 Hz), 8.02 (d, 1H, J = 7.8 Hz). Melting point: 220-221°C Calcd for $C_{18}H_{26}FN_3O_3S$: C,56.38; H,6.83; F,4.95; N,10.96; S,8.36. Found: C,56.41; H,6.90; F,4.96; N,11.07; S,8.36.

Compound Ij-159

[Formula 526]

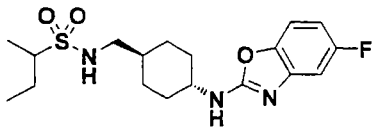


^{1}H-NMR (DMSO-d_6) δ: 0.91-1.08 (m, 2H), 1.16-1.46 (m, 3H), 1.27 (s, 9H), 1.77-1.87 (m, 2H), 1.98-2.10 (m, 2H), 2.89 (t, 2H, J = 6.0 Hz), 3.38-3.54 (m, 1H), 6.88 (t, 1H, J = 5.7 Hz), 6.90-7.00 (m, 1H), 7.19 (dd, 1H, J = 8.7, 5.1 Hz), 7.34 (dd, 1H,

J = 8.7, 2.7 Hz), 7.88 (d, 1H, J = 7.5 Hz). Anal. Calcd for $C_{18}H_{26}FN_3O_3S$: C,56.38; H,6.83; F,4.95; N,10.96; S,8.36. Found: C,56.39; H,6.93; F,4.98; N,11.09; S,8.29.

Compound Ij-160

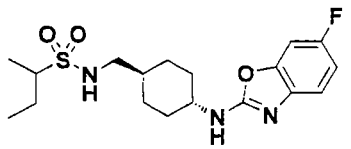
[Formula 527]



^{1}H-NMR (DMSO-d_6) δ: 0.95 (t, 3H, J = 7.8 Hz), 0.92-1.07 (m, 2H), 1.21 (d, 3H, J = 6.9 Hz), 1.20-1.47 (m, 4H), 1.77-1.96 (m, 3H), 1.98-2.08 (m, 2H), 2.79 (t, 2H, J = 6.3 Hz), 2.85-2.98 (m, 1H), 3.42-3.57 (m, 1H), 6.71-6.80 (m, 1H), 7.00 (t, 1H, J = 5.7 Hz), 7.06 (dd, 1H, J = 9.3, 2.7 Hz), 7.31 (dd, 1H, J = 8.7, 4.5 Hz), 8.02 (d, 1H, J = 7.8 Hz). Melting point: 172-173°C Anal. Calcd for $C_{18}H_{26}FN_3O_3S$: C,56.38; H,6.83; F,4.95; N,10.96; S,8.36. Found: C,56.37; H,6.84; F,5.04; N,11.12; S,8.14.

Compound Ij-161

[Formula 528]



^{1}H-NMR (DMSO-d_6) δ: 0.95 (t, 3H, J = 7.5 Hz), 0.92-1.08 (m, 2H), 1.21 (d, 3H, J = 6.9 Hz), 1.20-1.47 (m, 4H), 1.77-1.96 (m, 3H), 1.98-2.08 (m, 2H), 2.79 (t, 2H, J = 6.3 Hz), 2.85-2.98 (m, 1H), 3.38-3.56 (m, 1H), 6.90-6.98 (m, 1H), 7.00 (t, 1H, J = 6.0 Hz), 7.19 (dd, 1H, J = 8.7, 5.1 Hz), 7.33 (dd, 1H, J = 8.7, 2.7 Hz), 7.88 (d, 1H, J = 7.8 Hz). Melting point: 173-174°C Anal. Calcd for $C_{18}H_{26}FN_3O_3S$: C,56.38; H,6.83; F,4.95; N,10.96; S,8.36. Found: C,56.45; H,6.80; F,4.93; N,11.02; S,8.54.

[0085]

Experiment 1 Transportability through the blood-brain barrier and potential for drug-drug interactions through P-gp

Transportability of the compounds of this invention through the blood-

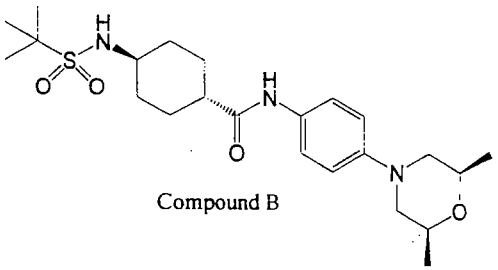
brain barrier (blood-brain partition coefficient; Kp) in mice (Jcl;C57BL/6J mice, ♂, 7 weeks) was defined from the difference in concentration of the compounds between in plasma and in brain after intravenous administration of the compounds (0.5 mg/2 mL/kg). The brain Kp value of Compound (I-72) ($Kp_{Cont.}$) was 1.29 showing high transportability through the blood-brain barrier.

To examine the potential for drug-drug interactions through P-gp in vivo, the Kp values of compounds of this invention with (Kp_{CsA}) or without ($Kp_{Cont.}$) cyclosporin A (20 mg/kg), a P-gp inhibitor, were calculated. The Kp_{CsA} value of Compound (I-72) was 1.14, and the calculated Kp_{CsA} / $Kp_{Cont.}$ ratio was 0.9. The result indicate that Compound (I-72) has no significant potential for drug-drug interactions through P-gp in mice.

[0086]

On the other hand the potential for drug-drug interactions through P-pg of amide compound B which has similar structure of Compound (I-72) was also examined in mice. The $Kp_{Cont.}$ and Kp_{CsA} were 0.04 and 0.84, respectively. The Kp_{CsA} / Kp_{Cont} ratio was more than 1.0 (i.e. 20.5), indicating that the compound is effectively excreted through P-gp from the brain to vessels, and that significant drug-drug interactions through P-gp could be induced in mice.

[Formula 529]



Compound B

[0087]

Experiment 2 Affinity for NPY Y5 receptor

cDNA sequence encoding a human NPY Y5 receptor (WO96/16542) was cloned in a vector (pME18S, Takebe et al. Mol. Cell. Biol. 8, 466-472). The obtained expression vector was transfected into CHO cells as a host by using Lipofect AMINE reagent (Trademark, Gico BRL Co., Ltd.) according to the instruction manual. The cells that stably express NPY Y5 receptor were obtained.

The membranes prepared from the CHO cells expressing NPY Y5 receptor, the compound of this invention and 30,000 cpm [^{125}I] peptide YY (60 pM of final

concentration: Amersham) were incubated in the assay buffer (20 mM HEPES-Hanks buffer containing 0.1% bovine serum albumin, pH 7.4) at 25 °C for 2 hours, and then the membrane was filtered from the mixture through a glassfilter (GF/C) presoaked with 1 % polyethyleneimine. After washing with 50 mM Tris-HCl buffer (pH 7.4), radioactivity retained on the filters was quantified with a gamma counter. Nonspecific binding was defined as the amount of radioactivity bound to the membranes after incubation in the presence of 200 nM of peptide YY. The 50 % inhibitory concentration of the test compound against the specific peptide YY binding (IC_{50} value) was calculated (Inui, A. et al. Endocrinology 131, 2090 - 2096 (1992)). The results are shown in Table 1.

The compounds of this invention inhibited the binding of peptide YY (NPY homologue) to NPY Y5 receptor, indicating that the compounds of this invention have an affinity for the NPY Y5 receptor.

[Table 1]

Compound No.	Binding IC_{50}(nM)	Compound No.	Binding IC_{50}(nM)
Ii-1	0.10	Ij-152	0.35
Ii-16	2.5	Ij-153	0.12
Ii-34	11	Ij-154	0.17
Ii-44	3.4	Ij-155	0.88
Ij-1	0.70	Ij-156	0.68
Ij-52	0.27	Ij-157	0.16
Ij-59	2.5	Ij-158	0.49
Ij-66	0.39	Ij-159	0.60
Ij-149	0.92	Ij-160	0.55
Ij-150	4.66	Ij-161	0.69
Ij-151	0.12		

[0088]

Experiment 3 Inhibitory effect on cAMP production in CHO cells

CHO cells expressing human NPY Y5 receptor were incubated in the presence of 0.1 mM isobutylmethylxanthine (SIGMA) and 0.2mM RO-201724 (Calbiochem) at 37 °C for 20 min. After the incubation the compound of this invention was added, and then the mixture was incubated for 10 min. Next, 50 nM NPY and 10 μM forskolin (SIGMA) were added, and the mixture was incubated for 30 min. After termination of the reaction by adding 1N HCl, the amount of cAMP in the supernatant was determined with a EIA kit (Amersham LIFE SCIENCE). The inhibitory activity of NPY against forskolin stimulated cAMP production was expressed as 100 % and the 50 % inhibitory concentration (IC50 value) of the compound of this invention against the NPY activity was calculated.

[0089]

Experiment 4

Using the membranes prepared from Y1-expression cells (human neuroblastoma, SK-N-MC) and the membranes prepared from Y2-expression cells (human neuroblastoma, SMS-KAN), the experiment was carried out in a similar way as Experiment 2 to determine the affinity of the compounds for NPY Y1 and NPY Y2 receptor. The results showed that the compounds of this invention had no significant affinity for their receptors, indicating high selectivity for NPY Y5

receptor.

[0090]

Experiment 5

Under diethylether anesthesia the skull of male C57BL/6J mice (12-14 week old, 25-30g) was exposed by making an incision about 1-cm long from external occipital crest to nasal dorsum, and then drilled in the 1-mm lateral position to the left following 1-mm posterior from bregma. After recovery from anesthesia mice were dosed with either 0.5% hydroxypropylmethyl cellulose solution (vehicle, Shin-Etsu Chemical Co., Ltd) or the compounds of this invention suspended in the 0.5% hydroxypropylmethyl cellulose solution. At one hour after the treatment, each animal received saline or a NPY Y5 receptor specific agonist, [cPP$^{1-7}$, NPY$^{19-23}$, Ala^{31}, Aib^{32}, Gln^{34}]-hPancreatic Polypeptide (0.1 nmol/1.5 μL saline/mouse) through the skull opening using a canula. Residual food was measured at 2 and 4 hours after the treatment. The inhibition ratio of Y5 agonist-induced food intake by the compounds was calculated as follows; inhibition ratio (%)=[1-(food intake (g) by the compound treated and Y5 agonist received mice - food intake (g) by the vehicle treated and saline received mice)/(food intake (g) by the vehicle treated and Y5 agonist received mice-food intake (g) by the vehicle treated and saline received mice)]x100. As shown in Table 2, the compounds at 1.5mg/kg or 6 mg/kg caused a significant inhibition in Y5 agonist induced-food intake compared to the 0.5% hydroxypropylmethyl cellulose solution. The inhibition ratios 4 hours after dosing are shown in Table 2.

[0091]

[Table 2]

Compound No.	Inhibition ratio	Compound No.	Inhibition ratio
Ii-45	76.2%	Ij-153	73.0%
Ii-55	64.3%	Ij-154	81.3%
Ij-4	88.2%	Ij-155	56.1%*
Ij-110	90.3%	Ij-156	90.4%
Ij-149	62.6%	Ij-158	70.5%
Ij-150	25.3%	Ij-159	83.2%
Ij-151	78.4%*	Ij-160	36.6%*
Ij-152	62.6%*	Ij-161	15.8%*

* Dose: 1.5mg/kg

[0092]

Experiment 6

Prior to administration of the compounds of this invention, male C57BL/6J mice were given a high-fat diet to induce obese. The high-fat diet-induced obese mice (13-14 week old, body weight 28-33g) were dosed with 0.5% hydroxypropylmethyl cellulose solution (vehicle, Shin-Etsu Chemical Co., Ltd) or the compounds of this invention suspended in the 0.5% hydroxypropylmethyl cellulose solution twice a day (b.i.d.) for 3 weeks with the same diet. The changes in body weight were monitored daily. As shown in Figure 1 and 2, the compounds of this invention at 6mg/kg b.i.d. resulted in a significant suppression of body weight gain compared to the 0.5% hydroxypropylmethyl cellulose solution (vehicle).

[0093]

Formulation Example

The following Formulation Examples are only exemplified and not intended to limit the scope of this invention.

Formulation Example 1 Tablets

Compound (I-1)	15 mg
Starch	15 mg
Lactose	15 mg
Crystalline cellulose	19 mg
Polyvinyl alcohol	3 mg
Distilled water	30 ml

Calcium stearate 3 mg

All of the above ingredients except for calcium stearate are uniformly mixed. Then the mixture was crushed, granulated and dried to obtain a suitable size of granules. Next, calcium stearate was added to the granules. Finally, tableting was performed under a compression force.

[0094]

Formulation Example 2 Capsules

Compound (I-2)	10 mg
Magnesium stearate	10 mg
Lactose	80 mg

The above ingredients were mixed uniformly to obtain powders or fine granules, and then the obtained mixture was filled in capsules.

[0095]

Formulation Example 3 Granules

Compound (I-3)	30 g
Lactose	265 g
Magnesium Stearate	5 g

After the above ingredients are mixed uniformly, the mixture was compressed. The compressed matters were crushed, granulated and sieved to obtain suitable size of granules.

Industrial Applicability

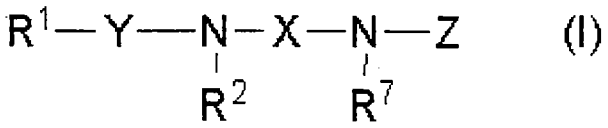
[0096]

As shown in the above Experiments, the compounds for this invention have NPY Y5 receptor antagonistic activity. Therefore, this invention are very useful as an anorectic or anti-obesity composition.

Claims

[1] An anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 1]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

Y is -S(O)n- wherein n is 1 or 2, or -CO-,

R^2 is hydrogen or optionally substituted lower alkyl,

R^1 and R^2 taken together may form lower alkylene,

R^7 is hydrogen or optionally substituted lower alkyl,

X is optionally substituted lower alkylene,

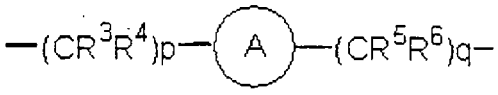
optionally substituted lower alkenylene,

optionally substituted -CO-lower alkylene,

optionally substituted -CO-lower alkenylene or

a group of the formula:

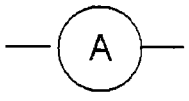
[Formula 2]



wherein R^3, R^4, R^5 and R^6 are each independently hydrogen or optionally substituted lower alkyl,

a group of the formula:

[Formula 3]



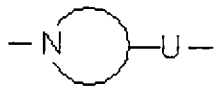
is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted arylene or optionally substituted heterocyclediyl,

p and q are each independently an integer between 0 and 2, and

either p or q is not 0,

$-NR^2-X-$ may be a group of the formula:

[Formula 4]



wherein a group of the formula:

[Formula 5]



is piperidinediyl, piperazinediyl, pyridinediyl, pyrazinediyl, pyrrolidinediyl or pyrroledіyl, and U is lower alkylene or lower alkenylene,

Z is optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino, optionally substituted lower alkoxy, optionally substituted carbocyclyl or optionally substituted heterocyclyl, and

provided that Z is not fused heterocyclyl consisting of three rings or optionally substituted thiazolyl or optionally substituted quinazolinyl.

[2] The anorectic or anti-obesity composition of Claim 1 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein R^1 is lower alkyl.

[3] The anorectic or anti-obesity composition of Claim 1 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Y is $-S(O)_2-$.

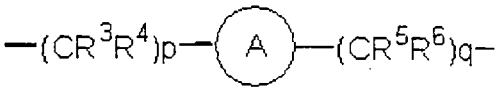
[4] The anorectic or anti-obesity composition of Claim 1 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

[5] The anorectic or anti-obesity composition of Claim 1 comprising a compound, pharmaceutically acceptable salt or solvate thereof,

wherein

X is a group of the formula:

[Formula 6]



, and

R^1 is optionally substituted C2 to C10 alkyl.

[6] The anorectic or anti-obesity composition of Claim 5 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted heterocyclyl..

[7] The anorectic or anti-obesity composition of Claim 5 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein a group of the formula:

[Formula 7]



is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene or optionally substituted piperidinylene.

[8] The anorectic or anti-obesity composition of Claim 5 comprising a compound, pharmaceutically acceptable salt or solvate thereof,

wherein a group of the formula:

[Formula 8]



is optionally substituted cyclohexylene or optionally substituted piperidinylene, p and q are each independently 0 or 1, and either p or q is not 0.

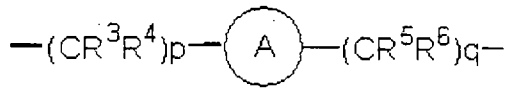
[9] The anorectic or anti-obesity composition of Claim 7 or 8 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted lower alkyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyrazolyl, optionally substituted isoxazolyl, optionally substituted oxadiazolyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl or optionally substituted fused heterocycle consisting of two rings.

[10] The anorectic or anti-obesity composition of Claim 1 comprising a compound, pharmaceutically acceptable salt or solvate thereof,

wherein

X is a group of the formula:

[Formula 9]



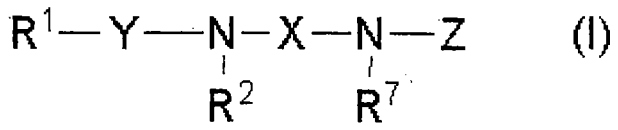
, and

p+q is 1 or 2.

[11] The anorectic or anti-obesity composition of Claim 10 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein p+q is 1.

[12] The anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 10]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

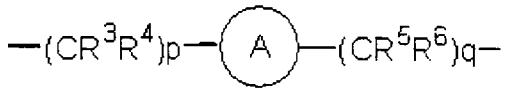
Y is $-S(O)_2-$,

R^2 is hydrogen or optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:

[Formula 11]



wherein

R^5 and R^6 are each independently hydrogen,

a group of the formula:

[Formula 12]



is optionally substituted cycloalkylene,

p is 0, and

q is 1 or 2,

Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl, and provided that a compound wherein Z is fused heterocyclyl consisting of three rings or optionally substituted pyrimidinyl is excluded.

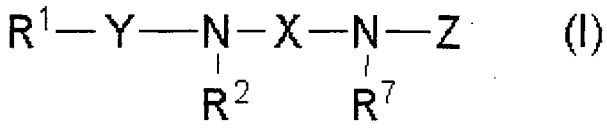
[13] The anorectic or anti-obesity composition of Claim 12 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted phenyl, optionally substituted indanyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted

pyrimidinyl, optionally substituted pyrazolyl, optionally substituted isoxazolyl, optionally substituted oxadiazolyl or optionally substituted fused heterocycle consisting of two rings.

[14] The anorectic or anti-obesity composition of Claim 12 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzoxazolyl, optionally substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzimidazolyl, optionally substituted thiazolopyridyl, optionally substituted isoxazolinonyl, optionally substituted oxazolinonyl, optionally substituted benzoxadinonyl or optionally substituted benzoxyazepinonyl.

[15] The anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 13]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

R^1 is optionally substituted lower alkyl,

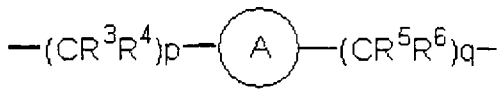
Y is $-S(O)_2-$,

R^2 is hydrogen or optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:

[Formula 14]



wherein R^3 and R^4 are each independently hydrogen,

a group of the formula:

[Formula 15]



is optionally substituted cycloalkylene,

p is 1 or 2, and

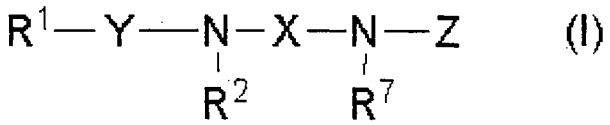
q is 0,

Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl, and provided that a compound wherein Z is fused heterocyclyl consisting of three rings, optionally substituted thiazolyl or optionally substituted quinazolinyl is excluded.

[16] The anorectic or anti-obesity composition of Claim 15 comprising a compound, pharmaceutically acceptable salt or solvate thereof, wherein Z is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl or optionally substituted oxazolopyridyl.

[17] An anorectic or anti-obesity composition comprising a compound of the formula (I):

[Formula 16]



(I)

a pharmaceutically acceptable salt or solvate thereof,

wherein

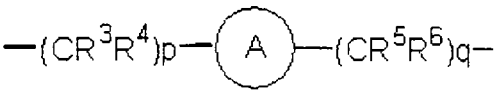
Y is $-S(O)_2-$,

R^2 is hydrogen or optionally substituted lower alkyl,

R^7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:

[Formula 17]



wherein

R^3 and R^4 are each independently hydrogen,

a group of the formula:

[Formula 18]



is optionally substituted cycloalkylene,

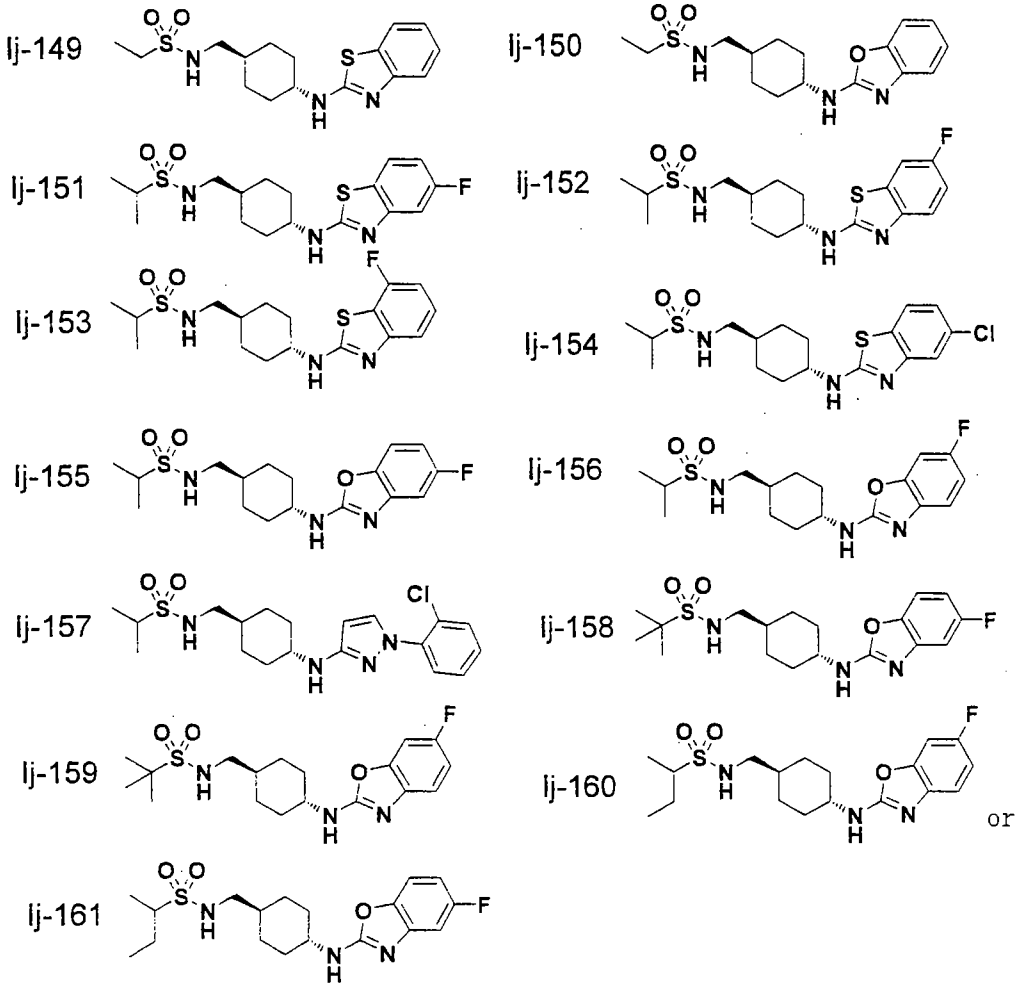
p is 1 or 2, and

q is 0, and

Z is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl or optionally substituted oxazolopyridyl.

[18] A compound of the formula:

[Formula 19]



or

a pharmaceutically acceptable salt or solvate thereof.

[19] A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of Claim 18.

[20] A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of Claim 18 and exhibiting NPY Y5 receptor antagonistic activity.

[21] An anorectic or anti-obesity composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of Claim 18.